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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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International Organization for Standardization
Case postale 56 • CH-1211 Genève 20 • Switzerland
Internet central@iso.ch
X.400 c=ch; a=400net; p=iso; o=isocs; s=central

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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.

8 Routine moist heat sterilization

8.1 Steam sterilization process control

8.1.1 The accuracy and reliability of instrumentation used to monitor each production cycle shall be periodically checked for compliance with their specification.

8.1.2 Documented procedures for the routine monitoring of the sterilization cycle shall be provided.

8.1.3 For each cycle, a record shall be retained of the following:

a) date;
b) sterilizer identification;
c) cycle identification;
d) operator identification;
e) description of the load and batch number;
f) cycle start time (real time);
g) chamber pressures throughout the cycle as a function of elapsed time;
h) chamber temperatures throughout the cycle as a function of elapsed time;

8.2 Change control

There shall be documented procedures in place to ensure that no changes take place in equipment, process, or materials that could affect the sterilization process. If such changes do occur as a planned event, the new sterilization cycle shall be validated. Process failures that cannot be attributed to lack of adherence to process specifications shall be examined to determine the need for validation.

8.3 Periodic testing

Sterilizers shall be tested periodically in accordance with a documented plan.

8.4 Cycle evaluation

The efficacy of the process cycle shall be determined by evaluation of the attainment of physical parameters.

NOTE — The routine testing of samples (sterility testing) or the use of biological indicators is not recommended, except in a limited number of special applications. These practices are of limited value in routine control of moist heat sterilization and should always be considered in combination with the attainment of physical parameters.

8.5 Release of sterilized products

8.5.1 A system to differentiate between processed and unprocessed items shall be used.

8.5.2 A system shall be established and maintained for release of product after sterilization. The system shall ensure that the validated sterilization cycle has been reproduced within the specified limits. Each release decision shall be documented, including identification of the person making the decision.

8.5.3 For each load, the release documentation shall:

a) specify the load or include a reference to the specification for the load;
b) include records from routine testing;
c) include records from the sterilization cycle.

8.5.4 Non-conforming product shall be handled in accordance with the requirements of ISO 9001 or ISO 9002.

8.6 Audit of operations

Production and quality control procedures and all records shall be reviewed at least once every 12 months. Competent personnel not directly involved in these procedures shall ensure that the process specifications and data established during validation remain valid.

8.7 Corrective action

Procedures and documentation for corrective action shall comply with ISO 9001. Any deviations from specifications or procedures identified during operations, audits, calibrations or maintenance shall be reviewed by a designated person to determine the proper steps and corrective action required. Any corrective action taken shall be documented.

8.8 Records

Records to demonstrate that products have been sterilized in accordance with all specifications shall be produced and maintained as specified in ISO 9001 and ISO 13485 or ISO 9002 and ISO 13488.

Annex A
(informative)

Guidance

A.1 Scope
No guidance is offered.

A.2 Normative references
No guidance is offered.

A.3 Definitions
No guidance is offered.

A.4 General

This section provides guidelines for personnel qualification, training and education, as well as minimum criteria for personnel health, personal hygiene and attire. These are key elements in minimizing bioburden, containing contamination and assuring an effective sterilization process.

A.4.1 Responsibilities and training of personnel

Supervision of process: Managers should be qualified by education and experience to administer the sterilization function of a health care facility. Managers are responsible for the establishment of policies and procedures for all phases of sterilization and for budgetary accountability. Managers should provide their employees with education in the basics of Central Service. Orientation and on-the-job training should be based on the procedures and equipment used within the facility. Documentation of education and training should record personnel competence for all phases of the process.

Education, training and competency should be monitored and documented for:

a) safe receipt of contaminated items;
b) decontamination and cleaning;
c) inspection;
d) preparation and assembly;
e) packaging/wrapping;
f) loading of the sterilizer;
g) operation of the sterilizer;
h) monitoring of the cycle (physical, as well as chemical and/or biological);
i) correct handling after sterilization;
j) storage;
k) distribution;
l) documentation of the process;
m) quality assurance.

The manager should provide coaching and feedback to correct errors and to assure compliance with policies and procedures.

Supervisory personnel: All preparation and sterilization activities, including decontamination, inspection, preparation, packaging, sterilization, storage, and distribution should be monitored. Personnel assigned to supervisory functions should be prepared for this responsibility by education, training and experience. Moist heat sterilization is a process that should be supervised by personnel having extensive health care experience in the fields of sterilization, processing and infection control. This should include participation in continuing education programmes and courses with content that includes information on government regulations, personnel and material management, as well as content directly related to the sterilization process.

Health and personal hygiene: Written policies on personal hygiene should be developed and communicated to employees. Hand washing and hand treatment procedures should be identified. Careful attention to personal hygiene will minimize the potential for cross-infection. Written policies should be established regarding the reporting, treatment and disposition of employees who could transmit infections or who are at risk of acquiring infections.

