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Sterilization of health care products — Requirements for validation and routine control of moist heat sterilization in health care facilities

Stérilisation des produits de santé — Exigences pour la validation et le contrôle pratique de la stérilisation en chaleur humide dans les locaux de soins de santé

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Contents

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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.

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.

International Standard ISO 13683 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

Annexes A, B and C of this International Standard are for information only.

Introduction

Persons having responsibility for safe sterile health care products should be aware of available sterilization processes, methods of control, and physical characteristics of the product to be sterilized. Products produced under controlled conditions will have microorganisms on them and are, by definition, non-sterile. The purpose of sterilization is to destroy these microbiological contaminants. After sterilization, however, there is always a finite probability that a microorganism could survive regardless of the treatment applied. As a consequence, sterility of a processed item is defined in terms of the probability of the occurrence of a single viable microorganism surviving on the item.

Requirements for a quality system for the design, development, production, supply, installation and servicing of health care products are given in the ISO 9000 series of standards.

The ISO 9000 series of standards designates certain processes used in the manufacture of health care products as "special" in that the result cannot be fully verified by subsequent inspection or testing of the product. Sterilization is an example of a special process, because efficacy cannot be verified by inspection or testing of the product. For this reason, sterilization processes must be validated before use, the process routinely monitored and the equipment maintained.

Sterilization of health care products — Requirements for validation and routine control of moist heat sterilization in health care facilities

1 Scope

1.1 Inclusions

1.1.1 This International Standard specifies requirements for the use of moist heat in sterilization process development, validation of the sterilization process, and control of routine sterilization in either a health care facility or a facility contracted by a health care organization.

1.1.2 This International Standard covers all moist heat processes in health care facilities in which the sterilant is either steam, steam/air mixtures or pressurized water.

NOTE — While the general requirements of this International Standard can apply to the sterilization of pharmaceutical products, other technical or regulatory requirements may also apply.

1.2 Exclusions

1.2.1 This International Standard does not describe a quality assurance system for the control of all stages of production.

NOTE — Attention is drawn to the International Standards for quality systems (ISO 13485 or ISO 13488) which control all stages of production including the sterilization process. It is not a requirement of this International Standard to have a complete quality system during production, but certain elements of such a system are required and these are normatively referenced at appropriate places in the text.

1.2.2 Except for general requirements, this International Standard does not provide detailed requirements for all equipment used within a sterilization system (e.g. washing equipment).

1.2.3 This International Standard does not address sterilization processes that employ a chemical/steam mixture as the sterilant.

1.2.4 This International Standard does not apply to industrial moist heat sterilization, which is addressed by ISO 11134.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 9001:1994, *Quality systems — Model for quality assurance in design, development, production, installation and servicing.*

ISO 9002:1994, *Quality systems — Model for quality assurance in production, installation and testing.*

ISO 10012-1:1992, *Quality assurance requirements for measuring equipment — Part 1: Metrological confirmation system for measuring equipment*

ISO 11138-1:1994, *Sterilization of health care products — Biological indicators — Part 1: General.*

ISO 11138-3:1995, *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization.*

ISO 11607:1997, *Packaging for terminally sterilized medical devices*

ISO 13485:1996, *Quality systems — Medical devices — Particular requirements for the application of ISO 9001.*

ISO 13488:1996, *Quality systems — Medical devices — Particular requirements for the application of ISO 9002.*

IEC 1010-1:1990, *Safety requirements for electrical equipment for measurement, control, and laboratory use — Part 1: General requirements.*

IEC 1010-2-041:1996, *Safety requirements for electrical equipment for measurement, control, and laboratory use — Part 2-041: Particular requirements for autoclaves using steam for the treatment of medical materials and for laboratory purposes.*

3 Definitions

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

3.1 air-steam mixture: Uniform mixture of air and saturated steam used in some sterilization processes.

NOTE — Air is used to compensate for pressures generated within sealed containers that exceed saturated steam pressures.

3.2 bioburden: Population of viable microorganisms on a raw material, component, a finished product and/or a package.

3.3 certification: Documented review and approval process.

3.4 D value: Exposure time required under a defined set of conditions to cause a 1-logarithm (to the base 10) or 90% reduction in the population of a particular microorganism.

3.5 electromechanical control: System that uses mechanical means (e.g. cams or punch cards) to time and initiate electrical signals.

