American National Standard

ANSI/AAMI/ISO 11135-1:2007

Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices

Association for the Advancement of Medical Instrumentation

Objectives and uses of AAMI standards and recommended practices

It is most important that the objectives and potential uses of an AAMI product standard or recommended practice are clearly understood. The objectives of AAMI's technical development program derive from AAMI's overall mission: the advancement of medical instrumentation. Essential to such advancement are (1) a continued increase in the safe and effective application of current technologies to patient care, and (2) the encouragement of new technologies. It is AAMI's view that standards and recommended practices can contribute significantly to the advancement of medical instrumentation, provided that they are drafted with attention to these objectives and provided that arbitrary and restrictive uses are avoided.

A voluntary *standard* for a *medical device* recommends to the manufacturer the information that should be provided with or on the product, basic safety and performance criteria that should be considered in qualifying the device for clinical use, and the measurement techniques that can be used to determine whether the device conforms with the safety and performance criteria and/or to compare the performance characteristics of different products. Some standards emphasize the information that should be provided with the device, including performance characteristics, instructions for use, warnings and precautions, and other data considered important in ensuring the safe and effective use of the device in the clinical environment. Recommending the disclosure of performance characteristics often necessitates the development of specialized test methods to facilitate uniformity in reporting; reaching consensus on these tests can represent a considerable part of committee work. When a drafting committee determines that clinical concerns warrant the establishment of *minimum* safety and performance criteria, referee tests must be provided and the reasons for establishing the criteria must be documented in the rationale.

A *recommended practice* provides guidelines for the use, care, and/or processing of a medical device or system. A recommended practice does not address device performance *per se*, but rather procedures and practices that will help ensure that a device is used safely and effectively and that its performance will be maintained.

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a frame of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards health care professionals, it may be useful to the manufacturer in better understanding the environment in which a medical device will be used. Also, some recommended practices, while not addressing device performance criteria, provide guidelines to industrial personnel on such subjects as sterilization processing, methods of collecting data to establish safety and efficacy, human engineering, and other processing or evaluation techniques; such guidelines may be useful to health care professionals in understanding industrial practices.

In determining whether an AAMI standard or recommended practice is relevant to the specific needs of a potential user of the document, several important concepts must be recognized:

All AAMI standards and recommended practices are *voluntary* (unless, of course, they are adopted by government regulatory or procurement authorities). The application of a standard or recommended practice is solely within the discretion and professional judgment of the user of the document.

Each AAMI standard or recommended practice reflects the collective expertise of a committee of health care professionals and industrial representatives, whose work has been reviewed nationally (and sometimes internationally). As such, the consensus recommendations embodied in a standard or recommended practice are intended to respond to clinical needs and, ultimately, to help ensure patient safety. A standard or recommended practice is limited, however, in the sense that it responds generally to perceived risks and conditions that may not always be relevant to specific situations. A standard or recommended practice is an important *reference* in responsible decision-making, but it should never *replace* responsible decision-making.

Despite periodic review and revision (at least once every five years), a standard or recommended practice is necessarily a static document applied to a dynamic technology. Therefore, a standards user must carefully review the reasons why the document was initially developed and the specific rationale for each of its provisions. This review will reveal whether the document remains relevant to the specific needs of the user.

Particular care should be taken in applying a product standard to existing devices and equipment, and in applying a recommended practice to current procedures and practices. While observed or potential risks with existing equipment typically form the basis for the safety and performance criteria defined in a standard, professional judgment must be used in applying these criteria to existing equipment. No single source of information will serve to identify a particular product as "unsafe". A voluntary standard can be used as one resource, but the ultimate decision as to product safety and efficacy must take into account the specifics of its utilization and, of course, cost-benefit considerations. Similarly, a recommended practice should be analyzed in the context of the specific needs and resources of the individual institution or firm. Again, the rationale accompanying each AAMI standard and recommended practice is an excellent guide to the reasoning and data underlying its provision.

In summary, a standard or recommended practice is truly useful only when it is used in conjunction with other sources of information and policy guidance and in the context of professional experience and judgment.