Personnel should be made aware of any health risks associated with the specific tasks to which they are assigned. Procedures should be developed to minimize these risks. Procedures should be documented.

A.4.2 Clothing

Appropriate attire minimizes the introduction of microorganisms from personnel to items being processed. All personnel working in the preparation, sterilization and sterile storage areas should wear clean clothing, which should be changed at least daily. Controlled laundering of garments reduces the risk of transferring microorganisms. Procedures should be developed to assure that these recommendations are carried out.

When specifying clothing, consideration should be given to the following:

a) potential for soiling during processing activity;
b) potential for cross-contamination between areas;
c) which garments should be changed and how often.

Special consideration should be given to the clothing worn by personnel in the decontamination and packaging areas. In the decontamination area, clothing should be selected to reduce the risk of transfer of microorganisms to personnel during processing. In the packaging area, clothing should be selected to reduce the particulate contamination on the devices being processed.

A.4.3 Product considerations

When selecting a health care product, consideration should be given to the manufacturer's recommendations for reprocessing and to the specific processes available within the facility, to ascertain that these are compatible. Where the manufacturer has specified a maximum number of reprocessing cycles for a product, a system of tracking the number of reprocessings should be developed and records should be kept for each such product. Whenever possible, decontamination and cleaning should be accomplished in machines designed for this purpose. Moist thermal treatment is preferred over other methods for this step in the process.

A.4.4 Packaging considerations

For further information on packaging material requirements, see ISO 11607.

Materials used for packaging should be compatible with the contained product. In developing selection procedures for packaging materials, consideration should also be given to:

a) resistance to tearing;
b) allowing for aseptic presentation;
c) containing the minimal possible levels of toxic ingredients, non-fast dyes and lint without compromising the quality of the product; and
d) not generating any gases that could restrict the removal of air and penetration of steam.

A.5 Equipment

NOTE — The national regulations in the country of use have precedence when considering the design of equipment or processes for sterilization of health care products.

A.5.1 Documentation

A.5.1.1 Identification

No guidance is offered.

A.5.1.2 Safety

Written instructions should be available to alert the user to potential hazards associated with equipment use. These safety features should be described in the literature accompanying the equipment. (See IEC 1010-1 and IEC 1010-2-041.)

A.5.1.3 Manuals and instructions

Information related to validation of software can be found in a document under preparation by IEC/SC 65A, *System aspects*, which has been given the provisional title, *Functional safety — Safety related systems — Part 3: Software requirements*.

A.5.1.4 Additional information

No guidance is offered.

A.5.2 Sterilizer performance, utilities, components, accessories and controls

A.5.2.1 Performance

Evidence that a sterilizer complies with its specification may be obtained from the manufacturer, generated by the user or from a third party.

A.5.2.2 Utilities

A.5.2.2.1 The sterilizer should be designed to operate with saturated steam or preset air-steam mixtures. Where saturated steam is used, the steam supplied to the sterilizer should have a dryness value not less than 0,95, containing not more than 3,5 % volume fraction of non-condensable gases and not superheated more than 5 °C. To ensure continued steam quality, the steam, on condensing, should not contain contaminants in a quantity that could impair the sterilization process, harm the sterilizer or compromise the product integrity. The steam boiler and transmission lines should be of sufficient size and capacity to provide adequate steam pressure and volume to the sterilizer. The steam pressure fluctuation before the sterilizer pressure-reduction valve should not exceed 10% and the reduction ratio should not be greater than 2 to 1. Steam and air traps should be installed to remove condensate and non-condensable gases from the steam piped to the sterilizer. Information regarding the tolerance of product should be obtained from the manufacturer.

A.5.2.2.2 The sterilizer should be designed to operate with a compressed air supply, free of liquid water, filtered to 5 µm and contains not more than 0,5 mg of oil per cubic metre of free air. Compressed air should be passed through a microbiologically retentive filter at the point of use. The filter should retain not less than 99,5 % of particles greater than 0,3 µm.

A.5.2.2.3 For sterilizers where the operating cycle requires the admission of air directly from the atmosphere into the chamber, the air should be admitted through a filter that retains not less than 99,5 % of particles greater than 0,3 µm.

Sealed products may not require air admitted to the chamber to be filtered microbiologically. Permeable packaging under conditions of vacuum, heat and humidity can, however, allow microbiological penetration which would not occur under normal conditions. Also, normally sealed packaging can breathe if heat-induced expansion of components and/or internal vacuums, caused by cooling of air in the product, occur.

A.5.2.2.4 The feed water for steam production and the water for direct cooling should be free from contaminants in a concentration that could impair the sterilization process, harm the sterilizer, damage the products to be sterilized or create any health hazard. See Table A.1 for typical limiting values of contaminants. The water for the vacuum system should be supplied at a temperature compatible with the performance of the sterilizer (e.g. 15 °C), and should be of a hardness value less than or equal to 0,2 mmol/l with a pH of not less than 6,5.

