BS EN ISO 17665:2024

BSI Standards Publication

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

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National foreword

This British Standard is the UK implementation of EN ISO 17665:2024. It is identical to ISO 17665:2024. It supersedes BS EN ISO 17665-1:2006, DD CEN ISO/TS 17665-2:2009 and PD ISO/TS 17665-3:2013, which are withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/198, Sterilization and Associated Equipment and Processes.

A list of organizations represented on this committee can be obtained on request to its committee manager.

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For the Great Britain market (England, Scotland and Wales), if UK Government has designated this publication for conformity with UKCA marking (or similar) legislation, it may contain an additional National Annex. Where such a National Annex exists, it shows the correlation between this publication and the relevant UK legislation. If there is no National Annex of this kind, the relevant Annex ZA or ZZ in the body of the European text will indicate the relationship to UK regulation applicable in Great Britain. References to EU legislation may need to be read in accordance with the UK designation and the applicable UK law. Further information on designated standards can be found at www.bsigroup.com/standardsandregulation.

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UK Government is responsible for legislation. For information on legislation and policies relating to that legislation, consult the relevant pages of www.gov.uk.

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English Version

Sterilization of health care products - Moist heat - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 17665:2024)

Stérilisation des produits de santé - Chaleur humide - Exigences pour le développement, la validation et le contrôle de routine d'un procédé de stérilisation des dispositifs médicaux (ISO 17665:2024)

Sterilisation von Produkten für die Gesundheitsfürsorge - Feuchte Hitze - Anforderungen an die Entwicklung, Validierung und Lenkung der Anwendung eines Sterilisationsverfahrens für Medizinprodukte (ISO 17665:2024)

This European Standard was approved by CEN on 3 December 2023.

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European foreword

This document (EN ISO 17665:2024) has been prepared by Technical Committee ISO/TC 198 "Sterilization of health care products" in collaboration with Technical Committee CEN/TC 204 “Sterilization of medical devices” the secretariat of which is held by BSI.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by November 2024, and conflicting national standards shall be withdrawn at the latest by November 2024.

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

This document supersedes EN ISO 17665-1:2006 and CEN ISO/TS 17665-2:2009.

This document has been prepared under a standardization request addressed to CEN by the European Commission. The Standing Committee of the EFTA States subsequently approves these requests for its Member States.

For the relationship with EU Legislation, see informative Annex ZA or ZB, which is an integral part of this document.

Any feedback and questions on this document should be directed to the users’ national standards body/national committee. A complete listing of these bodies can be found on the CEN website.

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Türkiye and the United Kingdom.

Endorsement notice

The text of ISO 17665:2024 has been approved by CEN as EN ISO 17665:2024 without any modification.

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Annex ZA
(informative)

Relationship between this European standard and the General Safety and Performance Requirements of Regulation (EU) 2017/745 aimed to be covered

This European standard has been prepared under M/575 to provide one voluntary means of conforming to the General Safety and Performance Requirements of Regulation (EU) 2017/745 of 5 April 2017 concerning medical devices [OJ L 117] and to system or process requirements including those relating to quality management systems, risk management, post-market surveillance systems, clinical investigations, clinical evaluation or post-market clinical follow-up.

Once this standard is cited in the Official Journal of the European Union under that Regulation, compliance with the normative clauses of this standard given in Table ZA.1 and application of the edition of the normatively referenced standards as given in Table ZA.2 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding General Safety and Performance Requirements of that Regulation, and associated EFTA Regulations.

Where a definition in this standard differs from a definition of the same term set out in Regulation (EU) 2017/745, the differences shall be indicated in this Annex Z. For the purpose of using this standard in support of the requirements set out in Regulation (EU) 2017/745, the definitions set out in this Regulation prevail. In this context, the definition of 'medical device' in this standard is a modified version of the definition prepared by the Global Harmonization Task Force with modification to the Note in the definition.

Where the European standard is an adoption of an International Standard, the scope of this standard can differ from the scope of the European Regulation that it supports. As the scope of the applicable regulatory requirements differ from nation to nation and region to region, the standard can only support European regulatory requirements to the extent of the scope of the European regulation for medical devices (EU) 2017/745).

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Regulation (EU) 2017/745. This means that risks have to be 'reduced as far as possible', 'reduced to the lowest possible level', 'reduced as far as possible and appropriate', 'removed or reduced as far as possible', 'eliminated or reduced as far as possible', 'removed or minimized as far as possible', or 'minimized', according to the wording of the corresponding General Safety and Performance Requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with General Safety and Performance Requirements 1, 2, 3, 4, 5, 8, 9, 10, 11, 14, 16, 17, 18, 19, 20, 21 and 22 of the Regulation.

NOTE 3 When a General Safety and Performance Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

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Table ZA.1 — – Correspondence between this European standard and Annex I of Regulation (EU) 2017/745 [OJ L 117] and to system or process requirements including those relating to quality management systems, risk management, post-market surveillance systems, clinical investigations, clinical evaluation or post-market clinical follow-up

General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s) / sub-clause(s) of this EN	Remarks / Notes
11.3	4,5,6,7,8,9,10,11,12	This standard provides requirements for the development, validation and routine control of a sterilization process using moist heat for medical devices, including requirements that the medical device is safe and performs as intended after treatment. It could also be applied to the development, validation and routine control of a process for attainment of a specific microbial state other than sterility. This General Safety and Performance Requirement is addressed only with regard to devices for which treatment by moist heat is appropriate. This relevant General Safety and Performance Requirement is only partly addressed in this European Standard. Design and packaging for maintenance of a specific microbial state during transportation and storage are not covered. Aspects of manufacture other than those related to attainment of a specific microbial state using moist heat are not covered.
11.4 first sentence only	4,5,6,7,8,9,10,11,12	This standard provides requirements for the development, validation and routine control of a sterilization process using moist heat for medical devices, including requirements that the sterilized medical device is safe and performs as intended after sterilization. This General Safety and Performance Requirement is addressed only with regard to devices for which sterilization by moist heat is appropriate. This relevant General Safety and Performance Requirement is only partly addressed in this European Standard. Design and packaging for maintenance of sterility during transportation and storage are not covered. Aspects of manufacture other than those related to attainment of sterility by moist heat are not covered. Evidence that the integrity of the packaging

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General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s) / sub-clause(s) of this EN	Remarks / Notes
		is maintained to the point of use is not covered.
11.5	4,5,6,7,8,9,10,11,12	This standard provides requirements for the development, validation and routine control of a sterilization process using moist heat for medical devices, including requirements that the sterilized medical device is safe and performs as intended after sterilization. This General Safety and Performance Requirement is addressed only with regard to devices for which sterilization by moist heat is appropriate. This relevant General Safety and Performance Requirement is only partly addressed in this European Standard. Packaging for maintenance of sterility is not covered. Aspects of manufacture other than those related to attainment of sterility using moist heat are not covered.

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Table ZA.2 — Applicable Standards to confer presumption of conformity as described in this Annex ZA

Column 1 Reference in Clause 2	Column 2 International Standard Edition	Column 3 Title	Column 4 Corresponding European Standard Edition
ISO 11140-1	ISO 11140-1:2014	Sterilization of health care products — Chemical indicators — Part 1: General requirements	EN ISO 11140-1:2014
ISO 11140-3	ISO 11140-3:2007	Sterilization of health care products — Chemical indicators — Part 3: Class 2 indicator systems for use in the Bowie and Dick-type steam penetration test	EN ISO 11140-3:2009
ISO 11140-4	ISO 11140-4:2007	Sterilization of health care products — Chemical indicators — Part 4: Class 2 indicators as an alternative to the Bowie and Dick-type test for detection of steam penetration	EN ISO 11140-4:2007
ISO 11140-5	ISO 11140-5:2007	Sterilization of health care products — Chemical indicators — Part 5: Class 2 indicators for Bowie and Dick-type air removal tests	None For applicable standard edition see Column 2
ISO 11140-6	ISO 11140-6:2022	Sterilization of health care products — Chemical indicators — Part 6: Type 2 indicators and process challenge devices for use in performance testing of small steam sterilizers.	EN ISO 11140-6:2022
ISO 11607-1	ISO 11607-1:2019	Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems	EN ISO 11607-1:2020+A11:2022
ISO 11607-2	ISO 11607-2:2019	Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes	EN ISO 11607-2:2020+A11:2022
ISO 11737-1	ISO 11737-	Sterilization of health care	EN ISO 11737-1:2018+A1:2021

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Column 1 Reference in Clause 2	Column 2 International Standard Edition	Column 3 Title	Column 4 Corresponding European Standard Edition
	1:2018/amd1:2021	products — Microbiological methods — Part 1: Determination of a population of microorganisms on products	
ISO 11737-2	ISO 11737-2:2019	Sterilization of health care products — Microbiological methods — Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process	EN ISO 11737-2:2020
ISO 11138-1	ISO 11138-1:2017	Sterilization of health care products — Biological indicators — Part 1: General requirements	EN ISO 11138-1:2017
ISO 11138-3	ISO 11138-3:2017	Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization processes	EN ISO 11138-3:2017

The documents listed in the Column 1 of Table ZA.2, in whole or in part, are normatively referenced in this document and are indispensable for its application. The achievement of the presumption of conformity is subject to the application of the edition of Standards as listed in Column 4 or, if no European Standard Edition exists, the International Standard Edition given in Column 2 of Table ZA.2.

