TECHNICAL SPECIFICATION

ISO/TS 17665-2

First edition
2009-01-15

Sterilization of health care products — Moist heat —

Part 2: Guidance on the application of ISO 17665-1

Stérilisation des produits de santé — Chaleur humide —

Partie 2: Directives relatives à l'application de l'ISO 17665-1

Reference number
ISO/TS 17665-2:2009(E)

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Published in Switzerland

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

In other circumstances, particularly when there is an urgent market requirement for such documents, a technical committee may decide to publish other types of document:

— an ISO Publicly Available Specification (ISO/PAS) represents an agreement between technical experts in an ISO working group and is accepted for publication if it is approved by more than 50 % of the members of the parent committee casting a vote;

— an ISO Technical Specification (ISO/TS) represents an agreement between the members of a technical committee and is accepted for publication if it is approved by 2/3 of the members of the committee casting a vote.

An ISO/PAS or ISO/TS is reviewed after three years in order to decide whether it will be confirmed for a further three years, revised to become an International Standard, or withdrawn. If the ISO/PAS or ISO/TS is confirmed, it is reviewed again after a further three years, at which time it must either be transformed into an International Standard or be withdrawn.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO/TS 17665-2 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

ISO 17665 consists of the following parts, under the general title *Sterilization of health care products — Moist heat*:

— *Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

— *Part 2: Guidance on the application of ISO 17665-1* [Technical Specification]

Introduction

The guidance given in this Technical Specification is not intended as a checklist for assessing compliance with ISO 17665-1. This guidance is intended to assist in obtaining a uniform understanding and implementation of ISO 17665-1 by providing explanations and acceptable methods for achieving compliance with specified requirements. It highlights important aspects and provides examples. Methods other than those given in this guidance may be used. However, the use of alternative methods has to be demonstrated to be effective in achieving compliance with ISO 17665-1.

The main body of this document is applicable to all settings where moist heat sterilization is carried out. The annexes to this guidance document also specify detailed means of implementing the requirements of ISO 17665-1 and represent current best practices.

The numbering of the clauses in the main body of this Technical Specification corresponds to that in ISO 17665-1.

Medical devices reprocessed in health care facilities include a wide variety of product with varying levels of bioburden. Appropriate and thorough cleaning and, where necessary for safe handling, decontamination processes are essential prior to presenting product for sterilization. Mixed product loads are common in healthcare facilities with throughput volumes dictated by historical and predicted demand for sterile product.

Health care facilities do not normally specify sterilization processes for any individual medical device. Also, it is impractical for health care facilities to determine bioburden on a medical device. It is important that specified instruments be disassembled before decontamination and thoroughly inspected after completion of the sterilization process. Reassembly and assessment of functionality are also needed. Therefore, the medical device manufacturer's instructions (see ISO 17664[23]) should be followed for all aspects of cleaning, disinfection, packaging and sterilization. Many devices can be fully immersed and can be washed and disinfected in automated equipment (see ISO 15883[19-22]). For devices that cannot be fully immersed and that cannot tolerate thermal decontamination, alternative methods of disinfection should be used to ensure safe handling. Such procedures and policies should be in place to ensure that medical devices undergo appropriate reprocessing. Particular attention needs to be paid to the drying and storage of sterile medical devices. Requirements for packaging of medical devices are covered in ISO 11607-1[8] and ISO 11607-2[9].

If multiple sterilization cycles can lead to degradation and limit the useful life of a medical device, the manufacturer will specify the number of reprocessing cycles that can normally be tolerated.

When selecting a medical device, priority should be given to properties such as ease of cleaning and disassembly.

Additional guidance specific to health care is offered in Annex D of this Technical Specification.

Sterilization of health care products — Moist heat —

Part 2:
Guidance on the application of ISO 17665-1

1 Scope

This Technical Specification provides general guidance on the development, validation and routine control of moist heat sterilization processes and is intended to explain the requirements set forth in ISO 17665-1. The guidance given in this Technical Specification is provided to promote good practice related to moist heat sterilization processes and to assist those developing and validating a moist heat sterilization process according to ISO 17665-1.

NOTE 1 The structure of the main body of this ISO Technical Specification (Clauses 1 to 12) corresponds to the structure of ISO 17665-1, so that the guidance given under a particular clause or subclause of this part of ISO 17665 applies to the requirements given in the corresponding clause or subclause of ISO 17665-1. For example, guidance for subclause 5.2 of ISO 17665-1:2006 is given in 5.2. This guidance is provided in addition to the guidance given in ISO 17665-1:2006, Annex A. See also Annexe E.

NOTE 2 Special considerations specific to sterilization processes performed in health care facilities are given in Annex D.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 17665-1:2006, *Sterilization of health care products — Moist heat — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

NOTE The normative references in ISO 17665-1 refer to published standards, the content of which should be used to assist in demonstrating compliance to the clause in which they are cited. Some are required mainly for moist heat sterilization in industry or for manufacturers of moist heat sterilizers and could go beyond typical practice for those performing sterilization in health care facilities.

ISO 17665-1 specifies a number of methods and procedures that can be used to monitor sterilization processes. The equipment required will normally be commercially available. A number of the normative references cited describe the specification and test methods used by commercial suppliers to qualify their products. The user of such products should ensure that purchased products comply with these standards, but will not normally need to refer to the standards.

ISO 17665-1 specifies the use of packaging complying with ISO 11607-1 and ISO 11607-2. Healthcare facilities should purchase packaging complying with these International Standards.

One method of process validation specified in ISO 17665-1 is based on the determination of bioburden. The ISO 11737[6],[7] series specifies a number of microbiological methods used during this process. Health care facilities would not normally utilize this approach for process validation.

3 Terms and definitions

For the purposes of this Technical Specification, the terms and definitions given in ISO 17665-1 and the following apply.

3.1
tests for sterility
technical operation defined in pharmacopoeia performed on product following exposure to a sterilization process

4 Quality management system elements

The guidance offered in Annex A of ISO 17665-1:2006 applies.

NOTE For additional considerations specific to health care facilities, see Clause D.2.

5 Sterilizing agent characterization

5.1 Sterilizing agent

5.1.1 Moist heat is water at elevated temperatures. Moist heat may be provided as saturated steam or can be generated in situ by applying thermal energy to water already present in the product. Moisture acts as the medium for transferring thermal energy to microorganisms.

5.1.2 Contaminants suspended in the sterilizing agent can be both toxic and corrosive and may generate a barrier between the microorganism and the sterilizing agent. They originate from water, that is heated or evaporated into steam or from contact between materials and the sterilizing agent during generation and transport to the sterilizer (see Clause 6, Clause 7 and Annex A). If the level of contaminants in the sterilizing agent can be affected by the quality of the feed water to the steam generation system, the feed water quality should be specified.

5.2 Microbicidal effectiveness

The microbicidal activity of moist heat is based on the temperature and the duration of contact between water molecules and microorganisms.

For the purpose of moist heat sterilization there are a number of acceptable time and temperature combinations recognised by some pharmacopoeias. These combinations include but are not limited to those listed in Table 1. All combinations listed are based on the concept of overkill with a safety factor that has been established for saturated steam or water in contact with the microorganism. Superheated steam behaves more like a dry gas and has a low microbicidal effectiveness compared with saturated steam. Superheated steam can result from pressure reduction and/or thermodynamic compression of saturated steam. It can also occur from the rehydration of parts of the sterilization load, particularly those parts containing natural fibres. Superheated steam conditions can be minimized by engineering of the steam supply system, for example by:

a) having a series of pressure reduction stages from the supply pipe to the sterilizer chamber and ensuring the pressure reduction ratio for each stage does not exceed 2:1;

b) ensuring steam velocity does not exceed 25 m/s;

c) ensuring materials made from natural fibres are pre-conditioned to a humidity greater than 40 % RH prior to sterilization.

Table 1 — Examples of minimum temperatures and times established for adequate levels of microbial lethality in sterilization processes

Temperature °C	Time min
121	15
126	10
134	3

5.3 Material effects

Material effects are generally limited to deformation and fracture caused by the temperatures and pressures of the sterilizing agent.

5.4 Environmental considerations

Principles of an environmental management system can be applied to a moist heat sterilization process. ISO 14001[11] provides a specification for an environmental management system. ISO 14040[12] provides guidance on designing a life cycle assessment study. The presence of noxious substances in the exhausts from the sterilizer should be considered. Further guidance on this clause is given in E.3 of ISO 14937:—[15].

6 Process and equipment characterization

NOTE The purpose of this activity is to characterize the entire sterilization process and the equipment necessary to deliver the sterilization process safely and reproducibly.

6.1 Process

6.1.1 General

A sterilization process should be specified for each product family and/or load configuration presented for sterilization.

Process parameters should apply to the equipment used. They should be optimised to ensure that for defined product families specified exposure conditions will be routinely obtained throughout the sterilizer chamber, and the maximum temperatures and rates of change of process variable (e.g. temperature and pressure) will not cause damage or degradation to the product.

The sterilization process specification should include all the process parameters that define the exposure profile throughout the operating cycle. It should also include the ones used to verify reproducibility. The portion of the operating cycle over which lethality is established should be identified, and the upper and lower limits of each process parameter that can affect both this lethality and the performance of the medical device should be defined.

Provision should be made to record data for judging the effectiveness and suitability of a routine sterilization process. The accuracy of measurement should be related to the tolerances of the process parameters.

If it is proposed to use an existing sterilization process to treat a new medical device, the existing sterilization process should be detailed and contain information and data sufficient to enable process definition (see Clause 8) to be carried out for the proposed new medical device(s) or loading configuration. The challenge identified for the new medical device or loading condition should be less than or equal to the challenge from the existing sterilization load(s). For some product families, assurance that defined exposure conditions will be reproduced might only be possible if the size of the sterilization load and the load configuration have been clearly defined.

If biological indicators and chemical indicators are to be used, they should not replace routine monitoring, measurement of process variables and any periodic tests.

Compatibility of a new medical device to the least favourable sterilization process conditions should be assessed. Such assessment should include process parameter tolerances, uncertainties of measurement associated with process parameters and the quality of the services (see Annex A).

Any restrictions on the size and mass of the sterilization load and its configuration should be identified and included in the operating instructions.

The relationship between the temperature measured at the reference measuring point and the temperature measured in the sterilization load should be known for each product family.

The performance of a medical device can be affected by contaminants on its surface. The contaminants and maximum acceptable concentration(s) contained in each fluid coming into contact with the medical device should be specified and included in the sterilization process specification. Some of the contaminants and their maximum levels which need to be considered are identified in Annex A.

6.1.2 Saturated steam processes

Steam may be generated in, or admitted to a sterilizer chamber from an external source. Air in the sterilizer chamber will be gradually removed by gravity displacement, active flow or by forced evacuation. The presence of saturated steam will be obtained at the measurement location, e.g. the chamber discharge, when the measured temperature is coincident with the temperature of saturated steam calculated from the pressure (see Annex C). Both temperature and pressure are process variables, and the point of temperature measurement is defined as the reference measuring point.

If variations in process parameters and/or the amount of non-condensable gas remaining in the sterilizer chamber at the end of air removal can result in an ineffective process, the sterilizer manufacturer or designated person (see A.4.2 in ISO 17665-1:2006) should provide adequate information to the user and should include:

— the upper and lower limits for each process parameter, and the method used for air removal;

— sources of non-condensable gas;

— test methods, test frequency and acceptance criteria for sterilization process evaluation.

The removal of air from the sterilizer chamber by either active flow or by gravity displacement is only predictable for simple solid medical devices. Air removal is unpredictable for medical devices such as instruments containing lumens, heavy solid masses and instruments and textiles contained within their primary packaging. For such medical devices, an operating cycle that employs forced or dynamic air removal should be used. An example is one that employs a number of vacuum and/or steam pulses to serially dilute the air from the sterilizer chamber and medical device(s). During each pulse, steam will move into and out of the medical device and the condensing steam will re-evaporate and cause a dynamic ‘scouring’ of the residual air contained in packages, crevices and lumens. The number of pulses, the upper and lower pressures associated with each pulse, the rate of change of pressure and temperature, and the interval of time between each change, are process variables and will play a part in effecting air removal. When assigning the suitability of a product family to a sterilization process, the combination of these pressures and temperature changes, the rates of change, and the duration of each change should be considered.