Test procedures should be written and tests should be carried out as frequently as necessary to assure that the limits specified in the Table A.1 are not exceeded.

Provisions should be made for preventing or removing any residues (e.g., microbiological residues) that can build up in the steam generator. This can be done, for example, by controlling the contamination of feedwater, or by a system to remove residues from the steam generator.

A.5.2.2.5 Electrical power supplied to the sterilizer should permit acceptable and reliable performance of the system. Electrical power supplied to the sterilizer should be installed in conformance with applicable codes and regulations. Electrical power quality and continuous electrical power for sterilization measurement and control systems can be achieved by providing line voltage conditioning.

A.5.2.3 Components

The design of piping systems should take into account the need for drainage and, when required, sterilization of the piping. Additional considerations include the elimination of dead legs, the proper sloping of lines and placement of other system components, and any other measures necessary to minimize retention of water in the system and microbial growth. The quality of connections should preclude leakage. Lines should not connect directly to a drain without an atmospheric break to avoid back-siphoning. Interconnection between water cooling systems and all other systems, such as compressed air, must be designed to prevent back flow. Pumps used to circulate cooling water which require lubrication of their seals should use water equal in quality to that being pumped. Heat exchangers should be designed to deter leakage of external media into the circulation system. If the water level is controlled as part of the sterilizing process, appropriate water-level controllers and alarms should be provided.

Table A1. Typical limiting values of contaminants of steam and/or water in contact with product and or product packaging

evaporate residue	≤ 15 mg/l
silica	≤ 2 mg/l
iron	≤ 0,2 mg/l
cadmium	≤ 0,005 mg/l
lead	≤ 0,05 mg/l
rest of heavy metals	≤ 0,1 mg/l
chloride	≤ 3 mg/l
phosphate	≤ 0,5 mg/l
conductivity	≤ 50 µS/cm
pH	6,5 to 8
appearance	colourless, clean, without sediment
hardness	≤ 0,1 mmol/l

Ports should be adequately sized, properly located, and sufficient to provide necessary connections for the process monitoring and testing systems. Chamber safety relief ports must be designed and placed so they will not be blocked. All ports should be clearly identified.

A.5.2.4 Accessories

No guidance is offered.

A.5.2.5 Control and monitoring systems

A.5.2.5.1 The chamber temperature should be measured using a thermal sensor located in a position that has a known relationship to the temperature occurring in the useable chamber space. Resistance temperature detectors (RTDs) or thermocouple sensor signals are generally accepted.

In saturated steam sterilization, the controlled chamber temperature correlates with the indicated chamber pressure.

An automatic measurement and monitoring system may provide either analog or digital data. This system may be used with manually recorded data to document the following process parameters and events, where applicable:

a) date;
b) sterilizer identification;
c) load traceability identification (e.g. lot number or cycle number);
d) cycle selected, if more than one programmed cycle available;
e) operator identification;
f) cycle start time (real time);
g) chamber pressure as a function of elapsed time;
h) chamber temperature as a function of elapsed time;
i) exposure phase start time;
j) exposure phase end time;
k) cooling time, final temperature, or both.

Mechanical control monitors include time-, temperature- and pressure-recording devices and gauges. When time, temperature and pressure records are provided, the operator should ensure, at the beginning of the cycle, that the record is marked with the date, the sterilizer identification number and the identification of the operator initiating the cycle. At the end of the cycle, and before items are released for use, the operator should examine the record to verify that cycle parameters were met, and mark it to allow later identification of the approving operator.

A.5.2.5.2 Most temperature sensors measure temperature within the exhaust line of the sterilizer, not at the centre of packs. For liquid loads, a representative location would be inside a container of similar size and shape and containing liquid of similar viscosity. Improper load configuration or package composition can interfere with the air evacuation and steam penetration; conditions that will not be revealed in the temperature recording. Therefore, mechanical monitoring and other indicators of sterilizer performance should never be considered a substitute for careful adherence to validated packaging and loading procedures.

A.5.2.6 Control programs

No guidance is offered.

A.5.3 Performance of instruments

The ability of the sterilization system to control the required process variables depends on the design of the total system, performance characteristics of the measurement and control instrumentation, and on calibration.

A.5.3.1 Instrument accuracy

The temperature control device should:

— be either digital or analog;
— have an accuracy of ± 1 % over the scale range 50 °C to 150 °C;
— be adjusted to ± 0,5 °C at the sterilization temperature;
— have broken-sensor protection;
— be adjustable *in situ* by the use of a key, code or tool without dismantling the instrument.

The pressure control device should:

— be either digital or analog;
— have an accuracy of ± 1,6 % or better over the scale range 0 bar to 5 bar absolute (0 kPa to 500 kPa);
— have broken-sensor protection;
— be adjustable *in situ* by the use of a key, code or tool without dismantling the instrument.