WARNING 1 — Presumption of conformity stays valid only as long as a reference to this European Standard is maintained in the list published in the Official Journal of the European Union. Users of this standard should consult frequently the latest list published in the Official Journal of the European Union.

WARNING 2 — Other Union legislation may be applicable to the product(s) falling within the scope of this standard.

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Annex ZB
(informative)

Relationship between this European standard and the General Safety and Performance Requirements of Regulation (EU) 2017/746 aimed to be covered

This European standard has been prepared under M/575 to provide one voluntary means of conforming to the General Safety and Performance Requirements of Regulation (EU) 2017/746 of 5 April 2017 concerning *in vitro* diagnostic medical devices [OJ L 117] and to system or process requirements including those relating to quality management systems, risk management, post-market surveillance systems, performance studies, clinical evidence or post-market performance follow-up.

Once this standard is cited in the Official Journal of the European Union under that Regulation, compliance with the normative clauses of this standard given in Table ZB.1 and application of the edition of the normatively referenced standards as given in Table ZA.2 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding General Safety and Performance Requirements of that Regulation, and associated EFTA Regulations.

Where a definition in this standard differs from a definition of the same term set out in Regulation (EU) 2017/746, the differences shall be indicated in the Annex Z. For the purpose of using this standard in support of the requirements set out in Regulation (EU) 2017/746, the definitions set out in this Regulation prevail. In this context, the definition of 'medical device' in this standard is a modified version of the definition prepared by the Global Harmonization Task Force with modification to the Note in the definition.

Where the European standard is an adoption of an International Standard, the scope of this standard can differ from the scope of the European Regulation that it supports. As the scope of the applicable regulatory requirements differ from nation to nation and region to region, the standard can only support European regulatory requirements to the extent of the scope of the In vitro Diagnostic Regulation (EU) 2017/746).

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Regulation (EU) 2017/746. This means that risks have to be 'reduced as far as possible', 'reduced to a level as low as reasonably practicable', 'reduced to the lowest possible level', 'reduced as far as possible and appropriate', 'removed or reduced as far as possible', 'eliminated or reduced as far as possible', 'prevented' or 'minimized', according to the wording of the corresponding General Safety and Performance Requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with General Safety and Performance Requirements 1, 2, 3, 4, 5, 8, 10, 11, 13, 15, 16, 17, 18 and 19 of the Regulation.

NOTE 3 When a General Safety and Performance Requirement does not appear in Table ZB.1, it means that it is not addressed by this European Standard.

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Table ZB.1 — Correspondence between this European standard and Annex I of Regulation (EU) 2017/746 [OJ L 117] and to system or process requirements including those relating to quality management systems, risk management, post-market surveillance systems, performance studies, clinical evidence or post-market performance follow-up.

General Safety and Performance Requirements of Regulation (EU) 2017/746	Clause(s) / sub-clause(s) of this EN	Remarks / Notes
11.2	4,5,6,7,8,9,10,11,12	This standard provides requirements for the development, validation and routine control of a sterilization process using moist heat for medical devices, including requirements that the sterilized medical device is safe and performs as intended after sterilization. It could also be applied to the development, validation and routine control of a process for attainment of a specific microbial state other than sterility. This General Safety and Performance Requirement is addressed only with regard to devices for which treatment by moist heat is appropriate. This relevant General Safety and Performance Requirement is only partly addressed in this European Standard. Design and packaging for maintenance of sterility or another specific microbial state during transportation and storage are not covered. Aspects of manufacture other than those related to attainment of sterility or another specific microbial state using moist heat are not covered.
11.3	4,5,6,7,8,9,10,11,12	This standard provides requirements for the development, validation and routine control of a sterilization process using moist heat for medical devices, including requirements that the sterilized medical device is safe and performs as intended after sterilization. This General Safety and Performance Requirement is addressed only with regard to devices for which sterilization by moist heat is appropriate. This relevant General Safety and Performance Requirement is only partly addressed in this European

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General Safety and Performance Requirements of Regulation (EU) 2017/746	Clause(s) / sub-clause(s) of this EN	Remarks / Notes
		Standard. Packaging for maintenance of sterility is not covered. Aspects of manufacture other than those related to attainment of sterility using moist heat are not covered.

WARNING 1 — Presumption of conformity stays valid only as long as a reference to this European standard is maintained in the list published in the Official Journal of the European Union. Users of this standard should consult frequently the latest list published in the Official Journal of the European Union.

WARNING 2 — Other Union legislation may be applicable to the product(s) falling within the scope of this standard.

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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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 204, *Sterilization of medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

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

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

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

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

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

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Introduction

A sterile medical device is one that is free of viable microorganisms. International Standards that specify requirements for validation and routine control of sterilization processes require when it is necessary to supply a sterile medical device, that adventitious microbiological contamination of a medical device prior to sterilization be minimized. Even so, medical devices produced under standard manufacturing conditions, can, prior to sterilization, have microorganisms on them, albeit in low numbers. Such medical devices are non-sterile. The purpose of sterilization is to inactivate the microbiological contaminants and thereby transform the non-sterile medical devices into sterile ones.

The kinetics of inactivation of a pure culture of microorganisms by physical and/or chemical agents used to sterilize medical devices generally can best be described by an exponential relationship between the number of microorganisms surviving and the extent of treatment with the sterilizing agent; inevitably this means that there is always a finite probability that a microorganism can survive regardless of the extent of treatment applied. For a given treatment, the probability of survival is determined by the number and resistance of microorganisms and by the environment in which the organisms exist during treatment. It follows that the sterility of any one product in a population subjected to sterilization processing cannot be ensured and the expression of sterility of a processed population is defined in terms of the probability of there being a viable microorganism present on a product item.

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

This document describes requirements that, if met, will provide a moist heat sterilization process intended to sterilize medical devices, which has appropriate microbicidal activity. Furthermore, conformance with the requirements, ensures this activity is both reliable and reproducible so that predictions can be made, with reasonable confidence, that there is a low level of probability of there being a viable microorganism present on product after every sterilization process is complete. Specification of this probability is a matter for regulatory authorities and can vary from country to country (see, for example, EN 556-1 and ANSI/AAMI ST67).

Generic requirements of the quality management system for design and development, production, installation and servicing are given in ISO 9001 and particular requirements for quality management systems for medical device production are given in ISO 13485. The standards for quality management systems recognise that, for certain processes used in manufacturing, the effectiveness of the process cannot be fully verified by subsequent inspection and testing of the product. Sterilization is an example of such a process. For this reason, sterilization processes are validated for use, the performance of the sterilization process is monitored routinely, and the equipment is maintained.

Exposure to a properly validated, accurately controlled, monitored and recorded sterilization process is not the only factor associated with the provision of reliable assurance that the product is sterile and, in this regard, suitable for its intended use. Attention is therefore given to a number of factors including:

a) the microbiological status of either incoming raw materials or components, or both;

b) the validation and routine control of any cleaning and disinfection procedures used on the product;

c) the control of the environment in which the product is manufactured, assembled and packaged;

d) the control of equipment and processes;

e) the control of personnel and their hygiene;

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f) the manner and materials in which the product is packaged;

g) the conditions under which product is stored.

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

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

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

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

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

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

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

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

1 Scope

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

1.1 Inclusions

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

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

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

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

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

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

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

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

1.2 Exclusions

1.2.1 This document does not specify requirements for development, validation, and routine control of a process for inactivating the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeldt-Jakob disease.