3.6 environmental control: System established in product manufacturing areas to control bioburden.

NOTE — Such a system can include air and fluid filters, surface disinfection, personnel uniforms and administrative procedures.

3.7 F value: Measure of the microbiological inactivation capability of a heat sterilization process.

3.8 F_o value: F value calculated at 121° C (234° F) with a z value of 10° C and a D value of 1 minute.

3.9 health care facility: Organization, including its service subcontractors, that provides any form of health care to patients.

3.10 health care products: Term encompassing medical devices, medicinal products (pharmaceuticals and biologics) and *in vitro* diagnostics.

3.11 microbiological challenge: Biological indicators, biological-indicator test packs, or inoculated products that contain known populations of microorganisms and which can be used in testing sterilization cycles.

3.12 porous material: Material or configuration that requires steam penetration into the product for sterilization to occur.

3.13 primary packaging: Element of the packaging system that maintains the sterility of the product.

3.14 process lethality: Capability of the sterilization process to destroy microorganisms.

NOTE — This can be determined by measurements of microbial death or by establishing and measuring the required physical parameters.

3.15 commissioning: Obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification and that it functions within pre-determined limits when operated in accordance with operational instructions.

3.16 recommissioning: Repetition of part or all of the commissioning test requirements for the purpose of reconfirming process reliability.

3.17 revalidation: Repetition of part or all of the validation test requirements for the purpose of reconfirming process reliability.

3.18 saturated steam: Water vapour in a state of equilibrium between condensation and evaporation.

3.19 simulated product load: Load that is used as an alternative to the actual product load and that represents an equal or greater challenge to the process.

3.20 sterile: State of being free from viable microorganisms.

NOTE — In practice no such absolute statement regarding the absence of microorganisms can be proven (see **sterilization**).

3.21 sterilization: Validated process used to render a product free of all forms of viable microorganisms.

NOTE — In a sterilization process, the nature of microbiological death is described by an exponential function. Therefore, the presence of microorganisms on any individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero.

3.22 sterilization cycle: Defined sequence of operational steps designed to achieve sterilization that are carried out in a sealed chamber.

3.23 sterilization process development: Studies conducted to develop a reproducible process by which the product can be sterilized to the desired probability of a non-sterile unit without damage.

3.24 validation: Documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications.

NOTE — Validation covers three activities: commissioning, verification of process specification and performance qualification.

3.25 z value: Number of degrees of temperature required for a 1-logarithm (to the base 10) change in the D-value.

3.26 sterilization system: Total of procedures and equipment including sterilization, needed to render a possibly soiled or contaminated product sterile and safe for use.

3.27 chamber furniture: Means inside the sterilizer chamber for supporting the load.

4 General

4.1 Responsibilities and training of personnel

Responsibility for the installation, operation, maintenance and periodic testing of moist heat sterilizers, for the validation and routine control of moist heat sterilization, and for the release of sterilized product shall be assigned to qualified personnel. The criteria for selection of personnel shall be based on requirements in one of the following: ISO 9001 [or ISO 13485] or ISO 9002 [or ISO 13488].

4.2 Clothing

Outer clothing to be used in each area of the sterile processing department shall be specified and documented.

4.3 Product considerations

Moist heat sterilization processes shall only be used with products that are designed to be compatible with the physical conditions and changes occurring in the sterilizer chamber. This information shall be documented and shall be either obtained from the product supplier or generated by the health care facility.

For products designed for reuse, documented evidence demonstrating that procedures recommended for the decontamination, cleaning and sterilization of the product are effective shall be obtained from the supplier. These procedures shall be evaluated during validation.

4.4 Packaging considerations

4.4.1 General

4.4.1.1 The packaging materials and procedures shall be specified.

4.4.1.2 Packaging materials shall be selected to be compatible with the environmental conditions within the sterilizer throughout the cycle.

4.4.1.3 Packaging materials shall comply with ISO 11607.

4.4.2 Packaging permeability

The packaging shall permit the attainment of sterilizing conditions on or within the product either by the removal of air and penetration of steam, or by heat transfer for nonpermeable packaging such as vials containing aqueous liquids.

When handled according to instructions, packaging shall protect the product from physical damage and shall maintain the sterility of the health care product up to the point of use.

