TERVISHOIUTOODETE STERILISEERIMINE. MADALATEMPERATUURNE AUR JA FORMALDEHÜÜD. NÕUDED MEDITSIINISEADME STERILISEERIMISPROTSESSI VÄLJATÖÖTAMISEKS, VALIDEERIMISEKS JA RUTIINSEKS KONTROLLIKS

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

EESTI STANDARDI EESSÕNA

NATIONAL FOREWORD

See Eesti standard EVS-EN ISO 25424:2019 +A1:2022 sisaldab Euroopa standardi EN ISO 25424:2019 ja selle muudatuse A1:2022 ingliskeelset teksti.	This Estonian standard EVS-EN ISO 25424:2019 +A1:2022 consists of the English text of the European standard EN ISO 25424:2019 and its amendment A1:2022.
Standard on jõustunud sellekohase teate avaldamisega EVS Teatajas. Euroopa standardimisorganisatsioonid on teinud Euroopa standardi rahvuslikele liikmetele kättesaadavaks 20.11.2019, muudatus A1 25.05.2022.	This standard has been endorsed with a notification published in the official bulletin of the Estonian Centre for Standardisation and Accreditation. Date of Availability of the European standard is 20.11.2019, for A1 25.05.2022.
Muudatusega A1 lisatud või muudetud teksti algus ja lõpp on tekstis tähistatud sümbolitega ⟦A1⟩ ⟨A1⟧. Standard on kättesaadav Eesti Standardimis-ja Akrediteerimiskeskusest.	The start and finish of text introduced or altered by amendment A1 is indicated in the text by tags ⟦A1⟩ ⟨A1⟧. The standard is available from the Estonian Centre for Standardisation and Accreditation.

Tagasisidet standardi sisu kohta on võimalik edastada, kasutades EVS-i veebilehel asuvat tagasiside vormi või saates e-kirja meiliaadressile standardiosakond@evs.ee.

ICS 11.080.01

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 25424 + A1

November 2019, May 2022

ICS 11.080.01

Supersedes EN ISO 25424:2011

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 (ISO 25424:2018 + 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 (ISO 25424:2018 + 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 (ISO 25424:2018 + ISO 25424:2018/Amd 1:2022)

This European Standard was approved by CEN on 4 November 2019. Amendment A1 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 giving this European Standard and its amendment the status of a 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.

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CEN-CENELEC Management Centre: Rue de la Science 23, B-1040 Brussels

Ref. No. EN ISO 25424:2019 E
+ EN ISO 25424:2019/A1:2022 E

European foreword

This document (EN ISO 25424:2019) 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 May 2020, and conflicting national standards shall be withdrawn at the latest by May 2020.

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 25424:2011 with a revised European Foreword and European Annexes ZA, ZB and ZC, and additional European Annexes ZD and ZE.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s).

For the relationship with EU Directive(s) see informative Annex ZA, ZB, ZC, ZD or ZE, which is an integral part of this document.

The following referenced documents are indispensable for the application of this document. For undated references, the edition of the referenced document (including any amendments) listed below applies. For dated references, only the edition cited applies. However, for any use of this standard within the meaning of Annex ZA, ZB, ZC, ZD or ZE the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this should be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard as listed below.

NOTE The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

Table – Correlation between normative references and dated EN and ISO standards

Normative references as listed in Clause 2 of the ISO standard	Equivalent dated standard	
	EN	ISO
ISO 11138-1:2017	EN ISO 11138-1:2017	ISO 11138-1:2017
ISO 11138-5:2017	EN ISO 11138-5:2017	ISO 11138-5:2017
ISO 11140-1:2014	EN ISO 11140-1:2014	ISO 11140-1:2014
ISO 11737-1	EN ISO 11737-1:2006	ISO 11737-1:2006
ISO 11737-2:2009	EN ISO 11737-2:2009	ISO 11737-2:2009

NOTE One standard normatively referred to by EN ISO 25424:2019 is undated. The referred standards also include normative references to other dated and undated standards. For undated normative references, it should always be assumed that the latest edition applies.