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

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

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

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

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

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

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

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

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

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

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 11607-2, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

ISO 11737-1, *Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products*

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

3 Terms and definitions

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

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

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

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

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

[SOURCE: ISO 11139:2018, 3.9]

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

[SOURCE: ISO 11139:2018, 3.18]

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

[SOURCE: ISO 11139:2018, 3.23]

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

[SOURCE: ISO 11139:2018, 3.29]

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

[SOURCE: ISO 11139:2018, 3.31]

3.6
chamber
part of equipment in which a load is processed

[SOURCE: ISO 11139:2018, 3.36]

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

[SOURCE: ISO 11139:2018, 3.43]

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

[SOURCE: ISO 11139:2018, 3.58]

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

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

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

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

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

3.11
correction
action to eliminate a detected nonconformity

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

[SOURCE: ISO 11139:2018, 3.64]

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

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

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

[SOURCE: ISO 11139:2018, 3.65]

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

[SOURCE: ISO 11139:2018, 3.72]

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

[SOURCE: ISO 11139:2018, 3.74]

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

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

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

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

3.16
development
act of elaborating a specification

[SOURCE: ISO 11139:2018, 3.79]

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

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

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

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

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

[SOURCE: ISO 11139:2018, 3.106]

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3.19
establish
determine by theoretical evaluation and confirm by experimentation

[SOURCE: ISO 11139:2018, 3.107]

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

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

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

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

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

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

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

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

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

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

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

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

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

[SOURCE: ISO 11139:2018, 3.116]

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

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

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

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

[SOURCE: ISO 11139:2018, 3.132]

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

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

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

[SOURCE: ISO 11139:2018, 3.220.2]

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

[SOURCE: ISO 11139:2018, 3.155]

3.31
load configuration
distribution and orientation of a load

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

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

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

[SOURCE: ISO 11139:2018, 3.165]

3.33
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, or software, material, or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

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

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

— investigation, replacement, modification, or support of the anatomy, or of a physiological process;

— supporting or sustaining life;

— control of conception;

— disinfection of medical devices;

— providing information by means of in vitro examination of specimens derived from the human body;

and does not achieve its primary intended action by pharmacological, immunological, or metabolic means, but which may be assisted in its intended function by such means

Note 1 to entry: Products which may be considered to be medical devices in some jurisdictions, but not in others include:

— items specifically intended for cleaning or sterilization of medical devices;

— pouches, reel goods, sterilization wrap, and reusable containers for packaging of medical devices for sterilization;

— disinfection substances;

— aids for persons with disabilities;

— devices incorporating animal and/or human tissues;

— devices for in vitro fertilization or assisted reproduction technologies.

[SOURCE: ISO 11139:2018 and Amd 1:2024, 3.166]

3.34
microorganism
entity of microscopic size, encompassing bacteria, fungi, protozoa and viruses

[SOURCE: ISO 11139:2018, 3.176]

3.35
moist heat
thermal energy in the presence of moisture used as the sterilizing agent to achieve the specified requirements for sterility

3.36
non-condensable gas
NCG
air and/or other gas which will not liquefy under the conditions of a saturated steam sterilization process

[SOURCE: ISO 11139:2018, 3.183, modified — Added “sterilization” and abbreviation NCG.]

3.37
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO 11139:2018, 3.220.3]

3.38
operating cycle
complete set of stages of a process that is carried out, in a specified sequence

Note 1 to entry: Loading and unloading are not part of the operating cycle.

[SOURCE: ISO 11139:2018, 3.188]

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3.39
overkill approach
method of defining a sterilization process that achieves a maximal sterility assurance level (SAL) for product substantially less than 10^{-6}

[SOURCE: ISO 11139:2018, 3.190]

3.40
packaging system
combination of a sterile barrier system and protective packaging

[SOURCE: ISO 11139:2018, 3.192]

3.41
performance qualification
PQ
process of establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements

[SOURCE: ISO 11139:2018, 3.220.4]

3.42
plateau period
equilibration time plus the holding time

[SOURCE: ISO 11139:2018, 3.195]

3.43
porous
<sterilizer load> permeable to water, air or other fluids

[SOURCE: ISO 11139:2018, 3.197]

3.44
preconditioning
treatment of product, prior to the operating cycle, to attain specified values for temperature, relative humidity, and/or other process variables

[SOURCE: ISO 11139:2018, 3.200]

3.45
preventive action
action to eliminate the cause of a potential nonconformity or other potential undesirable situation

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

Note 2 to entry: Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence.

[SOURCE: ISO 11139:2018, 3.203]

3.46
process challenge device
PCD
item providing a defined resistance to a cleaning, disinfection, or sterilization process and used to assess performance of the process

Note 1 to entry: For the purpose of this document, the item can be product, simulated product or other reference device. The item can contain a physical indicator, biological indicator or chemical indicator.

[SOURCE: ISO 11139:2018, 3.205, modified — Note 1 to entry has been added.]

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3.47
process parameter
specified value for a process variable

Note 1 to entry: The specification for a process includes the process parameters and their tolerances.

[SOURCE: ISO 11139:2018, 3.211]

3.48
process variable
chemical or physical attribute within a cleaning, disinfection, packaging, or sterilization process, changes in which can alter its effectiveness

Note 1 to entry: For the purposes of this document, process variables are conditions within a sterilization process, changes in which alter microbicidal effectiveness, i.e. exposure time and temperature in the presence of moist heat.

[SOURCE: ISO 11139:2018, 3.213, modified — EXAMPLES have been deleted and Note 1 to entry has been added.]

3.49
product
tangible result of a process

EXAMPLE Raw material(s), intermediates, sub-assembly(ies), healthcare product(s).

[SOURCE: ISO 11139:2018, 3.217]

3.50
product family
group or subgroup of product characterized by similar attributes determined to be equivalent for evaluation and processing purposes

Note 1 to entry: See Annex G.

[SOURCE: ISO 11139:2018, 3.218, modified — Note 1 to entry has been added.]

3.51
reference load
specified load created to represent combinations of items that provide defined challenge(s) to a process

[SOURCE: ISO 11139:2018, 3.226]

3.52
reference measurement point
location of the sensor controlling the operating cycle

[SOURCE: ISO 11139:2018, 3.227]

3.53
reference microorganism
microbial strain obtained from a recognized culture collection

[SOURCE: ISO 11139:2018, 3.228]

3.54
reproducibility
condition of measurement, out of a set of conditions that includes different locations, processors, measuring systems, and replicate measurements on the same or similar objects

Note 1 to entry: The different measuring systems may use different measurement procedures.

Note 2 to entry: A specification should give the conditions changed and unchanged to the extent practical.

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3.55
requalification
repetition of part or all of validation for the purpose of confirming the continued acceptability of a specified process

[SOURCE: ISO 11139:2018, 3.220.5]

3.56
saturated steam
water vapour in a state of equilibrium between its liquid and gas phases

[SOURCE: ISO 11139:2018, 3.241]

3.57
saturated steam sterilization
validated process which involves the direct contact of saturated steam as the sterilizing agent on product surfaces to achieve the specified requirements for sterility

[SOURCE: ISO 11139:2018 and Amd 1:2024, 3.368]

3.58
services
supplies from an external source, needed for the function of equipment

EXAMPLE Steam, electricity, water, compressed air, drainage.

[SOURCE: ISO 11139:2018, 3.252, modified — EXAMPLES have been added.]

3.59
specify
stipulate in detail within an approved document

[SOURCE: ISO 11139:2018, 3.259]

3.60
spore log reduction
SLR
negative exponent to the base 10 describing the decrease in the number of spores

Note 1 to entry: It is expressed as a logarithm.

[SOURCE: ISO 11139:2018, 3.260

3.61
sterile
free from viable microorganisms

[SOURCE: ISO 11139:2018, 3.271]

3.62
sterile barrier system
SBS
minimum package that minimizes the risk of ingress of microorganisms and allows aseptic presentation of the sterile contents at the point of use

[SOURCE: ISO 11139:2018, 3.272]

3.63
sterility
state of being free from viable microorganisms

Note 1 to entry: In practice, no such absolute statement regarding the absence of microorganisms can be proven.

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[SOURCE: ISO 11139:2018, 3.274]

3.64
sterility assurance level
SAL
probability of a single viable microorganism occurring on an item after sterilization

Note 1 to entry: It is expressed as the negative exponent to the base 10.

Note 2 to entry: The term SAL takes a quantitative value, generally 10^{-6} or 10^{-3}. When applying this quantitative value to assurance of sterility, an SAL of, for example, 10^{-6} has a lower value but provides a greater assurance of sterility than an SAL of 10^{-3}.

[SOURCE: ISO 11139:2018, 3.275, modified — Note 2 to entry has been added.]

3.65
sterilization
validated process used to render product free from viable microorganisms

Note 1 to entry: In a sterilization process, the nature of microbial inactivation is exponential and thus, the survival of a microorganism on an individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero.