Whenever the measured temperature exceeds the theoretical temperature calculated from measured pressure as described in Annex C, superheated steam may be present. The presence of superheated steam may be detrimental to the medical device and or its packaging and may compromise the sterilization process.

Effective air removal from lumens, porous loads and other complex designs incorporating enclosed spaces is difficult. The physical conditions required for effective air removal are influenced by length, width and shape of lumen, wall thickness, material of the product, mass, density, the packaging system and other items in the same packaging system. A sterilization process that removes air from the sterilizer chamber to a low level

may fail to remove sufficient air from a lumen to permit steam penetration. Dalton's law states that the total pressure in an enclosed space is equal to the sum of the partial pressures of the individual gases present. In theory the temperature in a sterilizer chamber containing a mixture of steam and residual air will be lower than the calculated temperature derived from the pressure in accordance with steam table values (see Annex C). However there is evidence to show that an amount of residual air sufficient to cause a process failure in a sterilization load may only depress steam temperature by as little as 0,01 °C. As a consequence the differences between the temperature measured at the temperature measurement point and the temperature calculated from the sterilizer chamber pressure using steam table values (see Annex C) may not be adequate to detect the small volumes of air which could concentrate in lumens or enclosed spaces and prevent steam penetration. Under such circumstances adequate air removal and steam penetration should be predicted from data obtained from a steam penetration test and/or a process monitoring device.

A steam penetration test is designed for a specified product family(ies) and is used to check that the amount of non-condensable gas remaining in the sterilizer chamber at the commencement of the plateau period will not obstruct the presence of saturated steam on the surfaces of the medical device for the duration of the holding time. The efficiency of the air removal system, air leakage into the sterilizer chamber and non-condensable gas carried by the steam contribute to this amount. Air leakage into the sterilizer chamber and non condensable gases carried by the steam can be checked by tests (see for example, Annex A and EN 285[25]). The total presence of non-condensable gas is monitored by the steam penetration test.

A steam penetration test may be based upon temperature measurement, biological indicators or chemical indicators, as applicable. The test system should provide a challenge representative of the product family(ies) it represents. A number of steam penetration and air removal test devices are available. Performance requirements for chemical indicators can be found in ISO 11140-3[55], ISO 11140-4[56], ISO 11140-5[57], ISO 11140-6 [1)] and EN 285[25]. Guidance on the selection and use of chemical indicators is given in ISO 15882[18]. Requirements for biological indicators are found in ISO 11138-3[4]. Guidance on the selection and use of biological indicators is found in ISO 14161[13].

A reference load can consist of a single medical device type, medical devices from different product families or medical devices assigned to different product families but assembled into a single package. For any reference product or medical device, difficulty in air removal and the challenge to the sterilization process should not be less than that for any medical device in the product family(ies) assigned to the sterilization process (see also Annex A and Annex B).

If it is proposed to use a process challenge device (e.g. an air detector or other monitoring device) to represent a product family(ies), then the validity of the device when exposed to the sterilization process should be established by the process challenge device manufacturer, sterilizer manufacturer or designated person (see A.4.2 of ISO 17665-1:2006).

6.1.3 Contained product processes

A product may be heated in a water immersion cycle, a water spray cycle, a cycle with an air and steam mixture, a cycle with steam and gravity displacement, or a cycle with forced air removal. Air and steam mixtures are often used to prevent distortion or fracture of the sterilized container caused by the internal pressure generated from heating both the water-based solution and air in any sealed container.

The energy required to heat up a sterilization load to the defined sterilization temperature depends on the product family, the size of a sterilization load and its initial temperature. Heat transfer will depend on the heating medium, its contact with the product container, the material of the container and container support system, and the temperature difference at the heat transfer site. The type of product family and the load configuration will have a major influence on temperature differences between containers. These differences may be minimized by increasing the flow and distribution of the heating medium by forced circulation. Mass flow and homogeneity of the heat transfer medium throughout the sterilizer chamber can be verified by process variables such as fan speed, circulation pressure and flow. Temperature of the heat transfer medium at the outlet should be identified as a process variable. If steam is used, the temperature of the steam environment should also be handled as a process variable. Consideration may need to be given to ensure the

1) ISO 11140-6 is under development and is based on EN 867-5[27].

heat transfer medium is pyrogen free and free of chemical impurities that may cause spotting on packaging. In addition, the heat transfer medium may need to be sterile during cooling and the period of the operating cycle for which lethality is claimed.

The temperature distribution within the product container will depend on the shape of the container, viscosity of the product, conduction through the container wall and product, and convection within the product. Large product containers will need longer times to heat up and cool down, which could restrict the size of container that can be used for products sensitive to prolonged exposure.

During the sterilization process, the locations of the product containers exhibiting the highest and lowest temperatures during the heating phase and the highest and lowest temperatures during the cooling phase in the sterilization load should be identified. The temperatures measured in these locations should be treated as process variables; however, if either location cannot be reproduced, a statistical approach may need to be used to ensure the specified lethality is consistently attained while maintaining product integrity.

6.2 Equipment

NOTE For additional considerations specific to health care facilities, see D.3.2.

6.2.1 Regional and national standards for sterilizing equipment have been published (e.g. EN 285), which recommend materials that can be used in the construction of a sterilizer. Materials used by a manufacturer for the construction of a sterilizer can be based on the sterilization process delivered by the sterilizer and the product family(ies) that will be sterilized. The materials chosen should minimize corrosion and any contaminant that can be released during routine operation. Steam, heat transfer, fluids or air used to pressurize the sterilizer chamber can carry corrosive and toxic agents. These should be identified and maximum permissible levels specified (see Annex A). Protection of materials by filming amines such as hydrazine should not be used as an alternative to the correct choice of material and the control of corrosive contaminants.

It is preferable that sterilization records be established independent from the automatic controller and indicating instruments. A system that combines recording, control and indication may lead to an ineffective sterilization process being interpreted as effective. Independent recorders are characterized by separate measurement, data processing and printing of values. Interchange of informative data between the recorder and the controller for other purposes is not excluded.

An air detector may be fitted to a sterilizer that uses vacuum and steam pulsing to remove air during the air removal stage of a saturated steam sterilization process. It is used to predict whether non-condensable gas remaining in the sterilizer chamber at the commencement of the plateau period could accumulate in parts of the sterilization load (e.g. lumens) and cause a failure of the sterilization process in these parts. The setting of the air detector is based on the defined process parameters and the product family(ies) that the sterilization process is designed to process**.** Non-condensable gas identified by an air detector may also contain gas released when a product or its packaging is heated. Air detector tests are specified in Annex A and EN 285.

6.2.2 The specification for the equipment should include sufficient information to perform a process definition for a new product or loading configuration. (See Clause 8).

6.2.3 A sterilization process delivered in accordance with its specification is dependant upon the quality of the services provided. During maximum demand, pressure measured at the connection to the sterilizer for each fluid, gas or steam service should not fall below the minimum specified by the sterilizer manufacturer. For example, the efficiency of a water ring vacuum pump and a heat exchanger deteriorates with falling water pressure and rising water temperature. Microbial contamination can occur if air entering the sterilizer chamber contains particles greater than 0,2 µm. If services are provided by another party, recommendations from the sterilizer manufacturer should be followed and conformity confirmed.

Local regulations for environmental considerations could govern the discharge of high temperature effluent from the sterilizer chamber into the public sewer system, the leakage of the materials used to generate the sterilizing agent, the particulates released from the product and/or packaging during sterilization, and the volume of water used during the process.

Safety is part of equipment design and operation. Reference should be made to IEC 61010-2-040[24] and national regulations.

6.2.4 Systems such as containers, shelving, racks and carriers designed to support and/or contain the medical device should not unduly restrict uniform steam distribution, circulation of heat transfer fluid, removal of residual air, drainage of condensate or drainage of water. The system should also prevent damage to the medical device and/or its packaging and retain the integrity of the sterilization load.

6.2.5 No guidance offered.

6.2.6 Software design should be structured. Guidance is given in Good Automated Manufacturing Practice, Guide For Validation Of Automated Systems In Pharmaceutical Manufacturing (GAMP 4)[39].

7 Product definition

NOTE For additional considerations specific to health care facilities, see Clause D.4.

7.1 During product design, consideration should be given to the procedures for disassembly (if appropriate), cleaning, disinfection, inspection and sterilization.

Guidance and methods for the cleaning and disinfection of medical devices prior to sterilization are addressed in the ISO 15883 series of standards[19-22]. Information to be provided by a medical device manufacturer for the reprocessing of a medical device is given in ISO 17664[25].

7.2 The major function of a package is to ensure that the medical device remains sterile until opened for use. Packaging should withstand the stresses that occur during a sterilization process, remain secure, and should not have a negative effect on the quality of the medical device (for example, by generating particles). Packaging for a medical device sterilized by saturated steam should meet the requirements of ISO 11607[8],[9]. For non-permeable packaging (e.g. vials, ampoules, flexible pouches), the material and design should permit heat transfer to the product and, if a closure is fitted, it should remain secure and sealed.

Secondary packaging should protect the product during customary handling and distribution. If secondary packaging is exposed to the sterilization process it should retain its ability to protect the product and should not be adversely affected by the sterilization process.

If, at the end of a sterilization process, controlled conditions are required for the equilibration of a medical device and its packaging to atmospheric conditions, the method by which this is to be achieved (e.g. in an environmentally controlled chamber or room) should be defined.

7.3 No guidance offered.

7.4 A medical device that is to be sterilized can be characterized by its shape, mass, materials of construction, moving parts and packaging. A contained product will be characterized by formulation, volume and viscosity. Its container can be characterized by size, material and closure.

A study should be carried out to assign a product to a product family. The extent of this study can be reduced by first reviewing the process parameters already established for an existing sterilization process, by employing a validated cleaning process (if applicable), and by comparing the new product to those products already assigned to the sterilization process.

7.5 No guidance offered.

7.6 Exposure of a medical device to the sterilizing agent should not cause the design parameters for each material used in the construction of the medical device to exceed its maximum or minimum permissible values. As temperature rises, materials weaken and are more susceptible to physical stresses or mechanical forces. Differential expansion through low heat-conductive materials, or the expansion and contraction of dissimilar materials in contact with each other, can cause an increase in material and joint stresses.

7.7 No guidance offered.

7.8 The heat sensitivity of a liquid product can dictate the maximum fill volume, material and size of the container that can be used. The stability and sterility of the liquid should be assessed from temperature mapping studies carried out in the proposed container when the liquid is exposed to at least the upper limits of the proposed sterilization process profile.

Medical devices that are to be reprocessed can suffer accumulative changes such as surface cracking caused by differential expansion through a thick material, brittleness or delamination. Crevices and lumens can retain organic, chemical and biological contaminants that could cause material reactions or be unpredictably removed during use. Many materials that are subject to repeated moist heat sterilization have a long history of safe use, are known to be suitable and have longevity (e.g. stainless steel). Other materials however, might have limited lifespans and require further study. Reference should be made to ISO 10993-1[1], ISO 10993-17[2], ISO 17664[23] and ISO 14971[17].

7.9 An evaluation should establish that, after processing, a medical device will perform as intended and will be safe for use. The evaluation should consider mechanical, chemical, electrical, toxicological, physical, biological and morphological properties. Intended additives, process contaminants, process residues, leachable substances and degradation products should be considered for their relevance to the safety of the device and its packaging. Corrosion on some materials can occur if steam is generated from water of low pH or if the water contains a contaminant such as chlorides and silicates. For example, rubber can become oxidised in the presence of residual air at elevated steam temperatures. Dehydrated cellulosic materials can rehydrate during steam sterilization causing exothermic superheat in the material and in the vicinity of the material.

7.10 No guidance offered.

8 Process definition

NOTE For additional considerations specific to health care facilities, see Clause D.5.

8.1 The purpose of this activity is to deliver the required sterility assurance level to every part of the sterilizer load by ensuring that contaminating microorganisms are maintained in contact with moisture at a specified temperature for a specified time.

Effectiveness and reproducibility of a sterilization process can be defined by conditions that can be controlled and confirmed by physical measurement. If a condition changes and this can affect the sterility assurance level, this condition can be identified as a process variable and the value at which the change occurs, a process parameter.