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, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 25424:2018 has been approved by CEN as EN ISO 25424:2019 without any modification.

A1 Amendment A1 European foreword

This document (EN ISO 25424:2019/A1:2022) 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 Amendment to the European Standard EN ISO 25424:2019 shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by November 2022, and conflicting national standards shall be withdrawn at the latest by November 2022.

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 has been prepared under a Standardization Request given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive(s) / Regulation(s).

For the relationship with EU Regulation(s) see informative Annex ZA and ZB, which are integral parts 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.

The following referenced documents are indispensable for the application of this document. For undated references, the edition of the referenced document (including any amendments) listed below applies. For dated references, only the edition cited applies. However, for any use of this standard within the meaning of Annex ZA and ZB the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this should be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard as listed in table ZA.2.

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Endorsement notice

The text of ISO 25424:2018/Amd 1:2022 has been approved by CEN as EN ISO 25424:2019/A1:2022 without any modification. A1

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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 on 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 the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This second edition cancels and replaces the first edition (ISO 25424:2009), which has been technically revised. The main changes compared to the previous edition are as follows:

— alignment with EN 14180:2014;

— alignment with ISO 14937:2009;

— alignment of definitions with ISO 11139:2018;

— addition of relevant literature.

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.

Amendment A1 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.

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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.

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

1 Scope

1.1 Inclusions

1.1.1 This document specifies requirements for the development, validation and routine control of a low temperature steam and formaldehyde (LTSF) sterilization process for medical devices using a mixture of low temperature steam and formaldehyde as sterilizing agent and which operates below ambient pressure.

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

1.1.2 This document is intended to be applied by process developers, manufacturers of sterilization equipment, manufacturers of medical devices to be sterilized and the organizations with responsibility for sterilizing medical devices (see ISO 14937:2009, Table E.1).

1.2 Exclusions

1.2.1 This document does not specify requirements for the 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. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

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

1.2.2 This document does not specify requirements for designating a medical device as “STERILE”. Such requirements are given in EN 556-1.

1.2.3 This document does not specify a quality management system for the control of all stages of production of medical devices.

NOTE It is not a requirement of this document to have a complete quality management system during manufacture or reprocessing, but those elements of such a system that are required are normatively referenced at appropriate places in the text. Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices including the sterilization process. Further guidance is given in E.4 of ISO 14937:2009.

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

NOTE 1 Safety requirements for sterilizers are specified in IEC 61010-2-040.

NOTE 2 Attention is also drawn to the existence in some countries of regulations stipulating safety requirements.

1.2.5 This document does not cover analytical methods for determining levels or residues of formaldehyde and/or its reaction products.

NOTE 1 Attention is drawn to EN 14180.

NOTE 2 Attention is drawn to the possible existence in some countries of statutory regulations specifying limits for the level of formaldehyde residues on medical devices and products.

1.2.6 This document does not cover preparatory measures that might be necessary before sterilization such as cleaning, disinfection and packing.

NOTE For reprocessable medical devices, the manufacturer(s) of these devices can supply information on the preparatory measures (see ISO 17664).

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, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11138-5:2017, *Sterilization of health care products — Biological indicators — Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes*

ISO 11140-1, *Sterilization of health care products — Chemical indicators — Part 1: General requirements*

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 medical devices — 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 terminological databases for use in standardization at the following addresses:

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

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

3.1
bioburden
population of viable microorganisms on or in *product* 〚A1〛 *deleted text* 〚A1〛 and/or sterile barrier system

[SOURCE: ISO 11139:2018, 3.23]

3.2
biological indicator
BI
test system containing viable microorganisms providing a specified resistance to a specified *sterilization process* 〚A1〛 *deleted text* 〚A1〛

[SOURCE: ISO 11139:2018, 3.29, modified — "BI" has been added.]