[SOURCE: ISO 11139:2018, 3.277]

3.66
sterilization cycle
predetermined sequence of stages performed in a sterilizer to achieve product free of viable microorganisms

[SOURCE: ISO 11139:2018, 3.279]

3.67
sterilization process
series of actions or operations needed to achieve the specified requirements for sterility

Note 1 to entry: This series of actions includes pre-treatment of product (if necessary), exposure, under specified conditions, to the sterilizing agent and any necessary post treatment. The sterilization process does not include any cleaning, disinfection or packaging operations that precede sterilization.

[SOURCE: ISO 11139:2018, 3.284]

3.68
sterilization temperature
minimum temperature on which the evaluation of the sterilization efficacy is based

[SOURCE: ISO 11139:2018, 3.286]

3.69
sterilizing agent
physical or chemical entity, or combination of entities having sufficient microbicidal activity to achieve sterility under defined conditions

[SOURCE: ISO 11139:2018, 3.288]

3.70
temperature band
<moist heat sterilization> temperature range, the minimum of which is the sterilization temperature

Note 1 to entry: The upper limit of the temperature band can be specified in standards and/or can take into account product compatibility.

[SOURCE: ISO 11139:2018, 3.293.1, modified — Note 1 to entry added.]

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3.71
test for sterility
technical operation defined in a pharmacopoeia performed on product following an aseptic process or exposure to a sterilization process

[SOURCE: ISO 11139:2018, 3.298]

3.72
test of sterility
technical operation performed as part of development, validation or requalification to determine the presence or absence of viable microorganisms on product or portions thereof

[SOURCE: ISO 11139:2018, 3.299]

3.73
validation
confirmation process, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled

Note 1 to entry: The objective evidence needed for a validation is the result of a test or other form of determination such as performing alternative calculations or reviewing documents.

Note 2 to entry: The word "validated" is used to designate the corresponding status.

Note 3 to entry: The use conditions for validation can be real or simulated.

[SOURCE: ISO 11139:2018, 3.313]

3.74
verification
confirmation, through provision of objective evidence, that specified requirements have been fulfilled

Note 1 to entry: The objective evidence needed for a verification can be the result of an inspection or of other forms of determination such as performing alternative calculations, monitoring or reviewing documents.

Note 2 to entry: The word "verified" is used to designate a corresponding status.

[SOURCE: ISO 11139:2018, 3.314]

3.75
works test
series of technical operations performed prior to delivery to demonstrate compliance of a piece of equipment with its specification

[SOURCE: ISO 11139:2018, 3.325]

3.76
***z* value**
change in temperature of a thermal sterilization or disinfection process that produces a tenfold change in *D* value

Note 1 to entry: It is expressed in degrees Celsius (°C).

[SOURCE: ISO 11139:2018, 3.326]

4 General

4.1 The development, validation and routine control of a sterilization process is a critical element in product realization of a health care product. To ensure the consistent implementation of the requirements specified in this document, the necessary processes shall be established, implemented and maintained.

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Processes of particular importance in relation to the development, validation and routine control of a sterilization process include but are not limited to:

— control of documentation, including records;

— assignment of management responsibility;

— provision of adequate resources, including competent human resources and infrastructure;

— control of product provided by external parties;

— identification and traceability of product throughout the process;

— control of non-conforming product.

NOTE ISO 13485 covers all stages of the lifecycle of medical devices in the context of quality management systems for regulatory purposes. National and/or regional regulatory requirements for the provision of health care products can require the implementation of a full quality management system and the assessment of that system by a recognized conformity assessment body.

4.2 A process shall be specified for the calibration of all equipment, including instrumentation for test purposes, used in meeting the requirements of this document.

NOTE ISO 10012 specifies requirements for a system of calibration and ISO 13485 includes requirements for the control of monitoring and measuring equipment.

5 Sterilizing agent characterization

5.1 Sterilizing agent

5.1.1 The purpose of this activity is to:

a) define the sterilizing agent;

b) demonstrate its microbicidal effectiveness;

c) identify the factors that influence microbicidal effectiveness;

d) assess the effects that exposure to the sterilizing agent has on materials;

e) identify requirements for safety of personnel and protection of the environment.

This activity may be undertaken in a test or prototype system. Where this occurs, the final equipment specification shall be relatable to the results of experimental studies undertaken in the test or prototype equipment.

5.1.2 For the purposes of this document, the sterilizing agent shall be moist heat. A specification for the sterilizing agent shall be documented.

NOTE See definitions of moist heat (3.35), saturated steam sterilization (3.57) and contained product sterilization (3.10) with regard to the sterilizing agent.

5.1.3 Limiting values for any contaminants contained within the sterilizing agent shall be included in the sterilizing agent specification. Contaminants contained within the sterilizing agent shall not impair the efficacy of the sterilization process or the safety of the product for its intended use.

NOTE See A.5.4 and C.10 for guidance on contaminants which can be considered.

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5.2 Microbicidal effectiveness

If moist heat is used outside of the range of conditions that are widely recognised, then the microbicidal effectiveness shall be established and documented.

NOTE The microbial inactivation achieved by moist heat and its use in sterilization processes has been comprehensively documented and is available in the published literature (see [43] and [61]). If moist heat is used outside of the range of conditions that are widely recognised then its ability to achieve microbial inactivation can be established using the approach described in Annex B (e.g. bioburden or bioburden/biological indicator or overkill approach) or in ISO 14937:2009, 5.3.

5.3 Effects on materials

The effect of exposure to moist heat on the physical and/or chemical properties of materials and on their biological safety shall be assessed.

NOTE The effects of moist heat on a wide variety of materials used to manufacture medical devices have been comprehensively documented (see [28]) and such documentation is of value to those designing and developing medical devices that are to be sterilized by moist heat. Studies of the effects of a moist heat process on a product are implemented during the product design stage. See Clauses 6, 7 and 8. Table A.1 outlines the roles and responsibilities for each normative section and Annexes F and H give guidance for health care facilities and industrial settings.

5.4 Environmental consideration

Moist heat is not normally considered as having a significant environmental effect. However, the potential impact on the environment of the operation of the sterilization process shall be assessed and any measures necessary to protect the environment shall be identified. This assessment, including potential impact (if any) and measures for control (if identified), shall be documented.

6 Process and equipment characterization

6.1 General

6.1.1 The purpose of this activity is to specify the entire sterilization process and the equipment necessary to reproducibly deliver the sterilization process.

6.2 Process characterization

6.2.1 The process variables for moist heat sterilization shall be time and temperature in the presence of moist heat sufficient to ensure microbial inactivation. All sterilization processes shall be specified.

NOTE Pressure is not a process variable in a moist heat sterilization process since it has no bearing on microbial inactivation. Pressure is a cycle variable which is employed to control the operating cycle.

6.2.2 Process characterization, at a minimum, shall include:

a) identifying the type of moist heat sterilization cycle to be used and documenting the process variables and the process parameters and their tolerances;

NOTE 1 See the Scope, 6.3 and 6.4 for types of moist heat sterilization cycle and Annex D for examples of moist heat sterilization cycles.

b) identifying the cycle variables for the selected moist heat sterilization cycle and documenting the cycle variables, cycle parameters and their tolerances;

NOTE 2 The data developed in product definition (see Clause 7) can impact the characterization of the sterilization process.

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NOTE 3 This clause considers all cycle variables and their cycle parameters, 6.2.2 d) considers specific cycle variables and cycle parameters used to ensure efficacy, safety and reproducibility of the sterilization cycle.

c) description of each operating cycle, including specified process parameters and their tolerances;

d) the specific cycle variables and their cycle parameters used to ensure process efficacy, safety and reproducibility including their tolerances (see A.6.1);

e) the process variables and cycle variables that are measured and used to verify that the sterilization cycle will be delivered;

f) the products, including their SBS and packaging system, product families and representative load configurations that can be sterilized;

NOTE 4 Information on the product characteristics and product families can be found in Annex G.

g) any restrictions on the load, such as size, mass and configuration, as applicable;

h) requirements for the preconditioning of the load prior to sterilization, if such preconditioning is necessary to ensure the efficacy of the sterilization process (e.g. equilibration of the load at a specified temperature and humidity);

i) requirements for the post sterilization cycle treatment, if such treatment is included in the sterilization process specification (e.g. allowing the load to cool in a controlled environment);

j) the location of the reference measuring point;

k) the minimum frequency of use of process monitoring tools, e.g. physical sensors, biological indicators, chemical indicators, process challenge devices (PCDs);

l) the maximum quantity of each contaminant that can be present in any liquid, air, gas or steam admitted to the chamber if the contaminant can adversely affect the product, its SBS or packaging system or the efficacy of the sterilization cycle, e.g. the maximum amount of water that can be suspended in the steam entering the chamber shall be specified if that can cause an adverse effect on the product or its SBS or packaging system.

