

Technical Information Report

AAMI TIR16: 2009/(R)2013

Microbiological aspects of
ethylene oxide sterilization

Microbiological aspects of ethylene oxide sterilization

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Association for the Advancement of Medical Instrumentation

Abstract: Addresses various microbiological aspects of the development and validation of an ethylene oxide sterilization process. Does not address the various factors that can have an effect on the bioburden of the product and on the sterilization process. Provides additional guidance to ANSI/AAMI/ISO 11135-1:2007 and ANSI/AAMI/ISO TIR11135-2:2008 for medical device manufacturers, including those that use contract sterilization facilities or contract sterilization operations.

Keywords: sterilization, microbiological aspects, validation, ethylene oxide, bioburden, performance qualification

AAMI Technical Information Report

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Comments on this technical information report are invited and should be sent to AAMI, Attn: Standards Department, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

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Contents

	Page
Glossary of equivalent standards	v
Committee representation	vii
Foreword	x
1 Scope	1
2 Terms and definitions	1
3 Process and equipment characterization	1
3.1 Sterilization equipment	1
3.2 Process characterization — Physical parameters	1
3.2.1 Introduction	1
3.2.2 EO concentration	1
3.2.3 Relative humidity	2
3.2.4 Temperature	2
3.2.5 EO exposure time	2
4 Process definition	3
4.1 Considerations for process definition	3
4.1.1 Ethylene oxide exposure parameters	3
4.1.2 Product packaging	3
4.1.3 Process development method	3
4.1.4 Sampling considerations for process development studies	3
4.1.5 Methods for microbial enumeration and fraction negative studies in a pilot or a production chamber	4
4.1.5.1 Enumeration or fraction negative study approaches	4
4.1.5.2 Establishing relationship between pilot chamber and production	5
4.1.5.3 Parameter	5
4.2 Methods for process definition	6
4.2.1 Methods for estimating cycle lethality	6
4.2.1.1 Direct enumeration	6
4.2.1.2 Fraction-negative method	6
4.2.2 Biological indicator/bioburden approach	7
4.2.3 Overkill methods	8
4.2.3.1 Half-cycle method	8
4.2.3.2 Cycle calculation approach	9
4.2.4 Other approaches—Absolute bioburden method of cycle development	10
4.2.4.1 Bioburden isolates approach	10
4.2.4.2 Product sample approach	10
4.3 Sterilization process definition troubleshooting	11
4.3.1 Obtaining all positives	11
4.3.1.1 Methods to obtain all positives with a new process	11
4.3.1.2 Methods to obtain all positives in an existing cycle	11
4.3.2 Obtaining a linear slope in the lethality curve	11
4.3.3 Obtaining all negatives	11
4.4 Process challenge devices	12
4.4.1 Types of PCDs	12
4.4.1.1 Internal PCDs (IPCDs)	12
4.4.1.2 External PCDs (EPCDs)	12
4.4.2 Appropriateness of the PCD	13
4.4.3 Examples of PCDs	13
4.4.3.1 Examples of internal PCDs	13
4.4.3.2 Examples of external PCDs that have been used throughout the industry	13
4.4.3.3 PCDs for product families	13
5 Validation	14
5.1 Microbiological performance qualification (MPQ)	14
5.1.1 General considerations	14
5.1.2 Validation cycle selection criteria	14

5.1.3	Placement and handling of PCDs, test samples, and sensors	14
5.1.3.1	General.....	14
5.1.3.2	Cycle monitoring equipment	14
5.1.3.3	Product handling, shipping, and testing.....	15
5.2	Sterilization loads—general considerations	15
5.2.1	Packaging	15
5.2.2	Full and partial loads	16
5.2.3	Mixed loads	16
5.2.4	Reuse of loads	16
5.3	Simulation of anticipated process conditions	16
5.4	Release of validation loads	16
5.5	Release of small batches or lots	17
6	Maintaining process effectiveness	17
6.1	Failure investigation	17
6.1.1	Sterilization process or equipment issues	17
6.1.1.1	Potential process differences.....	17
6.1.1.2	Potential equipment differences	18
6.1.1.3	Potential process utility differences	18
6.1.2	Product issues.....	18
6.1.2.1	Product design or materials.....	18
6.1.2.2	Product bioburden	18
6.1.3	Microbiological testing issues.....	18
6.1.3.1	Test laboratory.....	18
6.1.3.2	Biological Indicators (BIs)	18
6.2	Requalification	19
	Bibliography	20