5 Equipment

5.1 Documentation

5.1.1 Identification

Each sterilizer and steam generator shall have one or more information plates, permanently fastened and marked, that provide the following information in the language agreed by the user:

a) name and address of the manufacturer;
b) serial number or other system identification;
c) chamber design pressure and maximum working temperature;
d) jacket pressure rating (if applicable);
e) stamp of inspection authority and vessel identification mark;
f) date of primary pressure testing of the vessel;
g) pressure vessel standard to which the vessel was constructed and tested, if applicable.

5.1.2 Safety

Documentary evidence shall be provided to demonstrate that the sterilization system complies with the safety requirements specified in IEC 1010-1 and IEC 1010-2-041.

5.1.3 Manuals and instructions

Documentation provided with each identified sterilizer shall be written in the language or languages agreed to by the user and shall include:

a) instructions for the installation of the sterilization system sufficient to ensure safe and effective operation of the equipment;
b) a list of materials of construction of the vessel and chamber furniture in contact with the sterilant;
c) instructions for safe and effective operation, including the vessel temperature and pressure limits;
d) instructions and recommended schedules for routine preventive maintenance, including a list of replacement parts and special tools for maintenance.
e) chamber drawings sufficient to define configuration and hardware, pipework and control system schematic drawings, recommended installation drawings, and a list defining all significant components;

f) process-control logic and/or software documentation necessary to operate and maintain the equipment control system (see 5.2.6).
g) release and revision of software, including proof of validation.

5.1.4 Additional information

The user shall obtain and maintain documentation of any installation testing.

5.2 Sterilizer performance, utilities, components, accessories and controls

5.2.1 Performance

The user shall obtain evidence to demonstrate that the sterilizer complies with its specification.

5.2.2 Utilities

5.2.2.1 Steam purity and quality shall be specified and demonstrated not to impair the proper function of the product being sterilized. These parameters shall be documented.

5.2.2.2 The purity of the compressed air used in the sterilization chamber shall be such that the safety of the product is not impaired. This shall be documented.

5.2.2.3 Ambient air admitted to the chamber to relieve the vacuum shall pass through a microbiologically retentive filter. Specification of the filter shall be documented.

5.2.2.4 Water used in the sterilizer as a means of direct cooling of product shall be specified and shall be verified not to contaminate the product. This shall be documented.

5.2.2.5 Electrical power supplied to the sterilization system shall comply with the sterilizer manufacturer's specification. This shall be documented.

5.2.3 Components

The user shall ensure that the positioning of components and the materials selected for construction of the sterilization system minimize the potential for microbiological or chemical contamination. This shall be documented.

5.2.4 Accessories

The user shall select chamber furniture that is designed to allow uniform steam penetration and/or heat transfer, and the drainage of condensate.

5.2.5 Control and monitoring systems

5.2.5.1 The control system shall maintain the temperature within a specified range appropriate for the particular moist heat sterilization process being carried out.

The following process parameters shall be automatically controlled and monitored as a function of elapsed time:

a) chamber temperature;
b) chamber pressure;
c) rate of change of chamber temperature and pressure.

The result of the monitoring shall be recorded.

The monitoring and process control systems shall either be independent or designed in a manner that will cause a warning to occur during or at the end of the cycle if the difference between a set and a measured value exceeds specified limits. The recording made of the monitoring shall be sufficient to allow subsequent analysis.

5.2.5.2 The sensor(s) used for process control and monitoring shall be placed in a position determined by temperature distribution studies to be representative of the conditions throughout the load.

5.2.6 Control programs

The user shall ensure that programs used to control and monitor the sterilization process, whether microprocessor or electromechanically based, are validated. The control program shall be evaluated by procedures designed to demonstrate the correctness of the program logic in both process simulated conditions and actual sterilizer use. Any subsequent changes shall be similarly documented and be evaluated to assess whether revalidation is required.

5.3 Performance of instruments

5.3.1 Instrument accuracy

5.3.1.1 The accuracy of instrumentation shall be specified.

5.3.1.2 Accuracy of instruments used for validation shall exceed the required accuracy of the controller and monitoring system.

5.3.1.3 Temperature and pressure sensors shall be selected, installed and used in a manner which will ensure that the stated accuracy is attained.

5.3.2 Calibration standards

The accuracy of standards used to calibrate process measurement instruments shall be specified and calibration shall be traceable to a national reference standard as specified in ISO 9001 and ISO 9002, and shall comply with ISO 10012-1.

