SLOVENSKI STANDARD
oSIST prEN ISO 11135:2023

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Sterilizacija izdelkov za zdravstveno nego - Etilenoksid - Zahteve za razvoj, validacijo in rutinsko kontrolo sterilizacijskih postopkov za medicinske pripomočke (ISO/DIS 11135:2023)

Sterilization of health care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO/DIS 11135:2023)

Sterilisation von Produkten für die Gesundheitsfürsorge - Ethylenoxid - Anforderungen an die Entwicklung, Validierung und Lenkung der Anwendung eines Sterilisationsverfahrens für Medizinprodukte (ISO/DIS 11135:2023)

Stérilisation des produits de santé - Oxyde d'éthylène - Exigences de mise au point, de validation et de contrôle de routine d'un processus de stérilisation pour des dispositifs médicaux (ISO/DIS 11135:2023)

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

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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*.

This third edition cancels and replaces the second edition (ISO 11135:2014 and Amd1:2018), which has been technically revised.

The main changes are as follows:

— addition of informational guidance Annexes B, D, E, G, H, J and K;

— more defined requirements for microbiological performance qualification in Annex F;

— incorporation of relevant elements of ISO/TS 21387:2020 into Annexes A and H.

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. Medical devices produced under standard manufacturing conditions in accordance with the requirements for quality management systems (see for example ISO 13485) may, 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 can generally best be described by an exponential relationship between the numbers of microorganisms surviving and the extent of treatment with the ethylene oxide (EO); inevitably this means that there is always a finite probability that a microorganism may 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 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 an ethylene oxide sterilization process intended to sterilize medical devices, which has appropriate microbicidal activity. Furthermore, conformance with the requirements ensures that validations conducted following this document provide products that meet the defined requirements for sterile products with a high degree of confidence. The specification for 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 systems 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 recognize that, for certain processes used in manufacturing or reprocessing, 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 monitored routinely and the equipment is maintained and calibrated.

Exposure to a properly validated, accurately controlled 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 considerations including:

— the microbiological status of incoming raw materials and/or components;

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

— the control of the environment in which the product is manufactured or reprocessed, assembled and packaged;

— the control of equipment and processes;

— the control of personnel and their hygiene;

— the manner and materials in which the product is packaged;

— the conditions under which product is stored.

The type of contamination on a product to be sterilized varies and this impacts upon the effectiveness of a sterilization process. Products that have been used in a health care setting and are being presented for resterilization in accordance with the manufacturer's instructions (see ISO 17664-1) are a special case. There is the potential for such products 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, it is important to pay particular attention to the validation and control of the cleaning and

disinfection processes used during reprocessing. Mixed product loads are common in health care facilities with throughput volumes dictated by historical and predicted demand for sterile product.

The requirements are the normative parts of this document with which conformance is claimed. The guidance given in the informative annexes is not normative and is not provided as a checklist for auditors. Annexes A to K provide explanations and methods that are regarded as being suitable means for complying with the requirements for industry and health care facilities.

The guidance, in annexes, is intended for people who have a basic knowledge of the principles of EO sterilization. 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 comprises a number of discrete but interrelated activities; e.g. 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 in which 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 separate individuals and/or organizations, each of whom undertakes one or more of these activities. This document does not specify the particular individuals or organizations to carry out the activities.

It is important that patient safety be addressed by minimizing exposure to EO and its by-products during product use. ISO 10993-7 specifies limits for EO and ethylene chlorohydrin (ECH); however, no exposure limits are set for ethylene glycol (EG) because risk assessment indicates that when EO residues are controlled, it is unlikely that biologically significant residues of EG would be present.

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

1 Scope

1.1 Inclusions

This document specifies requirements for the development, validation and routine control of an ethylene oxide sterilization process for medical devices in both the industrial and health care facility settings, and it acknowledges the similarities and differences between the two applications.

NOTE 1 Among the similarities are the common need for quality systems, staff training, and proper safety measures. The major differences relate to the unique physical and organizational conditions in health care facilities, and to the initial condition of reusable medical devices being presented for sterilization.

NOTE 2 Health care facilities differ from medical device manufacturers in the physical design of processing areas, in the equipment used, and in the availability of personnel with adequate levels of training and experience. The primary function of the health care facility is to provide patient care; medical device reprocessing is just one of a myriad of activities that are performed to support that function.

NOTE 3 In terms of the initial condition of medical devices, medical device manufacturers generally sterilize large numbers of similar single-use medical devices. Health care facilities, on the other hand, handle and process both new medical devices and reusable medical devices of different types and with varying levels of bioburden. They are therefore faced with the additional challenges of cleaning, evaluating, preparing and packaging a medical device prior to sterilization. In this document, alternative approaches and guidance specific to health care facilities are identified as such.

NOTE 4 EO gas and its mixtures are effective sterilants for medical devices that are sensitive other modalities such as moist heat and ionizing radiation

NOTE 5 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.

