SLOVENSKI STANDARD
oSIST prEN 556-2:2023

01-marec-2023

Sterilizacija medicinskih pripomočkov - Zahteve za medicinske pripomočke, ki morajo biti označeni s "STERILNO" - 2. del: Zahteve za medicinske pripomočke, izdelane v aseptičnem okolju

Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 2: Requirements for aseptically processed medical devices

Sterilisation von Medizinprodukten - Anforderungen an Medizinprodukte, die als "STERIL" gekennzeichnet werden - Teil 2: Anforderungen an aseptisch hergestellte Medizinprodukte

Stérilisation des dispositifs médicaux - Exigences relatives aux dispositifs médicaux en vue d'obtenir l'étiquetage « STÉRILE » - Partie 2 : Exigences relatives aux dispositifs médicaux soumis à un traitement aseptique

Ta slovenski standard je istoveten z: **prEN 556-2**

ICS:

11.080.01	Sterilizacija in dezinfekcija na splošno	Sterilization and disinfection in general

oSIST prEN 556-2:2023 **en,fr,de**

EUROPEAN STANDARD
NORME EUROPÉENNE
EUROPÄISCHE NORM

DRAFT
prEN 556-2

January 2023

ICS 11.080.01

Will supersede EN 556-2:2015

English Version

Sterilization of medical devices - Requirements for medical devices to be designated ''STERILE" - Part 2: requirements for aseptically processed medical devices

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This draft European Standard is submitted to CEN members for enquiry. It has been drawn up by the Technical Committee CEN/TC 204.

If this draft becomes a European Standard, CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration.

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Recipients of this draft are invited to submit, with their comments, notification of any relevant patent rights of which they are aware and to provide supporting documentation.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
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Ref. No. prEN 556-2:2023 E

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European foreword

This document (prEN 556-2:2023) has been prepared by Technical Committee CEN/TC 204 “Sterilization of medical devices”, the secretariat of which is held by BSI.

This document is currently submitted to the CEN Enquiry.

This document will supersede EN 556-2:2015.

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 relationship with EU Directive(s) / Regulation(s), see informative Annexes ZA and ZB, which is an integral part of this document.

For relationship with EU Directive(s), see informative Annexes ZA and ZB, which are integral parts of this document.

EN 556, *Sterilization of medical devices — Requirements for medical devices to be designated "STERILE"*, is currently composed with the following parts:

— *Part 1: Requirements for terminally sterilized medical devices*;

— *Part 2: Requirements for aseptically processed medical devices* [this document].

EN 556-2:2023 includes the following significant technical changes with respect to EN 556-2:2015:

— definitions have been aligned with ISO 11139;

— the normative reference has been updated to the latest edition;

— informative Annex ZA has been replaced with Informative Annexes ZA and ZB giving the relationship with the European Regulations for medical devices and in vitro diagnostic medical devices respectively;

— the Bibliography has been updated.

For any use of this standard within the meaning of Annex ZA or 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.

Introduction

Medical devices designated 'STERILE' are prepared using appropriate and validated methods. Whenever possible, sterile medical devices are terminally-sterilized using a properly validated and controlled sterilization process (see EN 556-1, EN ISO 11135, EN ISO 11137-1, EN ISO 14160, EN ISO 14937, EN ISO 17665-1, EN ISO 20857 and EN ISO 25424). When a medical device is intended to be sterile but cannot be terminally sterilized, aseptic processing is the method of manufacture (see EN ISO 13408-1).

Aseptic processing necessitates that either:

a) the entire product is sterilized and then introduced into a sterilized package; or

b) components of the product are sterilized, then further processed/assembled, and the final product packed into a sterilized package.

Processing/assembly and packaging are carried out in a manner that minimizes the opportunity for items to become re-contaminated by carrying out these operations in a controlled environment in which microbial and particulate levels are maintained at or below defined limits and human intervention is minimized.

NOTE EN ISO 15223-1 specifies the label applied to aseptically processed medical devices as “STERILE A”.

1 Scope

This document specifies the requirements for an aseptically processed medical device to be designated 'STERILE'.

NOTE For the purpose of the EU Directive(s) for medical devices (see Bibliography), designating that a medical device is 'STERILE' is permissible when a validated manufacturing and sterilization process has been applied. Requirements for validation and routine control of aseptic processes are specified in EN ISO 13408-1. Specific requirements for the aseptic processing of solid medical devices and combination products are specified in ISO 13408-7.

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.

EN ISO 11135:2014,[1] *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014* incorporating amendment 1:2018*)*

EN ISO 11137-1:2015,[2] *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 11137-1:2006, including Amd 1:2013 and Amd 2:2015)*

EN ISO 13408-2:2018, *Aseptic processing of health care products — Part 2: Sterilizing filtration (ISO 13408-2:2018)*

EN ISO 13408-5:2011, *Aseptic processing of health care products — Part 5: Sterilization in place (ISO 13408-5:2006)*

EN ISO 13485:2016,[3] *Medical devices — Quality management systems — Requirements for regulatory purposes (ISO 13485:2016)*

EN ISO 14160:2021, *Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices (ISO 14160:2020)*

EN ISO 14937:2009, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices (ISO 14937:2009)*

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

EN ISO 20857:2013, *Sterilization of health care products — Dry heat — Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 20857:2010)*

[1] As impacted by EN ISO 11135:2014/A1:2019.

[2] As impacted by EN ISO 11137-1:2015/A2:2019.

[3] As impacted by EN ISO 13485:2016/AC:2018 and EN ISO 13485:2016/A11:2021.