5.3.3 Calibration program

The effective procedure shall be established, documented and maintained for the calibration of all controlling, indicating and recording instruments used for validation and routine control of the sterilization cycle. The procedure shall be based on the requirements given in ISO 9001 or ISO 9002.

5.4 Maintenance

5.4.1 Equipment shall be maintained in accordance with a documented planned preventive maintenance scheme.

5.4.2 Person(s) carrying out maintenance shall have documentary evidence demonstrating successful training in the skills needed to maintain the specified equipment.

5.4.3 The procedure for each planned maintenance task and the frequency with which it is carried out shall be specified and documented.

5.4.4 A sterilizer shall not be used to process health care products until scheduled maintenance, and necessary unscheduled tasks that are critical to proper sterilizer function have been satisfactorily completed and recorded.

5.4.5 Records of maintenance shall be retained in an equipment file.

5.4.6 The maintenance scheme, maintenance procedures and maintenance records shall be reviewed periodically by a designated person. This person shall be selected in accordance with the requirements given in ISO 9001 or ISO 9002.

6 Sterilization process development

6.1 All parts of the sterilization system shall be developed to be reproducible during routine production. Where applicable, these parts shall be included:

a) cleaning/decontamination;
b) inspection;
c) assembly;
d) packaging;
e) loading;
f) exposure to sterilization conditions;
g) unloading;
h) storage;
i) distribution.

6.2 Procedures and materials used in each part shall be documented and each task performed by trained personnel.

6.3 Except where compliance with the product specification would be compromised, sterilization by saturated steam shall be used.

Air-steam mixtures shall only be used in combination with effective circulation that creates a uniform heating medium throughout the sterilizer.

Reproducibility of the environment within the chamber shall be demonstrated.

6.4 The attainment of sterilizing conditions in the products processed in newly-developed moist heat sterilization cycles shall be demonstrated.

6.5 The evaluation of the efficacy of a sterilization cycle shall be based on the attainment of physical parameters.

6.6 Any microbiological testing performed shall be in addition to the measurement of physical parameters.

6.7 If indicator microorganisms are used, they shall be selected with reference to the sterilization process and shall meet the requirements of ISO 11138-1 and ISO 11138-3.

7 Sterilization process validation

7.1 The validation programme shall be performed using an approved protocol that conforms to the requirements outlined in ISO 9002.

7.2 Each sterilizer shall be commissioned upon installation. New products and new sterilization equipment or process conditions shall be validated.

7.3 Validation activities shall be assigned to a designated person experienced in this task.

7.4 The commissioning shall include:

a) demonstration of compliance with equipment construction specifications after installation;
b) documentation of the equipment (see 5.1);
c) demonstration of conformance of the quality and capacity of utilities;
d) verification of calibration of both operating and test instrumentation;
e) when applicable, demonstration of efficacy of air removal;
f) demonstration of compliance with performance specifications.

7.5 The performance qualification shall demonstrate that the sterilization process is reproducible and shall include:

a) demonstration of uniformity of physical parameters within specified limits throughout the chamber and load;
b) demonstration of the relationship between set control parameters and actual parameters measured in the load;
c) demonstration of the correlation of physical parameters to microbiological lethality using data taken from established literature or from original research;
d) demonstration of acceptable maximum and minimum loading;
e) demonstration of the acceptable limits of product mix within and across loads;
f) if simulated product loads are used, demonstration that the simulated product loads are representative of actual products;
g) demonstration that qualification loads that will be reused have returned to specified conditions before reuse.

7.6 The number of temperature sensors and cycles to be used for performance qualification and performance requalification shall be specified. Documented evidence shall be provided to demonstrate that this number is sufficient to establish that the process conforms to specifications generated during process development.

7.7 The calibration of temperature measurement systems used for validation shall be verified at least before and after each program of sequential tests.

7.8 At the completion of the validation, all data shall be formally reviewed, approved and certified by a designated person.

7.9 Revalidation shall be done whenever there has been a major repair to the sterilization system that could affect the efficacy of the process. Revalidation shall also be performed at least once every 12 months.

7.10 Procedures for revalidation, review and implementation of changes to the process, sterilization system (hardware and software), product or packaging shall be documented. The responsibility for determining the need for and extent of repetition of the original validation studies shall be assigned to trained personnel.

Modifications to equipment or control systems shall be evaluated to confirm that the process conditions delivered to the product load are comparable to those originally qualified.