Process variables should be defined and process parameters, including their tolerances, specified. The process parameters should characterize the conditions that will justify the prediction that the sterilizing agent will generate the required sterility assurance level in all parts of the product without causing any part to exceed its design limit.

For some medical devices the measurement of physical conditions (such as temperature) is not possible inside sterile barrier systems. For such medical devices the reproducible attainment of the defined sterility assurance level should be verified at a reference measurement point(s), for example, the drain for the measurement of sterilization temperature. In the case of a saturated steam process, evidence that establishes reproducibility of the sterilization process may be generated from the:

a) temperature and pressure at least at the turning points of pressure;

b) number of steam pulses;

c) pressure and/or temperature change rates;

d) exposure time;

e) air leakage into the sterilizer chamber;

f) steam quality.

The sterilization process may be developed in the production sterilizer or a in a research sterilizer. The process parameters for the defined sterilization process should be set at their least favourable but acceptable values for effective sterilization, for example, by using the lower tolerance limit for exposure time or by using the lowest allowable recirculation rate for a water immersion process.

8.2 A sterilization process based on the recommendations for a sterilization temperature and holding time specified in national and regional pharmacopoeias is sometimes chosen for processing a product(s) produced in the pharmaceutical and medical industries.

8.3 No guidance offered.

8.4 No guidance offered.

8.5 A biological indicator is a microbiological challenge of known resistance that is used to confirm sterilization process lethality at locations on or in product (see ISO 11138-1[3]) where it is placed. Microbiological process development and definition is discussed in Annex B and in ISO 17665-1:2006 Annexes B, C and D. When using biological indicators, consideration should be given to the entrapment of microorganisms in the product, contaminants in and/or on product, adverse reactions from the materials of construction and the difficulty in locating biological indicators in hollow devices and lumens.

Whenever biological indicators are used to confirm lethality in prescribed locations, the physical parameters measured during the sterilization process should always be used to verify that the defined sterilization process has been carried out.

8.6 No guidance offered.

8.7 No guidance offered.

8.8 A chemical indicator (see ISO 11140-1[54]) can be used as an element in sterilization process definition. It is used to demonstrate the attainment of process parameters in the location in which it is placed.

Chemical indicators show exposure by means of physical and/or chemical changes and are designed to react to one or more parameters of the sterilization process such as time of exposure, temperature and presence of moisture. The chemical indicator manufacturer should define exposure conditions that can cause the chemical indicator to reach its endpoint. Attainment of the chemical indicator's endpoint should not be regarded as an indication of attainment of an acceptable sterility assurance level, but rather one of many factors which should be taken into consideration when judging the acceptability of a sterilization process. Failure of a chemical indicator to reach its endpoint should be regarded as evidence of a sterilization process failure and be investigated. Guidance on the use of chemical indicators is found in ISO 15882[18].

8.9 Data generated from a reference device such as a process challenge device, and/or a reference device designed to mimic the attributes of the product or product family, may be used in the development of the process. For saturated steam processes factors that could require consideration are:

— materials of construction;

— mass;

— length and diameter of hollow devices and tubing;

— absorbency to moisture;

— thermal conductivity;

— safety margins associated with the challenge, and

— the means by which air dilution and steam penetration can be evaluated.

These factors can usually be assessed by the measurement of temperature in combination with the use of chemical indicators and/or biological indicators.

For contained products the reference device should mimic the temperature profile in the least favourable location within the product.

8.10 If a product has been assigned to a product family for which a sterilization process has been defined and this sterilization process is based on an established time/temperature relationship, additional biological assessment is generally unnecessary.

8.11 A sterilization process based on a defined biological challenge represented by biological indicators is used during sterilizer development by the food industry, pharmaceutical industry, medical device industry and in health care facilities. This method is known as the overkill method (see Annex D of ISO 17665-1:2006).

8.12 A sterilization process based on bioburden in its natural state or combined with biological indicators requires extensive biological studies followed by frequent biological screening of product and the environment. This method is generally used in the pharmaceutical and medical device industries. It is chosen if some attribute of the product or equipment has been demonstrated during product definition to be sensitive to moist heat sterilization processing. In this case, a minimum process is used to attain the conditions that will allow the product to be designated “sterile” without compromising product quality or function (see Annex B and Annex C of ISO 17665-1:2006). A test for the presence of viable microorganisms should be performed on sterilized carriers that have been contaminated with a known population of microorganisms having a known resistance.

8.13 No guidance offered.

9 Validation

9.1 General

9.1.1 A new sterilizer should be provided and installed in accordance with its drawings and specifications.

It could be acceptable to move elements of validation between installation qualification, operational qualification and performance qualification if, during planning of a specific validation, it is found to be more practical to do so.

The documented validation plan should be agreed upon and approved by the responsible parties before the validation study begins. The validation documents should be subjected to document history and change control procedures. (See 9.1.3 of ISO 17665-1:2006).

9.1.2 No guidance offered.

9.1.3 See 9.1.1, paragraph 3.

9.1.4 A temperature measurement chain should be verified using a calibration reference and a working standard. One example is an oil bath of known stable temperature traceable to a temperature reference standard. Whenever a number of sensors are immersed together in the oil bath, differences (i.e. errors in measured temperature between sensors) can be identified.

Whenever differences between measured temperatures are used to judge the results of a sterilization process, the error in each measurement should be known at the temperature at which comparison is to be made.

9.1.5 The calibration of an instrument(s) fitted to the sterilizer and the calibration of a measuring chain(s) used for control can often be verified at critical parts of the operating cycle by reference to measurements registered by test instrumentation used during a performance test.

9.1.6 See 9.2.3, paragraph 1.

9.1.7 No guidance offered.

9.1.8 See D.6.2.3 and D.6.3.

9.2 Installation qualification (IQ)

9.2.1 Equipment

Installation qualification will be necessary whenever a new sterilizing facility is to be commissioned or when an existing sterilizer is replaced or relocated. Some elements of installation qualification will be necessary when there are changes to an existing sterilizer which could affect the effectiveness of the sterilization process such as changing a door seal, steam supply modifications, vacuum pump replacement or refurbishment.

An installation qualification plan, which may form part of a validation master plan, should include procedures that will provide documented evidence that the sterilizer and documentation comply with the specification.

The sterilizer manufacturer should provide guidance for tests and routine monitoring of each fault recognition system as part of the sterilizer documentation, for example, a method by which a service fault may be caused or a method for creating retained air in the chamber.

9.2.2 Installation

The qualification plan should include procedures that will provide documented evidence that services connected to the sterilizer comply with the specification and the operating cycle is as specified by the sterilizer manufacturer.

9.2.3 Function

The provision and function of safety systems as required by IEC 61010-2-40[24] should be established after installation.

The qualification plan should include procedures that will provide documented evidence that during an operating cycle there is no evidence of a malfunction or leakage and that during maximum demand, the supply pressure for each service is at or above the minimum pressure specified by the sterilizer manufacturer.

The performance of fault recognition systems fitted by the sterilizer manufacturer should be verified.

The verification of calibration of measurement systems fitted to a sterilizer and the checking of each system used to register or enable the identification of a failure to attain a critical process parameter may be done at this stage and/or during operational qualification.

9.3 Operational qualification (OQ)

NOTE For additional considerations specific to health care facilities, see D.6.1.

9.3.1 An operational qualification plan, which may form part of a validation master plan, should include procedures that will provide documented evidence that:

a) the safety and fault recognition systems fitted to the sterilizer function in accordance with the specification;

b) the installed equipment operates within pre-determined limits;

c) the quality of each service complies with its specification;

d) the operating cycle is delivered as specified;

e) during an operating cycle there is no evidence of interference from, or to, other equipment;

f) the sound pressure at the site of installation does not exceed regional or national requirements;

g) when operated with an empty sterilizer chamber, the temperature and pressures recorded and indicated throughout the sterilization cycle on instruments fitted permanently to the sterilizer are within specified limits of the sterilization process;

h) there are no obvious leaks of steam, compressed air, water or effluent at any temperature or pressure within the working range of the sterilization cycle.

The maximum and minimum value for any process parameters should not exceed the permissible value specified by the medical device manufacturer(s).

If performance tests are recommended by the sterilizer manufacturer, they should be done during operational qualification and conformity with acceptance criteria defined by the sterilizer manufacturer should be verified.

If a manufacturer claims conformity to an equipment standard, tests performed during operational qualification should comply with the tests specified by the equipment standard.

If an existing sterilization process is to be used, its current performance status should be verified by demonstrating conformity with the results from previous performance tests carried out during installation qualification and operational qualification.

For saturated steam processes:

— Steam quality and air leakage into the sterilizer chamber can affect the efficiency of the sterilization process. Conformity to Clause 7 and Clause 8 of ISO 17665-1:2006 and/or the medical device manufacturer and sterilizer manufacturer's recommendations should be demonstrated.

— If a steam penetration test is required (see Clause 6 of ISO 17665-1:2006), conformity to the performance requirements and test procedures for the test should be demonstrated.

— If a steam penetration test is to be used routinely to check air removal and steam penetration, the validity of the test should be known, for example, compliance to recognised standards describing steam penetration tests such as ISO 11140-3[55], ISO 11140-4[56] or ISO 11140-5[57].

— If a process challenge device is to be used to represent a specific product, the sterilization process should be challenged with this device. It may be used alone or included with other tests. The instructions provided by the process challenge device manufacturer should be followed.

— If an air detector is to be used for routine monitoring it should be set during performance testing using a reference load. The air detector should cause a fault to be indicated if the process parameters for the reference load during air removal are not attained. The reference load should be representative of a worst case medical device and loading configuration.

— Annex A identifies the tests that should be done during operational qualification for a sterilization process using a parametric approach. Annex B identifies the tests that should be done during operational qualification for a sterilization process assessed by a biological approach.

— If the level of residual moisture within the product can affect its performance at the point of use (e.g. by facilitating microbial recontamination), a load dryness test should be carried out.

For contained products:

— heating, exposure and cooling profiles should be checked in an empty sterilizer chamber;

— cold spots and hot spots should be identified;

— conformity with the requirements for process parameters such as pump pressure, circulation and temperature should be verified.

9.3.2 No guidance offered.

9.4 Performance qualification (PQ)

NOTE For additional considerations specific to health care facilities, see D.6.2.

9.4.1 The purpose of performance qualification is to demonstrate that the sterilization process is capable of achieving a predetermined sterility assurance level for the subject load on a repeatable basis.

A performance qualification plan, which may form part of a validation master plan, should be provided.

9.4.2 No guidance offered.

9.4.3 Procedures should be included to provide documented evidence that the sterilization process will sterilize the product(s) assigned to the product family the sterilization process is designed to process.

If preheating of the sterilizer directly before use is recommended by the sterilizer manufacturer this should be stated and carried out before performance qualification is carried out.

The sterilizer load and load configuration should be as proposed for routine production. If reprocessing is intended, a load configuration and the least favourable combination of products from the product families assigned to the sterilization process should be used. Packaging should be that which will be used routinely.

Tests for sterility can be carried out on a final sterilized product that has been subjected to a sterilization process. Tests for sterility have little statistical relevance and should not be accepted as sole proof that a sterilization process is valid.

9.4.4 For saturated steam processes:

— Steam quality and air leakage into the sterilizer chamber can both have an impact on predefined process variables and should be known before commencing performance qualification (see operational qualification). If a steam penetration test such as a Bowie and Dick test is to be used, the results of the test should also be known.

— The validity of air dilution and steam penetration indirectly identified from the performance tests specified for installation qualification and operational qualification should be verified to be effective for a worst case sterilization load, loading configuration and medical device. Data from which judgement is to be made should be established from temperature measurements supplemented by chemical indicators and/or biological indicators positioned in difficult-to-sterilize locations. If a reference load and/or process challenge device is to be used as an alternative to this worst case load its validity as a greater challenge should be established. The types of medical device and loading configurations represented by these alternatives may be provided by the sterilizer manufacturer. A process challenge device should be packaged in the same type of packaging and using the same procedures as products routinely sterilized. The same device in a different packaging system (e.g. pouches and containers) may represent a different product family.

— Throughout the air removal and equilibration part of the operating cycle, the difference in temperature between the temperature measured at the reference measuring point and a measurement point(s) on the medical device or a reference load can be used to determine the presence of saturated steam at the measurement location. The plateau period is a combination of the equilibration time and the holding time. In most cases the holding time is the part of the operating cycle used to establish lethality.