NOTE 5 Properly engineered steam traps and separators can be used to remove water from the steam prior to injection into the chamber.

NOTE 6 The level of risk to the process and load associated with the presence of contaminants can depend upon the point in the process when maximum quantities occur.

6.2.3 The acceptable SAL for the process shall be specified.

NOTE 1 The specification for SAL can be based on the determination of the population and resistance of any bioburden which can be on the product at the start of the sterilization process.

NOTE 2 If a 10^{-6} SAL is specified for a product and an overkill approach with recognised time and temperature combinations for moist heat sterilization (see Table A.2) is used to achieve the SAL, then the maximum SAL for the product will be substantially less than 10^{-6}.

NOTE 3 See Annex B for guidance on the establishment and evaluation of a sterilization process primarily based on microbiological inactivation methods.

6.3 Saturated steam sterilization processes

In addition to the requirements in 6.1 and 6.2, the specification for a saturated steam sterilization process shall include:

a) the holding time and the minimum and maximum temperatures (and their locations) measured during this time for the reference load(s) in the chamber, including fixed chamber parts and specific loading accessories (e.g. trolleys, frames) intended for routine operation.

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b) the maximum difference between the temperature measured at the reference measuring point and the temperature determined from the measured chamber pressure using steam table values [see Annex E, Table E.1 and Formula (E.1)] during the holding time;

NOTE 1 The comparison between the measured temperature and that calculated from measured chamber pressure according to steam tables cannot be regarded as a substitute for the monitoring devices or procedures specified in 6.3 c), d) or e).

NOTE 2 See A.6.1.2.5 and Annex E for guidance on assigning a limit to the difference.

c) a description of and justified procedure for the steam penetration test used to verify that the level of residual NCG does not prevent the presence of the validated level of moist heat on the surfaces to be sterilized, for the product family(ies) known to restrict the penetration of steam by virtue of their material composition, mass, design or load configuration;

NOTE 3 The presence of residual NCG in the chamber can arise from:

— NCGs carried into the chamber in the steam supply;

— air leakage into the chamber during periods of vacuum;

— NCG remaining as a result of an inadequate air removal stage of the operating cycle.

d) a description of:

1) the PCD suitable for the sterilization process and not fitted to the sterilizer to demonstrate a specific characteristic of the sterilization process (e.g. air removal and steam penetration); or

2) for dynamic air removal cycles, the monitoring system fitted to the sterilizer for the detection of NCGs (e.g. an air detector), including its sensor location(s), and how to interpret its results;

NOTE 4 The specification for a saturated steam sterilization process normally includes a description of a PCD not fitted to the sterilizer [6.3 d) 1)] or a monitoring system fitted to the sterilizer [6.3 d) 2)] both used for the detection of NCG during each operating cycle. Specified, established and validated alternative methods for the detection of NCGs, particularly in an industrial setting where sterilization processes and load configurations are specified in detail, are also possible (but see E.2.3).

e) the reference load(s) to be used to confirm or judge the effectiveness of the sterilization process for an identified load [see 6.2.2 f)];

f) dryness of the reference load determined by a change in mass or by presence of perceptible moisture.

6.4 Contained product sterilization processes

In addition to the requirements in 6.1 and 6.2, the sterilization process specification shall include the following information for the load configuration justified to be the most difficult to sterilize:

a) details of the product(s) and its container(s) or, if applicable, reference product(s);

b) the size of the load and its location, orientation and support system within the chamber;

c) the temperature profiles and the locations from which they were determined for the period of the sterilization cycle for which lethality is claimed, and which shall be measured in the reference load and in the free space surrounding the load;

d) the maximum and minimum temperature and rates of change for the period of the sterilization cycle for which lethality is claimed;

e) the method for establishing the location where the maximum and minimum temperature can be measured.

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6.5 Equipment

6.5.1 Equipment used to deliver the sterilization process shall be specified. The specification shall include:

a) unique identification (e.g. manufacturer, model and serial number) and physical description of the equipment, together with any necessary ancillary items;

b) the materials of construction of any part of the equipment and any ancillary items that are used to contain and transport steam or any other gas or liquid into the chamber;

c) characteristics of filters (if used);

d) a record of cycle parameters that is independent from the process control (see ISO/TS 22421:2021, Annex B);

e) for each measuring chain used for control and recording;

   1) a description of the measuring chain;

   2) the characteristics and location of the sensor;

   3) the measurement range, resolution and accuracy.

f) where applicable, the rates of pressure change capability during each stage of the cycle;

   NOTE 1 The specification for the rates of pressure change during each stage of the operating cycle can be important as this can influence the integrity of a medical device and an SBS, or influence diffusive steam penetration into complex devices.

g) the fault(s) and failures recognised by the monitoring system, together with any visual, audible or recorded warnings or indications;

h) the safety features;

   NOTE 2 The specification can include safety features for the protection of personnel and the environment.

   NOTE 3 In some jurisdictions specific safety features can be required.

i) information and test results which can allow the user to establish the conformity of the equipment to local, regional, or national regulations applicable for installation and operation of the equipment including those for emissions into the environment;

   NOTE 4 Citation of appropriate standards can be included.

j) a description and acceptance criteria for the test to be used to determine the level of air leakage into the chamber if vacuum is used during the operating cycle;

k) a description of the device (e.g. air detector), if fitted, including its settings used to detect non-condensable gas that can be present in steam supplied to the chamber or remain in the chamber after the air removal stage of the sterilization cycle.

6.5.2 The operating procedures for the equipment and ancillary items shall be specified. The specification shall include:

a) the means by which allowed changes to the automatic controller programmes can be made;

b) step-by-step operating instructions;

c) action to be taken in case of a fault or failure indication;

d) the means by which an error in the results of a measurement for control, indication and/or recording can be identified, e.g. if a sensor becomes damaged an open circuit error will be reported;

e) the contact for technical support if applicable.

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6.5.3 The installation requirements for the equipment shall be specified. The specification shall include:

a) the location, space and the environment in which the equipment is to be installed;

b) installation instructions;

c) any restriction or precautions to be considered for intended operation of the equipment (e.g. required space for load carriers, maintenance access, ventilation);

d) details of each service necessary for the correct function of the equipment, including (if applicable);

   1) means of disconnecting services to the sterilizer;

   2) minimum and maximum pressure of services including, e.g. compressed air, water, steam;

   3) minimum and maximum temperature of services including, e.g. water;

   4) minimum and maximum flow rate for each service;

   5) any filtration requirements for each service, e.g. water, compressed air, steam;

   6) electrical requirements, e.g. phase requirements, minimum and maximum voltage and maximum current (amperes), expressed as phase to neutral or phase to phase, for the electrical supply;

   7) maximum level of NCG and liquid water in steam;

   8) maximum quantity of each contaminant which can be found in fluids supplied to the sterilizer, e.g. compressed air, water, steam.

e) the load bearing structures that are to support the principal heavy components of the equipment;

f) the materials of construction for the parts that transport steam, gas, air and water into the space in which the sterilizer is to be installed and into the sterilizer.

6.5.4 The load support system, if used, in the chamber shall be specified. This specification shall ensure that the system shall not inhibit the attainment of sterilizing conditions throughout the load or cause damage to product including its SBS or packaging system.

6.5.5 The sterilizer specification shall provide a description of how a failure in a control function does not lead to a failure in recording of process parameters resulting in an ineffective process appearing effective.

NOTE This can be achieved by monitoring systems which evaluate and compare data from process control, independent cycle recording, equipment specifications and hardware status indications for fault detection, indication and initiation of consecutive safety measures, as applicable.

6.5.6 The software used to control or monitor the process shall be prepared in accordance with a documented system that provides documented evidence that the software meets its design intention.

7 Product definition

7.1 The purpose of this activity is to define the product to be sterilized including the microbiological quality of the product before sterilization, and the manner in which the product is packaged and presented for sterilization.

7.2 Product and, as applicable, product family(ies) to be sterilized shall be specified.

NOTE For health care facilities, see F.7.2.

7.3 The criteria for defining and assigning a product to a product family shall be specified (see Annex G for guidance).

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7.4 The SBS or packaging system that is assigned to a product family shall be specified and conform to ISO 11607-1 and ISO 11607-2.

7.5 A system shall be defined, documented and maintained to ensure that the condition of the product presented for sterilization is controlled and does not compromise the effectiveness of the sterilization process, e.g. preconditioning the product in a controlled temperature and humidity environment. Also see A.7.5.

