

American National Standard



ANSI/ AAMI/ISO 11135:2014

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

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 healthcare 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.

INTERPRETATIONS OF AAMI STANDARDS AND RECOMMENDED PRACTICES

Requests for interpretations of AAMI standards and recommended practices must be made in writing, to the AAMI Vice President, Standards Policy and Programs. 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 11135:2014
(Combined revision of ANSI/AAMI/ISO 11135-1:2007
and ANSI/AAMI/ISO TIR11135-2:2007)

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

Approved 30 March 2015 by
Association for the Advancement of Medical Instrumentation

Approved 27 July 2015 by
American National Standards Institute

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.

CAUTION NOTICE: This AAMI standard may be revised or withdrawn at any time. AAMI procedures require that action be taken to reaffirm, revise, or withdraw this standard no later than five years from the date of publication. Interested parties may obtain current information on all AAMI standards by calling or writing AAMI.

All AAMI standards, recommended practices, technical information reports, and other types of technical documents developed by AAMI are *voluntary*, and their application is solely within the discretion and professional judgment of the user of the document. Occasionally, voluntary technical documents are adopted by government regulatory agencies or procurement authorities, in which case the adopting agency is responsible for enforcement of its rules and regulations.

Published by

Association for the Advancement of Medical Instrumentation
4301 North Fairfax Drive, Suite 301
Arlington, VA 22203

© 2015 by the Association for the Advancement of Medical Instrumentation

All Rights Reserved

This publication is subject to copyright claims of ISO, ANSI, and AAMI. No part of this publication may be reproduced or distributed in any form, including an electronic retrieval system, without the prior written permission of AAMI. All requests pertaining to this document should be submitted to AAMI. It is illegal under federal law (17 U.S.C. § 101, *et seq.*) to make copies of all or any part of this document (whether internally or externally) without the prior written permission of the Association for the Advancement of Medical Instrumentation. Violators risk legal action, including civil and criminal penalties, and damages of \$100,000 per offense. For permission regarding the use of all or any part of this document, contact AAMI, 4301 North Fairfax Drive, Suite 301, Arlington, VA 22203. Phone: (703) 525-4890; Fax: (703) 276-0793.

Printed in the United States of America

ISBN 1-57020-596-5

Contents

Page

Glossary of equivalent standards	vi
Committee representation	vii
Background of AAMI adoption of ISO 11135-1:2007	x
Foreword	xi
Introduction	xii
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	12
5.1 General.....	12
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	13
6.3 Equipment characterization	14
7 Product definition	15
7.1 General.....	15
7.2 Product safety, quality and performance	15
7.3 Microbiological quality.....	15
7.4 Documentation.....	16
8 Process definition	16
9 Validation	17
9.1 General.....	17
9.2 Installation qualification, IQ.....	17
9.2.1 Equipment	17
9.2.2 Installation qualification	17
9.3 Operational qualification, OQ.....	18
9.4 Performance qualification, PQ	18
9.4.1 General.....	18
9.4.2 Performance qualification — Microbiological.....	19
9.4.3 Performance qualification — Physical	19
9.5 Review and approval of validation	20
10 Routine monitoring and control	22
11 Product release from sterilization.....	24

12	Maintaining process effectiveness	24
12.1	General	24
12.2	Maintenance of equipment	24
12.3	Requalification	25
12.4	Assessment of change	25
12.5	Assessment of equivalence	25
12.5.1	Process Equivalence	25
12.5.2	Product	26
Annex A (normative)	Determination of lethal rate of the sterilization process — Biological indicator/bioburden approach	27
A.1	General	27
A.2	Procedure	27
Annex B (normative)	Conservative determination of lethal rate of the sterilization process — Overkill approach	28
B.1	General	28
B.2	Procedure	28
Annex C (informative)	Temperature sensors, RH sensors and biological indicator numbers	30
C.1	Temperature sensors	30
C.2	Humidity sensors	31
C.3	Biological Indicators	31
Annex D (informative)	Guidance on the application of the normative requirements	33
D.1	Scope	33
D.2	Normative references	33
D.3	Terms and definitions	33
D.4	Quality management systems	33
D.4.1	Documentation	33
D.4.2	Management responsibility	33
D.4.3	Product realization	34
D.4.4	Measurement, analysis and improvement — Control of non-conforming product	34
D.5	Sterilizing agent characterization	34
D.5.1	General	34
D.5.2	Sterilizing agent	35
D.5.3	Microbicidal effectiveness	35
D.5.4	Material effects	35
D.5.5	Safety and the environment	35
D.6	Process and equipment characterization	36
D.6.1	General	36
D.6.2	Process characterization	36
D.6.3	Equipment characterization	38
D.7	Product definition	40
D.7.1	General	40
D.7.2	Product safety, quality and performance	43
D.7.3	Microbiological quality	45
D.7.4	Documentation	45
D.8	Process definition	45
D.9	Validation	49
D.9.1	General	49