— For the test loads identified in Annex A the equilibration time is a measure of residual non-condensable gases present at the commencement of the plateau period. Increases in non-condensable gases will decrease the holding time and reduce the delivered lethality. The rate of pressure rise from vacuum to the commencement of the plateau period can affect the sensitivity of determination for the presence of saturated steam. A lower rate of pressure rise can result in heating of residual air, which would cause a smaller temperature difference and result in the misinterpretation of the recorded data relating to steam penetration.

— Heat penetration into each type of sterilizer load should be determined either from the temperature measured within a number of medical device packages or in a reference load. At least one temperature sensor should be situated adjacent to the temperature sensors connected to the recording instrument, indicating instrument and controller. If a sensor or indicator cannot be located at a position on a medical device known to be difficult to sterilize, the medical device may be substituted by a different type of medical device or process challenge device, provided that the challenge to the process from the alternative has been demonstrated to be equal to or greater than the medical device it is to represent. The number and the locations of the sensors to be used will depend on the type of sterilization load and the size of the sterilizer chamber. The sensors placed within the load should be located on or within those parts of the medical device from which air is difficult to remove. Caution should be exercised when interpreting thermometric data from within hollow or porous medical devices capable of entrapping air. Temperature measurement alone cannot differentiate between hot air and saturated steam. The presence of saturated steam may be judged from the rate of pressure rise and temperature rise and, if necessary, from the exposure of chemical indicators or biological indicators.

— Reproducibility within acceptable limits should be checked using a minimum of three replicate cycles (see 9.4.6 of ISO 17665-1:2006).

For contained product processes, the test load and its location in the sterilizer chamber should be as proposed for routine production. Heating, exposure and cooling profiles within the sterilizer chamber should be checked at least in positions adjacent to the containers as identified in operational qualification to attain the shortest and longest exposure. The profiles should then be checked within the reference product placed in these locations in a test load and loading configuration according to the proposed production load. Compliance with the critical parameters identified in Clause 8 should be verified. If an existing sterilization process is to be used for a new product family and/or loading configuration, the limits on exposure identified in Clause 7 should be observed and the attainment of microbiological effectiveness identified in Clause 8 should be verified. If process parameters change during subsequent development, microbiological effectiveness and the limits on exposure for the existing product familiy(ies) should be verified.

9.4.5 No guidance offered.

9.4.6 No guidance offered.

9.4.7 No guidance offered.

9.5 Review and approval of the validation

9.5.1 Data collected during validation should be reviewed and approved by a designated person organizationally independent of those conducting the tests, those preparing the validation report and those responsible for production.

9.5.2 Data used to confirm the sterilization process should include, where applicable:

a) the sterilizer specification and any subsequent changes to it;

b) the location and unique identification for the sterilizer, e.g. serial number together with name and address of the manufacturer, type of sterilizer and model reference;

c) documentation to demonstrate compliance with the safety specifications;

d) the pressure vessel certificate(s);

e) a maintenance manual and a planned maintenance schedule for the sterilizer;

f) the installation instructions;

g) the operating instructions;

h) copies of any declarations according to medical device regulations, if appropriate;

i) the validation master plan, validation protocol and validation report, together with all data recorded;

j) operational procedures for all maintenance, checks and tests;

k) details of any modification to the sterilizer, instrumentation or controls;

l) details of any faults found on the sterilizer and how they have been corrected;

m) the load configuration for each type of sterilizer load/product family;

n) for contained product and, if applicable, packaged product (e.g. containerized product) heat penetration studies for each type of sterilizer load/product family;

o) the parameters used to control the sterilization cycle and a copy of the specification for the sterilization process;

p) the identity of all personnel together with their professional qualifications (in terms of their competence to do the work) involved in validation:

— the programme for requalification, periodic testing and routine testing;

— training manuals for routine operating personnel;

— confirmation that the sterilizer is installed and connected to services according to specification;

— confirmation that the calibration of test equipment has been verified and the calibration of each measuring chain fitted to the sterilizer has been checked and, where necessary, adjusted;

— confirmation that the equipment has been tested and reproducibly delivers the defined sterilization process;

— the process parameters (including their tolerances) used to justify product release;

— the value set for an air detector and/or the interpretation of a biological indicator used alone or in combination with a process challenge device;

— for equipment that is in current use, the results of maintenance and confirmation that data from routine performance tests are satisfactory.

10 Routine monitoring and control

NOTE For additional considerations specific to health care facilities, see Clause D.7.

10.1 There should be an approved programme for routine monitoring and control. The outcome of all monitoring and control should be documented, reviewed, approved and retained.

10.2 Persons responsible for sterilization should ensure that before the sterilizer is used for production, they have evidence to show that scheduled maintenance has been satisfactorily completed. Evidence should also be available to show that performance qualification/periodic re-qualification reports include the types of sterilization load/product families to be sterilized.

10.3 See D.7.2 for considerations specific to health care facilities.

10.4 A profile for both chamber temperature and chamber pressure may be generated electronically or by assessment from the temperatures and pressures recorded throughout the operating cycle. The profile can then be used for comparison with the profiles obtained during validation.

If a biological indicator and/or chemical indicator is to be used for routine monitoring it should be placed at a location(s) demonstrated during validation to be the least accessible to the sterilizing conditions. Alternatively, the indicator(s) may be placed at a location demonstrated by one of the methods described in Annex C or Annex D of ISO 17665-1:2006 to present a challenge to the sterilization process sufficient for the lethality to be delivered in the least accessible part of the product.

10.5 Measurement of the sterilization temperature, the plateau period and the sterilizer chamber pressure is sufficient for unwrapped medical devices sterilized by saturated steam. If a medical device is wrapped and/or non-condensable gas can be trapped in a part such as a lumen, tubing or crevice, a daily steam penetration test should be used. A comparison of the measured and calculated temperature could be necessary to demonstrate the presence of saturated steam and to detect superheated steam conditions within the available space during the sterilization process. If a medical device is wrapped and/or non-condensable gas can be trapped in a part such as a lumen, tubing or crevice, F_0 calculated from chamber temperatures will not represent the lethality delivered and should not be used to judge the results of a sterilization process for this type of medical device. In addition to the measurement of process parameters, steam penetration should be assured for each operating cycle, for example, by using an air detector fitted to the sterilizer and/or a process challenge device. Both an air detector and a process challenge device should be verified as valid for the product in the sterilization load.

10.6 The temperature of fluid in reference containers in locations shown from a number of exploratory cycles to represent the coolest and hottest parts of the sterilization load can be used to predict the highest and lowest temperatures throughout a sterilization load of fluids. Temperature profiles generated for the sterilizer chamber and the circulating heat transfer fluid can sometimes be used to predict a reproducible temperature profile for the coolest product. Whenever temperatures are to be measured in reference containers located in a production load, wireless systems may be considered.

10.7 No guidance is offered.

11 Product release from sterilization

11.1 The result(s) of a scheduled periodic test(s) should be noted on release documentation.

Product release may be based on the comparison of the temperature profile for the sterilizer chamber with the temperature profile measured in either a reference product(s) or in a location(s) from which the temperature profile within the product can be predicted. Attainment of the specified values for sterilization temperature, plateau period, and sterilization temperature band in a location from which the holding time can be predicted can also be used for product release.

For medical devices sterilized by saturated steam, release based solely on sterilization temperature and holding time should be restricted to unwrapped medical devices.

If chemical indicators and/or biological indicators are used routinely, they should be treated as part of the release criteria and should be additional to the measurement of process parameters.

The integrity of packaging and containers should be visually checked after removal from the sterilizer. Damaged packaging and containers should be treated as non-conforming product. Similarly, a system should be in place to ensure wet packs are appropriately addressed in order to avoid recontaminated products entering the supply chain. Drying should be carried out in an environment in which particles and microbial contamination are controlled. A Class 7 Environment as defined in ISO 14644-1[14] might be suitable.

11.2 The identification of non-processed and processed goods may be achieved by physical barriers, pass through sterilizers and process indicators on the packaging.

12 Maintaining process effectiveness

12.1 Demonstration of continued effectiveness

Whenever records of routine monitoring, periodic testing and performance requalification indicate unacceptable deviations from data determined during validation, the cause should be identified and corrected, and the sterilizer requalified.

When a sterilizer is operated infrequently, the periods of inactivity can result in changes to the performance of the sterilizer or its associated services. This could result in the delivery of a process that does not conform with the specified process. If the sterilizer undergoes periods of inactivity, a review should be carried out to ascertain the consequences for process effectiveness, and the measures to be taken to redefine routine monitoring, testing or requalification to confirm process effectiveness. For example, the consequences of a weekend shut down or the effect of an energy conservation system should be considered.

12.2 Recalibration

NOTE For additional considerations specific to health care facilities, see D.9.1.

The interval between recalibration of each measuring chain should not exceed 12 months and should be reduced if there is unscheduled maintenance or evidence of inaccuracy.

12.3 Maintenance of equipment

NOTE For additional considerations specific to health care facilities, see D.9.2.

12.3.1 Periodically the sterilizer should be examined to confirm that the installation is still in accordance with the specification and that there is no evidence of malfunction. Checks and tests should also be carried out to demonstrate that the equipment remains safe (see IEC 61010-2-040[24]) and that the services are satisfactory.

12.3.2 A maintenance scheme should be developed from the schedules provided by the sterilizer manufacturer, instrument manufacturer(s) and equipment manufacturer(s), from the routine tasks and tests carried out in the plant and as a result of experience. A set of procedures should be developed for each sterilizer containing full instructions for each maintenance task. The maintenance scheme and frequency with which each task is performed should be based on the recommendations given by the manufacturer, the sterilizer usage and safety considerations.

12.3.3 Safety and functional checks should be done after each maintenance sequence is completed.

12.3.4 The effect of maintenance activities on the process should be evaluated. A successful repair should be confirmed by requalification.

12.4 Requalification

NOTE For additional considerations specific to health care facilities, see D.9.3.

Requalification is performed to confirm that process changes have not compromised the effectiveness of the sterilization process and that the data acquired during validation remains valid. To guard against unreported changes, the extent of, and the interval between each part of requalification should be determined from the type of sterilization process data obtained through periodic tests and from data that verifies that established process parameters are routinely reproduced. Typically, requalification is performed annually.

The extent of requalification will depend on the reasons for the inconsistency in performance; if a component is changed (see 12.5 of ISO 17665-1:2006), or the control system is modified, it could only be necessary to show repeatability of the qualified sterilization cycle. If, in the case of a wrapped goods and porous load process, the cause is shown to be a leak into the sterilizer chamber, it might only be necessary to repeat a leak test on the sterilizer chamber and then carry out a steam penetration test.

Performance requalification might also need to be performed after a change of product, product packaging or loading pattern, or when the data for the sterilizer load are not within specified limits.

If biological indicators are used during requalification, their performance should present a similar challenge to those used during validation. Any change that raises doubt about the effectiveness of the sterilization process should initiate a review.

To facilitate comparison of performance qualification and performance requalification data, it is normal for the same report format to be used.

12.5 Assessment of change

No additional guidance provided.

Annex A
(informative)

Evaluation of a sterilization process primarily based on the measurement of physical parameters

A.1 Introduction

A.1.1 Evaluation of a sterilization process by this method will normally be from the data generated from a series of performance tests. Each test should be designed to identify whether one or more of the performance requirements specified for the sterilization process has been attained.

The tests and performance requirements detailed in this annex are examples and relate to a sterilizer conforming to EN 285[25] and apply when test equipment and procedures meeting the requirements of EN 285 are used (see also 9.1.4 of ISO 17665-1:2006). Tests and performance requirements for small sterilizers are given in EN 13060[38].

Sterilizers conforming to either EN 285 or EN 13060 are primarily intended for use in health care, however, they can also be used in the production of medical devices.

A.1.2 For sterilizers not conforming to EN 285 or EN 13060, it may not be possible to attain all the acceptance criteria given in this annex. For such sterilizers, documented validation procedures could include tests and procedures from both this annex and Annex B. The data from the tests could then be used to verify the efficiency of the proposed sterilization process for treating the defined medical device(s). This approach can also be appropriate for demonstrating conformity with the requirements of medical device legislation (if required).

