



BSI Standards Publication

Sterilization of health care products — Low temperature steam and formaldehyde — Requirements for development, validation and routine control of a sterilization process for medical devices

National foreword

This British Standard is the UK implementation of EN ISO 25424:2019+A1:2022. It is identical to ISO 25424:2018, incorporating amendment 1:2022. It supersedes BS EN ISO 25424:2019, which is withdrawn.

The start and finish of text introduced or altered by amendment is indicated in the text by tags. Tags indicating changes to ISO text carry the number of the ISO amendment. For example, text altered by ISO amendment 1 is indicated by **A1** **A1**.

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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Amendments/corrigenda issued since publication

Date	Text affected
30 June 2022	Implementation of ISO amendment 1:2022 with CEN endorsement A1:2022

English Version

**Sterilization of health care products - Low temperature
steam and formaldehyde - Requirements for
development, validation and routine control of a
sterilization process for medical devices - Amendment 1
(ISO 25424:2018/Amd 1:2022)**

Stérilisation des produits de santé - Formaldéhyde
et vapeur à faible température - Exigences
pour le développement, la validation et le
contrôle de routine d'un procédé de stérilisation
pour dispositifs médicaux - Amendement
1 (ISO 25424:2018/Amd 1:2022)

Sterilisation von Produkten für die
Gesundheitsfürsorge - Niedertemperatur-Dampf-
Formaldehyd - Anforderungen an die Entwicklung,
Validierung und Routineüberwachung von
Sterilisationsverfahren für Medizinprodukte -
Änderung 1 (ISO 25424:2018/Amd 1:2022)

This amendment A1 modifies the European Standard EN ISO 25424:2019; it was approved by CEN on 28 December 2021.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for inclusion of this amendment into the relevant national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This amendment exists in three official versions (English, French, German).

A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

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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 a Commission's standardisation request 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](#) 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 EN ISO 25424 is a modified version of the definition prepared by the Global Harmonization Task Force with modification to the Note in the definition.

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 This [Annex ZA](#) is based on normative references according to the table of references in the European Foreword, replacing the references in the core text.

NOTE 4 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.

Table ZA.1 — – Correspondence between this European standard and Annex I of Regulation (EU) 2017/745 [OJ L 117]

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	<p>This standard provides requirements for the development, validation and routine control of a sterilization process using low temperature steam and formaldehyde 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 low temperature steam and formaldehyde is appropriate.</p> <p>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 by low temperature steam and formaldehyde are not covered.</p>

General Safety and Performance Requirements of Regulation (EU) 2017/745	Clause(s) / sub-clause(s) of this EN	Remarks / Notes
11.4 first sentence only	4,5,6,7,8,9,10,11,12	<p>This standard provides requirements for the development, validation and routine control of a sterilization process using low temperature steam and formaldehyde 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 low temperature steam and formaldehyde is appropriate.</p> <p>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 low temperature steam and formaldehyde are not covered. Evidence that the integrity of the packaging is maintained to the point of use is not covered.</p>
11.5	4,5,6,7,8,9,10,11,12	<p>This standard provides requirements for the development, validation and routine control of a sterilization process using low temperature steam and formaldehyde 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 low temperature steam and formaldehyde is appropriate.</p> <p>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 by low temperature steam and formaldehyde are not covered.</p>

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 11138-1	ISO 11138-1:2017	Sterilization of health care products — Biological indicators — Part 1: General requirements	EN ISO 11138-1: 2017
ISO 11138-5:2017	ISO 11138-5:2017	Sterilization of health care products — Biological indicators — Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes	EN ISO 11138-5:2017
ISO 11140-1	ISO 11140-1:2014	Sterilization of health care products — Chemical indicators — Part 1: General requirements	EN ISO 11140-1:2014
ISO 11737-1	ISO 11737-1:2018 amd1: 2021	Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products	EN ISO 11737-1:2018 amd1: 2021
ISO 11737-2	ISO 11737-2:2019	Sterilization of medical devices — Microbiological methods — Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process	EN ISO 11737-2:2020

The documents listed in the Column 1 of table [ZA.2], in whole or in part, are normatively referenced in this document, i.e. 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 this Other Union legislation may be applicable to the product(s) falling within the scope of standard. 