The time control device should have an accuracy of ± 1 % or better for time periods above 5 min and have an accuracy of ± 2,5 % or better for time periods of up to 5 min.

Where possible, the systematic errors should be quantified and corrected by applying the appropriate correction factors.

The accuracy of test instruments should be not less than the accuracy of the instruments fitted to the sterilizer and should exceed by at least a factor of three the accuracy of measurements required to judge the performance of the sterilizer.

A.5.3.2 Calibration standards

No guidance is offered.

A.5.3.3 Calibration program

No guidance is offered.

A.5.4 Maintenance

A.5.4.1 Sterilizers should be inspected and cleaned according to the manufacturer's written instructions. Examples of items requiring frequent care are recorders, door gaskets, the chamber drain screen, the internal chamber and external surfaces. All prescribed inspection and cleaning should be performed as specified in the manufacturer's written instructions.

Periodic inspection and cleaning reduces the frequency of sterilizer malfunction. Cleanliness of environmental surfaces in the loading and unloading area also reduces the risk of accidental contamination of sterile material.

A.5.4.2 The person carrying out the manufacturer's written instructions for preventive maintenance of the equipment should be qualified to do so. Attention should be given to maintenance and replacement of components subject to wear. Examples of these are recording devices (as applicable), filters, steam traps, drain pipes, valves, and door gaskets.

A.5.4.3 Lubrication of appropriate parts and replacement of expendable parts, such as steam traps, should be performed as needed by qualified personnel. Certain maintenance tasks could require the services of the manufacturer or other qualified service organization. The frequency of maintenance could depend on how often the equipment is used and could vary from facility to facility; the manufacturer's instructions should be consulted for guidance.

A.5.4.4 No guidance is offered.

A.5.4.5 A maintenance record should be kept for each sterilizer. The individual performing maintenance should document each maintenance activity on this record. The record should be kept at the location of the sterilizer. Included in this maintenance record should be sufficient information to identify the steam sterilizer and to establish a continuous history of all scheduled and unscheduled service.

A.5.4.6 No guidance is offered.

A.6 Sterilization process development

NOTE — See also Annex B, Sterilization cycles.

A.6.1 Health care products that are moist heat-sterilized in health care facilities may be either purchased from a supplier or developed within the health care facility. For products that are purchased, the following information should be obtained from the supplier:

— suitability of moist heat sterilization;
— maximum sterilization temperature;
— pressure and/or vacuum limitations, including rates of change;
— recommendations for cleaning, if applicable, to include disassembly (if required), cleaning agents and cleaning utensils;
— disassembly for sterilization, if applicable;
— estimate of the number of reprocessing cycles allowable, if reprocessing will contribute to product degradation.

For products developed and manufactured within the health care facility, the same information should be determined during product development.

Effective sterilization of health care products includes many aspects in addition to the sterilization cycle itself. These include:

— Cleaning. Cleaning should remove all visible debris and lubricants from the surface of the product and all interior passages (e.g., tubing or lumens). The cleaning process should also include areas not visibly contaminated to reduce ambient microorganisms. Special care should be given to lumina to assure adequate cleaning and removal of cleaning solutions. All surfaces should be rinsed and dried.

NOTE — In the cleaning process, it could be necessary to disassemble a product with multiple parts to adequately remove all debris.

— Inspection: After cleaning, components of the product, if applicable, and the assembled product should be inspected for cleanliness or any deterioration that could effect the safety and functionality.

— Assembly: After inspection, products should be placed in a configuration in which they can be sterilized. This could mean the collection of several items into a kit or set. To assure effective sterilization, some products could require partial disassembly, depending on the moist heat sterilization process being used.

In developing procedures for inspection and assembly, consideration should be given to practices that minimize contamination of the product by physical, chemical and microbiological means.

Prior to assembly and sterilization, porous materials should be allowed to equilibrate in an environment with a relative humidity range of 35 % to 70 % at room temperature. Temperature and humidity equilibration of packaging material and product facilitate air removal, sterilant (moist heat) penetration, and reduce the opportunity for superheating.

— Packaging (see 4.4 and A.4.4): Products should be packaged immediately after the assembly procedure. Storage and transport to the sterilizer should not cause damage to the package. Storage time before sterilization should be minimized and should be in an environment within the temperature and humidity ranges noted above.

— Loading: Acceptable product loading in the chamber should be documented. If only one type of product is permitted in the chamber, a loading diagram and maximum/minimum loading should be documented. Where mixed loads are permitted, acceptable product mix and load configuration should be determined and documented. Factors that can influence product mixing include the ability to withstand the sterilization process; the size and weight of packaged product; the configuration of packaged product; and the ability of steam to penetrate the package and product. (See also Table A.2.)

The product load should be arranged to allow contact of the sterilizing agent with every surface to be sterilized.