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 Technical Corrigendum 1 and 2	ANSI/AAMI ES60601-1:2005 ANSI/AAMI ES60601-1:2005/C1:2009 (amdt)	Major technical variations C1 Identical to Corrigendum 1 & 2
IEC 60601-1-2:2007	ANSI/AAMI/IEC 60601-1-2:2007	Identical
IEC 60601-2-2:2009	ANSI/AAMI/IEC 60601-2-2:2009	Identical
IEC 60601-2-4:2002	ANSI/AAMI DF80:2003	Major technical variations
IEC 60601-2-19:2009	ANSI/AAMI/IEC 60601-2-19:2009	Identical
IEC 60601-2-20:2009	ANSI/AAMI/IEC 60601-2-20:2009	Identical
IEC 60601-2-21:2009	ANSI/AAMI/IEC 60601-2-21:2009	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:2004/(R)2009	Major technical variations
IEC 60601-2-47:2001	ANSI/AAMI EC38:2007	Major technical variations
IEC 60601-2-50:2009	ANSI/AAMI/IEC 60601-2-50:2009	Identical
IEC 80601-2-30:2009 and Technical Corrigendum 1	ANSI/AAMI/IEC 80601-2-30:2009 and ANSI/AAMI/IEC 80601-2-30:2009/ C1:2009 (amdt) – consolidated text	Identical (with inclusion) C1 Identical to Corrigendum 1
IEC 80601-2-58:2008	ANSI/AAMI/IEC 80601-2-58:2008	Identical
IEC/TR 60878:2009	ANSI/AAMI/IEC TIR60878:2003	Identical
IEC/TR 62296:2009	ANSI/AAMI/IEC TIR62296:2009	Identical
IEC 62304:2006	ANSI/AAMI/IEC 62304:2006	Identical
IEC/TR 62348:2006	ANSI/AAMI/IEC TIR62348:2006	Identical
IEC/TR 62354:2009	ANSI/AAMI/IEC TIR62354:2009	Identical
IEC/TR 80002-1:2009	ANSI/IEC/TR 80002-1:2009	Identical
ISO 5840:2005	ANSI/AAMI/ISO 5840:2005	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001/(R)2004	Identical
ISO 7199:2009	ANSI/AAMI/ISO 7199:2009	Identical
ISO 8637:2004	ANSI/AAMI RD16:2007	Major technical variations
ISO 8638:2004	ANSI/AAMI RD17:2007	Major technical variations
ISO 10993-1:2009	ANSI/AAMI/ISO 10993-1:2009	Identical
ISO 10993-2:2006	ANSI/AAMI/ISO 10993-2:2006	Identical
ISO 10993-3:2003	ANSI/AAMI/ISO 10993-3:2003/(R)2009	Identical
ISO 10993-4:2002 and Amendment 1:2006	ANSI/AAMI/ISO 10993-4:2002/(R)2009 and Amendment 1:2006/(R)2009	Identical
ISO 10993-5:2009	ANSI/AAMI/ISO 10993-5:2009	Identical
ISO 10993-6:2007	ANSI/AAMI/ISO 10993-6:2007	Identical
ISO 10993-7:2008	ANSI/AAMI/ISO 10993-7:2008	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/(R)2008 ANSI/AAMI BE78:2002/A1:2006/(R)2008	Minor technical variations Identical
ISO 10993-11:2006	ANSI/AAMI/ISO 10993-11:2006	Identical
ISO 10993-12:2007	ANSI/AAMI/ISO 10993-12:2007	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)2009	Identical
ISO 10993-17:2002	ANSI/AAMI/ISO 10993-17:2002/(R)2008	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

