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Sterilization of health care products — Dry heat — Requirements for the development, validation and routine control of a sterilization process for medical devices

Stérilisation des produits de santé — Chaleur sèche — Exigences pour l'élaboration, la validation et le contrôle de routine d'un processus de stérilisation pour dispositifs médicaux

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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web 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 20857 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

Introduction

A sterile medical device is one that is free of viable microorganisms. International Standards that specify requirements for development, 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) may, prior to sterilization, have microorganisms on them, albeit in low numbers. Such products are non-sterile. The purpose of sterilization is to inactivate the microbiological contaminants and thereby transform the non-sterile products 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 may 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 product 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 product.

This International Standard describes requirements that, if met, will provide a dry heat sterilization process capable of sterilizing medical devices through appropriate microbicidal activity. This International Standard also describes requirements that, if met, will provide a dry heat depyrogenation process through an appropriate denaturation activity. Furthermore, such compliance permits prediction, with reasonable confidence, that there is a low probability of there being a viable microorganism present on the product after processing. Specification of this probability is a matter for regulatory authorities and may vary from country to country (see for example EN 556-1 and ANSI/AAMI ST67). Additionally, there will be a low probability of pyrogenic material of bacterial origin being present on the product after the application of a depyrogenation process.

Generic requirements of the quality management systems for design/development, production, installation and servicing are given in ISO 9001 and particular requirements for quality management systems for medical device production in ISO 13485. The standards for quality management systems recognise that, for certain processes used in manufacturing or reprocessing, the effectiveness of the process cannot be fully verified by subsequent inspection and testing of the product. Sterilization and depyrogenation are examples of such processes. For this reason, sterilization and depyrogenation processes are validated for use, the performance of the processes 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 the product is sterile and, in this regard, suitable for its intended use. Attention is therefore 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 product;

c) the control of the environment in which the product 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 product is packaged;

g) the conditions under which product is stored.

These factors also need consideration for the provision of reliable assurance of depyrogenation.

The type of contamination on the product to be sterilized varies and this variation influences the effectiveness of a sterilization and depyrogenation process. Product that has been used in a health care setting and is being presented for resterilization in accordance with the manufacturer's instructions (see ISO 17664) should be regarded as a special case. There is potential for such product 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 the informative annexes is not normative and is not provided as a check list for auditors. The guidance provides explanations as well as methods that are accepted as being suitable means for complying with the requirements. Approaches other than those given in the guidance may 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 and/or a depyrogenation 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 programmes of development and validation might be iterative. It is possible that performing these different activities will involve a number of separate individuals and/or organizations, each of whom undertake one or more of these activities. This International Standard does not specify the particular individuals or organizations to carry out the activities.

Sterilization of health care products — Dry heat — Requirements for 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 requirements for the development, validation and routine control of a dry heat sterilization process for medical devices.

NOTE Although the scope of this International Standard is limited to medical devices, it specifies requirements and provides guidance that might be applicable to other health care products.

1.1.2 Although this International Standard primarily addresses dry heat sterilization, it also specifies requirements and provides guidance in relation to depyrogenation processes using dry heat.

NOTE Dry heat is often used for the depyrogenation of equipment, components and health care products and its effectiveness has been demonstrated. The process parameters for sterilization and/or depyrogenation are time and temperature. Because the conditions for depyrogenation are typically more severe than those required for sterilization, a process that has been validated for product depyrogenation will result in product sterility without additional validation.

1.2 Exclusions

1.2.1 This International Standard does not specify requirements for the 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.

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

1.2.2 This International Standard does not apply to processes that use infrared or microwaves as the heating technique.

1.2.3 This International Standard does not detail a specified requirement for designating a medical device as "sterile."

NOTE Attention is drawn to national or regional requirements for designating medical devices as “sterile.” See, for example, EN 556-1 or ANSI/AAMI ST67.

1.2.4 This International Standard does not specify a quality management system for the control of all stages of production of medical devices.

NOTE It is not a requirement of this International Standard to have a complete quality management system during manufacture, but the elements of a quality management system that are the minimum necessary to control the sterilization process 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 of medical devices, including the sterilization process. Regional and national regulations for the provision of medical devices might require implementation of a complete quality management system and the assessment of that system by a third party.

1.2.5 This International Standard does not specify requirements for occupational safety associated with the design and operation of dry heat sterilization and/or depyrogenation facilities.

NOTE Requirements for operational safety are specified in IEC 61010-2-040. Additionally, safety regulations exist in some countries.

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 11138-4:2006, *Sterilization of health care products — Biological indicators — Part 4: Biological indicators for dry heat sterilization processes*

ISO 11140-1, *Sterilization of health care products — Chemical indicators — Part 1: General requirements*

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 11607-2, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

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, *Medical devices — Quality management systems — Requirements for regulatory purposes*

IEC 61010-1, *Safety requirements for electrical equipment for measurement, control, and laboratory use — Part 1: General requirements*

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*

3 Terms and definitions

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

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

[ISO/TS 11139:2006, definition 2.1]

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

[ISO/TS 11139:2006, definition 2.2]

3.3
biological indicator
BI
test system containing viable microorganisms providing a defined resistance to a specified sterilization process

[ISO/TS 11139:2006, definition 2.3]

3.4
calibration
set of operations that establish, under specified conditions, the relationship between values of a quantity indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards

[ISO/TS 11139:2006, definition 2.4]

3.5
change control
assessment and determination of the appropriateness of a proposed alteration to product or procedure

[ISO/TS 11139:2006, definition 2.5]

3.6
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]

3.7
correction
action to eliminate a detected nonconformity

NOTE A correction can be made in conjunction with a **corrective action** (3.8).