NOTE — Type of product is defined by similarity of the size, shape, weight, material make-up, and, for items with lumens, the length-to-bore ratio. It does not mean that all items must be exactly the same.

— Exposure to sterilization conditions: Selection of the type of sterilization cycle to be used depends upon the product configuration and the ability of the product and package to withstand temperatures, pressure stresses and total heat input.

Moist heat sterilization of health care products can be complex because of the heterogeneity of product types, product packaging, and vessel loading configurations that can be encountered. Factors that can influence moist heat sterilization of health care products are listed in Table A.2.

Multicomponent products can have surfaces where the steam penetration necessary for sterilization might not occur. In these cases it could be necessary to disassemble the product for sterilization. In extreme cases it could also be necessary to demonstrate that sterilization is possible using a microbiological challenge (see ISO 11137-2).

If packaged products are moist heat-sterilized, consideration should be given to adequate post-sterilization drying of the packaging material and package contents to maintain sterile barrier properties of the packaging.

Many similarities can exist among products and packages to be sterilized. For example, the only difference among several devices could be a slight modification in the length of tubing, or the presence of some accessory that has no effect on the product's suitability for sterilization. In addition, many product packages can be composed of the same material with only slight modifications in size. The general approach is to classify products and packages by their similarities and then to evaluate what conditions within a given classification provide the greatest challenge. Families of products and packages can be used in the development of product sterilization cycles, in certification of validation of sterilizers, and in the development of other quality assurance or product tests. The studies or rationale used to place a product in a particular product classification should be documented.

Determination of the most difficult surface to sterilize is generally done using temperature probes (e.g. thermocouples). These are positioned at suspected sites and the product is then exposed to the moist heat sterilization process. Areas of the product that are typically of concern are long lengths of tubing, narrow lumens, dead end spaces, the centre of porous loads, as well as the interior of large product masses.

Table A.2 — Factors that can influence or be affected by moist heat sterilization

Variables	Factors	Considerations
Packaging	Density per unit volume Hermetic seals Porosity Labelling	Moisture penetration Ability to adequately dry prior to cycle termination Seal strengths Retained moisture or condensation Maintenance of sterility Retention of product labels during process
Device or Component	Composition Complexity	Moisture absorption Design Thermal degradation Appropriateness of venting for air removal and subsequent drying Maintenance of sterility potential Loss of function
Sterilizer	Sterilizer load density, e.g., fully loaded or partially loaded sterilizer	Rate of steam penetration in the load Rate of post-sterilization drying

For products that are heat-sensitive, mathematical techniques and graphing methods have been developed so that process lethality (often expressed as F-Physical) can be calculated from product temperature data. The calculation of an F value derived from physical process parameters is explained in publications by the U.S. National Canners Association (U.S. National Canners Association 1969), the Parenteral Drug Association (PDA-1978), I.J. Pflug (1979) and HTM 2010 (1994). These techniques allow the microbiological lethality of the heat-up and cool-down phases of the process to be included in calculating the lethal effects of the cycle. When using these techniques, other factors might need to be considered, such as the reproducibility of the environment around the product and the accuracy of instrumentation. Generally, this will require an extensive study.

— Unloading: Unloading procedures should be developed to avoid damage to the package. At the conclusion of the sterilization cycle, the items in the load may still have steam vapour in them that would condense if the item had contact with a cooler surface. The load should be visually examined without touching any items immediately upon opening the sterilizer. If porous packaging is used and the product is visibly moist, the load should be rejected. Sterilizer loads should be removed from the chamber and allowed to further cool and dry before handling. This equilibration should take place in an area free of drafts and with restricted traffic patterns. Warm, moist packaging materials are more susceptible to damage. At the conclusion of the equilibration period, the load should again be examined for signs of wetness as items are moved to storage shelving.

Of particular concern are fluids in sealed containers. These products can cause serious injury if not handled appropriately immediately after sterilization. They should not be removed from the chamber until the fluid's temperature is well below its boiling point [i.e. 20 °C for fluids in glass containers and 10 °C for fluids in flexible containers (e.g. PVC bags)]. See IEC 1010-2-041 for additional guidance.

— Storage and distribution: Sterilized products should not be stored in areas subject to great fluctuations in humidity, pressure and/or temperature. The transportation and distribution system should be designed to avoid damage to the packaging. Where appropriate, an expiration date should be on the package and a system established to assure first-in, first-out usage.

A.6.2 No guidance is offered.

A.6.3 Cycle development studies may be performed in a research vessel if process equivalency with the production vessel is demonstrated.

Moist heat processes should be developed with the narrowest practical range of temperatures within the sterilization chamber. Prevacuum-saturated steam processes are inherently easier to control while, for example, a steam-air or pressurized water cycle can potentially have a greater temperature band. The number of repetitive cycles in a validation process could have to be adjusted based on the process to adequately demonstrate the control desired. Throughout the holding time, the temperature in the chamber:

a) should be within a 3 °C temperature band, with the sterilization temperature as the lower limit;
b) should not fluctuate by more than ± 1 °C;
c) should not differ from one another by more than 2 °C.