A.1.3 When selecting a test instrument for validation studies and routine testing, attention should be paid to the number and type of signal inputs required. Both temperature and pressure will need to be recorded. Other input signals could also be needed. For example, the small load test (see A.4) requires at least seven temperature signal inputs and one pressure signal input.

A.2 Hollow load test

A.2.1 This is a test for steam penetration into a medical device(s) containing lumens. The test is based on a hollow load test piece described in EN 285:2006, A1. This test complements the tests in which the standard test pack is specified (see A.3).

A.2.2 The result of the hollow load test is judged from exposure to a chemical indicator inserted into the test piece.

A.3 Standard test pack

A.3.1 The standard test pack is used for the small load test, the full load test, the Bowie and Dick test, air detector tests, load dryness tests for textiles and can be used with other materials to form a full load. The standard test pack is a reusable item that can be used for testing continuously if the requirements in A.3.3, A.3.6 and A.3.7 are met.

A.3.2 The standard test pack should be composed of plain cotton sheets, each bleached to a good white and having an approximate size of 900 mm $\times$ 1 200 mm. The number of threads per centimetre in the warp should be (30 $\pm$ 6) and the number of threads per centimetre in the weft (27 $\pm$ 5). The weight should be (185 $\pm$ 5) g/m^2 and the edges, other than selvedges, should be hemmed.

A.3.3 The sheets should be washed when new or soiled and should not be subjected to any fabric conditioning agent during laundering. The sheets should be dried and then allowed to equilibrate in an environment of between 20 °C to 30 °C and a relative humidity of 40 % to 60 %.

NOTE Fabric conditioning agents can affect the characteristics of the fabric and can contain volatiles that will contribute to the non-condensable gases in the sterilizer.

A.3.4 After equilibration the sheets should be folded to approximately 220 mm × 300 mm as illustrated in Figure A.1.

A.3.5 The sheets should be stacked to a height of approximately 250 mm after compression by hand. The pack should then be wrapped in a similar fabric and secured with tape not exceeding 25 mm in width. For sterilizers unable to accommodate more than one module the height of the stack should be approximately 150 mm.

A.3.6 The total weight of the standard test pack should be 7,0 kg ± 0,14 kg (approximately 30 sheets) and for the small pack 4,0 kg ± 0,16 kg (approximately 17 sheets).

After use, the sheets will become compressed. When the weight of sheets used to form a stack 250 mm high exceeds 7,14 kg, the sheets should be discarded. Similarly, for the smaller pack, when the weight of the sheets used to form a stack 150 mm high exceeds 4,16 kg the sheets should also be discarded.

A.3.7 Immediately before use the temperature and humidity at the centre of the test pack should be between 20 °C and 30 °C and the relative humidity between 40 % and 60 %. After use the pack should be removed from the sterilizer and aired in a similar environment.

A.3.8 Test packs comprising different materials and of different sizes and weights can be used provided equivalence with the requirements for the test in which the standard test pack is used is demonstrated (see ISO 11140-4[56]).

Dimensions in millimetres

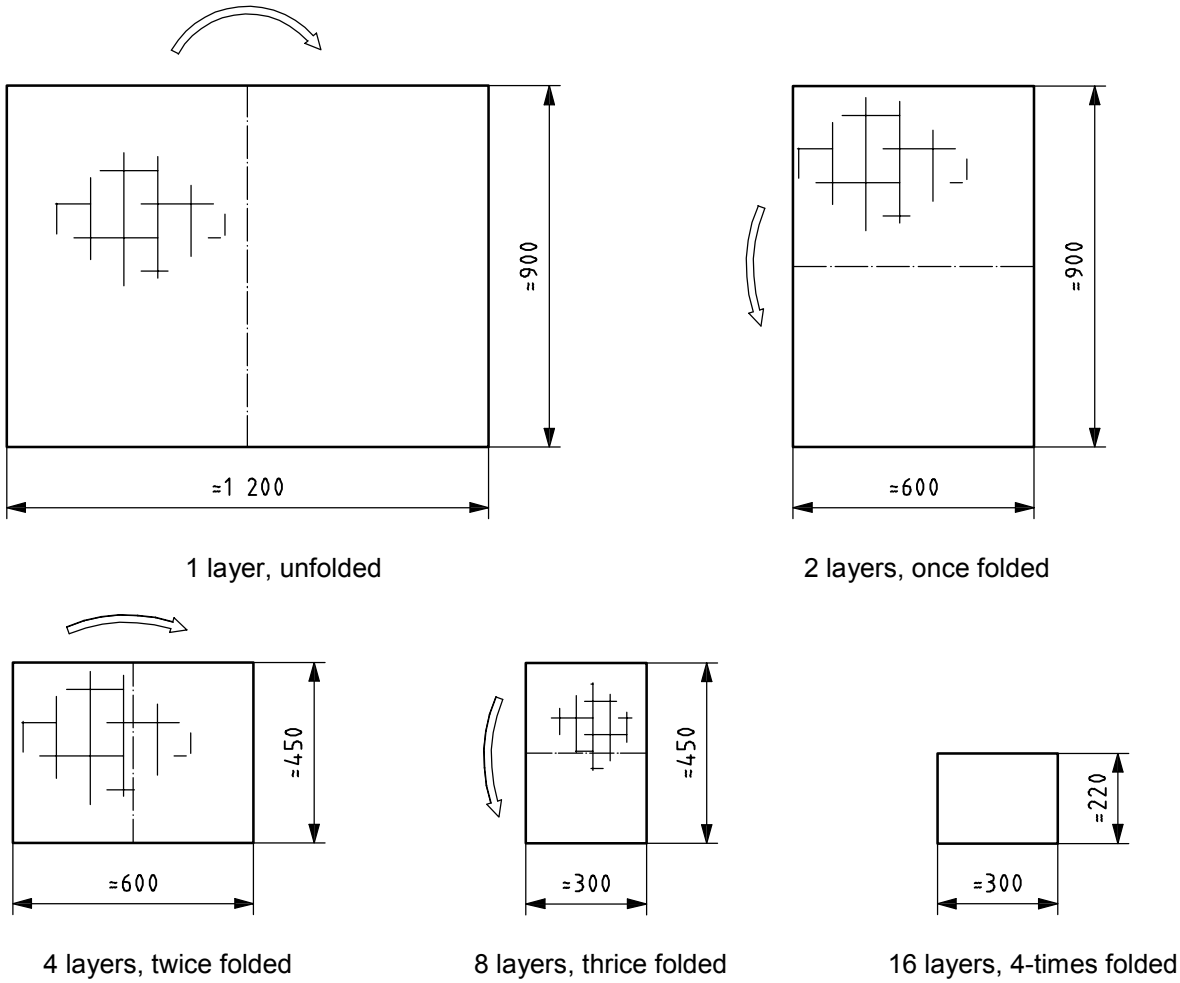

Figure A.1 — Folding each sheet

A.4 Thermometric tests

A.4.1 Small load thermometric test

A.4.1.1 This is a test for steam penetration into a standard test pack (see A.3). This test pack is used to identify a level of air removal sufficient to qualify the sterilization process for a wide range of cannula, metal and textile products. For this test a number of temperature sensors (5) are located at different levels within the standard test pack around the vertical axis. Figure 6 of EN 285:2006 provides an illustration of the temperature sensor locations.

A.4.1.2 Acceptance criteria for the test are as follows.

a) The sterilization temperature band should have a lower limit defined by the sterilization temperature and an upper limit of +3 °C.

b) The equilibration time should not exceed 15 s for sterilizer chambers up to 800 l usable space and 30 s for larger sterilizer chambers.

c) During the plateau period the temperature measured above the test pack should not exceed the temperature measured at the reference measurement point of the sterilizer chamber by more than 5 °C for the first 60 s and 2 °C for the remaining period.

d) Throughout the holding time the temperature measured at the reference measurement point of the sterilizer chamber, any temperature measured at the same instant within the test pack and the respective saturated steam temperature calculated from the chamber pressure should be within the sterilization temperature band and not differ from each other by more than 2 °C (see 6.1.2).

e) The holding time should be not less than 15 min, 10 min and 3 min for sterilization temperatures of 121 °C, 126 °C and 134 °C respectively.

A.4.2 Full load thermometric test

A.4.2.1 This is a test for steam penetration into the maximum size sterilizer load and complements the small load test. The textile test pack is located in the centre of a full load of textiles.

A.4.2.2 Acceptance criteria are the same as for the small load test, except that the temperature measurement above the test pack is omitted.

A.5 Bowie and Dick test

A.5.1 This test is a steam penetration test, similar to the small load test and intended for daily use. A chemical indicator meeting the requirements of ISO 11140-3[55] is placed in the centre of a standard test pack and a pass is identified from a uniform colour change to the indicator.

For the original work on which the Bowie and Dick test is based, see Bowie et al.[44].

A.5.2 The standard test pack described in A.3 offers a challenge to the sterilization process nominally the same as the challenge from the textile test pack described by Bowie. Indicators complying with ISO 11140-4[56] may be used as an alternative to the standard test pack for conducting the Bowie and Dick steam penetration test.

A.6 Air leakage flow rate test

The performance specification identified in A.2, A.4 and A.5 are based on achieving a low level of residual air. Air leakage into the sterilizer chamber will affect this level and should not cause the pressure in the sterilizer chamber to rise more than 0,13 kPa/min (1,3 mbar/min) when measured at a chamber pressure of 6kP (60mbar) or less.

A.7 Air detector tests (if fitted), small load, full load and function

A.7.1 These tests are used to set the air detector to register a fault whenever residual air is sufficient to cause a failure of the small load test (see A.4.1) and the full load test (see A.4.2).

A.7.2 The air detector should register a fault when, at the commencement of the equilibration time, residual air causes a difference of more than 2 °C between the lowest temperature measured in the standard test pack (used in the tests given in A.4.1 and A.4.2) and the temperature measured at the reference measurement point of the sterilizer chamber. For a sterilizer chamber too small to accommodate this test pack, a smaller version is used (see A.3).

A.8 Load dryness — Small and full load with textiles, full load with metal

These tests are used to verify that the design of the operating cycle, selection of the process parameters and the moisture contained in the steam are such that the level of moisture remaining in the load at the end of a sterilization process has not increased by more than 1 % for textiles and 0,2 % for metal.

A.9 Sound power test

Tests to determine sound pressure for use in calculating the sound power generated by the sterilizer will have been done by the sterilizer manufacturer in accordance with IEC 61010-2-040[24].

Sound pressure generated by the sterilizer in the environment in which the sterilizer is installed should be determined in accordance with ISO 3746[58] and conformity to local regulations for sonic noise in the environment verified.

A.10 Dynamic pressure test

This test is used to verify that the maximum rate of pressure change in the sterilizer chamber will not cause damage to packaging. The average pressure change for any 3 s interval during the sterilization process should not exceed 1 000 kPa/min (10 bar/min).

A.11 Steam quality tests

A.11.1 Non-condensable gas in the steam will affect air dilution in the sterilizer chamber. Moisture in the steam will affect residual moisture in the sterilizer load. Superheat in the steam will delay the presence of saturated steam. Wide variations in delivery pressure to the sterilizer is indicative of inadequate steam capacity and this can affect the validity of the 2 °C when judging the presence of saturated steam (see A.4). Contaminants can cause corrosion and deposit toxic substances on the product.

A.11.2 When tested by the methods given in EN 285 the following should apply to the quality of steam supplied to the sterilizer:

a) a maximum of 3,5 % by volume of non-condensable gas;

b) a minimum dryness value of 95 % (5 % moisture) for a sterilizer load containing metal and a minimum of 90 % (10 % moisture) for a sterilizer load containing textiles;

c) a maximum of 25 °C of superheat when expanded to atmospheric pressure;

d) contaminants in accordance with Tables A.1 and A.2;

e) fluctuations in steam pressure not exceeding ± 10 % of the nominal gauge pressure measured at the inlet to the final pressure reduction valve.

Table A.1 — Contaminants in condensate measured at the steam inlet to the sterilizer to be considered in relationship to the corrosion of materials

Determinand	Condensate
Silicate (SiO_2)	⩽ 0,1 mg/l
Iron	⩽ 0,1 mg/l
Cadmium	⩽ 0,005 mg/l
Lead	⩽ 0,05 mg/l
Rest of heavy metals except iron, cadmium, lead	⩽ 0,1 mg/l
Chloride (Cl^-)	⩽ 0,1 mg/l
Phosphate (P_2O_5)	⩽ 0,1 mg/l
Conductivity (at 25 °C)	⩽ 3 µS/cm
pH value (degree of acidity)	5 to 7
Appearance	Colourless clean without sediment
Hardness (Σ ions of alkaline earth)	⩽ 0,02 mmol/l
NOTE A method by which a sample of condensate can be taken is given in subclause 22.4 of EN 285:2006.	