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Requests for interpretations of AAMI standards and recommended practices must be made in writing, to the Manager for Technical Development. An official interpretation must be approved by letter ballot of the originating committee and subsequently reviewed and approved by the AAMI Standards Board. The interpretation will become official and representation of the Association only upon exhaustion of any appeals and upon publication of notice of interpretation in the "Standards Monitor" section of the *AAMI News*. The Association for the Advancement of Medical Instrumentation disclaims responsibility for any characterization or explanation of a standard or recommended practice which has not been developed and communicated in accordance with this procedure and which is not published, by appropriate notice, as an *official interpretation* in the *AAMI News*.

American National Standard

ANSI/AAMI/ISO 11135-1:2007
(Partial revision of ANSI/AAMI/ISO 11135:1994)

Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices

Approved 4 June 2007 by
Association for the Advancement of Medical Instrumentation

Approved 23 July 2007 by
American National Standards Institute Inc.

Abstract: Specifies requirements for the development, validation, and routine control of an ethylene oxide sterilization process for medical devices.

Keywords: EO, industrial sterilization, validation, routine control, medical device, product release, process control, process monitoring

AAMI Standard

This Association for the Advancement of Medical Instrumentation (AAMI) standard implies a consensus of those substantially concerned with its scope and provisions. The existence of an AAMI standard does not in any respect preclude anyone, whether they have approved the standard or not, from manufacturing, marketing, purchasing, or using products, processes, or procedures not conforming to the standard. AAMI standards are subject to periodic review, and users are cautioned to obtain the latest editions.

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Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. For each International Standard that has been adopted by AAMI (and ANSI), the table below gives the corresponding U.S. designation and level of equivalency to the International Standard. NOTE: Documents are sorted by international designation.

Other normatively referenced International Standards may be under consideration for U.S. adoption by AAMI; therefore, this list should not be considered exhaustive.

International designation	U.S. designation	Equivalency
IEC 60601-1:2005	ANSI/AAMI ES60601-1:2005	Major technical variations
IEC 60601-1-2:2007	ANSI/AAMI/IEC 60601-1-2:2007	Identical
IEC 60601-2-2:2006	ANSI/AAMI/IEC 60601-2-2:2006	Identical
IEC 60601-2-4:2002	ANSI/AAMI DF80:2003	Major technical variations
IEC 60601-2-19:1990 and Amendment 1:1996	ANSI/AAMI II36:2004	Major technical variations
IEC 60601-2-20:1990 and Amendment 1:1996	ANSI/AAMI II51:2004	Major technical variations
IEC 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 and Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:2004	Major technical variations
IEC 60601-2-50:2001	ANSI/AAMI/IEC 60601-2-50:2006	Identical
IEC/TR 60878:2003	ANSI/AAMI/IEC TIR60878:2003	Identical
IEC/TR 62296:2003	ANSI/AAMI/IEC TIR62296:2003	Identical
IEC 62304:2006	ANSI/AAMI/IEC 62304:2006	Identical
IEC/TR 62348:2006	ANSI/AAMI/IEC TIR62348:2006	Identical
ISO 5840:2005	ANSI/AAMI/ISO 5840:2005	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001/(R)2004	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996/(R)2002	Identical
ISO 8637:2004	ANSI/AAMI RD16:2007	Major technical variations
ISO 8638:2004	ANSI/AAMI RD17:2007	Major technical variations
ISO 10993-1:2003	ANSI/AAMI/ISO 10993-1:2003	Identical
ISO 10993-2:2006	ANSI/AAMI/ISO 10993-2:2006	Identical
ISO 10993-3:2003	ANSI/AAMI/ISO 10993-3:2003	Identical
ISO 10993-4:2002 and Amendment 1:2006	ANSI/AAMI/ISO 10993-4:2002 and Amendment 1:2006	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:2007	ANSI/AAMI/ISO 10993-6:2007	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995/(R)2001	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999/(R)2005	Identical
ISO 10993-10:2002 and Amendment 1:2006	ANSI/AAMI BE78:2002 ANSI/AAMI BE78:2002/A1:2006	Minor technical variations Identical
ISO 10993-11:2006	ANSI/AAMI/ISO 10993-11:2006	Identical
ISO 10993-12:2002	ANSI/AAMI/ISO 10993-12:2002	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999/(R)2004	Identical
ISO 10993-14:2001	ANSI/AAMI/ISO 10993-14:2001/(R)2006	Identical
ISO 10993-15:2000	ANSI/AAMI/ISO 10993-15:2000/(R)2006	Identical
ISO 10993-16:1997	ANSI/AAMI/ISO 10993-16:1997/(R)2003	Identical