Producing a saturated steam environment by air venting or gravity displacement of air leads to some uncertainty about achieving a single-component (i.e. steam) atmosphere. Removal of air from porous materials and trapped air spaces such as lumens is of greater concern. The loading pattern in the sterilizer chamber is critical, both to ensure air removal from the package and product, and to permit adequate steam penetration. Additional validation tests might be required for such cycles.

To preserve the integrity of the package, moist heat sterilization of sealed containers with liquid and gas phases can require external pressures greater than those provided for heating alone. If the contained liquid is water (or a solution with similar physical properties), the vapour pressure produced by heating during the heat-up and exposure phases cannot exceed the pressure of the heating media. It is typical to add external pressure greater than required to compensate during the heat-up and exposure phases. This compensates for the pressures within the sealed container caused by the interior temperatures and vapour pressure being greater than those of the cooling media.

Addition of air to the chamber can be used to produce the required overpressure. These systems, however, are difficult to run and validate. To ensure a homogeneous environment within the chamber, a forced mixing system is necessary. A load configuration that permits effective circulation between packages is also vital.

Pressurized water spray or submerged water processes can also be used. These processes avoid the air/steam mixing problems but not the problem of adequate distribution and flow of the heating media, and so are often run with high water flow rates to prevent significant top to bottom temperature and heat input deficiencies. The large volumes of water used can also require that water treatment, both microbiological (e.g., pyrogen control) and chemical, be performed to prevent substantial deposits on packaging.

A.6.4 Temperature data are collected during replicate runs done at the parameters known to result in the lowest process lethality (e.g., at minimum time and temperature). Other factors that can affect the process lethality derived during these studies can include, but are not limited to, initial product temperature, chamber/jacket temperature, duration of heat-up and cool-down periods, and load configuration.

A.6.5 Sterilization cycles in health care facilities should be selected from recognized time/temperature relationships that are based on an overkill sterilization process. Examples of exposure-phase timing in recognized saturated steam cycles are:

— 134 °C for a minimum holding time of 3 min;
— 121 °C for a minimum holding time of 15 min.

In exceptional circumstances, sterilization cycles using time/temperature relationships other than those recognized in the scientific and technical literature could need to be developed.

Time at temperature cycles, such as those given above, do not take into account the heat input during the product heat-up and cool-down when determining process lethality. For heat-labile products that cannot withstand recognized time/temperature relationships, the use of the F_o method can reduce the time at temperature and result in lower heat input for sensitive products.

Use of F_o to express cycle lethality assumes a reference temperature of 121 °C and a z value of 10 °C. Product temperature accumulated during the entire process (heating, holding time, and cooling) are converted to the equivalent lethality at 121 °C and mathematically or graphically integrated to derive a physical lethality value expressed as the equivalent minutes of exposure at 121 °C. For example, each minute at 114 °C has a lethal rate of 0,2 min at 121 °C, if $z = 10$ °C. Some software programs can calculate the process F value continuously during the sterilization cycle using input from one or more temperature sensors in the product.

The location of temperature sensor(s) used for routine monitoring of any moist heat sterilization cycle should be at the location within the load and chamber that is known to be the slowest to attain sterilization conditions. The rationale for placement of the sensor(s) should be documented. If the location slowest to attain sterilization conditions is unknown, then temperature distribution studies in the empty chamber, the loaded chamber, and within the load should be done to determine this location. Replicate cycles should be done to demonstrate reproducibility. If the size of the package or container, or the volume of fill is small, consideration should be given to the possible effects of heat conduction along the temperature sensor and into the product, and to the need to insert the sensor to the proper depth to minimize steam conduction errors. Small-gauge sensor wire can be used to minimize this heating effect.

Sterilization process development, therefore, consists of the following steps:

— select an appropriate cycle (see Annex B) based upon the product to be sterilized;
— determine the most difficult to sterilize location in the product;
— determine requirements for decontamination, cleaning, packaging, etc.;
— determine if the product can be placed in an existing product type grouping, and an existing sterilization cycle;
— confirm the effectiveness of the cycle by temperature measurement and, when appropriate, microbiological challenge.