Table A.2 — Contaminants in condensate from steam used by the sterilizer to be considered in relation to contamination of the load

Determinand	Clean steam condensate
Acidity or alkalinity	R[a]
Ammonium (NH_4)	⩽ 0,2 mg/l
Calcium and magnesium	R[a] (mg/l)
Heavy metals	⩽ 0,1 mg/l
Chloride (Cl^-)	⩽ 0,5 mg/l
Nitrate (NO_3)	⩽ 0,2 mg/l
Sulphate (SO_4)	R[a] (mg/l)
Oxidisable substances	R[a]
Residue on evaporation	⩽ 30 mg/l
Silicate (SiO_2)	⩽ 0,1 mg/l
Phosphate (P_2O_5)	⩽ 0,1 mg/l
Conductivity (25 °C)	⩽ 35 µS/cm
Bacterial endotoxins	⩽ 0,25 EU/ml
Appearance	Clear, colourless
[a] Reagent test specified in European Pharmacopoeia.	
NOTE A method by which a sample of condensate can be taken is given in subclause 22.4 of EN 285:2006.	

A.12 Water

The water supply should be of potable quality and fitted with a backflow protection device. Because of the effect of temperature on the performance of the vacuum system, the water temperature should not exceed 15 °C. The hardness value of water, Σ (ions of alkaline earth), should be between 0,7 mmol/l and 2,0 mmol/l. Hardness values outside these limits can cause scaling and corrosion problems.

A.13 Compressed air

The compressed air supply should be at a pressure of 600 kPa to 800 kPa (5 to 7 bar), free of liquid water, filtered to 25 µm and free from oil droplets greater than 2 µm.

A.14 Test programmes

The example shown in Table A.3 includes the tests needed to verify the attainment of defined process parameters and also to judge from the data whether non-condensable gas present in the sterilizer chamber during the plateau period is sufficient to prevent steam penetration into medical devices used in health care.

Table A.3 — Example of a schedule of tests for validation and periodic testing

Test	EN 285 reference	Installation qualification	Operational qualification	Performance qualification	Periodic testing
Safety tests and checks	Clause 11	××[b]	—	—	×[b]
Steam quality (A.11)					
— Non-condensable gases	13.3.2, 22.1		×	—	×[d]
— Dryness value	13.3.3, 22.2		×	—	×[d]
— Superheat	13.3.4, 22.3		×	—	×[d]
— Contaminants[a] (Tables A.1 and A.2)	Table E.2		×	—	×[d]
Thermometric tests (A.4)					
— Small load (A.4.1)	8.3.1.2, 16.1	—	××	—	×[c]
— Full load (A.4.2)	8.3.1.3, 16.2	—	××	—	×[d]
Hollow load test (A.2)	8.2.5, 15	—	××	—	×[d]
Bowie and Dick test (A.5)	8.3.2, 17	—	××	××	××[e]
Air leakage flow rate (A.6)	8.3.3, 18	—	××	—	××[c]
Air detector (if fitted) (A.7)					
— Small load	8.3.4.2, 19.2	—	××	—	×[d]
— Full load	8.3.4.3, 19.3	—	××	—	×[d]
— Function	8.3.4.4, 19.4	—	××	—	×[f]
Load dryness tests (A.8)					
— Small load textiles	8.4.1, 20.1	—	×	—	—
— Full load textiles	8.4.2, 20.2	—	×	—	—
— Metal	8.4.3, 20.3	—	×	—	—
Dynamic pressure test (A.10)	10, 23	—	—	—	×[b]
Product test	—	—	—	×[g]	×[d]

×× Tests that are suggested.

× Tests that may be considered.

— Tests that need not be performed.

[a] Compliance should be tested in accordance with acknowledged analytical methods.

[b] Specified by the manufacturer.

[c] At least three-monthly.

[d] At least annually.

[e] At least daily.

[f] At least weekly.

[g] Required if exposure to defined sterilizing conditions cannot be predicted from operational qualification tests.

Annex B
(informative)

Evaluation of a sterilization process primarily based on biological inactivation and an accompanying mechanical air removal procedure

B.1 Introduction

B.1.1 There are three general methods of moist heat sterilization employed (see Annexes B, C and D of ISO 17665-1:2006). Knowledge of these three methods allows the user to make an informed decision regarding which method to apply based upon knowledge of the product to be sterilized, whether or not the bioburden of microorganisms on the product have been characterized, and an understanding of the microbial risks involved from a sterilization failure.

B.1.2 The first method is generally known as the "bioburden method" for which the actual microbial challenge is identified and a moist heat process is defined whereby the moist heat parameters required to render the product free of that specific microbial challenge are developed. The product is then tested for sterility. This method is particularly applicable in cases where effects of the sterilizing conditions on the product should be minimized. (See Annex B, ISO 17665-1:2006).

B.1.3 The second method is generally known as the "combined biological indicator/bioburden method," for which the actual microbial challenge is identified, a more resistant biological indicator (BI) is selected as being an appropriate representative challenge, and a moist heat process is developed whereby the product may be assessed to be free of viable microorganisms based on the successful demonstration of inactivating the more resistant organisms of the biological indicator. This method is particularly applicable in cases where the bioburden is known and controlled as in many manufacturing operations. (See Annex C, ISO 17665-1:2006).

B.1.4 The third method is generally known as the "overkill method" for which the actual microbial challenge is unknown or cannot reasonably be measured, as is the case where reusable medical devices are reprocessed. This method may also be used where products for sterilization are durable and can readily withstand the conditions necessary to achieve sterilization. In the overkill method, an organism is selected as being representative of a significant challenge to a defined moist heat process. The defined process (i.e. saturated steam) is expressed in parametric terms (typically time and temperature coupled with the limit values for the steam) relating to the death kinetics of the biological organism selected. The limiting values of the parameters are defined (if applicable) and an acceptable lethal condition is defined. The acceptable minimum criterion (typically a holding time at a specified temperature) is determined and a safety factor is applied to the critical parameters in order to establish a recommended exposure condition for the product to be processed. Very large safety margins are typically employed for applications where the bioburden challenge is not accurately identified and the nature and mixture of products is variable. This method is particularly applicable in healthcare applications. (See Annex D of ISO 17665-1:2006).

Two examples of an overkill cycle are the following.

a) A sterilization process calculated to provide a minimum 12-log reduction of microorganisms having a D-value of 1 min at 121 °C. Validation of a sterilization process based on this value is often closely associated with an overkill cycle of 121 °C maintained for a period of 15 min.

b) A sterilization process that delivers lethality in excess of what is required to destroy the bioburden.

B.1.5 In health care each sterilizer should be periodically demonstrated to be capable of rendering products processed therein to be free from viable microorganisms that the medical devices routinely processed. Methods used to monitor the sterilization process provide the assurance of process integrity between biological challenges tests (see Table B.1).

B.2 Biological qualification of a sterilization process

B.2.1 A sterility assurance level (SAL) of at least 10^{-6} should be demonstrated. The sterility assurance level is the microbial control level of a process and is defined as the probability of a viable microorganism in or on a product, or the probability of a non-sterile unit. The physical limitations of microbiological measurement are such that, at best, we can only directly measure to a survival probability level of 10^{-1}. Since a sterilization process must be based on real data, strategies have been developed that allow us to design and qualify to a sterility assurance level of 10^{-6} using indirect measurement methods.

B.2.2 When sterilizing heat-stable materials an overkill approach is normally utilized. Its simplicity, robustness and ease of validation relative to other approaches should make it the default approach in all instances. (See Annex D of ISO 17665-1:2006.)

B.2.3 Acceptable results for three consecutive cycles of either half cycle or full cycle approach are required for each type of load. (See Annex D.4 of ISO 17665-1:2006.)

B.2.4 The biological indicators used in testing should contain heat resistant spores, such as *Geobacillus stearothermophilus* spores and should comply with applicable standards. (See ISO 11138-1 and ISO 11138-3 and Annex D.4.1 of ISO 17665-1:2006.)

B.3 Biological challenge

B.3.1 The biological challenge consists of sixteen freshly laundered, 100 % cotton towels, in good condition. After being folded, the towels are placed one on top of another, with folded ends alternating, to form a stack. One or more biological indicators are placed between the eighth and ninth towels in the approximate geometric centre of the pack (see ANSI/AAMI ST79[59]).

B.3.2 The biological challenge is placed flat (layers of towels horizontal) on a rack in the area of the sterilizer chamber that is least favourable to sterilization. For gravity-displacement sterilizers, the test is run in a fully loaded chamber. For dynamic-air-removal sterilizers, the test is run in an otherwise empty chamber.

B.3.3 A sterility assurance level of at least 10^{-6} should be demonstrated when the biological challenge is used. One method that can be applied to demonstrate an SAL of 10^{-6} is empirical overkill, based on a 12-log reduction of a micro organism with a D_{121} °C of 1 minute resulting in an F_{bio} of 12 (based on a reference z value of 10 °C. (See Pflug[53].)

B.3.4 Moisture retained by the fabric should not increase the pre-sterilization weight of the biological challenge by more than 3 %. There should be no visible wet spots on the fabric.

B.4 Mechanical air removal

B.4.1 The air-removal test and the leak-rate test are complementary to each other. A dynamic-air-removal sterilizer should meet the requirements of both tests. Neither test is applicable to gravity-displacement sterilizers.

B.4.2 The efficacy of the air removal system of a dynamic-air-removal sterilizer is tested using a steam penetration test similar to the Bowie-Dick test. (See ISO 11140-5).

B.4.3 When tested, a dynamic-air-removal sterilizer should exhibit an average leak rate of 1 mm of mercury (mmHg) per min or less over the measured time interval.

B.4.4 The steam penetration test pack consists of folded, 100 % cotton surgical towels that are clean and preconditioned. The towels should be folded and then placed one above the other.

B.4.5 A Bowie-Dick test indicator sheet is placed across the centre layer of the pack. A single two-ply fabric wrap, made of 100 % cotton is loosely applied (see ISO 11140-5).

B.4.6 The test pack is placed horizontally on the bottom front of the loading rack, near the door and over the chamber drain, in an otherwise empty chamber.

B.4.7 Table B.1 provides a schedule of tests for validation and routine testing.

Table B.1 — Example of a schedule of tests for validation and periodic testing

Test and Monitoring	Installation qualification	Operational qualification	Performance qualification	Routine test of the sterilizer	Periodic test of the sterilizer	Comments
Type tests and safety checks: pressure vessel electrical plumbing environmental	×					
Biological challenge test pack		×			×	× in otherwise empty chamber
Air removal test		×		×	×	× in otherwise empty chamber
Air leak test						Sterilizer manufacturer test
Physical monitors		×	×	×	×	
Monitoring, recording, control		×	×	×	×	
Independent sensor/recorder						Optional
Biological indicators		×	×	×	×	
Chemical indicators		×	×	×	×	
× = tests that should be considered.						

Annex C
(informative)

Temperature and pressure of saturated steam for use in moist heat sterilization

Theoretical steam temperature (see 6.1.2 b of ISO 17665-1:2006) can be determined directly from the steam tables shown below or calculated from Equation (C.1).

