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

*Stérilisation des produits de santé — Oxyde d'éthylène — Exigences
de développement, de validation et de contrôle de routine d'un
processus de stérilisation pour des dispositifs médicaux*





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Published in Switzerland

Contents

Page

Foreword	v
Introduction	vi
1 Scope	1
1.1 Inclusions	1
1.2 Exclusions	1
2 Normative references	2
3 Terms and definitions	3
4 Quality management systems	11
4.1 Documentation	11
4.2 Management responsibility	11
4.3 Product realization	11
4.4 Measurement, analysis and improvement — Control of nonconforming product	11
5 Sterilizing agent characterization	11
5.1 General	11
5.2 Sterilizing agent	12
5.3 Microbicidal effectiveness	12
5.4 Material effects	12
5.5 Safety and the environment	12
6 Process and equipment characterization	12
6.1 General	12
6.2 Process characterization	12
6.3 Equipment characterization	13
7 Product definition	14
7.1 General	14
7.2 Product safety, quality and performance	15
7.3 Microbiological quality	15
7.4 Documentation	15
8 Process definition	15
9 Validation	16
9.1 General	16
9.2 Installation qualification, IQ	17
9.3 Operational qualification, OQ	17
9.4 Performance qualification, PQ	18
9.5 Review and approval of validation	20
10 Routine monitoring and control	22
11 Product release from sterilization	23
12 Maintaining process effectiveness	23
12.1 General	23
12.2 Maintenance of equipment	24
12.3 Requalification	24
12.4 Assessment of change	24
12.5 Assessment of equivalence	25
Annex A (normative) Determination of lethal rate of the sterilization process — Biological indicator/bioburden approach	26
Annex B (normative) Conservative determination of lethal rate of the sterilization process — Overkill approach	27
Annex C (informative) Temperature sensors, RH sensors and biological indicator numbers	29

Annex D (informative) Guidance on the application of the normative requirements	32
Annex E (normative) Single Lot Release	74
Bibliography	76

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. www.iso.org/directives

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT), see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 198, *Sterilization of health care products*.

ISO 11135:2014 cancels and replaces ISO 11135-1:2007 and ISO/TS 11135-2:2008, both of which have been technically revised and condensed into a single standard.

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) might, 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 might 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.

ISO 11135 describes requirements that, if met, will provide an ethylene oxide sterilization process intended to sterilize medical devices, which has appropriate microbicidal activity. Furthermore, compliance with the requirements ensures that validations conducted following this International Standard will 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 maintained.

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) 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 ISO 11135 with which compliance is claimed. The guidance given in the informative annexes is not normative and is not provided as a checklist for auditors. The guidance in [Annex D](#) provides explanations and methods that are regarded as being suitable means for complying with the requirements for industry and health care facilities.

The guidance, in [Annex D](#), 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 compliance with the requirements of ISO 11135.

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 ISO 11135 have been grouped together and are presented in a particular order, ISO 11135 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 may 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 International Standard 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 normal 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.