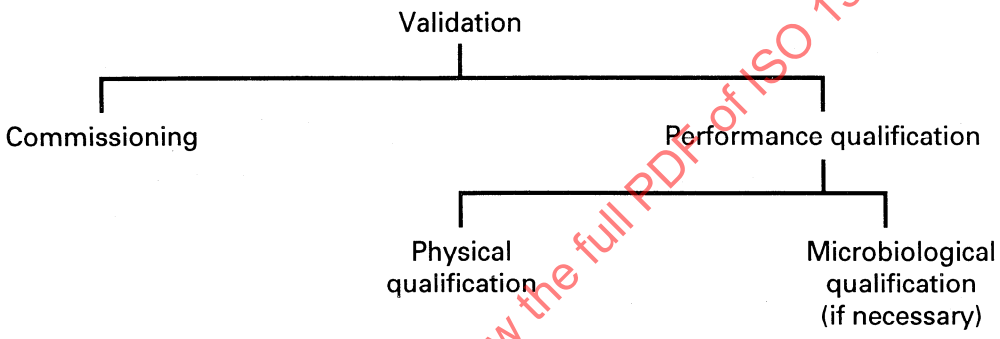
A.6.6 Moist heat sterilization is a probability function dependent on thermal energy, time, moisture content, the number of microorganisms associated with the product (bioburden), and the thermal resistance of those microorganisms. The "typical" cycles in A.6.5 are generally acceptable based upon a history of the resistance of "typical" bioburden microorganisms and assuming that preparation of the product (e.g. cleaning) has resulted in a low number of organisms.

Any microbiological testing done should be in accordance with ISO 11138 and ISO 11737-1.

A.6.7 No guidance is offered.

A.7 Validation

Validation is considered as a total process which consists of commissioning and performance qualification. The relationship between these terms is illustrated below:



A.7.1 The validation programme is performed to evaluate the reliability of a sterilization process. This requires the validation protocol to be explicit in what, when and how to measure. A major part of the protocol will also need to address the interpretation of the results. True objective validation is only possible if the requirements upon which the sterilization process will be judged are determined and fixed prior to the validation. Compliance with a quality system such as ISO 9002 will ensure clear and objective validation.

Careful attention should be given to assuring that physical parameters throughout the entire sterilization cycle (not just the exposure phase) are comparable to those set during cycle development. The conditioning phase could deliver significant lethality to the load. Likewise, successful drying of replicate loads will depend on consistency of the cooling and drying phases.

A.7.2 The analysis of the data obtained during validation will demonstrate that a given sterilization cycle in an identified sterilizer will or will not render a specified load sterile. Validation is, therefore, not just related to the sterilizer, but also to such factors as the load and its arrangement. Validation should be repeated every time significant changes are made. Examples of such changes are:

a) any change to the sterilization cycle;
b) changes in packaging or loading concepts;
c) changes in the material to be sterilized, such as changing from 100 % cotton to 50 % cotton/50 % polyester fabric; or
d) the addition of a new complex medical device.

The introduction of a new sterilizer is an important change, even if it replaces a similar sterilizer or is one of a number of sterilizers of the same type. Data from one sterilizer can never be used to demonstrate the proper function of another sterilizer.

Small changes over time eventually add up to large changes. The wear and tear on the sterilizer itself will also introduce changes. For these reasons, a periodic validation (e.g. once every twelve months) is advised.

A.7.3 No guidance is offered.

A.7.4 The commissioning plan should include procedures that will provide assurance that the sterilizer and its connected service utilities comply with the specifications and performance criteria and that the sterilizer is safe and fit for use.

A.7.5 The performance qualification is performed to demonstrate that the sterilizer is indeed capable of sterilizing the load. As there is a strong influence on the sterilization process, different loads and load modifications should be evaluated to determine the range of possible applications of the sterilizer. In this respect, it should be emphasized that certain loads and loading patterns will not be sterilizable in moist heat sterilization processes.

In general, one can state that homogeneous loads will be easier to define, and reduce the amount of validation work. Mixed loads (e.g. a combination of textiles and instruments) will require a range of measurements to ensure sure that any mix will be acceptable.

The performance qualification should be based on the loading protocols.

As the performance of the sterilizer is established through the measurement of physical parameters, the relation of these parameters to microbiological lethality should be documented.

In the case of saturated steam sterilization, there is an abundance of data available provided the results are within given limits. Typically, one would accept a maximum temperature difference between different points in the sterilization phase of not more than 2 °C. Combined with the requirement that the saturated steam temperature related to the pressure measured in the sterilization phase should be within these 2 °C in less than 15 s, one can demonstrate that saturated steam is being used and thereby avoid extensive additional research.

A.7.6 The homogenicity of the load and the loading pattern largely determine the number of temperature sensors needed. Practice has shown that one temperature sensor per 100 litre chamber volume with a minimum of five sensors is, in general, adequate to evaluate a sterilization cycle. Using steam air mixtures and/or mixed loads could require an increase in the number of sensors being used. At least one sensor should be placed next to the monitoring and control sensors, one should be placed in the free chamber space, and at least one should be placed on the non-heated part of the chamber wall. The latter sensor is used to determine the influence of the jacket on the load (e.g. to evaluate wet loads).

A.7.7 The quality of the entire validation depends on the accuracy and reliability of the temperatures and pressures measured. It is, therefore, essential that a good calibration according to an equipment-related-protocol is performed. Calibration should always be traceable to a national standard. It is not unusual for validation to be carried out in a number of measurement sessions that might be interrupted by production of already validated loads.

