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

Stérilisation des produits de santé — Chaleur humide — Exigences pour le développement, la validation et le contrôle de routine d'un procédé de stérilisation des dispositifs médicaux

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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 document 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*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 204, *Sterilization of medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This first edition cancels and replaces ISO 17665-1:2006, ISO/TS 17665-2:2009 and ISO/TS 17665-3:2013, which have been technically revised.

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

— combined ISO 17665-1, ISO/TS 17665-2 and ISO/TS 17665-3 into a single standard.

A list of all parts in the ISO 17665 series can be found on the ISO website.

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

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, can, 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 can 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 ensured and the expression of sterility of a processed population is defined in terms of the probability of there being a viable microorganism present on a product item.

The process variables for a moist heat sterilization process, i.e. those which contribute towards microbial lethality, are exposure to adequate temperature for a prerequisite time in the presence of moisture. Moist heat sterilization can be utilised as a saturated steam process, where saturated steam is allowed to directly contact all surfaces to be sterilized, or as a contained product sterilization process, where steam, steam mixed with air or other gas, or hot water under pressure are used as the heating medium in order to generate moist heat within the sealed contained product. The term saturated steam describes a theoretical state in which water and vapour are in equilibrium and that no other gases are present. In practice theoretical saturated steam state conditions are not achieved. Mixtures of steam and NCGs, albeit in very low levels, will be supplied to the sterilizer and employed as the sterilizing agent, moist heat.

This document describes requirements that, if met, will provide a moist heat sterilization process intended to sterilize medical devices, which has appropriate microbicidal activity. Furthermore, conformance with the requirements, ensures this activity 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 product after every sterilization process is complete. 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, monitored and recorded 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 either incoming raw materials or components, or both;

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.

The type of contamination on a product to be sterilized varies and this has an impact upon the effectiveness of a sterilization process. It is preferable that products that have been used in a health care setting and that are being presented for sterilization in accordance with the instructions for use (see ISO 17664-1) be regarded as special cases. There is the potential for such products to possess a wide range of contaminating microorganisms (bioburden) and either residual inorganic or organic contamination, or both, in spite of the application of a cleaning process. Hence, particular attention is given to the validation and control of the cleaning and disinfection processes used during processing. The ISO 15883 series provides requirements for and information on automated cleaning and disinfection processes.

This document describes the requirements for ensuring that the activities associated with the process of moist heat sterilization are performed properly. The requirements are the normative parts of this document with which conformance is claimed. The guidance given in the informative Annexes is not intended as checklists for assessing conformance with the requirements of this document. The guidance in the informative Annexes is intended to assist in obtaining a uniform understanding and implementation of the requirements in this document by providing explanations, rationales, examples and methods that are regarded as being suitable means for conforming with the requirements. Methods other than those given in the guidance can be used if they are effective in achieving conformance with the requirements of this document.

The development, validation and routine control of a sterilization process comprise a number of discrete but interrelated activities, e.g. calibration, equipment maintenance, product definition, process definition, installation qualification (IQ), OQ and PQ, during which, along with other characteristics, compatibility of product and materials will be ascertained. While the activities required by this document have been grouped together and are presented in a particular order, this document 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. It is possible that performing these different activities will involve a number of either separate individuals or organizations, or both, each of whom undertake one or more of these activities. This document does not specify the particular individuals or organizations who are responsible for carrying out the activities.

The requirements of this document are applicable to all settings where moist heat sterilization of medical devices is carried out. However, this document or part of it can be applied to the moist heat sterilization of other products.

Medical devices processed in an industrial setting can, in certain circumstances, be manufactured using standardised processes that result in product with a known and controlled bioburden prior to sterilization. Medical devices processed in health care facilities can include a wide variety of product with varying levels of bioburden. Appropriate and thorough cleaning and, where necessary for safe handling, decontamination processes, are used prior to presenting product for sterilization. Mixed product loads are common in facilities reprocessing medical devices with throughput volumes dictated by historical and predicted demand for sterile product.

Annex A provides guidance on the principles of moist heat sterilization and provides a rationale for the requirements. Specific guidance for health care facilities is given in Annex F and for industrial applications, in Annex H. The numbering and structure of the clauses in Annex F and Annex H correspond to the numbering and structure of the clauses in the normative requirements section of this document.

An overview of the purpose of each normative section is provided at the beginning of Clauses 5 to 12 (see ISO 14937). Table A.1 summarises the purpose of each normative section and suggests the roles and responsibilities for the organisations and personnel involved in each element of the development, validation and routine control of a moist heat sterilization process and moist heat sterilizer.

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

1 Scope

This document provides requirements for the development, validation and routine control of moist heat sterilization processes for medical devices. It also contains guidance which is intended to explain the requirements set forth in the normative sections. The guidance given is intended to promote good practice related to moist heat sterilization processes according to this document. The application within industrial and health care settings is considered.