[ISO 9000:2005, definition 3.6.6]

3.8
corrective action
action to eliminate the cause of a detected nonconformity or other undesirable situation

NOTE 1 There can be more than one cause for a nonconformity.

NOTE 2 Corrective action is taken to prevent recurrence whereas **preventive action** (3.27) is taken to prevent occurrence.

NOTE 3 There is a distinction between **correction** (3.7) and corrective action.

[ISO 9000:2005, definition 3.6.5]

3.9
D **value**
D_{10} **value**
time or radiation dose required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions

NOTE 1 For the purposes of this International Standard, D value refers to the exposure time necessary to achieve the 90 % reduction of the population of test microorganisms.

NOTE 2 Adapted from ISO/TS 11139:2006.

3.10
depyrogenation
validated process designed to remove or inactivate pyrogenic material, by a specified quantity, which is monitored by inactivation of endotoxin

NOTE For the purposes of the depyrogenation process, “inactivation” refers to loss of ability of biological material to cause a pyrogenic reaction.

3.11
depyrogenation process
series of actions or operations needed to achieve the specified requirements for removal or inactivation of pyrogens

3.12
establish
determine by theoretical evaluation and confirm by experimentation

[ISO/TS 11139:2006, definition 2.17]

3.13
exposure time
period for which the process parameters are maintained within their specified tolerances

[ISO/TS 11139:2006, definition 2.18]

3.14
F **value**
microbiological lethality of a sterilization process expressed in terms of the equivalent time, in minutes, at a temperature of 160 °C with reference to microorganisms with a z value of 20 °C.

NOTE 1 For dry heat, the F value for specific values of sterilization temperature, T, and z is referred to as F_H. Usually, F_H is the equivalent time in minutes at 160 °C delivered to product at temperature, T, assuming a z value of 20 °C. F_H can be determined by biological (F_{Bio}) or physical (F_{phys}) methods.

NOTE 2 The F_H for a process at temperature T, where T is other than 160 °C, may be determined by multiplying the lethal rate by the time at temperature T:

$$F_H = \Delta t \times L$$

where

F_H is the equivalent time in minutes at 160 °C, that has been delivered to the product by the process over time t;

Δt is the time in minutes at temperature T;

L is the lethal rate at temperature T.

3.15
fault
one or more of the process parameters lying outside of its/their specified tolerance(s)

[ISO/TS 11139:2006, definition 2.19]

3.16
fraction positive
quotient derived from the number of positive tests of sterility observed and the total number of tests of sterility performed (number of positive tests of sterility plus number of negative tests of sterility)

3.17
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]

3.18
inactivation
loss of ability of microorganisms to grow and/or multiply

[ISO/TS 11139:2006, definition 2.21]

NOTE For purposes of depyrogenation processes, “inactivation” refers to loss of ability of biologic material to cause a pyrogenic reaction.

3.19
inoculated carrier
supporting material on or in which a defined number of test microorganisms have been deposited

3.20
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]

3.21
lethal rate
L
expression of inactivation per unit time at temperature, T, expressed in terms of a reference temperature, T_{ref}

NOTE 1 L is expressed as minutes at the reference temperature, T_{ref}, per minute at T.

NOTE 2 Lethal rate at any temperature can be calculated using the equation $L = 10^{\frac{(T - T_{ref})}{z}}$

where

T is the delivered temperature;

T_{ref} is the reference temperature;

z is the change in temperature in degrees Celsius required to change a D value by a factor of 10.

3.22
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,

— disinfection of medical devices,

— providing information for medical purposes by means of *in vitro* examination of specimens derived from the human body

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 has been developped by the Global Harmonization Task Force (GHTF 2002).

3.23
microorganism
entity of microscopic size, encompassing bacteria, fungi, protozoa and viruses

[ISO/TS 11139:2006, definition 2.26]

NOTE A specific standard might not require demonstration of the effectiveness of the sterilization process in inactivating all types of microorganisms, identified in this definition, for development, validation and/or routine control of the sterilization process.

3.24
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]

3.25
parametric release
declaration that product is sterile, based on records demonstrating that the process parameters were delivered within specified tolerances

[ISO/TS 11139:2006, definition 2.29]

3.26
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 its specification

[ISO/TS 11139:2006, definition 2.30]

3.27
preventive action
action to eliminate the cause of a potential nonconformity or other undesirable potential situation

NOTE 1 There can be more than one cause for a potential nonconformity.

NOTE 2 Preventive action is taken to prevent occurrence whereas **corrective action** (3.8) is taken to prevent recurrence.

[ISO 9000:2005, definition 3.6.4]

3.28
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]

3.29
process parameter
specified value for a process variable

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

[ISO/TS 11139:2006, definition 2.34]

3.30
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]

3.31
product
result of a process

[ISO 9000:2005, definition 3.4.2]

NOTE For the purposes of sterilization standards, product is tangible and can be raw material(s), intermediate(s), sub-assembly(ies) and health care product(s)

3.32
product family
group or subgroup of product characterized by similar attributes such as mass, material, construction, shapes, lumens and/or packaging and that present a similar challenge to the sterilization process

3.33
requalification
repetition of part of validation for the purpose of confirming the continued acceptability of a specified process

[ISO/TS 11139:2006, definition 2.40]

3.34
specify
stipulate in detail within an approved document.

[ISO/TS 11139, definition 2.42]