D.9.2	Installation qualification	49
D.9.2.1	Equipment	49
D.9.2.2	Installation qualification	50
D.9.3	Operational qualification	51
D.9.4	Performance qualification	53
D.9.4.1	General.....	53
D.9.4.2	Performance qualification — Microbiological.....	54
D.9.4.3	Performance qualification — Physical	55
D.9.4.4	Review and approval of validation	56
D.10	Routine monitoring and control.....	57
D.11	Product release from sterilization.....	60
D.12	Maintaining process effectiveness.....	60
D.12.1	General.....	60
D.12.2	Maintenance of equipment	61
D.12.3	Requalification	62
D.12.4	Assessment of change	64
D.12.5	Assessment of equivalence	65
D.12.5.1	Process equivalence	65
D.12.5.2	Criteria for process equivalence	65
D.12.5.3	Determination of process equivalence	66
D.12.5.4	Process analysis and evaluation	66
D.12.5.5	Evaluation of preconditioning or aeration areas	66
D.12.5.6	Evaluation of sterilization chamber performance.....	66
D.12.5.7	Microbiological evaluation	67
D.12.5.8	Results evaluation.....	67
D.12.5.9	Maintenance of equivalence.....	68
D.12.5.10	Documentation	68
D.12.5.11	Product.....	68
D.12.5.11.1	Product family	68
D.12.5.11.2	Determination of adverse effects to product.....	69
D.12.5.11.3	Determination of product design effects.....	69
D.12.5.11.4	Determination of product material and characteristics effects.....	70
D.12.5.11.5	Determination of sterile barrier system effects	70
D.12.5.11.6	Determination of load configuration effects	70
D.12.5.11.7	Conclusions of product adoption evaluation.....	70
D.13	Guidance on Annex A — Determination of lethal rate of the sterilization process — Biological indicator/bioburden approach	70
D.13.1	[A.1] General	70
D.13.2	[A.2] Procedure.....	72
D.14	Guidance on Annex B — Conservative determination of lethal rate of the sterilization process — Overkill approach.....	73
D.14.1	[B.1] General	73
D.14.2	[B.2] Procedure.....	74
Annex E (normative)	Single Lot Release	75
E.1	General.....	75
E.2	Procedure	75
Bibliography		77

Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. AAMI maintains a current list of each International Standard that has been adopted by AAMI (and ANSI). Available on the AAMI website at the address below, this list gives the corresponding U.S. designation and level of equivalency to the International Standard.

www.aami.org/standards/glossary.pdf

Committee representation

Association for the Advancement of Medical Instrumentation Ethylene Oxide Sterilization Working Group

The adoption of ISO 11135:2014 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 Jeff Martin and Gerry O'Dell, played an active part in developing the ISO Standard.

Committee approval of this document does not necessarily imply that all committee members voted for its approval.

