
**Sterilization of health care products —
Ethylene oxide —**

Part 1:

**Requirements for development, validation
and routine control of a sterilization
process for medical devices**

Stérilisation des produits de santé — Oxyde d'éthylène —

*Partie 1: Exigences de développement, de validation et de contrôle de
routine d'un processus de stérilisation pour des dispositifs médicaux*



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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

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Contents

Page

Foreword.....	iv
Introduction	v
1 Scope	1
2 Normative references	2
3 Terms and definitions.....	2
4 Quality management systems	9
4.1 Documentation	9
4.2 Management responsibility	9
4.3 Product realization.....	9
4.4 Measurement, analysis and improvement — Control of nonconforming product	10
5 Sterilizing agent characterization	10
5.1 Sterilizing agent	10
5.2 Microbicidal effectiveness	10
5.3 Material effects	10
5.4 Environmental considerations	10
6 Process and equipment characterization	10
6.1 Process characterization	10
6.2 Equipment characterization.....	11
7 Product definition	12
7.1 General.....	12
7.2 Product safety and performance.....	12
7.3 Microbiological quality	12
7.4 Documentation	13
8 Process definition.....	13
9 Validation	14
9.1 Installation qualification.....	14
9.2 Operational qualification.....	14
9.3 Performance qualification.....	14
9.4 Varying load configurations	16
9.5 Review and approval of validation.....	16
10 Routine monitoring and control	18
11 Product release from sterilization.....	19
12 Maintaining process effectiveness	19
12.1 General.....	19
12.2 Maintenance of equipment	19
12.3 Requalification	19
12.4 Assessment of change.....	20
Annex A (normative) Determination of lethal rate of the sterilization process — Biological indicator/bioburden approach.....	21
Annex B (normative) Conservative determination of lethal rate of the sterilization process — Overkill approach.....	23
Annex C (informative) General guidance	25
Bibliography	41

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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 11135-1 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

ISO 11135 consists of the following parts, under the general title *Sterilization of health care products — Ethylene oxide*:

- *Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*
- *Part 2: Guidance on the application of ISO 11135-1*

For the purposes of this part of ISO 11135 the CEN annex regarding fulfilment of European Council Directives will be removed at publication stage.

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) 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; 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 part of 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 this activity is both reliable and reproducible so that it can be predicted, with reasonable confidence, that there is a low level of probability of there being a viable microorganism present on product after sterilization. Specification of this probability is a matter for regulatory authorities and may 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 recognise 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:

- 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 product;
- c) the control of the environment in which the product is manufactured or reprocessed, 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 product is packaged;
- g) 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) should be regarded as 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.

The requirements are the normative parts of this part 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 provides explanations and methods that are regarded as being suitable means for complying with the requirements. Methods other than those given in the guidance may be used if they are effective in achieving compliance with the requirements of this part 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 this part of ISO 11135 have been grouped together and are presented in a particular order, this part of 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 part of ISO 11135 does not specify the particular individuals or organizations to carry out the activities.

When determining the suitability of ethylene oxide (EO) for sterilization of medical devices, it is important that patient safety is addressed by minimizing exposure to residual EO, ethylene chlorohydrin (ECH) and ethylene glycol (EG) during normal product use (see ISO 10993-7).

Sterilization of health care products — Ethylene oxide —

Part 1:

Requirements for development, validation and routine control of a sterilization process for medical devices

1 Scope

This part of ISO 11135 specifies requirements for the development, validation and routine control of an ethylene oxide sterilization process for medical devices.

NOTE 1 Although the scope of this part of ISO 11135 is limited to medical devices, it specifies requirements and provides guidance that may be applicable to other health care products.

Sterilization processes validated and controlled in accordance with the requirements of this part of ISO 11135 are not assumed to be effective in inactivating the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeldt Jacob disease. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

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

This part of ISO 11135 does not detail a specified requirement for designating a medical device as sterile.

NOTE 3 Attention is drawn to national or regional requirements for designating medical devices as “sterile”. See for example EN 556-1 or ANSI/AAMI ST67.

This part of ISO 11135 does not specify a quality management system for the control of all stages of production of medical devices.

NOTE 4 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 part of ISO 11135 to have a complete quality management system during manufacture or reprocessing, but the elements of a quality management system that are the minimum necessary to control the sterilization process are normatively referenced at appropriate places in the text (see in particular Clause 4). National and/or regional regulations for the provision of medical devices might require implementation of a complete quality management system and the assessment of that system by a third party.

This part of ISO 11135 does not specify requirements for occupational safety associated with the design and operation of ethylene oxide sterilization facilities.

NOTE 5 For further information on safety, see examples in the Bibliography. National or regional regulations may also exist.

NOTE 6 Ethylene oxide is toxic, flammable and explosive. Attention is drawn to the possible existence in some countries of regulations giving safety requirements for handling ethylene oxide and for premises in which it is used.

This part of ISO 11135 does not cover sterilization by injecting ethylene oxide or mixtures containing ethylene oxide directly into individual product packages, or continuous sterilization processes.