A.7.8 A good interpretation of the results is only possible if the criteria have been set before validation is performed. Adapting the requirements on the basis of the validation results is in contradiction with any quality system or principle. If the sterilization process is not within the preset limits, it takes experience and expertise to interpret the results found and to be able to identify the problems causing noncompliance.

A.7.9 A periodic revalidation is advised (e.g. every 12 months) to make sure that unnoted changes—deliberate or by accident—are not neglected.

A.8 Routine moist heat sterilization

A.8.1 Steam sterilization process control

A.8.1.1 The basis of steam sterilization process monitoring is the measurement of physical parameters, i.e. time, temperature and pressure. In day-to-day routine, these physical parameters, as recorded during the cycle, are compared with the values determined during validation. The reproducibility of the cycle can only be determined if the instrumentation used for measurement functions correctly and is calibrated on a regular basis.

A.8.1.2 No guidance is offered.

A.8.1.3 These data are necessary to determine if the product can be released. It should, therefore, be accessible to the designated person making the product release decision. The records should be retained so that it is possible to demonstrate retrospectively that the load has been properly sterilized. Identification of the operator should be unique and restricted to the individual for traceability.

A.8.2 Change control

Judgements regarding the need for validation or repeat validation should only be made by a designated person qualified for this task.

A.8.3 Periodic testing

Not every process failure is easily read from the recorder charts. Periodic tests (e.g., thermometric tests, steam penetration and air removal tests, and vacuum leakage tests) are performed to check for the most common process failures and the adequacy of the monitoring system. The frequency of testing should be established using information supplied by the sterilizer manufacturer. For example, steam penetration and air removal tests are usually performed daily in sterilizers with assisted air removal, and vacuum leak testing is done weekly. Not only the results of individual tests, but also the trends established by these results should be evaluated. Individual test results will detect failure to meet specifications. Evaluation of test result trends might detect pending failures before they result in process failures.

A.8.4 Cycle evaluation

Where the design of the product is such that the environment in contact with the surfaces to be sterilized cannot be realistically determined, microbiological methods may be used. Such circumstances can occur, for example, in instruments or tubing with long lumina.

A.8.5 Release of sterilized product

A.8.5.1 This can be done, for example, by using process indicators on each package, placed so that they are visible from the outside of the package, or by establishing a logistic system that does not allow the mixing of sterilized and non-sterilized products.

A.8.5.2 Where reliable process measurement and control can be documented for the entire sterilization process, and correlated with sterility assurance, sterilized product can be released if a review of the monitoring data from the sterilization cycle indicates conformity with validated physical parameters. Such parametric release is based on having procedures in place to ensure there are no changes in equipment, product, packaging, or processes that could inadvertently affect the efficacy of the sterilization process.

Annex B

(informative)

Sterilization cycles

NOTE — This annex describes cycles typically used in the moist heat sterilization process. Diagrams are conceptual and give examples only.

B.1 Saturated steam/vented systems

This sterilization process is used for products that can tolerate process temperatures at saturated steam pressure. It is primarily intended for surface contact sterilization, as air removal from fabrics and cavities is uncertain. An example of a chamber temperature and pressure profile for a vented saturated steam cycle is given in Figure B.1.

This process consists of three major phases.

a) Heating phase: With the vent open, saturated steam is admitted or generated in the chamber until the desired conditions are met—normally determined by the measurement of temperature. The vent then closes and saturated steam continues to be admitted or generated in the chamber until the exposure temperature and corresponding saturated steam pressure are attained.

b) Exposure phase: The sterilizing temperature is maintained in the chamber by saturated steam for the prescribed exposure time.

c) Cooling phase: This phase can differ for various types of product. The chamber can be vented to the atmosphere or, when solutions are cooled, filtered compressed air might be admitted to the chamber to prevent rapid depressurization. This phase is completed when the pressure in the chamber is at atmosphere and also, in the case of sealed containers, when a safe temperature is reached.

B.2 Saturated steam/forced air removal

This process is intended to sterilize products consisting of porous materials, and/or items having cavities where air is difficult to remove. An example of a chamber temperature and pressure profile is given in Figure B.2.

a) Air removal phase: Air is removed from the chamber and load by either a deep vacuum, a number of vacuum pulses, or a combination of vacuum or steam pulses.
b) Charge phase: Saturated steam enters the chamber until the sterilization temperature and pressure are attained.
c) Exposure phase: The sterilizing temperature and pressure are maintained in the chamber by saturated steam for the specified exposure time.
d) Exhaust phase: Steam is exhausted from the chamber, and a vacuum is drawn to a predetermined level.
e) Drying phase: For products that are required to be dry, the temperature in the jacket and the vacuum in the chamber are maintained for a predetermined period.
f) Vacuum relief phase: Air is admitted to the chamber through a microbiologically-retentive filter until atmospheric pressure is reached.