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

Cochairs Jeff Martin
 Gerry O'Dell

Members Erin Armstrong, B Braun of America Inc
 Ed Arscott, NAMSA
 Anne Booth, Booth Scientific Inc
 Lloyd Brown, Covidien
 Tim Carlson, Becton Dickinson & Company
 Sarah Chamberlain, Accuratus Labs Services
 Denny Christensen, Mesa Laboratories Biological Indicator Division- Bozeman Facility
 Gary Cranston, Consulting & Technical Services/PCS
 Elaine Daniell, CR Bard
 Douglas Davie, Sterilization Validation Services
 Darci Diage, Direct Flow Medical Inc
 Mary Ann Drosnock, Healthmark Industries Company Inc
 Paul Fioriti, Company for Individuals
 William FitzGerald, FitzGerald & Associates Ltd
 Dan Floyd, Nelson Laboratories Inc
 Lisa Foster, Aduvo QS & SA Consulting
 Zory Glaser, Johns Hopkins University-School of Public Health
 Mike Groendyk, Javelin Medical
 Doug Harbrecht, Sterility Assurance LLC
 Arthur Harris, Cook Inc
 Deborah Havlik, Hospira Worldwide Inc
 Jason Hedrick, Medtronic Inc WHQ Campus
 Krista Howard, WL Gore & Associates Inc
 Danny Hutson, CareFusion
 Nupur Jain, Intuitive Surgical Inc
 Carolyn Kinsley, LexaMed Ltd
 Karen Kowalczyk, Centurion Sterilization Services
 Christine Loshbaugh, Edwards LifeSciences
 Jeff Martin, Alcon Laboratories Inc
 Ted May, Andersen Products Inc
 Patrick McCormick, Bausch & Lomb Inc
 David McGoldrick, Abbott Laboratories
 Rusty Mills, GE Healthcare
 Gary Mitchel, Johnson & Johnson
 Sarah Mowitt, Mowitt, Sarah - 322573
 Gerry O'Dell, Gerry O'Dell Consulting
 Dave Parente, Ecolab
 Michelle Peterson, Stryker Instruments Division
 Nancy Rakiewicz, IUVO BioScience
 Beth Ridgeway, Mesa Laboratories Biological Indicator Division- Bozeman Facility
 Manny Saavedra, Halyard Health
 Jon Seulean, Terumo BCT

Mark Seybold, Baxter Healthcare Corporation
 Harry Shaffer, Sterilization Consulting Services
 David Silor, Zimmer Inc
 Bill South, Steris Corporation
 Michael Sprague, Ethide Laboratories Inc
 Sopheak Srun, Quality Tech Services Inc
 Ralph Stick, WuXi AppTec Inc
 Fenil Sutaria, Medline Industries Inc
 Radhakrishna Tirumalai, US Pharmacopeia Convention Inc
 Steven Turtill, FDA/CDRH
 Craig Wallace, 3M Healthcare
 Richard Warburton, Company for Individuals
 Bud Weisman, Fresenius Medical Care
 Beverly Whitaker, Indigo Consulting Group LLC
 Stacy Wiehle, Boston Scientific Corporation
 Dennis Wildes, St Jude Medical Inc
 Bill Young, Sterigenics International

Alternates

August Baur, Centurion Sterilization Services
 MarJean Boyter, Fresenius Medical Care
 Robert Bradley, Mesa Laboratories Biological Indicator Division- Bozeman Facility
 Carolyn Braithwaite-Nelson, Spectranetics Corporation
 Trabue Bryans, BryKor LLC
 Susan Bullis, Johnson & Johnson
 Greg Bush, Alcon Laboratories Inc
 Claudia Camp, Stryker Instruments Division
 Greg Crego, IUVO BioScience
 Jeffrey Delgaudio, Covidien
 Jessica Desmond, Accuratus Labs Services
 John DiCaro, Covidien
 Dave Dion, Cardinal Health (MP&S)
 David Dominguez, CareFusion
 Brian Drumheller, CR Bard
 Steven Elliott, FDA/CDRH
 Diane Faivre-Swiat, Cardinal Health (MP&S)
 Naomi Gamm, St Jude Medical Inc
 Scott Giraud, Medtronic Inc WHQ Campus
 Ken Gordon, Steris Corporation
 David Hilliker, ChemDAQ Inc
 Nichole Jackson, Ecolab
 Chris Kobus, GE Healthcare
 Ezra Koski, Terumo BCT
 Jim Kulla, LexaMed Ltd
 Wesley Lantz, Zimmer Inc
 John Lindley, Andersen Products Inc
 Paul Littley, Nelson Laboratories Inc
 Ronald Lulich, 3M Healthcare
 Joseph Mello, Ethide Laboratories Inc
 Laurie Nawrocki, NAMSA
 Susumu Nozawa, Becton Dickinson & Company
 Koyejo Obadina, Abbott Laboratories
 Mike Padilla, Sterigenics International
 Andrew Porteous, Baxter Healthcare Corporation
 Tyrone Rouse, Halyard Health
 Matthew Russell, Cook Inc
 Arnie Shechtman, Medline Industries Inc
 Jade Schiesser, Quality Tech Services Inc
 Mike Schoene, Bausch & Lomb Inc
 Brian Wallace, Intuitive Surgical Inc
 Daryl Woodman, Andersen Products Inc
 Bryan Worwa, Boston Scientific Corporation
 Cas Woss, FitzGerald & Associates Ltd

