DRAFT INTERNATIONAL STANDARD ISO/DIS 17665

ISO/TC **198** Secretariat: **ANSI**

Voting begins on: **2004-07-29** Voting terminates on: **2004-12-29**

INTERNATIONAL ORGANIZATION FOR STANDARDIZATION • МЕЖДУНАРОДНАЯ ОРГАНИЗАЦИЯ ПО СТАНДАРТИЗАЦИИ • ORGANISATION INTERNATIONALE DE NORMALISATION

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

Stérilisation des produits de santé — Chaleur humide — Élaboration, validation et contrôle de routine d'un processus de stérilisation des dispositifs médicaux

ICS 11.080.01

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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.

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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 17665 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This standard cancels and replaces ISO 11134:1994 and ISO 13683:1997.

Introduction

A sterile medical device is one which 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 minimised. 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 standard describes requirements which will enable the demonstration that a moist heat sterilization process intended to sterilize medical devices has appropriate microbicidal activity, and that this activity is both reliable and reproducible, such that the relationship for the inactivation of microorganisms can be extrapolated with reasonable confidence to low levels of probability of there being a viable microorganism present on a product after sterilization. This standard does not specify the maximal value to be taken by this probability; specification of this probability is a matter for Regulatory Authorities and may vary from country to country (see, for example, EN 556 or ANSI/AAMI ST67).

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 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 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, and,

g) the conditions under which product is stored.

The type of contamination on a product to be sterilized varies and this impacts upon the effectiveness of a sterilization process. Products that have been used in a health care setting and are being presented for resterilization in accordance with the manufacturer's instructions (see ISO 17664) should be regarded as a special case. There is the potential for such products 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 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 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 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 programs of development and validation may 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 — Moist heat — 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 moist heat sterilization process for medical devices.

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

1.1.2 Moist heat sterilization processes covered by this standard include but are not limited to:

a) saturated steam venting systems;

b) saturated steam active air removal systems;

c) air steam mixtures;

d) water spray; and

e) water immersion.

1.2 Exclusions

1.2.1 Sterilization processes validated and controlled in accordance with the requirements of this standard should not be assumed to be effective in inactivating the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeld-Jakob disease. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

NOTE (See, for example, EN 12442-1, -2 and -3)

1.2.2 This standard 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 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 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 standard to have a full 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 or reprocessing of medical devices, including the sterilization process. National and/or regional regulations for the provision of medical devices might require a complete the implementation of a full quality management system and the assessment of that system by a third party.

1.2.5 This standard does not specify requirements for occupational safety associated with the design and operation of moist heat sterilization 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 11138-1, Sterilization of health care products — Biological indicators — Part 1: General Requirements

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

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

ISO 11140-3, Sterilization of health care products — Chemical indicators — Part 3: Class 2 indicators for steam penetration test sheets

ISO 11140-4, Sterilization of health care products — Chemical indicators — Part 4: Class 2 indicators for steam penetration test packs

ISO 11140-5, Sterilization of health care products — Chemical indicators — Part 5: Class2 indicators for air removal test sheets and packs

ISO 11737-1, Sterilization of medical devices — Microbiological methods — Part 1: Determination of population of microorganisms on product

ISO 11737-2, Sterilization of medical devices — Microbiological methods — Part 2: Tests of Sterility performed in the validation of a sterilization process

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

ISO 17664, Sterilization of medical devices — Information to be provided by the manufacturer for the processing of resterilizable medical devices

3 Terms and definitions

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

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

3.2
automatic controller
device that, in response to pre-determined operating cycle variables, operates the sterilizer sequentially through the required stages of the operating cycle(s)

3.3
bioburden
population of viable microorganisms on and/or in a product and/or a package
[ISO TS 11139:2001]

3.4
biological indicator
viable microorganisms inoculated onto a carrier and contained within a primary pack, ready for use and providing defined resistance to a specified sterilisation process under defined conditions.

3.5
biological indicator system
test system containing viable microorganisms providing a defined resistance to a specified sterilization process

3.6
calibration
set of operations which establish under specified conditions the relationship between values indicated by a measuring system, or values represented by a material measure or a reference material, and the corresponding values of that quantity obtained from a reference standard.
[ISO TS 11139:2001]

3.7
chemical indicator
test system that reveals change in one or more process variables based on a chemical or physical change resulting from exposure to a sterilization process
[ISO TS 11139:2001]

3.8
contained product
product in which the environment within the sterilizer during any stage of the sterilization process does not come into direct contact with the product

NOTE The environment within the sterilizer is used for heating and cooling purposes only, not for achieving the sterilization effect, for example, a solution in a sealed bottle.

3.9
correction
action to eliminate a detected nonconformity

NOTE A correction can be made in conjunction with corrective action.