EN ISO 25424:2019,[4] *Sterilization of medical devices — Low temperature steam and formaldehyde — Requirements for development, validation and routine control of a sterilization process for medical devices (ISO 25424:2018)*

ISO 22441:2022, *Sterilization of health care products — Low temperature vaporized hydrogen peroxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

3 Terms and definitions

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

3.1
aseptic processing
handling of sterile product, containers and/or devices in a controlled environment, in which the air supply, materials, equipment and personnel are regulated to maintain sterility

[SOURCE: EN ISO 13408-1:2015, 3.4]

3.2
bioburden
population of viable microorganisms on or in product and/or sterile barrier system

[SOURCE: EN ISO 11139:2018, 3.23]

3.3
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;

— 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;

[4] As impacted by EN ISO 25424:2019/A1:2022.

— 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 13485:2016, 3.11, modified — The first two list items in Note 1 to entry have been added.]

3.4
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: EN ISO 11139:2018, 3.220.4]

3.5
process simulation
exercise that mimics the manufacturing process or portions of the process in order to demonstrate the capability of that process

Note 1 to entry: Other terms for process simulation include media fill, simulated process fill, simulated filling operation, broth trial, broth fill.

[SOURCE: EN ISO 11139:2018, 3.212]

3.6
requalification
repetition of part or all of validation for the purpose of confirming the continued acceptability of a specified process

[SOURCE: EN ISO 11139:2018, 3.274]

3.7
sterility
state of being free from viable micro-organisms

[SOURCE: EN ISO 11139:2018, 3.274]

3.8
sterile
free from viable microorganisms

[SOURCE: EN ISO 11139:2018, 3.271]

3.9
terminally sterilized
condition of a product that has been exposed to a sterilization process in its sterilized barrier system

[SOURCE: ISO 11139:2018, 3.296]

3.10
test for sterility
technical operation specified in a pharmacopoeia performed on product following an aseptic process or exposure to a sterilization process

Note 1 to entry: For the purpose of this document, the Pharmacopoeia that applies is the European Pharmacopoeia.

[SOURCE: ISO 11139:2018, 3.298 modified, Note 1 to entry has been added]

3.11
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 9000:2015, 3.8.13, modified — "process" has been added to the definition.]

4 Requirements

4.1 Validation and routine control

For an aseptically processed medical device, the following shall apply:

a) the manufacturing environment in which the aseptic process is conducted is specified and records demonstrating compliance with the specification throughout the conduct of the process are prepared and maintained;

b) the processes employed to sterilize product, components, equipment and packaging are validated and routinely controlled in compliance with EN ISO 11135:2014, EN ISO 11135:2014/A1:2019, EN ISO 11137-1:2015, EN ISO 11137-1:2015/A2:2019, EN ISO 14160:2021, EN ISO 13408-2:2018, EN ISO 13408-5:2011, EN ISO 14937:2009, EN ISO 17665-1:2006, EN ISO 20857:2013, EN ISO 25424:2019, EN ISO 25424:2019/A1:2022, or ISO 22441:2022, as applicable;

NOTE 1 Usually such sterilization processes are validated and routinely controlled to achieve a probability of a viable microorganism surviving on a sterilized item of 10^{-6} or less.

c) the requirements for the competence of personnel and methods for their training are specified and records demonstrating that the specified competence has been achieved are prepared and maintained;

d) the interventions that are permitted to occur in the aseptic process are identified, documented and validated;

e) records of all interventions occurring within the aseptic process are prepared and maintained;

f) process simulations are conducted initially in performance qualification and at a specified frequency thereafter;

g) when process simulations are undertaken, the observed frequency of occurrence of a non-sterile unit in initial performance qualification shall not be greater than that specified in Table 1 and thereafter not greater that specified in Table 2;

h) tests for sterility are carried out on product after aseptic processing and test results are interpreted against the acceptance criteria described in the European Pharmacopoeia. Records of the performance and outcomes of tests for sterility are prepared and maintained.

NOTE 2 EN ISO 13408-1 specifies detailed requirements for and guidance on the quality of the manufacturing environment, the training of personnel, the management of interventions, the performance of tests for sterility and the performance of process simulations.

NOTE 3 ISO 13408-7 specifies detailed requirements for and guidance on the quality of the manufacturing environment, the training of personnel, the management of interventions, the performance of tests for sterility and the performance of process simulations for medical devices and combination products.

NOTE 4 The target for process simulation is to obtain zero contaminated units. When a contaminated unit occurs, an investigation to identify its origin is carried out.

NOTE 5 For aseptically processed semi-solids, powders, solid medical devices, microspheres, liposomes and other formulations, evaluation by use of traditional process simulation using liquid media filling might not be possible. In such cases surrogate procedures that represent the operations as closely as possible might be developed and justified. These procedures might include processing of a sterile surrogate as normal with subsequent immersion in sterile media or some other means of simulation where sterility of the surrogate is determined after it has been subjected to the total aseptic process.

NOTE 6 Permission for acceptance of a frequency of occurrence of non-sterile units greater than that shown in Tables 1 and 2 or other approaches to demonstrate acceptable assurance of sterility for aseptically-processed medical devices can be sought through appropriate regulatory bodies. Such permission depends on the individual situation, including consideration of risk management activities undertaken by the manufacturer of the medical device (see EN ISO 14971).

Table 1 — Acceptance limits and actions for occurrence of non-sterile units in process simulations in initial performance qualification

Minimum number of simulations	Number of units filled per simulation	Number of contaminated units in any of the simulations	Number of simulations having contaminated units	Action
3	Less than 5 000	0	0	Accept
		1 or more	1 or more	Investigate, Implement corrective measures, repeat initial performance qualification