NOTE Microbiological, organic and inorganic contamination can be considered when defining the system. See C.10.2 and Annexes F and H for further guidance.

7.6 If biological indicators are used for evaluation of a contained product sterilization process, evidence of any effect the composition of the contained product can have on the measured resistance (*D* value) of a biological indicator used to evaluate the sterilization process shall be established.

7.7 A dedicated PCD shall be specified. Alternatively, a reference device identified as an appropriate challenge and its SBS or packaging system, shall be specified. For example, product that can be used to represent a specific characteristic(s) of the product.

7.8 The limiting value(s) for each process and cycle variable to which the product and its SBS or packaging system (if used) can be exposed, shall be specified.

NOTE 1 Exceeding the limiting values can have an adverse effect on either the performance of the product or its packaging, or both.

NOTE 2 If an SBS is not used (e.g. sterilization of a load in a dental office where the items are used immediately after processing) sterility will not be maintained once the sterilizer door is opened.

7.9 If the level of moisture present in the product and/or its packaging system prior to sterilization can affect the efficacy of the sterilization process, the limiting value(s) shall be specified.

7.10 The safety, performance and stability of a product in its SBS or packaging system, and where applicable, product potency, after exposure to the sterilization process, shall continue to meet documented specifications.

7.11 If the product is a reusable medical device, the instructions for use shall be consulted for any limitations relating to end-of-life indicators or the number of processing cycles which they can be subjected to (see ISO 17664-1).

7.12 If the integrity of the product can be affected by a contaminant(s) or process residue (e.g. moisture) remaining on the product or packaging after sterilization, the contaminant or process residue shall be specified along with the maximum acceptable limit allowed.

7.13 An operating procedure shall be specified to ensure that the condition of the product and, if used, its SBS or packaging system presented for sterilization will not compromise the effectiveness of the sterilization process. This procedure shall include at least the following elements:

a) cleaning and where applicable disinfection of re-useable product by a validated process;

   NOTE When processing reusable product, cleaning and disinfection will also reduce the risk of infectious hazards to operators.

b) cleaning and, where applicable, disinfection of re-useable SBSs where used, using a validated process;

c) cleaning of single use product during manufacturing, where applicable, by a validated process;

d) any further preconditioning prior to the sterilization cycle identified as necessary for specific product;

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e) characteristics and limitations of load configurations;

f) if required, verification of the integrity of the SBS before exposure to the sterilization process;

g) an estimation of bioburden in accordance with ISO 11737-1 when a sterilization process is established using the bioburden approach.

7.14 The integrity of the SBS or packaging system after exposure to the sterilization process shall be ensured.

NOTE The integrity of the SBS can be ensured by using either a validation approach or a post process test approach.

8 Process definition

8.1 The purpose of this activity is to define the sterilization process by providing a detailed specification for the sterilization cycle to be applied to defined product without compromising the safety, quality and performance of that product.

8.2 The sterilization process shall be specified, including process variables and process parameters and their tolerances. During the establishment of this sterilization process, process parameters and appropriate cycle parameters shall be measured and used, to confirm reproducibility.

8.2.1 If a saturated steam sterilization cycle is to be used, during the holding time the maximum difference between the temperature measured at the reference measuring point and the temperature measured at the surfaces in or on the product to be sterilized shall be specified.

EXAMPLE A temperature difference of 2 K can be considered acceptable. Alternatively, maximum temperature difference is determined based on risk assessment for product attribute.

8.2.2 If an existing validated sterilization process, including the sterilization cycle, is intended to be used to sterilize defined product, process and equipment documentation shall be reviewed to ensure the identified variables in 6.2, 6.3 and 6.4 have been included in the process specification for routine production.

8.3 The sterilization process shall be established from at least one of the following:

a) data supplied in the instructions for use accompanying the medical device (see ISO 17664-1), the sterilizer and, if used, the SBS;

NOTE This is the common approach for process definition in health care facilities.

b) similarity with a product that is already assigned to a product family (see Annex G);

c) development of an operating cycle that will deliver the specified SAL.

8.4 The SAL to be achieved by the sterilization process on and/or within a product shall be specified and shall meet a pre-defined requirement. National specifications for the SAL can apply.

NOTE The SAL specified can be a range with the maximum value representing the maximal SAL required to be achieved by the sterilization process.

8.4.1 The SAL attained on and/or within the product during the sterilization process shall be by means of one of the following;

a) established by knowledge of the bioburden and its resistance (see B.2 and B.3);

b) determined by an “overkill” method (see B.4);

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c) defined by demonstrating that during the holding time all parts of the product that are intended to be sterile are exposed to process parameters selected from an official national or regional pharmacopoeia;

NOTE This is a common approach in a health care facility.

8.4.2 The SAL attained on and/or within the product during the sterilization process shall be deemed to be equal to or exceed the requirements specified in 8.4.1 c) provided that:

a) the product is assigned to a relevant product family;

b) a relevant sterilization process is specified;

c) the equilibration time does not exceed the maximum for products assigned to the same product family.

8.5 The sterilization process shall not expose the product and its SBS or packaging system (if used) beyond the limiting process and cycle parameters or contaminants.

8.6 If a saturated steam sterilization process is to be used, the level of residual air and NCG at the commencement of the holding time shall not prevent the attainment of moist heat on all surfaces of the product intended to be sterilized, including the surfaces in cavities, lumens and tubing.

8.7 If biological indicators are used to establish the sterilization process:

a) they shall conform with ISO 11138-1 and ISO 11138-3;

b) the microorganism, population, resistance and method of presentation shall be identified and shall take into account the expected or established product bioburden;

c) the location of biological indicators within the sterilization load and acceptance criteria post-exposure to the sterilization process shall be specified.

8.7.1 The selected biological indicator or inoculated product may have populations and resistance values lower than the minimum values specified in ISO 11138-3:2017, Clause 9 in order to obtain a specified BI microbiological challenge, but they shall otherwise meet the requirements of ISO 11138-1 and ISO 11138-3 (also see Annex B).

NOTE The BI microbiological challenge is calculated as the product of the logarithm to the base ten of the initial population of microorganisms and the D value (BI microbiological challenge = $\log N_0 \times D_{121}$-value ; see F_{BIO}).

8.7.2 The method of presentation can include inoculated product or the placement of inoculated carrier(s) within the product.

NOTE 1 Conformance of the biological indicator to ISO 11138-1 and ISO 11138-3 does not apply to the inoculation of the PCD/reference device.

NOTE 2 A test for the ability to sterilize defined medical devices includes test specifications is given in Clauses 6 and 7.

8.8 For contained product, the effect of the product and its packaging system on the resistance of the test microorganism when exposed to the proposed sterilization process shall be known and considered for evaluation.

NOTE For contained products, the nature of the product (e.g. 5 % dextrose solution) and the packaging (e.g. a flexible intravenous infusion bag) can alter the resistance of the test microorganism.

8.9 If chemical indicators are used as part of the establishment of the sterilization process;

a) they shall conform to the relevant part(s) of the ISO 11140 series;

b) they shall be appropriate for their intended purpose;

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c) the location of chemical indicators within the load shall be specified;

d) the acceptance criteria shall be specified;

e) they shall not adversely affect the medical device by reaction, contamination and/or transfer before, during or after the sterilization process.

8.10 If a PCD is to be used to assess the efficacy of the specified characteristics of a sterilization process, the validity of the PCD, test methodology(ies) and acceptance criteria shall be established and documented.

8.11 For a sterilization process established by microbiological methods (see B.2, B.3 and B.4), the following apply:

a) bioburden determination shall be performed in accordance with ISO 11737-1 if the bioburden (B.2) or bioburden / biological indicator (B.3) approaches are used;

b) when the bioburden method (B.2) is followed, tests of sterility shall be performed in accordance with ISO 11737-2;

c) product used in establishing the process shall be representative of that to be processed routinely;

d) equipment used shall be capable of reproducibly delivering a combination of process parameters with less lethality than the routine sterilization process (unless the full cycle overkill approach described in B.4.6 is used), such that the level of inactivation of microorganisms results in a population that allows extrapolation with regard to the total result.

NOTE These approaches are more commonly used in an industrial setting.

8.12 If, after exposure to the sterilization process, treatment of the product and its packaging is required in order to maintain sterility, this treatment shall be specified.

8.13 Calibration, equipment maintenance, performance test(s) and acceptance criteria (where applicable) intended to ensure that the sterilization process remains reproducible shall be specified.