International designation	U.S. designation	Equivalency
ISO 10993-17:2002	ANSI/AAMI/ISO 10993-17:2002	Identical
ISO 10993-18:2005	ANSI/AAMI BE83:2006	Major technical variations
ISO/TS 10993-19:2006	ANSI/AAMI/ISO TIR10993-19:2006	Identical
ISO/TS 10993-20:2006	ANSI/AAMI/ISO TIR10993-20:2006	Identical
ISO 11135-1:2007	ANSI/AAMI/ISO 11135-1:2007	Identical
ISO 11137-1:2006	ANSI/AAMI/ISO 11137-1:2006	Identical
ISO 11137-2:2006 (2006-08-01 corrected version)	ANSI/AAMI/ISO 11137-2:2006	Identical
ISO 11137-3:2006	ANSI/AAMI/ISO 11137-3:2006	Identical
ISO 11138-1: 2006	ANSI/AAMI/ISO 11138-1:2006	Identical
ISO 11138-2: 2006	ANSI/AAMI/ISO 11138-2:2006	Identical
ISO 11138-3: 2006	ANSI/AAMI/ISO 11138-3:2006	Identical
ISO 11138-4: 2006	ANSI/AAMI/ISO 11138-4:2006	Identical
ISO 11138-5: 2006	ANSI/AAMI/ISO 11138-5:2006	Identical
ISO/TS 11139:2006	ANSI/AAMI/ISO 11139:2006	Identical
ISO 11140-1:2005	ANSI/AAMI/ISO 11140-1:2005	Identical
ISO 11140-3:2007	ANSI/AAMI/ISO 11140-3:2007	Identical
ISO 11140-4:2007	ANSI/AAMI/ISO 11140-4:2007	Identical
ISO 11140-5:2007	ANSI/AAMI/ISO 11140-5:2007	Identical
ISO 11607-1:2006	ANSI/AAMI/ISO 11607-1:2006	Identical
ISO 11607-2:2006	ANSI/AAMI/ISO 11607-2:2006	Identical
ISO 11737-1: 2006	ANSI/AAMI/ISO 11737-1:2006	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO 11737-3:2004	ANSI/AAMI/ISO 11737-3:2004	Identical
ISO 13485:2003	ANSI/AAMI/ISO 13485:2003	Identical
ISO 14155-1:2003	ANSI/AAMI/ISO 14155-1:2003	Identical
ISO 14155-2:2003	ANSI/AAMI/ISO 14155-2:2003	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998	Identical
ISO 14161:2000	ANSI/AAMI/ISO 14161:2000	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO/TR 14969:2004	ANSI/AAMI/ISO TIR14969:2004	Identical
ISO 14971:2007	ANSI/AAMI/ISO 14971:2007	Identical
ISO 15223-1:2007	ANSI/AAMI/ISO 15223-1:2007	Identical
ISO 15225:2000 and A1:2004	ANSI/AAMI/ISO 15225:2000/(R)2006 and A1:2004/(R)2006	Identical
ISO 15674:2001	ANSI/AAMI/ISO 15674:2001	Identical
ISO 15675:2001	ANSI/AAMI/ISO 15675:2001	Identical
ISO 15882:2003	ANSI/AAMI/ISO 15882:2003	Identical
ISO/TR 16142:2006	ANSI/AAMI/ISO TIR16142:2006	Identical
ISO 17664:2004	ANSI/AAMI ST81:2004	Major technical variations
ISO 17665-1:2006	ANSI/AAMI/ISO 17665-1:2006	Identical
ISO 18472:2006	ANSI/AAMI/ISO 18472:2006	Identical
ISO/TS 19218:2005	ANSI/AAMI/ISO 19218:2005	Identical
ISO 25539-1:2003 and A1:2005	ANSI/AAMI/ISO 25539-1:2003 and A1:2005	Identical

Committee representation

Association for the Advancement of Medical Instrumentation

Ethylene Oxide Sterilization Working Group

The adoption of ISO 11135-1:2007 as an AAMI standard was initiated by the Ethylene Oxide Sterilization Working Group of the AAMI Sterilization Standards Committee (AAMI/ST), which also functions as a U.S. Technical Advisory Group to the relevant work in the International Organization for Standardization (ISO). U.S. representatives from the AAMI Ethylene Oxide Sterilization Working Group (U.S. Sub-TAG for ISO/TC 198/WG 1), chaired by Charles "Phil" Cogdill and Carolyn Kinsley, played an active part in developing the ISO Standard.