AAMI Sterilization Standards Committee

<i>Cochairs</i>	Victoria M. Hitchins, PhD, FDA/CDRH William E. Young, Boston Scientific Corporation
<i>Members</i>	Trabue D. Bryans, AppTec Nancy Chobin, RN CSPDM, St Barnabas Healthcare System Charles Cogdill, Boston Scientific Corporation Ramona Conner, RN MSN CNOR, Association of Perioperative Registered Nurses Jacqueline Daley, Association for Professionals in Infection Control and Epidemiology Kimbrell Darnell, CR Bard Lisa Foster, Sterigenics International James M. Gibson, Jr., JM Gibson Associates Joel R. Gorski, PhD, NAMSA Deborah A. Havlik, Hospira Inc Victoria M. Hitchins, PhD, FDA/CDRH Danny Hutson, Cardinal Health (MP&S) Lois Atkinson Jones, MS, (Independent Expert) Susan G. Klacik, AS BS, IAHCSMM Byron J. Lambert, PhD, Abbott Laboratories Colleen Patricia Landers, RN, Canadian Standards Association David Liu, Johnson & Johnson Jeff Martin, Alcon Laboratories Inc Patrick J. McCormick, PhD, Bausch & Lomb Inc Susie McDonald, American Society for Healthcare Central Service Professionals Thomas K. Moore, Getinge USA Barry F.J. Page, Cook Endoscopy Nancy J. Rakiewicz, Ethox International Inc Phil M. Schneider, 3M Healthcare Michael H. Scholla, Dupont Nonwovens Mark Seybold, Baxter Healthcare Corporation Andrew Sharavara, Propper Manufacturing Co Inc William N. Thompson, TYCO Healthcare John W. Walker, STERIS Corporation James L. Whitby, MA, MB, FRCP, University of Western Ontario Thelma Wilcott, Becton Dickinson & Company Martell Kress Winters, BS SM, Nelson Laboratories Inc
<i>Alternates</i>	Lloyd Brown, TYCO Healthcare Lina C. Bueno, Dupont Nonwovens Dave Dion, Cardinal Health (MP&S) Thomas J. Frazar, Johnson & Johnson Kathy Hoffman, Sterigenics International Clark W. Houghtling, STERIS Corporation Jim Kaiser, Bausch & Lomb Inc Joseph J. Lasich, BS, Alcon Laboratories Inc Chiu S. Lin, PhD, FDA/CDRH Natalie Lind, IAHCSMM Lisa N. Macdonald, Becton Dickinson & Company Ralph Makinen, Boston Scientific Corporation Mary S. Mayo, CR Bard David Ford McGoldrick, BS, Abbott Laboratories Jerry R. Nelson, MS PhD, Nelson Laboratories Inc Janet M. Prust, 3M Healthcare Mike Sadowski, Baxter Healthcare Corporation Ralph Stick, AppTec Jason Voisinnet, Ethox International Inc Valerie Welter, Hospira Inc William E. Young, Boston Scientific Corporation

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 11135:2014

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.

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 original edition of the standard was published in 1994, and the document is now in its third edition. The new edition combines the previous standard—ISO 11135-1, which contained the normative requirements for validation and routine control—with ISO/TS 11135-2, which contained the bulk of the guidance for ethylene oxide sterilization. (These ISO documents had also been adopted by AAMI as an American National Standard and a Technical Information Report [TIR], respectively.)

The AAMI Ethylene Oxide Sterilization Working Group (AAMI ST/WG 01) considered adoption of the standard concurrent with the development of the U.S. position on the third edition of ISO 11135 and, after publication of the ISO standard, agreed to adopt this new edition.

AAMI had previously published a series of TIRs providing additional guidance on ethylene oxide sterilization and, at the time of the adoption of ISO 11135:2014, these TIRs were being revised to ensure alignment with this new standard. In addition, a new TIR was being developed to explain the differences between this new edition and the earlier standard and guidance document it replaces.

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 that 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, 4301 North Fairfax Drive, Ste 301, Arlington, VA 22203

NOTE—Beginning with the foreword on page xi, this American National Standard is identical to ISO 11135-1:2014, except for two minor errors in the ISO version that have been corrected in this adoption (and which are indicated in footnotes in sections C.1 and D.12.5).

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

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. 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 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 that 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; and
- 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.



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 International Standard 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 medical devices that have been produced from virgin material. Health care facilities, on the other hand, must handle and process both new medical devices and reusable medical devices of different descriptions 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 International Standard, alternative approaches and guidance specific to health care facilities are identified as such.