9 Validation

9.1 General

9.1.1 The purpose of this activity, is to demonstrate that the sterilization process established in the process definition can be delivered effectively and reproducibly to the load. Validation consists of several identified stages: installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ). IQ is undertaken to demonstrate that the sterilization equipment and any ancillary items have been supplied and installed in accordance with their specification. OQ is carried out either with unloaded equipment or using appropriate test materials to demonstrate the capability of the equipment to deliver the sterilization process that has been defined. PQ is the stage of validation that uses product to demonstrate that the equipment consistently operates in accordance with predetermined criteria and the process yields product that is sterile and meets the specified requirements.

9.1.2 Each stage of validation shall be carried out in accordance with a documented procedure.

NOTE 1 Carrying out all the elements of validation (IQ, OQ, PQ) cannot be regarded as a substitute for routine monitoring as specified in Clause 10.

NOTE 2 For further information and examples see C.14, F.9.1.2, F.9.2, and H.9.1.2.

9.1.3 It shall be verified that each item of test equipment used to perform validation conforms with its specification.

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9.1.4 Any modifications to product, packaging, equipment, or sterilization process carried out during validation shall be recorded and justified, and the specification(s) changed accordingly (see Clause 12).

NOTE Modifications can invalidate regulatory conformity status for sterilizer equipment in some jurisdictions.

9.1.5 The measuring chain for each test instrument used for validation shall have:

a) documented evidence of calibration, traceable to a national standard and equipment maintenance in accordance with the instructions for use;

b) a calibration status verified according to the technical and applicable management requirements carried out at a value(s) used to control the sterilization process and judge the results of the test in which the measuring chain is used.

NOTE National calibration reference standards are often mutually recognized and traceable to international reference standards with recognized fixed points.

9.1.6 The correlation between readings from sterilizer instruments and independent test instruments for validation at the similar sensor locations shall be confirmed.

9.1.7 If the equipment could have been affected by packaging, transportation or installation activities after certified final inspection tests at the manufacturing site, conformance with related specifications shall be verified during validation (IQ and OQ).

9.1.8 During IQ, OQ or PQ, as applicable, it shall be verified that fault recognition and operational safety systems function and conform with their performance specifications. Verification can be carried out as far as possible without compromising the safety, functional integrity and certified conformity of the sterilizer.

NOTE Suitable procedures for testing the fault recognition and operational safety systems can be available in the sterilizers technical documentation.

9.1.9 If an existing sterilizer with a validated sterilization process is to be used to process a new product, the IQ and OQ stages of the existing validation may be accepted, provided that changes have not been made to the equipment since the existing validation.

9.2 Installation qualification (IQ)

9.2.1 Installation qualification shall demonstrate that the equipment and ancillary items have been installed in accordance with their specification.

NOTE Additional regional, national and local regulations can also apply.

9.2.2 It shall be verified that the installation of the equipment, ancillary items and the supply of the services conform with their specifications.

9.3 Operational qualification (OQ)

9.3.1 Operational qualification shall demonstrate that the equipment will deliver the specified sterilization process(es).

9.3.2 The rationale for the number and locations of the temperature sensors used to demonstrate that requirements are met for temperature distribution in the chamber and, if used, the test load in place in the chamber shall be documented. The OQ may be performed with a test load.

NOTE If the guidance in Annex C is followed, this can include a test load.

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9.3.3 Prior to OQ, the calibration of all instrumentation (including any test instruments) used for monitoring, controlling, indicating or recording of the sterilization process shall be verified.

9.4 Performance qualification (PQ)

9.4.1 Performance qualification shall demonstrate that product has been exposed to the specified sterilization process, including the specified sterilizing agent, by the equipment to be used for routine sterilization.

9.4.2 Performance qualification shall verify that the conditions required to achieve the specified SAL have been met.

9.4.3 Rationale shall be documented for the number and locations of temperature sensors, biological indicators and/or chemical indicators used to demonstrate that requirements are met throughout the load.

9.4.4 Checks shall include and verify that:

a) the IQ and OQ were successful;

b) the SBS or packaging system is the same as, or is a greater challenge to that intended for routine production;

c) the load configuration conforms with 6.2.2 f) and g) and is considered to be representative or more challenging to the sterilization process than the routine load;

d) the test load, if used, represents product that will be routinely processed and that is assigned to a product family(ies) compatible with the one(s) assigned to the sterilization cycle or that represents the product families considered to be a greater challenge to the sterilization process;

e) the load configuration and any required preconditioning conforms with 6.2.2 f), g) and h) and 7.13;

f) if varying load configurations will be used, the extent to which the variation affects the sterilization process shall be evaluated to ensure that all product exposed to the sterilization process achieves the required SAL.

9.4.5 For each of the following, studies shall establish:

a) conformity to the sterilization process identified during process definition and the limiting process parameters of the process variables identified for the product, SBS or packaging system;

b) data as required for the condition of the product and SBS (as applicable) as presented to the sterilization process;

c) the temperature profile(s) on and throughout product located in representative positions in the load;

d) the temperatures measured during the plateau period;

e) the equilibration time;

f) the minimum and maximum temperatures during the holding time and their locations including:

— at the reference measurement point;

— on the surface of/ in the load;

— calculated from the measured chamber pressure according to steam table values, if applicable (see Annex E).

For saturated steam sterilization processes, national or regional requirements should be taken into consideration when defining the maximum permissible difference between the measured temperature

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and the temperature determined from measured chamber pressure according to steam tables. See Annex E and, for example, EN 285.

NOTE 1 If a difference between the measured temperature and the temperature determined from measured chamber pressure exists, this can indicate a process failure. If there is no difference between the measured temperature and the temperature determined from measured chamber pressure this cannot be regarded as an indication of an acceptable process. Other information is required to confirm process acceptability.

g) the holding time;

h) the response of chemical indicators according to their instructions for use, when used;

i) that the response of the chemical indicator or biological indicator or sensor contained in the PCD according to its instructions for use (if used) is acceptable;

NOTE 2 PCDs are discussed in greater detail in Annex A (air removal indicator) and in Annex B (microbiological indicator).

j) the integrity of the SBS when used.

NOTE 3 Product is normally wrapped in an SBS or packaging system. However, medical devices can be sterilized unwrapped if they are immediately and aseptically transferred to the point of use (e.g. the sterile field in an operating room) after removal from the sterilizer.

9.4.6 If, in addition to the measurement of physical parameters, the sterilization process is to be verified by microbiological methods, then it shall be qualified and one of the following methods shall be used:

a) bioburden method;

b) combined bioburden/biological indicator method; or

c) overkill method.

NOTE 1 See Annex B.

NOTE 2 The bioburden and bioburden/biological indicator methods are also known as product specific approaches.

When the bioburden is not known or measurable, a process based on an overkill approach shall be used provided that the product is stable when exposed to the specified process conditions.

9.4.7 The reproducibility of the sterilization process shall be demonstrated to ensure the required SAL is consistently delivered to the load. Either a defined load (e.g. a contained product load) or load configuration(s) considered to be the most challenging to the sterilization process (e.g. a load configuration containing defined product families for saturated steam sterilization) shall be exposed to at least three consecutive sterilization processes to demonstrate that the sterilization process is reproducible within its specification and specified tolerances.

NOTE Three consecutive sterilization processes does not necessarily mean one after the other. See Annexes F and H for additional information on the interpretation of this subclause.

9.4.8 If, during the sequence of three consecutive cycles specified in 9.4.7, a failure occurs and this can be attributed to factors not relevant to the effectiveness of the sterilization process being validated (see example below), the failure shall be documented as unrelated to the performance of the sterilization process and the cycle omitted from the sequence.

EXAMPLE Failure of external services, e.g. electricity, steam, water, compressed air or a failure of external monitoring equipment.

9.4.9 Non-conformance with the sterilization process specification during PQ shall be reviewed and corrected.

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9.5 Review and approval of validation

9.5.1 Information gathered or produced during IQ, OQ and PQ shall be reviewed for conformity to the acceptance criteria specified for each stage of the validation process. The outcome of this review shall be documented and approved.

9.5.2 The sterilization process specification shall be confirmed. This specification shall include the criteria for designating the sterilization process used for a particular product or load as conforming, and shall document at least the following:

a) the sterilizer including the associated services;

b) the cycle parameters of the cycle to be used;

c) the product family(ies) that can be processed;

d) the load configuration(s) (including orientation, size and mass);

e) the procedures for any preconditioning of product, if used;

f) a description of the SBS or packaging system and methods of packaging;

g) the distribution and orientation of medical devices within a package containing multiple medical devices, if applicable;

h) the periodic tests and equipment maintenance activities necessary to indicate delivery of a reliable process;

i) the PCD and the product family(ies) for which it is relevant;

j) the bioburden, if applicable.