Approval of this document does not necessarily imply that all working group members voted for its approval.

At the time this document was published, the **AAMI Ethylene Oxide Sterilization Working Group** had the following members:

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NOTE—Participation by federal agency representatives in the development of this standard does not constitute endorsement by the federal government or any of its agencies.

Background of ANSI/AAMI adoption of ISO 11135-1:2007

The International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of this standard.

The first edition of ISO 11135 was developed by ISO Technical Committee 198 to fill a need for an international standard for ethylene oxide sterilization of health care products. The standard was published in 1994 and was followed by several technical information reports developed in AAMI to provide guidance on ISO 11135. Resulting from a systematic review of ISO 11135:1994 (adopted in the U.S. as ANSI/AAMI/ISO 11135:1994), ISO/TC 198 decided to revise the document by splitting it into two parts under the general title *Sterilization of health care products—Ethylene oxide.* The two parts are:

— Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices; and

— Part 2: Guidance on the application of ISO 11135-1

Concurrent with the development of the U.S. position on the ISO 11135 series, the AAMI Ethylene Oxide Sterilization Working Group (AAMI ST/WG 01) decided to adopt the two parts verbatim.

The requirements for validation and routine control are contained in the normative section of Part 1, and the methods for microbiological performance qualification, originally presented as guidance in Annexes A and B of the 1994 version are now normative. Part 1 contains limited guidance in Annex C, with the bulk of the guidance presented in Part 2.

Other revisions to the 1994 version found in Part 1 include:

— Changes to the requirements for parametric release validation,

— Clarification of the physical performance qualification requirements,

— Requirements for the use of a research or pilot sterilizer,

— Consideration of the environmental impact of EO sterilization, and

— Addition of a requirement to define systems to ensure the microbiological quality and cleanliness of the products presented for sterilization and to estimate bioburden at defined intervals, in accordance with ANSI/AAMI/ISO 11737-1.

In addition, content from some of the AAMI technical information reports developed since the first edition was published has been incorporated into the current ISO 11135 series.

U.S. participation in ISO/TC 198 is organized through the U.S. Technical Advisory Group for ISO/TC 198, administered by the Association for the Advancement of Medical Instrumentation (AAMI). The United States made a considerable contribution to this standard.

As used within the context of this standard, “shall” indicates requirements to be followed strictly in order to conform to the standard; “should” indicates that among several possibilities, one is recommended as particularly suitable, without mentioning or excluding others, that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action is undesirable but not prohibited; “may” is used to indicate that a course of action is permissible within the limits of the standard; “can” is used as a statement of possibility and capability; “must” is used only for those situations which cannot be otherwise, as in the example “Monday must follow Sunday.”

The concepts incorporated in this standard should not be considered inflexible or static. This standard, like any other, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as technological advances are made and as new data comes to light. Suggestions for improving this standard are invited. Comments on this standard are invited and should be sent to AAMI, Attn: Standards Department, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

NOTE—Beginning with the foreword on page xi, this American National Standard is identical to ISO 11135-1:2007.

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 fulfillment 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 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:

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 program 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 Creutzfeld 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.

This part of ISO 11135 does not cover analytical methods for determining levels of residual ethylene oxide and/or its reaction products.

NOTE 7 For further information see ISO 10993-7.

NOTE 8 Attention is drawn to the possible existence of regulations specifying limits for the level of ethylene oxide residues present on or in medical devices and products.

2 Normative references

The following referenced documents are indispensable for the application 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 10012, *Measurement management systems — Requirements for measurement processes and measuring equipment*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

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

ISO 11138-1:2006, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11138-2:2006, *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 medical devices — 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 validation of a sterilization process*

ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

ISO 14161, *Sterilization of health care products — Biological indicators — Guidance for the selection, use, and interpretation of results*

ISO 14937:2000, *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*