NOTE 4 EO gas and its mixtures are effective sterilants that are primarily used for heat- and/or moisture-sensitive medical devices that cannot be moist heat sterilized.

NOTE 5 Although the scope of this International Standard is limited to medical devices, it specifies requirements and provides guidance that can be applicable to other health care products.

1.2 Exclusions

1.2.1 This International Standard 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 International Standard 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 International Standard 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 International Standard to have a full quality management system during manufacture or reprocessing. The necessary elements are normatively 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 might require the implementation of a full quality management system and the assessment of that system by a third party.

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

NOTE 1 For further information on safety, see examples in the Bibliography. National or regional regulations may also exist.

NOTE 2 EO is toxic, flammable, and explosive. Attention is drawn to the possible existence in some countries of regulations giving safety requirements for handling EO and for premises in which it is used.

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

NOTE See ISO 14937 for these types of EO processes.

1.2.6 This International Standard 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, in whole or in part, are normatively referenced in this document and are indispensable for its application. 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 10993-7, *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 11138-2:2009, *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 definition, validation and maintenance of a sterilization process*

ISO 13485:2003/Cor 1:2009, *Medical devices — Quality management systems — Requirements for regulatory purposes — Technical Corrigendum 1*

3 Terms and definitions

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

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.

3.2

aeration area

either a chamber or a room in which aeration occurs

3.3

bioburden

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

[SOURCE: ISO/TS 11139:2006, definition 2.2]

3.4

biological indicator

test system containing viable microorganisms providing a defined resistance to a specified sterilization process

[SOURCE: ISO/TS 11139:2006, definition 2.3]

3.5

calibration

set of operations that establish, under specified conditions, the relationship between values of a quantity indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards

[SOURCE: ISO/TS 11139:2006, definition 2.4]

3.6

chemical indicator

test system that reveals a change in one or more pre-defined process variables based on a chemical or physical change resulting from exposure to a process

[SOURCE: ISO/TS 11139:2006, definition 2.6]

3.7

conditioning

treatment of product within the sterilization cycle, but prior to ethylene oxide admission, to attain a predetermined temperature and relative humidity

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 3.27, preconditioning.

3.8

D value

D_{10} value

time or dose required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions

[SOURCE: ISO/TS 11139:2006, definition 2.11]

NOTE 1 to entry: For the purposes of this International Standard, the *D* value is the exposure time required to achieve 90 % inactivation of the population of the test organism.

3.9

development

act of elaborating a specification

[SOURCE: ISO/TS 11139:2006, definition 2.13]

3.10

dew point

The temperature at which the saturation water vapor pressure is equal to the partial pressure of the water vapor in the atmosphere

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

3.11

establish

determine by theoretical evaluation and confirm by experimentation

[SOURCE: ISO/TS 11139:2006, definition 2.17]

3.12

ethylene oxide (EO) injection time

duration of the stage beginning with the first introduction of the EO (mixture) into the chamber to the completion of that injection

3.13

exposure time

period for which the process parameters are maintained within their specified tolerances

[SOURCE: ISO/TS 11139:2006, definition 2.18]

NOTE 1 to entry: For the purpose of calculation of cycle lethality, it is the period of sterilization between the end of EO injection and the beginning of EO removal.

3.14

fault

one or more of the process parameters lying outside of its/their specified tolerance(s)

[SOURCE: ISO/TS 11139:2006, definition 2.19]

3.15

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

3.16

fractional cycle

a cycle in which the exposure time to EO gas is reduced compared to that specified in the sterilization process

3.17

half cycle

a cycle in which the exposure time to EO gas is reduced by 50 % compared to that specified in the sterilization process

3.18

health care facility

HCF

governmental and private organizations and institutions devoted to the promotion and maintenance of health, and the prevention and treatment of diseases and injuries

EXAMPLE A health care facility can be a hospital, nursing home, extended care facility, free-standing surgical centre, clinic, medical office, or dental office.

3.19

health care product

medical device(s), including *in vitro* diagnostic medical device(s), or medicinal product(s), including biopharmaceutical(s)

[SOURCE: ISO/TS 11139:2006, definition 2.20]

3.20

installation qualification

IQ

process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification

[SOURCE: ISO/TS 11139:2006, definition 2.22]

3.21

medical device

any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of

- diagnosis, prevention, monitoring, treatment, or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for an injury,
- investigation, replacement, or modification or support of the anatomy or of a physiological process,
- control of conception,
- disinfection of medical devices,
- providing information for medical purposes by means of *in vitro* examination of specimens derived from the human body,

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological, or metabolic means, but which may be assisted in its function by such means

[SOURCE: ISO 13485:2003, definition 3.7]

3.22

microorganism

entity of microscopic size, encompassing bacteria, fungi, protozoa, and viruses

NOTE 1 to entry: A specific standard might not require demonstration of the effectiveness of the sterilization process in inactivating all types of microorganisms, identified in the definition above, for validation and/or routine control of the sterilization process.