1.1 Inclusions

Moist heat sterilization processes covered by this document include, but are not limited to:

a) saturated steam sterilization in which air is removed by passive purging (gravity displacement principle);

b) saturated steam sterilization in which air is removed by active air removal (dynamic air removal, pre-vacuum/fractionated vacuum principle);

c) contained product sterilization in which heat transfer is achieved by steam or steam-air mixtures;

d) contained product sterilization in which heat transfer is achieved by water sprays;

e) contained product sterilization in which heat transfer is achieved by water immersion.

NOTE 1 See Annex D where the processes are explained further.

NOTE 2 Although the scope of this document is limited to medical devices, it specifies requirements and provides guidance that can be applicable to other health care products and industrial applications.

1.2 Exclusions

1.2.1 This document does not specify requirements 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.

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

NOTE 2 Specific regulations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

1.2.2 This document does not apply to those sterilization processes that are based on a combination of moist heat with other biocidal agents (e.g. formaldehyde) as the sterilizing agent.

1.2.3 This document does not detail a specified requirement for designating a medical device as “sterile.”

NOTE National or regional requirements can designate medical devices as “sterile.” See, for example, EN 556-1 or ANSI/AAMI ST67.

1.2.4 This document does not specify requirements for occupational safety associated with the design and operation of moist heat sterilization facilities.

NOTE There can be applicable national or regional regulations for operational safety.

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 11138-1:2017, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11138-3:2017, *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization processes*

ISO 11140 (all parts), *Sterilization of health care products — Chemical indicators*

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 health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products*

ISO 11737-2, *Sterilization of health care products — Microbiological methods — Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process*

3 Terms and definitions

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

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

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

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

3.1
air detector
device designed to detect the presence of non-condensable gases in the chamber or in a stream of steam and condensate

[SOURCE: ISO 11139:2018, 3.9]

3.2
automatic controller
device that directs the equipment sequentially through required stages of the cycle in response to programmed cycle parameters

[SOURCE: ISO 11139:2018, 3.18]

3.3
bioburden
population of viable microorganisms on or in a product and/or sterile barrier system

[SOURCE: ISO 11139:2018, 3.23]

3.4
biological indicator
test system containing viable microorganisms providing a defined resistance to a specified sterilization process

[SOURCE: ISO 11139:2018, 3.29]

3.5
calibration
operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by the measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication

[SOURCE: ISO 11139:2018, 3.31]

3.6
chamber
part of equipment in which a load is processed

[SOURCE: ISO 11139:2018, 3.36]

3.7
chemical indicator
test system that reveals change in one or more pre-specified process variables based on a chemical or physical change resulting from exposure to a process

[SOURCE: ISO 11139:2018, 3.43]

3.8
conditioning
treatment of product prior to the exposure stage to attain a specified temperature, relative humidity, or other process variable throughout the load

[SOURCE: ISO 11139:2018, 3.58]

3.9
contained product
load for which the ambient media within a chamber do not come into direct contact with the item to be processed

Note 1 to entry: The environment within the sterilizer is used for heating and cooling purposes only, not for achieving the sterilization effect, e.g. a solution in a sealed bottle.

3.10
contained product sterilization
validated process where indirect contact of a heating medium on the external surfaces of contained product is used to create moist heat internally to achieve the specified requirements for sterility within the contained product

Note 1 to entry: The environment within the sterilizer is used for heating and cooling purposes only, not for achieving the sterilization effect, e.g. a solution in a sealed bottle.

[SOURCE: ISO 11139:2018/Amd1:2024, 3.332, modified — Note 1 to entry added.]

3.11
correction
action to eliminate a detected nonconformity

Note 1 to entry: A correction can be made in advance of, in conjunction with or after a corrective action.

[SOURCE: ISO 11139:2018, 3.64]

3.12
corrective action
action to eliminate the cause of a nonconformity and to prevent recurrence

Note 1 to entry: There can be more than one cause for a nonconformity.

Note 2 to entry: Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence.

[SOURCE: ISO 11139:2018, 3.65]

3.13
cycle parameter
value of a cycle variable including its tolerance used for control, monitoring, indication, and recording of an operating cycle

[SOURCE: ISO 11139:2018, 3.72]

3.14
cycle variable
property used to control, monitor, indicate, or record an operating cycle

[SOURCE: ISO 11139:2018, 3.74]

3.15
***D* value**
D_{10} value
time or dose required under stated conditions to achieve inactivation of 90 % of a population of the test microorganisms

Note 1 to entry: For the purposes of this document, *D* value refers to the exposure period necessary to achieve 90 % reduction.