Table C.1 — Temperature and pressure of saturated steam for use in moist heat sterilization

Pressure mB[a]	**Temperature**, T °C[a]	**Pressure** MPa[a]	T **from** P using –273,27 °C as absolute zero[b]	**Deviation from steam tables**[c]
1 014,2	100	0,101 42	99,997 1	–0,002 87
1 050,9	101	0,105 09	100,998 1	–0,001 85
1 088,7	102	0,108 87	101,999 3	–0,000 71
1 127,7	103	0,112 77	103,002 5	0,002 456
1 167,8	104	0,116 78	104,004 4	0,004 372
1 209	105	0,120 9	105,004 5	0,004 526
1 251,5	106	0,125 15	106,007 1	0,007 106
1 295,1	107	0,129 51	107,006 8	0,006 789
1 340,1	108	0,134 01	108,009 8	0,009 813
1 386,3	109	0,138 63	109,011 0	0,011 046
1 433,8	110	0,143 38	110,012 1	0,012 132
1 482,6	111	0,148 26	111,012 5	0,012 517
1 532,8	112	0,153 28	112,013 7	0,013 662
1 584,3	113	0,158 43	113,013 0	0,013 041
1 637,3	114	0,163 73	114,014 0	0,013 976
1 691,8	115	0,169 18	115,015 8	0,015 808
1 747,7	116	0,174 77	116,016 2	0,016 17
1 805,1	117	0,180 51	117,016 4	0,016 372
1 864	118	0,186 4	118,015 9	0,015 913
1 924,5	119	0,192 45	119,016 0	0,015 968
1 986,7	120	0,198 67	120,017 6	0,017 586
2 050,4	121	0,205 04	121,017 1	0,017 056
2 115,8	122	0,211 58	122,017 1	0,017 072
2 182,9	123	0,218 29	123,017 1	0,017 112
2 251,7	124	0,225 17	124,016 7	0,016 702
2 322,2	125	0,232 22	125,015 4	0,015 407

Table C.1 (*continued*)

Pressure mB[a]	**Temperature**, T °C[a]	**Pressure** MPa[a]	T **from** P using –273,27 °C as absolute zero[b]	**Deviation from steam tables**[c]
2 394,6	126	0,239 46	126,015 6	0,015 56
2 468,8	127	0,246 88	127,015 3	0,0152 71
2 544,8	128	0,254 48	128,014 1	0,0141 23
2 622,7	129	0,262 27	129,013 0	0,0130 03
2 702,6	130	0,270 26	130,012 7	0,012 71
2 784,4	131	0,278 44	131,011 5	0,011 547
2 868,2	132	0,286 82	132,010 3	0,010 329
2 954,1	133	0,295 41	133,009 8	0,009 792
3 042	134	0,304 2	134,008 4	0,008 352
3 132	135	0,313 2	135,006 8	0,006 761
3 224,2	136	0,322 42	136,005 7	0,005 699
3 318,5	137	0,331 85	137,003 7	0,003 686
3 415,1	138	0,341 51	138,002 4	0,002 44
3 513,9	139	0,351 39	139,000 5	0,000 526
3 615	140	0,361 5	139,998 6	–0,001 42

[a] Extracted from ASME “International Steam Tables for Industrial Use” based on the IAPWS “Industrial Formulation 1997 for the Thermodynamic Properties of Water and Steam” (IAPWS-IF97).

[b] Indicates the temperature derived from Equation (C.1).

[c] The deviation of the calculated value using Equation (C.1) from the stated steam table value.

$$T = 42{,}677\ 6 + [-3\ 892{,}7/(\ln P - 9{,}486\ 54)] - 273{,}27 \qquad \text{(C.1)}$$

where

T is the the theoretical steam temperature, in degrees centigrade;

P is the the measured pressure, in megapascals;

A figure of –273,27 °C is used for the value of absolute zero (zero K). This value is used to compensate for a 0,1 °C offset between calculated theoretical temperature created by the formula and those prescribed in the current steam tables.

Linear interpolation between data points may be used to derive intermediate values.

Example calculation:

For $P = 0{,}205\ 04$ MPa and $T = 121$ °C

$\ln P = -1{,}584\ 550$

$\ln P + (-9{,}486\ 54) = -1{,}584\ 55 + (-9{,}486\ 54) = -11{,}071\ 09$

$3\ 892{,}7/-11{,}071\ 09 = 351{,}609\ 4$

$42{,}677\ 6 + 351{,}609\ 4 = 394{,}287\ 05$ K

$= 394{,}287\ 05 - 273{,}27 = 121{,}017\ 1$ °C

Annex D
(informative)

Special considerations for health care settings

D.1 Introduction

This annex offers additional guidance that may be used in a health care setting for the validation of a sterilization process that is to be used for reprocessing.

D.2 Quality management system elements
(additional guidance for ISO 17665-1:2006, 4.1)

D.2.1 The manager with executive authority should have the responsibility for:

a) introducing a quality system, review at regular intervals and ensure that the quality system is understood, implemented and maintained with current information;

b) defining roles and responsibilities, tasks and processes to be undertaken;

c) ensuring that the chain of accountability is clearly identified;

d) ensuring that a change in a process is verified and documented;

e) ensuring that staff performance reviews are established and implemented;

f) ensuring that resources are made available for trained personnel, supervision, work activities and quality audits.

D.2.2 The manager with executive authority should understand the benefits to the facility of a quality system, including financial, and is responsible for:

a) designating personnel trained in the performance of quality audits and the implementation of quality improvement initiatives;

b) defining staff and management responsibilities;

c) defining the qualifications, competency and responsibility of each person authorized (authorized person) designated to carry out specific task(s);

d) ensuring qualification, education and training of personnel;

e) introducing an infection prevention and control programme including procedures and protocols;

f) making provision for worker health and safety;

g) defining procedures for subcontractors, including whether they operate within or outside the health care facility, if applicable;

h) defining continuous quality assurance and competency assessment procedures;

i) ensuring that procedures are in place for control and monitoring of all phases of the operation and that there is documentation to ensure adherence to standards, guidelines and regulations; one example is implementing procedures for storage conditions, cleaning and disinfecting agents, and ensuring that they are being used according to instructions on their label;

j) ensuring that purchased sterilizers conform to legal requirements and its specification (see ISO 17665-1:2006, 6.2);

k) ensuring that sterilizers are installed correctly and safely with regard to proper functioning, safety of personnel and environmental protection;

l) ensuring that the service required for proper operation of the sterilization equipment meet the specifications of the sterilizer manufacturer;

m) ensuring that newly installed sterilizers are subject to a documented scheme of validation comprising installation qualification, operational qualification and performance qualification tests before they are put into service;

n) ensuring that sterilizers are subject to a documented scheme of periodic tests at yearly, quarterly, weekly and (in some cases) daily intervals;

o) ensuring that sterilizers have a maintenance service contract or in-house inspection and maintenance programme staffed by fully trained and qualified personnel;

p) ensuring that procedures for production, quality control and safe working are documented and adhered to in accordance with statutory requirements and accepted best practice;

q) ensuring that procedures for dealing with malfunctions, accidents and dangerous occurrences are documented and adhered to;

r) ensuring that the sterilizer manufacturer's recommendations for regular maintenance and periodic inspections are followed and documented (see Clause 12 and also 12.3 of ISO 17665-1:2006);

s) ensuring that each measuring chain fitted to, or used with, the sterilization equipment is periodically calibrated, inspected, checked and maintained; the calibration of the equipment should be carried out using instruments calibrated and traceable to national standards;

t) ensuring that the sterilizer manufacturer supplies information/schedules on any parts or components that require routine replacement and that this is made available to the user.

D.2.3 The manager with executive authority should be aware of operational aspects such as:

a) work area design (decontamination, preparation, sterilization and sterile storage areas), environmental controls, hand washing facilities, work surfaces, traffic control, personal protective equipment and dress code;

b) medical device preparation;

c) cleaning and disinfection;

d) reassembly and functional testing of complex devices;

e) packaging;

f) sterilizer loading, operation, unloading and product release;

g) storage and distribution;

h) need for a traceability system for each medical device;

i) sterility assurance and sterility maintenance;

j) purchase agreements;

k) maintenance and sterilizer quality assurance;

l) management and reporting of incidents requiring attention or action;

m) the sterilization of a medical device(s) according to its product family and/or the manufacturer's recommendations;

n) the sterilization of a medical device(s) that is (are) difficult to clean or sterilize.

D.2.4 The manager with executive authority should be aware of requirements for sterilization process documentation and should ensure that this documentation includes:

a) regular quality audits of the documentation system;

b) accessibility to the staff;

c) standard operating procedures and have pertinent information for all critical steps of the sterilization process;

d) manuals, diagrams and visual keys that should be available and readily accessible to staff;

e) all procedural and equipment audits and reports;

f) all changes to processes; the changes should be documented, approved and communicated to the appropriate staff in a timely manner.

D.3 Process and equipment characterization
(additional guidance for ISO 17665-1:2006, Clause 6)

D.3.1 Process (additional guidance for ISO 17665-1:2006, 6.1)

D.3.1.1 Two approaches to the evaluation of sterilization processes are described in Annex A and Annex B.

D.3.1.2 If the presence of sterilizing conditions on the medical device(es) cannot be predicted from the tests detailed in Annex A, a combination of the tests prescribed in Annex A and Annex B may be necessary.

D.3.2 Equipment (additional guidance for ISO 17665-1:2006, 6.2.)

Sterilizers for use in health care facilities should be equipped with a sterilization process(es) designed to sterilize a range of medical devices routinely used in a health care facility.

D.4 Product definition in health care facilities
(additional guidance for ISO 17665-1:2006, Clause 7)

D.4.1 Additional guidance on ISO 17665-1:2006, 7.1

It is unlikely that a health care facility will be involved in the design and development of a medical device. It is more likely that the health care facility will be faced with the choice of purchasing commercialized products. In certain circumstances the health care facility could be involved in the design and development of a new or modified medical device. Under such circumstances the product family should be identified and the requirements of ISO 17665-1 followed.

D.4.2 Additional guidance on ISO 17665-1:2006, 7.3

A health care facility will often combine several commercialized products into one pack. The product family for this combination should be identified. In most cases the product family identified should align with the product family for the medical device in the pack known to be the one most difficult to sterilize.

D.4.3 Additional guidance on ISO 17665-1:2206, 7.10

Use of devices that are difficult to clean and/or disassemble should be carefully considered prior to purchase because only a cleaned device can be successfully sterilized. Instructions for reprocessing should be provided by the medical device manufacturer. For instruments predating the publication of ISO 17664[23], regional or national guidelines for cleaning, decontamination and sterilization of such medical devices should be followed.

D.5 Process definition
(additional guidance for ISO 17665-1:2006, Clause 8)

D.5.1 Additional guidance on ISO 17665-1:2006, 8.1

D.5.1.1 A sterilization process based on the recommendations for a sterilization temperature and holding time specified in national and regional pharmacopoeias and/or developed from process parameters specified by the sterilizer and/or medical device manufacturer is used for reprocessing in health care facilities.

D.5.1.2 Standards for sterilizers suitable for processing a wide range of medical devices have been developed. A sterilization process that conforms to the performance requirements detailed in a relevant standard may be recommended by the medical device manufacturer.

D.5.1.3 A dissimilar but existing sterilization process that previously has been defined to treat the product family to which the new medical device is assigned may be used providing that the size, design and construction material of the new medical device fits into the product family range.

D.5.1.4 A health care facility will often combine several commercialized products into one pack. Under these circumstances the facility should take into account the instructions for reprocessing issued for each of the individual medical devices that make up the pack and the product families to which each medical device is assigned. The health care facility should consider the recommendations of individual suppliers of commercialized products for reprocessing in relation to their existing sterilization process(es). It might be possible to use an existing sterilization process, or it could be necessary to develop a new sterilization process based on the medical device manufacturer's recommendations. Any deviation for the proposed sterilization process should be agreed with the medical device manufacturer or validated by a designated person (see D.8.3.1 and A.4.2 in ISO 17665-1:2006).

D.5.1.5 If the intended sterilization process is neither recommended by the medical device manufacturer nor previously defined to treat the product family to which the new device fits, a detailed comparison between the new product and products already defined to the intended sterilization process should take place. The comparison should include physical characteristics supplemented with thermal and biological assessment when applicable.

D.5.2 Additional guidance on ISO 17665-1:2006, 8.3

Physical parameters and exposure restrictions identified by the medical device manufacturer(s) should be observed for each medical device. Failure to follow a manufacturer's reprocessing instructions can affect the performance of, and invalidate any warranties related to, the medical device.

D.5.3 Additional guidance on ISO 17665-1:2006, 8.4

For many medical devices, air removal is a critical factor when predicting the presence of saturated steam in locations that are difficult to sterilize. Relevant tests and acceptance criteria for factors that can affect steam penetration are identified in Annex A and Annex B.

D.5.4 Additional guidance on ISO 17665-1:2006, 8.12

A sterilization process based on bioburden is, in most cases, impractical and unsuitable for medical devices intended to be reprocessed.