[SOURCE: ISO/TS 11139:2006, definition 2.26]

3.23

operational qualification

OQ

process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO/TS 11139:2006, definition 2.27]

3.24

overkill approach

approach using sterilization process that delivers a minimum of 12 Spore Log Reduction (SLR) to a biological indicator having a resistance equal to or greater than the product bioburden

3.25

parametric release

declaration that product is sterile, based on records demonstrating that the process parameters were delivered within specified tolerances

[SOURCE: ISO/TS 11139:2006, definition 2.29]

NOTE 1 to entry: This method of process release does not include the use of biological indicators.

3.26

performance qualification

PQ

process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting its specification

[ISO/TS 11139:2006, definition 2.30]

3.27

preconditioning

treatment of product, prior to the sterilization cycle, in a room or chamber to attain specified conditions for temperature and relative humidity

3.28

process challenge device

PCD

item designed to constitute a defined resistance to a sterilization process and used to assess performance of the process

[SOURCE: ISO/TS 11139:2006, definition 2.33]

NOTE 1 to entry: For the purpose of this International Standard, a PCD can be product, simulated product, or other device that is inoculated directly or indirectly. See 7.1.6 and D.7.1.6.

NOTE 2 to entry: In this International Standard, a distinction is made between an internal PCD and an external PCD. An internal PCD is used to demonstrate that the required product SAL is achieved. A PCD located within the confines of the product or product shipper case is an internal PCD, whereas a PCD located between shipper cases or on the exterior surfaces of the load is an external PCD. An external PCD is an item designed to be used for microbiological monitoring of routine production cycles.

3.29

process parameter

specified value for a process variable

NOTE 1 to entry: The specification for a sterilization process includes the process parameters and their tolerances.

[SOURCE: ISO/TS 11139:2006, definition 2.34]

3.30

process variable

condition within a sterilization process, changes in which alter microbicidal effectiveness

EXAMPLE Time, temperature, pressure, concentration, humidity, wavelength.

[SOURCE: ISO/TS 11139:2006, definition 2.35]

3.31

processing category

collection of different product or product families that can be sterilized together

NOTE 1 to entry: All products within the category have been determined to present an equal or lesser challenge to the sterilization process than the process challenge device for that group.

3.32

product

result of a process

[ISO 9000:2005, definition 3.4.2]

NOTE 1 to entry: For the purposes of sterilization standards, product is tangible and can be raw material(s), intermediate(s), sub-assembly(ies), and health care products.

3.33

product family

group of product possessing characteristics that allow them to be sterilized using defined process conditions

3.34

product load volume

defined space within the usable chamber volume occupied by product

3.35

recognized culture collection

depository authority under the Budapest Treaty on *The International Recognition of the Deposit of Microorganisms for the Purposes of Patent and Regulation*

[SOURCE: ISO/TS 11139:2006, definition 2.38]

3.36

reference microorganism

microbial strain obtained from a recognized culture collection

[SOURCE: ISO/TS 11139:2006, definition 2.39]

3.37

requalification

repetition of part of validation for the purpose of confirming the continued acceptability of a specified process

[SOURCE: ISO/TS 11139:2006, definition 2.40]

3.38

reusable medical device

medical device designated or intended by the manufacturer as suitable for reprocessing and re-use

NOTE 1 to entry: This is not a medical device that is designated or intended by the manufacturer for single use only.

3.39

services

supplies from an external source, needed for the correct function of equipment

EXAMPLE Electricity, water, compressed air, drainage.

[SOURCE: ISO/TS 11139:2006, definition 2.41]

3.40

single use medical device

medical device designated or intended by the manufacturer for one-time use only

3.41

specify

stipulate in detail within an approved document

[SOURCE: ISO/TS 11139:2006, definition 2.42]

3.42

Spore-log-reduction

SLR

log of initial spore population, N_0 , minus the log of the final population, N_u

[SOURCE: ISO 14161:2009, definition 3.19]

NOTE 1 to entry: Describing the reduction in the number of spores on a biological indicator or inoculated item produced by exposure to specified conditions.