NOTE 6 See Annex A for guidance on Clauses 1 to 12.

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 detail a specified requirement for designating a medical device as sterile.

NOTE Attention is drawn to national or regional requirements for designating medical devices as “sterile”. See for example EN 556–1 or ANSI/AAMI ST67.

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

NOTE The effective implementation of defined and documented procedures is necessary for the development, validation and routine control of a sterilization process for medical devices. Such procedures are commonly considered to be elements of a quality management system. It is not a requirement of this document to have a full quality management system during manufacture or reprocessing. The necessary elements are referenced at appropriate places in the text (see, in particular, Clause 4). Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production or reprocessing of medical devices. National and/or regional regulations for the provision of medical devices can require the implementation of a full quality management system and the assessment of that system by a third party.

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

NOTE EO is toxic, flammable and explosive. National or regional regulations exist in some countries concerning safety requirements for the handling of EO and for premises in which EO is used. Refer to the Bibliography for further information on safety.

1.2.5 This document does not cover sterilization by injecting EO or mixtures containing EO directly into packages or a flexible chamber.

NOTE See ISO 14937 for validation of these types of EO processes.

1.2.6 This document does not cover analytical methods for determining levels of residual EO and/or its reaction products.

NOTE 1 For further information see ISO 10993-7.

NOTE 2 Attention is drawn to the possible existence of national or regional regulations specifying limits for the level of EO residues present on or in medical devices.

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 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

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

ISO 11138-2, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide 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 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
aeration
part of the sterilization process during which ethylene oxide and/or its reaction products desorb from the medical device until predetermined levels are reached

Note 1 to entry: This can be performed within the sterilizer and/or in a separate chamber or room.

[SOURCE: ISO 11139:2018, 3.7]

3.2
aeration area
either a chamber or a room in which aeration occurs

3.3
assurance of sterility
qualitative concept comprising all activities that provide confidence that product is sterile

[SOURCE: ISO 11139:2018, 3.17]

3.4
batch
defined quantity of a product intended or purported to be uniform in character and quality produced during a specified cycle of manufacture

[SOURCE: ISO 11139:2018, 3.21]

3.5
bioburden
population of viable microorganisms on or in product and/or sterile barrier system

[SOURCE: ISO 11139:2018, 3.23]

3.6
biological indicator
test system containing viable microorganisms providing a specified resistance to a specified sterilization process

[SOURCE: ISO 11139:2018, 3.29]

3.7
calibration
operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by 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]

3.8
chamber
part of equipment in which a load is processed

[SOURCE: ISO 11139:2018, 3.36]

3.9
chamber pre-heating
process that raises the temperature of internal chamber surfaces prior to the commencement of an operating cycle

[SOURCE: ISO 11139:2018, 3.37]

3.10
chamber reference temperature
temperature at a specified point within the chamber

[SOURCE: ISO 11139:2018, 3.38]

3.11
chamber volume
enclosed space of a chamber, including the volume of nozzles to the first connection or weld, and excluding the volume of permanent internal parts

[SOURCE: ISO 11139:2018, 3.318.1]

3.12
change control
assessment and determination of the appropriateness of a proposed alteration to product, process, or equipment

[SOURCE: ISO 11139:2018, 3.39]

3.13
chemical indicator
test system that reveals a 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]

3.14
conditioning
treatment of product prior to the exposure phase to attain a specified temperature, relative humidity, or other process variable throughout the load

Note 1 to entry: This part of the sterilization cycle can be carried out either at atmospheric pressure or under vacuum.

Note 2 to entry: See *preconditioning* (3.45).

[SOURCE: ISO 11139:2018, 3.58]

3.15
control
regulation of variables within specified limits

[SOURCE: ISO 11139:2018, 3.63]

3.16
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]

3.17
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]

3.18
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]

3.19
cycle variable
property used to control, monitor, indicate, or record an operating cycle

[SOURCE: ISO 11139:2018, 3.74]

3.20
***D* value**
D_{10} value
time or dose required under stated conditions to achieve inactivation of 90 % of a population of the test microorganisms

[SOURCE: ISO 11139:2018, 3.75]

3.21
development
act of elaborating a specification

[SOURCE: ISO 11139:2018, 3.79]

3.22
dew point
temperature at which the saturation water vapour pressure is equal to the partial pressure of the water vapour in the atmosphere

Note 1 to entry: Any cooling of the atmosphere below the dew point would produce water condensation.

[SOURCE: ISO 11139:2018, 3.80]

3.23
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

[SOURCE: ISO 11139:2018, 3.105]

3.24
establish
determine by theoretical evaluation and confirm by experimentation

[SOURCE: ISO 11139:2018, 3.107]

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]

3.26
flushing
procedure by which the ethylene oxide is removed from the load and chamber by either multiple alternate admissions of filtered air, inert gas or steam and evacuations of the chamber or continuous passage of filtered air, inert gas or steam through the load and chamber