D.6 Validation
(additional guidance for ISO 17665-1:2006, Clause 9)

D.6.1 Operational qualification
(additional guidance for ISO 17665-1:2006, 9.3.1)

D.6.1.1 Whenever new equipment is installed, existing equipment is modified to deliver a new sterilization process, or a service is changed, the sterilizer manufacturer, or the party having responsibility for the sterilization process, should define the product family(ies) that can be treated and the performance requirements and tests that are to be used to verify the efficiency of the sterilization process. Modifications to the sterilization process that can affect this efficiency include changes to process parameters.

D.6.1.2 Performance requirements and tests may be needed to establish:

a) *effective air dilution obtained from the sterilization process:* this can be predicted from the operating cycle; reproducibility will be affected by air leakage into the sterilizer chamber, non-condensable gas in the steam and the rate of change of temperature in the sterilizer chamber and sterilizer load;

b) *contaminants that are deposited on the medical device*: this can be predicted from the contaminants suspended in the steam;

c) *steam penetration into those parts of the medical device from which air is difficult to remove*: this can be predicted by comparing the temperature measured in a reference device to the temperature measured at the reference measuring point; the reference device should offer a similar challenge to the medical device(s) it represents and the method should be verified by chemical indicators or biological indicators positioned in the reference device and/or medical device;

d) *load dryness for wrapped goods:* this can be determined by both visual inspection and mass increase.

D.6.1.3 If an existing sterilization process is to be used to treat a new medical device and/or loading configuration, conformity to the performance requirements established during the original or subsequent operational qualification should be verified before performance qualification is carried out. This may be done by reference to data obtained during routine processing and/or periodic tests or by a repeat of operational qualification.

D.6.2 Performance qualification
(additional guidance on ISO 17665-1:2006, 9.4)

D.6.2.1 Additional guidance for ISO 17665-1:2006, 9.4.1

D.6.2.1.1 The efficiency and reproducibility of the sterilization process and process parameters should be known for the whole range of product family(ies) and load configuration(s) that the sterilization process is designed to treat.

D.6.2.1.2 The sterilization load most difficult to sterilize should be identified from the range of medical devices, product families and loading configurations that the sterilizing process may treat. Advice on characterizing for difficulty should be available from the medical device manufacturer(s) and/or sterilizer manufacturer.

D.6.2.1.3 Performance qualification should be carried out on this sterilization load and if successful may be deemed to be valid for other combinations from this range.

D.6.2.1.4 If dampness occurs on a medical device, specific orientation and/or location may be necessary.

D.6.2.1.5 Some medical devices may need pre-treatment such as equilibration to atmospheric or other specific temperature and humidity.

D.6.2.2 Additional guidance for ISO 17665-1:2006, 9.4.2

The number of sensors used should ensure that sufficient data are recorded to demonstrate the effectiveness of the process. Experience has shown that for a typical health care sterilization load and chamber usable space (ca. 400 l), 5 to 12 temperature sensors may be sufficient.

D.6.2.3 Additional guidance for ISO 17665-1:2006, 9.4.4

Data for identifying limits for process parameters and acceptance criteria for periodic tests should be determined from data obtained from the tests carried out during performance qualification. This should include thermometric data and data from the results from chemical indicators and/or biological indicators placed in the locations that are difficult to access. A judgement whether the measured temperature is in air or steam should also be made.

D.6.3 Review and approval of the validation
(additional guidance for ISO 17665-1:2006, 9.5.2)

Data should be presented to confirm that:

a) there is a specification for each test used during operational qualification and performance qualification, and that acceptance criteria for each test has been met;

b) if a test(s) is (are) to be carried out periodically to verify that the efficiency of the sterilization process remains within specification, and that this test and its performance requirements have been derived from data gained during operational qualification and performance qualification and requalification if necessary;

c) the product family(ies) represented by the worst case sterilization load for sterilization has been identified;

d) if a restriction on presentation and/or location has been identified, this restriction is reflected in they description of the load configuration.

D.7 Routine monitoring and control
(additional guidance for ISO 17665-1:2006, Clause 10)

D.7.1 Additional guidance for ISO 17665-1:2006, 10.1

D.7.1.1 Routine monitoring and control activities can be divided according to the frequency with which they should be performed. The activities should include, if appropriate:

a) an air leakage flow rate test to establish the level of air leakage into the sterilizer chamber;

b) a check to confirm that scheduled and unscheduled maintenance has been satisfactorily completed;

c) a steam penetration test to judge the effect that residual air and non-condensable gas will have on the efficiency of the sterilization process;

d) a check to confirm that the sterilizer load/product family(ies) to be sterilized is (are) included in the performance qualification/periodic re-qualification reports;

e) a check to confirm that during the sterilization process, all the process parameters are within their specified tolerances;

f) a check to confirm that chemical indicators and/or biological indicators respond as specified;

g) a check to confirm that process challenge devices, air detectors or process monitoring systems have responded as specified;

h) a check to confirm that, when the sterilizer is unloaded, all the packages are seen to be undamaged, dry, correctly marked and the process chemical indicator on each pack has reached their acceptance criteria.

D.7.1.2 A sterilization load will generally consist of medical devices from a number of product families with variations between each cycle. Residual non-condensable gas indirectly identified by periodic tests is such that within limits, instantaneous steam penetration occurs in a sterilizer load that has a resistance to steam penetration equal to or less than the resistance from the worst case sterilization load. Based on this level of air dilution, random loading configurations are permitted, and any restriction is generally limited to residual dampness. For a single product family and load configuration, reproducibility within small tolerances may be appropriate and will have been established during performance qualification. A medical device should always be assigned to a product family that is included in the processing list for the sterilization process. A product family may consist of a single medical device or a group of similar medical devices.

D.7.2 Additional guidance for ISO 17665-1:2006, 10.3

It is essential that any change that can affect air dilution is identified by means such as a process challenge device and/or air detection and a steam penetration test.

D.8 Product release from sterilization
(additional guidance for ISO 17665-1:2006, 11.1)

D.8.1 An audit trail for equipment, product and sterilization process should be in place. One example is as follows.

The sterilizer should be fit for purpose and this should be noted on the release documentation. This declaration should be based on and include:

a) successful scheduled maintenance;

b) conformity to the performance requirements for the current periodic tests and routine tests;

c) no change to the steam supply system and other services;

d) conformity to the performance requirements for routine processing has been met for recent production cycles.

D.8.2 A successful sterilization process should include:

a) conformity to the requirements for the environment in the preparation, packaging and sterilization areas;

b) conformity to the requirements for staff hygiene and control;

c) conformity to the procedures for the preparation, packaging and marking of medical devices;

d) each medical device or group of medical devices assigned to a product category(ies);

e) each sterilization load validated for the intended sterilization process;

NOTE Providing the sterilization load presenting the greatest challenge to the sterilization process has had successful performance qualification, sterilization loads with less of a challenge may be classed as validated.

f) the attainment of the prescribed sterilization temperature and plateau period;

g) a record of the whole operating cycle and its cycle number;

h) a specified response for chemical indicators, if used;

i) confirmation that each pack is visibly dry and undamaged.

D.8.3 The markings on each pack and if appropriate each medical device should enable:

a) identification of the sterilizer used;

b) the cycle number of the sterilization process;

c) identification of the pack;

d) identification of being 'processed'.

D.8.4 A failure of a periodic test including the daily Bowie and Dick test, if applicable, should trigger quarantine of the sterilizer. If biological indicators have been used, recovery of viable microorganisms should result in quarantine of product whilst an investigation into the cause is conducted. The investigation can result in a decision to destroy the product and/or recall product already released.

D.9 Maintaining process effectiveness
(additional guidance for ISO 17665-1:2006, Clause 12)

D.9.1 Recalibration
(additional guidance for ISO 17665-1:2006, 12.2)

Verification of calibration of each measuring chain should be carried out:

a) annually,

b) after unscheduled maintenance or repair of the measuring chain and

c) if there is evidence of inaccuracy of the measuring chain.

D.9.2 Maintenance of equipment
(additional guidance for ISO 17665-1:2006, 12.3.1)

Maintenance or changes to a service, such as a central steam generator, should be notified to the user because, for example, changes to the water treatment to a boiler could cause the level of non-condensable gas, moisture and/or chemical contaminants to exceed the specified maximum. Such changes should be assessed for their impact on creating a non-conformity with the process specification and if necessary, corrective action taken and documented.

D.9.3 Requalification

(additional guidance for ISO 17665-1:2006, 12.4.1)

If applicable, routine operational requalification and performance requalification should, typically, be performed annually (for example see Table A.3). Operational requalification should be a repeat of some or all of the operational qualification tests. Performance requalification should be a repeat of a performance qualification study for at least one of the sterilization loads routinely processed and for which performance qualification records are available. If the values established are within the same limits as in the original validation study or in the preceding requalification study, reproducibility should be deemed to be acceptable.

Annex E
(informative)

Index of normative clauses/subclauses of ISO 17665-1 and cited references or related guidance given in ISO 17665-1 and ISO/TS 17665-2

NOTE This table provides an index of cited references in clauses/subclauses of ISO 17665-1 and related guidance given in Annex A of ISO 17665-1:2006 or the main body of this Technical Specification and special considerations for health care facilities given in Annex D of this Technical Specification.

Normative clause/subclause in ISO 17665-1:2006	Cited references in ISO 17665-1:2006	Related guidance provided in Annex A of ISO 17665-1:2006	Related guidance provided in the main body (Clauses 1-12) of ISO/TS 17665-2	Special considerations/ guidance for health care facilities provided in ISO/TS 17665-2, Annex D
4 Quality management systems		A.1.2.4		
4.1 Documentation	Applicable subclauses of ISO 13485	A.4.1		
4.2 Management responsibility		A.4.2		D.2
4.3 Product realization	Applicable subclauses of ISO 13485 Applicable clauses of ISO 10012	A.4.3		
4.4 Measurement, analysis and improvement — Control of non-conforming product	Applicable subclauses of ISO 13485	A.4.4		
5 Sterilizing agent characterization		A.5	5	
5.1 Sterilizing agent			5.1	
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5.3 Materials effects			5.3	
5.4 Environmental considerations			5.4	
6 Process and equipment characterization		A.6	6	
6.1 Process			6.1	D.3.1
6.1.1 General			6.1.1	
6.1.2 Saturated steam processes			6.1.2	

Normative clause/subclause in ISO 17665-1:2006	Cited references in ISO 17665-1:2006	Related guidance provided in Annex A of ISO 17665-1:2006	Related guidance provided in the main body (Clauses 1-12) of ISO/TS 17665-2	Special considerations/ guidance for health care facilities provided in ISO/TS 17665-2, Annex D
6.1.3 Contained product processes		A.6	6.1.3	D.3.1
6.2 Equipment			6.2	D.3.2
7 Product definition	ISO 11607-1 ISO 11607-2 ISO 11737-1	A.7	7	D.4
8 Process definition	ISO 17665-1 Annexes B, C, D ISO 11138-1 ISO 11138-3 Applicable parts of ISO 11140 series ISO 11737-1 ISO 11737-2 ISO 17664	A.8	8	D.5
9 Validation		A.9	9	D.6
9.1 General			9.1	
9.2 Installation qualification (IQ)			9.2	
9.2.1 Equipment			9.2.1	
9.2.2 Installation			9.2.2	
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9.3 Operational qualification (OQ)			9.3	D.6.1
9.4 Performance qualification (PQ)	ISO 17665-1:2006, Annexes B, C and D EN 285		9.4	D.6.2
9.5 Review and approval of validation			9.5	D.6.3
10 Routine monitoring and control		A.10	10	D.7
11 Product release from sterilization		A.11	11	D.8
12 Maintaing process effectiveness		A.12	12	D.9
12.1 Demonstration of continued effectiveness			12.1	
12.2 Recalibration			12.2	D.9.1

Normative clause/subclause in ISO 17665-1:2006	Cited references in ISO 17665-1:2006	Related guidance provided in Annex A of ISO 17665-1:2006	Related guidance provided in the main body (Clauses 1-12) of ISO/TS 17665-2	Special considerations/ guidance for health care facilities provided in ISO/TS 17665-2, Annex D
12.3 Maintenance of equipment		A.12	12.3	D.9.2
12.4 Requalification			12.4	D.9.3
12.5 Assessment of change				

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