For Direct Enumeration:

$$\text{SLR} = \log N_0 - \log N_u$$

where

N_0 is the initial population;

N_u is the final population.

For Fraction Negative:

$$\text{SLR} = \log N_0 - \log [\ln (q/n)]$$

where

- N_0 is the initial population;
 q is the number of replicate samples tested;
 n is the number of samples negative for growth.

If there are no survivors, the true SLR cannot be calculated. The SLR can be reported as “greater than” $\log N_0$ if one surviving organism is used.

3.43

sterile

free from viable microorganisms

[SOURCE: ISO/TS 11139:2006, definition 2.43]

3.44

sterile barrier system

minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use

[SOURCE: ISO/TS 11139:2006, definition 2.44]

3.45

sterility

state of being free from viable microorganisms

NOTE 1 to entry: In practice, no such absolute statement regarding the absence of microorganisms can be proven.

NOTE 2 to entry: See 3.47, sterilization.

[SOURCE: ISO/TS 11139:2006, definition 2.45]

3.46

sterility assurance level

SAL

probability of a single viable microorganism occurring on an item after sterilization

NOTE 1 to entry: The term SAL takes a quantitative value, generally 10^{-6} or 10^{-3} . When applying this quantitative value to assurance of sterility, an SAL of 10^{-6} has a lower value but provides a greater assurance of sterility than an SAL of 10^{-3} .

[SOURCE: ISO/TS 11139:2006, definition 2.46]

3.47

sterilization

validated process used to render product free from viable microorganisms

NOTE 1 to entry: In a sterilization process, the nature of microbial inactivation is exponential and thus the survival of a microorganism on an individual item can be expressed in terms of probability. While this probability can be reduced to a very low number, it can never be reduced to zero.

NOTE 2 to entry: See 3.46, sterility assurance level.

[SOURCE: ISO/TS 11139:2006, definition 2.47]

3.48

sterilization cycle

treatment in a sealed chamber, which includes air removal, conditioning (if used), injection of ethylene oxide, inert gas (if used), exposure to ethylene oxide, removal of ethylene oxide and flushing (if used), and air/inert gas admission

3.49

sterilization load

product to be, or that has been, sterilized together using a given sterilization process

[SOURCE: ISO/TS 11139:2006, definition 2.48]

3.50

sterilization process

series of actions or operations needed to achieve the specified requirements for sterility

[SOURCE: ISO/TS 11139:2006, definition 2.49]

NOTE 1 to entry: This series of actions or operations includes preconditioning (if necessary), exposure to the ethylene oxide under defined conditions, and any necessary post-treatment required for the removal of ethylene oxide and its by-products. It does not include any cleaning, disinfection, or packaging operations that precede the sterilization process.

3.51

sterilization specialist

person with technical knowledge of the sterilization technology being utilized and its effects upon materials and microorganisms

3.52

sterilizing agent

physical or chemical entity, or combination of entities having sufficient microbicidal activity to achieve sterility under defined conditions

[SOURCE: ISO/TS 11139:2006, definition 2.50]

3.53

survivor curve

graphical representation of the inactivation of a population of microorganisms with increasing exposure to a microbicidal agent under stated conditions

[SOURCE: ISO/TS 11139:2006, definition 2.51]

3.54

test for sterility

technical operation defined in a Pharmacopoeia performed on product following exposure to a sterilization process

[SOURCE: ISO/TS 11139:2006, definition 2.53]

3.55

test of sterility

technical operation performed as part of development, validation, or requalification to determine the presence or absence of viable microorganisms on product or portions thereof

[SOURCE: ISO/TS 11139:2006, definition 2.54]

3.56

usable chamber volume

defined space within the sterilizer chamber, which is not restricted by fixed or mobile parts and which is available to accept the sterilization load

NOTE 1 to entry: The volume allowed for gas circulation around the load inside the chamber is not included as usable space.

3.57

validation

documented procedure for obtaining, recording, and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications

[SOURCE: ISO/TS 11139:2006, definition 2.55]

3.58

virgin material

material that has not been previously used or subjected to processing other than for its original production

4 Quality management systems

4.1 Documentation

4.1.1 Procedures for development, validation, routine control, and product release from sterilization shall be specified.

4.1.2 Documents and records required by this International Standard shall be reviewed and approved by designated personnel (see 4.2.1). Documents and records shall be controlled in accordance with the applicable clauses of ISO 13485.