International designation	U.S. designation	Equivalency
ISO 11135-1:2007	ANSI/AAMI/ISO 11135-1:2007	Identical
ISO/TS 11135-2:2008	ANSI/AAMI/ISO TIR11135-2:2008	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 11737-2:2009	ANSI/AAMI/ISO 11737-2:2009	Identical
ISO 13408-1:2008	ANSI/AAMI/ISO 13408-1:2008	Identical
ISO 13408-2:2003	ANSI/AAMI/ISO 13408-2:2003	Identical
ISO 13408-3:2006	ANSI/AAMI/ISO 13408-3:2006	Identical
ISO 13408-4:2005	ANSI/AAMI/ISO 13408-4:2005	Identical
ISO 13408-5:2006	ANSI/AAMI/ISO 13408-5:2006	Identical
ISO 13408-6:2006	ANSI/AAMI/ISO 13408-6:2006	Identical
ISO 13485:2003	ANSI/AAMI/ISO 13485:2003/(R)2009	Identical
ISO 14155-1:2003	ANSI/AAMI/ISO 14155-1:2003/(R)2008	Identical
ISO 14155-2:2003	ANSI/AAMI/ISO 14155-2:2003/(R)2008	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998/(R)2008	Identical
ISO 14161:2009	ANSI/AAMI/ISO 14161:2009	Identical
ISO 14708-3:2008	ANSI/AAMI/ISO 14708-3:2008	Identical
ISO 14708-4:2008	ANSI/AAMI/ISO 14708-4:2008	Identical
ISO 14937:2009	ANSI/AAMI/ISO 14937:2009	Identical
ISO/TR 14969:2004	ANSI/AAMI/ISO TIR14969:2004	Identical
ISO 14971:2007	ANSI/AAMI/ISO 14971:2007	Identical
ISO 15223-1:2007 and A1:2008	ANSI/AAMI/ISO 15223-1:2007 and A1:2008	Identical
ISO 15225:2000 and A1:2004	ANSI/AAMI/ISO 15225:2000/(R)2006 and A1:2004/(R)2006	Identical
ISO 15674:2009	ANSI/AAMI/ISO 15674:2009	Identical
ISO 15675:2009	ANSI/AAMI/ISO 15675:2009	Identical
ISO 15882:2008	ANSI/AAMI/ISO 15882:2008	Identical
ISO 15883-1:2006	ANSI/AAMI ST15883-1:2009	Major technical variations
ISO/TR 16142:2006	ANSI/AAMI/ISO TIR16142:2005	Identical
ISO 17664:2004	ANSI/AAMI ST81:2004	Major technical variations
ISO 17665-1:2006	ANSI/AAMI/ISO 17665-1:2006	Identical (with inclusions)
ISO/TS 17665-2:2009	ANSI/AAMI/ISO TIR17665-2:2009	Identical
ISO 18472:2006	ANSI/AAMI/ISO 18472:2006	Identical
ISO/TS 19218:2005	ANSI/AAMI/ISO 19218:2005	Identical
ISO 22442-1:2007	ANSI/AAMI/ISO 22442-1:2007	Identical
ISO 22442-2:2007	ANSI/AAMI/ISO 22442-2:2007	Identical
ISO 22442-3:2007	ANSI/AAMI/ISO 22442-3:2007	Identical
ISO 25539-1:2003 and A1:2005	ANSI/AAMI/ISO 25539-1:2003/(R)2009 and A1:2005/(R)2009	Identical
ISO 25539-2:2008	ANSI/AAMI/ISO 25539-2:2008	Identical
ISO 81060-1:2007	ANSI/AAMI/ISO 81060-1:2007	Identical
ISO 81060-2:2009	ANSI/AAMI/ISO 81060-2:2009	Identical

Committee representation

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

This technical information report (TIR) was developed by the Association for the Advancement of Medical Instrumentation (AAMI) Industrial Ethylene Oxide Sterilization Working Group under the auspices of the AAMI Sterilization Standards Committee. Working Group approval of the TIR does not necessarily imply that all committee members voted for its approval.

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

<i>Cochairs</i>	Charles Cogdill, Boston Scientific Corporation Gerry A. O'Dell, MS, Gerry O'Dell Consulting
<i>Members</i>	Anne F. Booth, MS, Conmed Corp Lloyd Brown, Covidien Tim Carlson, Becton Dickinson & Company Bradley J. Catalone, PhD, Olympus America Inc. Dennis E. Christensen, BS, Process Challenge Devices LLC Charlie Christianson, St Jude Medical Inc. Charles Cogdill, Boston Scientific Corporation Gary N. Cranston, Consulting & Technical Services/PCS Elaine Daniell, CR Bard Douglas D. Davie, Sterilization Validation Services Darci Diage, Direct Flow Medical Inc. Shawn A. Doyle, Sterilator Company Inc. William F. FitzGerald, PE, FitzGerald & Associates Ltd Dan B. Floyd, RM, Nelson Laboratories Inc. Zory R. Glaser, PhD MPH CSPDM, Independent Expert Arthur C. Harris, Cook Inc. Deborah A. Havlik, Hospira Worldwide Inc. Danny Hutson, Cardinal Health (MP&S) Jim Kaiser, Bausch & Lomb Inc. Bert Kingsbury, Terumo Medical Corporation Carolyn L. Kinsley, LexaMed Karen A. Kowalczyk, Centurion Sterilization Services Christine Loshbaugh, Edwards LifeSciences Ted May, Andersen Products Inc. David Ford McGoldrick, BS, Abbott Laboratories Craig A. Meadows, Medtronic Inc. Joseph M. Mello, Ethide Laboratories Inc. Russell D. Mills, Zimmer Inc. Gary Mitchel, PE, Johnson & Johnson Sarah A. Mowitt, Independent Expert Gerry A. O'Dell, MS, Gerry O'Dell Consulting Ken Paddock, Baxter Healthcare Corporation Dave Parente, NAMSA Manuel Saavedra, Jr., Kimberly-Clark Corporation Zenius V. Seliokas, Stericon Inc. Jon Seulean, CaridianBCT Sterilization Services Inc. Barb Smith, Getinge USA Bill South, Steris Corporation Ralph Stick, WuXi AppTec Radhakrishna S. Tirumalai, US Pharmacopeia Convention Inc. Steven E. Turtill, FDA/CDRH Jason Voisinet, Ethox International Inc. Craig A. Wallace, 3M Healthcare P. Richard Warburton, ChemDAQ Inc. Richard L. Weisman, Fresenius Medical Care Renal Therapies Group Casimir John Woss, PhD, Alcon Laboratories Inc.