3.10
corrective action
action to eliminate (or elimination of) the cause of a potential non-conformity or other undesirable situation

NOTE 1 Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence.

NOTE 2 There is a distinction between correction and corrective action.

3.11
D value; D_{10} value
Time, in minutes, required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions

3.12
development
act of elaborating a specification in preparation for validation
[ISO TS 11139:2001]

3.13
environmental control
engineering and/or procedural systems that maintain conditions in manufacturing areas within specified limits

NOTE Such systems may include air and fluid filters, surface disinfection, personnel uniforms and administrative procedures.

[ISO TS 11139:2001]

3.14
equilibration time
period which elapses between the attainment of the sterilization temperature at the reference measuring point and the attainment of the sterilization temperature at all points within the sterilizer load

3.15
establish
determine by theoretical evaluation and confirm by experimentation
[ISO TS 11139:2001]

3.16
exposure time
period for which the process parameters are maintained within their specified tolerances
[ISO TS 11139:2001]

3.17
fault
one or more of the process parameters which lies outside of its/their specified tolerance(s)
[ISO/TS 11139:2001]

3.18
F_0 value
microbiological lethality of a sterilization process expressed in terms of the equivalent heating time, in minutes, at a temperature of 121.1 °C with reference to microorganisms with a z value of 10 °C.

3.19
health care product
medical device (including in vitro diagnostic medical device) and medicinal product (including biopharmaceuticals
[ISO TS 11139:2001]

3.20
holding time
period for which the temperatures at the reference measurement point and at all points within the sterilizer load are continuously within the sterilization temperature band

3.21
inoculated carrier
supporting material on or in which a defined number of test microorganisms have been deposited

3.22
Installation Qualification (IQ)
process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification
[ISO TS 11139:2001]

3.23
load configuration
specified configuration within the sterilization chamber of the items of chamber furniture and the numbers, types, distribution and orientation of product presented for sterilization

3.24
maintenance
combination of all technical and associated administrative actions intended to retain an item at/or restore it to a state in which it can perform its required function

3.25
medical device
instrument, apparatus, implement, machine, appliance, implant, in-vitro reagent or calibrator, 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 purpose(s) of

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

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

— investigation, replacement or 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

NOTE This definition has been developed by the Global Harmonization Task Force (GHTF)

[ISO13485:2003]

3.26
measuring chain
series of elements of a measuring instrument or measuring system that constitutes the path of the measurement signal from the input (quantity subject to measurement) to the output (the result of the measurement)

3.27
microorganism
entity of microscopic size, encompassing bacteria, fungi, protozoa and viruses

NOTE A specific standard might not require the demonstration of the effectiveness of the sterilization process in inactivation of all types of microorganism identified in the definition above during validation or routine control of the sterilization process.

[ISO TS 11139:2001]

3.28
moist heat
heat that is derived from water, either as a liquid or as steam under pressure, for the purpose of achieving microbial lethality

3.29
non-condensable gas
air and/or other gas which will not condense under the conditions of saturated steam sterilization

3.30
Operational Qualification (OQ)
process of obtaining and documenting evidence that the installed equipment operates within predetermined limits when used in accordance with its operational procedures
[ISO TS 11139:2001]

3.31
operating cycle
complete set of stages of the process that is carried out in the sequence as regulated by the automatic controller

3.32
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 11139:2001]

3.33
preventive action
action to eliminate (or elimination of) the cause of a potential non-conformity or other undesirable potential situation

NOTE Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence.

3.34
plateau period
equilibration time plus the holding time

3.35
process challenge device
item designed to constitute a defined resistance to a sterilization process, and used to assess the effective performance of the process
[ISO TS 11139:2000]

3.36
process parameter
specified value for a process variable

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

[ISO TS 11139:2000]

3.37
process variable
condition within a sterilization process, changes in which alter microbicidal effectiveness

NOTE Process variables may include, for example, time, temperature, pressure, humidity

3.38
product
raw material(s), intermediate(s), sub-assembly(ies) and health care product(s)

NOTE A product may be considered to be a number of different items all contained within the same packaging.

3.39
product family
groups or subgroups of product characterized by similar attributes such as mass, material, construction, shapes, lumens and which present a similar challenge to the sterilization process

3.40
reference load
specified sterilization load(s) made up to represent difficult combinations of items to be sterilized.

3.41
reference measuring point
point where the temperature sensor used for the operating cycle control is located

3.42
reference microorganism
microbial strain obtained from a recognized culture collection

NOTE Recognised culture collections are maintained under the international depository authority under the *Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent And Regulation*.

3.43
requalification
repetition of part of validation for the purpose of confirming the continued acceptability of a specified sterilization process
[ISO TS 11139:2001]

3.44
saturated steam
water vapour in a state of equilibrium between condensation and evaporation