4.2 Management responsibility

4.2.1 The responsibility and authority for implementing and meeting the requirements described in this International Standard shall be specified. Responsibility shall be assigned to competent personnel in accordance with the applicable clauses of ISO 13485.

4.2.2 If the requirements of this international standard are undertaken by organizations with separate quality management systems, the responsibilities and authority of each party shall be specified.

When a HCF contracts out the sterilization of reusable medical devices, it is the HCF's responsibility for validation and release of the sterilized product.

4.3 Product realization

4.3.1 Procedures for purchasing shall be specified. These procedures shall comply with the applicable clauses of ISO 13485.

4.3.2 Procedures for identification and traceability of product shall be specified. These procedures shall comply with the applicable clauses of ISO 13485.

4.3.3 A system complying with the applicable clause(s) of ISO 13485 or ISO 10012 shall be specified for the calibration of all equipment, including instrumentation for test purposes, used in meeting the requirements of this International Standard.

4.4 Measurement, analysis and improvement — Control of nonconforming product

Procedures for control of product designated as nonconforming and for correction, corrective action, and preventive action shall be specified. These procedures shall comply with the applicable clauses of ISO 13485.

5 Sterilizing agent characterization

5.1 General

The purpose of this activity is to define the sterilizing agent, demonstrate its microbicidal effectiveness, identify the factors that influence microbicidal effectiveness, assess the effects that exposure to the sterilizing agent has on materials, and identify requirements for safety of personnel and protection of the environment. This activity may be undertaken in a test or prototype system. Where this occurs, the final equipment specification (see 6.3) shall be relatable to the results of experimental studies undertaken in the test or prototype equipment. For the purposes of this International Standard, the sterilizing agent is EO.

5.2 Sterilizing agent

The sterilizing agent specification shall include, if appropriate, conditions of storage to maintain the EO within its specification for the duration of the stated shelf life.

5.3 Microbicidal effectiveness

Microbicidal effectiveness data shall be developed if it is proposed to use the EO outside of the range of compositions that are widely recognized or if a novel diluent is to be used.

NOTE The inactivation of microorganisms by EO has been comprehensively documented in literature. This literature provides knowledge of the manner in which the process variables affect microbial inactivation. Reference to these general studies on microbial inactivation is not required by this International Standard.

5.4 Material effects

The effects of EO on a wide variety of materials used to manufacture medical devices have been comprehensively documented, and such documentation is of value to those designing and developing medical devices that are to be sterilized by EO. This International Standard does not require the performance of specific studies on material effects but does require performance of studies of the effects of EO on product (see Clause 7).

5.5 Safety and the environment

5.5.1 Either a material safety data sheet (MSDS) or analogous safety information shall be made available for EO and its diluents (if any). Measures necessary to protect the health and safety of personnel shall be identified.

5.5.2 The potential effect on the environment of the operation of the sterilization process shall be assessed, and measures to protect the environment shall be identified. This assessment, including potential impact and measures for control, shall be documented.

5.5.3 Users of EO shall comply with applicable local, national, and international requirements regarding the emission and disposal of EO and its diluents, as well as any by-products.

6 Process and equipment characterization

6.1 General

6.1.1 The purpose of this activity is to define the entire sterilization process and the equipment necessary to deliver the sterilization process safely and reproducibly.

6.1.2 If an existing process has been used to sterilize product, this activity is not required; however, the process and equipment should be reviewed to ensure the identified variables in 6.2 and 6.3 have been included in the process specification for routine production.

6.2 Process characterization

6.2.1 Process characterization, at a minimum, shall include:

- a) identifying the phases that are necessary for an EO sterilization process;
- b) identifying the process variables for each phase; and
- c) documenting the process variables.

NOTE The data developed in product definition (see Clause 7) can impact the characterization of the sterilization process.

6.2.2 The phases of the sterilization process include:

- a) preconditioning (if used);
- b) the sterilization cycle; and
- c) aeration (if used).

6.2.3 The process variables for preconditioning (if used) include at a minimum:

- a) time;
- b) temperature;
- c) humidity; and
- d) transfer time.

6.2.4 The process variables for the sterilization cycle include:

- a) exposure time;
- b) temperature;
- c) humidity;
- d) EO concentration; and
- e) pressure.

6.2.5 The process variables for aeration (if used) include at a minimum:

- a) time; and
- b) temperature.