10 Routine monitoring and control

10.1 Routine monitoring

10.1.1 The purpose of this activity is to demonstrate that the validated and specified sterilization process has been delivered to the product for each sterilization process that is carried out.

10.1.2 Routine monitoring and control shall be performed on each operating cycle in order to demonstrate that the process variables for moist heat sterilization are attained.

10.1.3 Delivery of an effective sterilization process shall be verified by confirming that recorded data from routine monitoring are within specified tolerances measured by physical sensors together with the results from chemical indicators and/or biological indicators and/or PCDs, if used.

10.2 Operational status

The operational status of the equipment shall be verified by evidence from the following periodic tests:

a) air leakage into the chamber;

b) quality of steam or heat transfer media admitted to the chamber (which can include checks for, e.g. NCG, conductivity of feed water, contaminant(s), moisture content);

c) automatic control (e.g. a test to verify that the operating cycle continues to function correctly);

EXAMPLE A record of the timings of each stage along with pressure maximum and minimum values for each air removal and steam admission pulse.

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d) a steam penetration test using a defined test load which shall be conducted using devices independent of the sterilizer and the sterilizer control;

NOTE 1 The steam penetration test comes in many forms including Bowie and Dick tests and hollow PCDs both of which can contain an indicator.

NOTE 2 For equipment or processes not intended for hollow or porous items (i.e. those which do not entrain air) a steam penetration test cannot be required.

10.3 Process verification

For verification of a successful process, any fault indication, defined failure message and further relevant information provided by the monitoring system (e.g. fault indication system, process evaluation system) shall be documented and evaluated with respect to possible detrimental impact on the reliability of the process outcome.

10.4 Evaluation of additional data for saturated steam sterilization processes

For saturated steam sterilization processes, evaluation of additional data and information shall include:

NOTE 1 Evaluation can be carried out automatically by a validated software system or by visual examination of recorded data.

a) the duration when the temperature at the reference measurement point is at or above the sterilization temperature;

NOTE 2 If the data recording system reports that the validated duration has been achieved this can be regarded as meeting the requirement.

b) temperature at the reference measurement point and chamber pressure during the plateau period and, when available, the temperature determined from measured chamber pressure according to steam table values (see Annex E) during the holding time;

c) for all stages of the operating cycle:

— the chamber pressure;

— the temperature measured at the reference measurement point;

— the chamber temperature if provided;

NOTE 3 Printed records can provide a summary of the information above, assisting conformity assessment.

d) the results obtained from a PCD containing an indicator sensor designed to assess a specific characteristic of the sterilization process, such as adequacy of air removal and steam penetration, if used [see 6.3 c) and d)];

e) the results obtained from a process monitoring system (e.g. an air detector) fitted to the sterilizer as part of process control, if used, [see 6.3 c) and e)];

f) results of inspection procedures employed to confirm the dryness and integrity of the SBS or packaging systems of the load.

NOTE 4 This can involve direct inspection of every package as can happen, for example, in a health care facility or can involve a risk assessment and qualification exercise (which can involve a sampling and inspection plan) as can, for example, be used in an industrial setting.

10.5 Evaluation of additional data for contained product sterilization processes.

For sterilization processes for contained product, evaluation of the data shall include:

a) the temperature(s) measured in the PCD that represents the product in the load, having a known thermal relationship to the contained product or load, if used as part of process control;

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b) the temperature at the reference measurement point and the chamber pressure for all stages of the operating cycle;

c) the temperature measured in the product during the heating stage, plateau period and cooling stage if used as part of process control and monitoring;

d) the time of the plateau period;

e) the holding time;

f) the integrated lethality, F_0, if used;

g) the value(s) for the process parameter(s) for homogeneity of the heating media in the chamber.

10.6 Record retention

All records shall be retained in accordance with specified procedures (see A.10.10).

11 Product release from sterilization

11.1 The purpose of this activity is to specify procedures for establishing if product exposed to a sterilization process can be released into use.

11.2 Procedures (e.g. standard operating procedures, also known as SOPs) for the review of records and product release from the sterilization process shall be specified and documented. The procedure(s) shall define the requirements for designating a sterilization process as conforming. If a requirement is not met, product shall be designated as non-conforming and handled in accordance with standard operating procedures.

NOTE 1 Suitably trained and qualified individuals can perform product release (see 4.1, A.10.2 and Annexes F and H).

NOTE 2 Examples of nonconformance include a process or cycle parameter being out of specification, a growth positive biological indicator or a chemical indicator failing to meet its endpoint. An acceptable test for sterility cannot be used as confirmatory evidence of process success. See also Annex F and H for further guidance.

11.3 A system shall be specified to ensure that processed and non-processed items are clearly differentiated.

12 Maintaining process effectiveness

12.1 Purpose

The purpose of this activity is to ensure that the products to be sterilized are presented for sterilization in accordance with its specifications, configurations and pre-conditioning requirements as stated in the validation documentation. In addition, it shall be confirmed, that appropriate periodic tests calibration of measuring chains, equipment maintenance, any required requalification and an assessment of any changes, has been carried out.

12.2 Demonstration of continued effectiveness

12.2.1 Product presented for sterilization shall conform with:

a) the product identified during product definition;

b) the load configuration as defined during PQ;

c) if specified during PQ, any pre-conditioning of the load.

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12.2.2 Successful completion of periodic tests, calibrations, equipment maintenance tasks and requalification carried out at specified intervals shall be verified.

12.2.3 If the sterilization process makes use of a vacuum, an air leakage test shall be defined and carried out at specified intervals.

12.2.4 If the sterilization process relies on the removal of air from the chamber and load to achieve rapid and even penetration of steam into the load, an air removal and steam penetration test shall be carried out each day before the sterilizer is used [see 10.2 d].

NOTE 1 The steam penetration test is carried out using a device having a defined challenge to air removal and steam penetration for the process.

NOTE 2 If the sterilizer is used continuously for production of product, the test can be done at least every 24 h.

12.2.5 For applications using saturated steam sterilization in which defined loads known not to inhibit the penetration of steam, are being processed, alternative methods may be used to confirm steam penetration based on specified physical measurements and a risk assessment of the likelihood of process failure.

12.2.6 Product shall conform to bioburden requirements if the sterilization process was established by the bioburden microbiological method (see B.2) or bioburden/biological indicator microbiological method (see B.3).

12.3 Recalibration

The accuracy and reliability of each measuring chain used to control, monitor, indicate, or record the sterilization process shall be verified periodically in accordance with standard operating procedures.

12.4 Equipment maintenance

12.4.1 Preventative equipment maintenance shall be planned and performed in accordance with documented procedures.

Calibration, equipment maintenance, performance test(s) and acceptance criteria (where applicable) intended to ensure that the sterilization process remains reproducible shall be specified as part of the process (see 8.13).

12.4.2 Equipment shall not be used to process product until all specified equipment maintenance tasks have been satisfactorily completed and recorded.

12.4.3 The equipment maintenance plan, procedures and records shall be retained and reviewed at specified intervals by a responsible person. The results of the review shall be documented.

12.5 Requalification

12.5.1 Requalification of a sterilization process shall be carried out for defined product and specified equipment, at defined intervals and after the assessment of any change determined to require requalification. The extent to which requalification is carried out shall be justified.

12.5.2 Requalification procedures shall be specified, and records of requalification shall be retained (see 4.1).

12.5.3 Requalification data shall be reviewed against specified acceptance criteria in accordance with documented procedures.

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12.5.4 Requalification records shall be retained and reviews of requalification data together with corrections made and corrective actions taken shall be documented.

12.6 Assessment of change

12.6.1 Any change shall be assessed for its impact on the safety of the equipment (hardware and software), specified process and cycle parameters, and the effectiveness of the sterilization process. Changes to be considered shall include:

a) replacement of a part which can cause a process parameter to change;

b) replacement of a part which can cause an increase in leakage into the chamber;

c) variation of homogeneity of the process variables in the usable chamber space of the sterilizer;

d) new or modified software for process or cycle control and monitoring and/or hardware replacement or modification of the automatic controller or its software;

e) any change to a process or cycle parameter;

f) any change to services and the outcome of equipment maintenance on a service;

g) any change of the SBS or packaging system or packaging procedures used;

h) any change of load configuration;

i) any change of product manufacturing processes, product materials or source of materials or design of product;

j) any change of equipment maintenance procedures.

12.6.2 The outcome of the assessment, including the rationale for the decisions reached and the extent of changes made to the sterilization process, product or requalification requirements, if any, shall be documented.

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