Note 2 to entry: The definition of *D* value assumes that a plot of $\log_{10}$ of population versus time of exposure is linear within accepted tolerances.

[SOURCE: ISO 11139:2018, 3.75, modified — Notes to entry have been added.]

3.16
development
act of elaborating a specification

[SOURCE: ISO 11139:2018, 3.79]

3.17
equilibration time
period between the attainment of defined sterilization process parameters at the reference measurement point and the attainment of the specified sterilization process parameters at all points within the load

Note 1 to entry: For the purposes of this document the process parameter to which this definition refers is temperature.

Note 2 to entry: Equilibration time is also known as sterilization time lag.

[SOURCE: ISO 11139:2018, 3.105, modified — Notes to entry have been added.]

3.18
equipment maintenance
combination of all technical and associated administrative actions intended to keep equipment at a state in which it can perform its required function, or restore it to such a state

[SOURCE: ISO 11139:2018, 3.106]

3.19
establish
determine by theoretical evaluation and confirm by experimentation

[SOURCE: ISO 11139:2018, 3.107]

3.20
evaluation
systematic and objective comparison of the measured results either with one another or with a specification to be met in initial, intermediate and final tests

Note 1 to entry: Evaluation analyses the level of achievement of both expected and unexpected results by examining the results chain, processes, contextual factors and causality using appropriate criteria. An evaluation provides credible, useful evidence-based information that enables the timely incorporation of its findings, recommendations and lessons into the decision-making processes of organizations and stakeholders.

[SOURCE: ISO 9022-1:2016, 2.10, modified — Added "systematic and objective" at the beginning of the definition and Note 1 to entry has been added.]

3.21
exposure stage
cycle stage between the introduction of the sterilizing or disinfecting agent into the chamber and when the agent is removed or neutralised

Note 1 to entry: For the purposes of this document the exposure stage only includes that part of the process for which microbial lethality is claimed.

[SOURCE: ISO 11139:2018 & Amd 1:2024, 3.111, modified — Note 1 to entry has been added]

3.22
F_o value
measure of microbiological lethality delivered by a moist heat sterilization process expressed in terms of the equivalent time, in minutes, at a temperature of 121,1 °C with reference to microorganisms with a z value of 10 °C

[SOURCE: ISO 11139:2018, 3.113.1, modified — 10 K was replaced by °C (by convention, z value is expressed in °C).]

3.23
F_{BIO} value
expression of the resistance of a biological indicator calculated as the product of the logarithm to base 10 of the initial population of microorganisms and the D value

[SOURCE: ISO 11139:2018, 3.113.2, modified — "to base 10" added to the definition]

3.24
$F_{BIOLOGICAL}$ value
expression of the delivered lethality of a process, measured in terms of actual kill of microorganisms on or in a biological indicator challenge system

Note 1 to entry: $F_{BIOLOGICAL}$ can be calculated by multiplying the D_{121} value by the difference between the log to the base ten of the starting population and the log to the base ten of the enumerated population after processing.

3.25
fault
situation in which one or more of the process or cycle parameters is/are outside its/their specified tolerance(s)

[SOURCE: ISO 11139:2018, 3.116]

3.26
health care facility
HCF
dedicated setting where health care professionals deliver services for care of patients

EXAMPLE Hospitals, free standing ambulatory surgical centres, nursing homes, extended care facilities, medical, dental and physician offices or clinics and other specialized treatment facilities.

[SOURCE: ISO 11139:2018 and Amd 1:2024, 3.339]

3.27
health care product
medical device, including in vitro diagnostic medical device, or medicinal product, including biopharmaceutical

[SOURCE: ISO 11139:2018, 3.132]

3.28
holding time
<moist heat sterilization> period for which the temperatures at the reference measurement point and all points within the load are continuously within the sterilization temperature band

[SOURCE: ISO 11139:2018 & Amd 1:2024, 3.133.1]

3.29
installation qualification
IQ
process of establishing by objective evidence that all key aspects of the process equipment and ancillary system installation comply with the approved specification

[SOURCE: ISO 11139:2018, 3.220.2]

3.30
load
product, equipment or materials to be processed together within an operating cycle

[SOURCE: ISO 11139:2018, 3.155]

3.31
load configuration
distribution and orientation of a load

Note 1 to entry: For the purposes of this document the definition refers to the placement of a load in the chamber and includes fixed chamber parts and the numbers and types of product presented for sterilization.

[SOURCE: ISO 11139:2018, 3.156, modified — Note 1 to entry has been added.]

3.32
measuring chain
series of elements of a measuring instrument or measuring system, which constitutes the path of the measurement signal from the input (quantity subject to measurement) to the output (the result of the measurement)

[SOURCE: ISO 11139:2018, 3.165]

3.33
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, or software, material, or other similar or 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;