Annex ZB (informative)

A1 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 a Commission's standardisation request 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](#) 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 this 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 EN ISO 25424 is a modified version of the definition prepared by the Global Harmonization Task Force with modification to the Note in the definition.

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 This [Annex ZB](#) is based on normative references according to the table of references in the European Foreword, replacing the references in the core text.

NOTE 4 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.

Table ZB.1 — – Correspondence between this European standard and Annex I of Regulation (EU) 2017/746 [OJ L 117]

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	<p>This standard provides requirements for the development, validation and routine control of a sterilization process using low temperature steam and formaldehyde 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 low temperature steam and formaldehyde is appropriate.</p> <p>This relevant General Safety and Performance Requirement is only partly addressed in this European Standard. Design and packaging for maintenance of a 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 by low temperature steam and formaldehyde are not covered.</p>

General Safety and Performance Requirements of Regulation (EU) 2017/746	Clause(s) / sub-clause(s) of this EN	Remarks / Notes
11.3	4,5,6,7,8,9,10,11,12	<p>This standard provides requirements for the development, validation and routine control of a sterilization process using low temperature steam and formaldehyde 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 low temperature steam and formaldehyde is appropriate.</p> <p>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 by low temperature steam and formaldehyde are not covered.</p>

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 documents 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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

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).

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.

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 in accordance with the requirements for quality management systems (see, for example, ISO 13485) could, 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 nonsterile 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 survives 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 medical device in a population subjected to sterilization processing cannot be guaranteed and the sterility of a processed population is defined in terms of the probability of there being a viable microorganism present on a medical device.

This document describes requirements that, if met, will provide a sterilization process with appropriate microbicidal activity intended to sterilize medical devices. Furthermore, conformity with the requirements ensures that the sterilization process 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 a medical device after sterilization. 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 sterilization process is not the only factor associated with the provision of reliable assurance that a processed medical device is sterile and, in this regard, suitable for its intended use. Attention is also given to a number of factors including:

- a) the microbiological status of incoming raw materials and/or components;
- b) the validation and routine control of any cleaning and disinfection procedures used on the medical device;
- c) the control of the environment in which the medical device is manufactured, assembled and packaged;
- d) the control of equipment and processes;
- e) the control of personnel and their hygiene;
- f) the manner and materials in which the medical device is packaged;
- g) the conditions under which the medical device is stored.

The type of contamination on a medical device to be sterilized varies, and this influences the effectiveness of a sterilization process. Medical devices that have been used in a health care setting and that are being presented for resterilization in accordance with the manufacturer's instructions

(see ISO 17664) should be regarded as special cases. There is the potential for such medical devices to possess a wide range of contaminating microorganisms and residual inorganic and/or organic contamination in spite of the application of a cleaning process. Hence, particular attention has to be given to the validation and control of the cleaning and disinfection processes used during reprocessing.

The requirements are the normative parts of this document with which conformity is claimed. The guidance given in [Annex C](#) is not normative and is not provided as a checklist for auditors. The guidance provides explanations and methods that are regarded as being a suitable means for conforming with the requirements. Methods other than those given in the guidance can be used if they are effective in achieving conformity with the requirements of this document.

The development, validation and routine control of a sterilization process comprise a number of discrete but interrelated activities, for example, calibration, maintenance, product definition, process definition, installation qualification, operational qualification and performance qualification. While the activities required by this 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. The responsibility for carrying out the activities required by this document will vary from case to case. This document requires that the responsibilities of the various parties be defined (see [4.3](#)) but does not specify to whom the responsibilities are allocated. [Annex C](#) provides guidance on allocation of responsibility.

Activities required by this document could also give rise to an environmental burden that can be considered and minimized, e.g. by utilizing flexibility in planning. Environmental aspects are addressed in [Annex D](#) of this document.

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