Stephen C. Yeadon, BS, Kinetic Concepts Inc.
William T. Young, Sterigenics International

Alternates Jennifer R. Asleson, Becton Dickinson & Company
August Baur, Centurion Sterilization Services
John Broad, NAMSA
Delores Bruce, Steris Corporation
Trabue D. Bryans, WuXi AppTec
Susan Bullis, Johnson & Johnson
Kate Davenport, Baxter Healthcare Corporation
John DiCaro, Covidien
Brian R. Drumheller, CR Bard
Joseph R. Durbin, Hospira Worldwide Inc.
Mark Fischer, Nelson Laboratories Inc.
David Michael Gasparik, Cardinal Health (MP&S)
Thomas L. Hansen, Terumo Medical Corporation
Donna Horner, Abbott Laboratories
Brent Huberty, St Jude Medical Inc.
Ezra Koski, A, CaridianBCT Sterilization Services Inc.
John M. Kuchinski, FDA/CDRH
James P. Kulla, BS MS, LexaMed
Richard Lenz, Medtronic Inc.
John Lindley, Andersen Products Inc.
Ralph Makinen, Boston Scientific Corporation
Jeff Martin, Alcon Laboratories Inc.
Janette Martinez, BS, Edwards LifeSciences
Michael E. Mattison, Getinge USA
Michael A. Padilla, BSME, Sterigenics International
Frank Peacock, Jr., Bausch & Lomb Inc.
Jeff Peltier, Boston Scientific Corporation
Nancy Rakiewicz, Ethox International Inc.
Tyrone S. Rouse, Kimberly-Clark Corporation
Matthew Russell, Cook Inc.
David Silor, Zimmer Inc.
Larry Talapa, 3M Healthcare

AAMI also acknowledges the **Task Group**, comprised of the following members, for its special contribution in the development of this document:

Task Group Leader Craig Wallace, 3M Healthcare

Task Group Members Lloyd Brown, Covidien
Delores Bruce, Steris Corporation
Deborah Havlik, Hospira Worldwide, Inc.
Carolyn Kinsley, LexaMed
Tyrone Rouse, Kimberly-Clark Corporation
Casimir Woss, Alcon Laboratories Inc.

At the time this document was published, the **AAMI Sterilization Standards Committee** had the following members:

Cochairs Victoria M. Hitchins, PhD, FDA/CDRH
William E. Young, Boston Scientific Corporation

Members Trabue D. Bryans, WuXi AppTec
Peter A. Burke, PhD, Steris Corporation
Nancy Chobin, RN CSPDM, Independent Expert
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
Joel R. Gorski, PhD, NAMSA

Deborah A. Havlik, Hospira Worldwide Inc.
Victoria M. Hitchins, PhD, FDA/CDRH
Danny Hutson, Cardinal Health (MP&S)
Lois Atkinson Jones, MS, Independent Expert
Susan G. Klacik, CCSMC FCS ACE, IAHCSSM
Byron J. Lambert, PhD, Abbott Laboratories
Colleen Patricia Landers, RN, Canadian Standards Association
Lisa N. Macdonald, Becton Dickinson & Company
Jeff Martin, Alcon Laboratories Inc.
Patrick J. McCormick, PhD, Bausch & Lomb Inc.
Rainer Newman, Johnson & Johnson
Janet M. Prust, 3M Healthcare
Nancy Rakiewicz, Ethox International Inc.
Michael H. Scholla, Dupont Nonwovens
Mark Seybold, Baxter Healthcare Corporation
Andrew Sharavara, PhD, Propper Manufacturing Co Inc.
Mark N. Smith, Getinge USA
William N. Thompson, Covidien
James L. Whitby, MA MB FRCP, Independent Expert
Martell Kress Winters, BS SM, Nelson Laboratories Inc.

Alternates

Lloyd Brown, Covidien
Glenn W. Calvert, Becton Dickinson & Company
Dave Dion, Cardinal Health (MP&S)
Steven J. Elliott, WuXi AppTec
Thomas J. Frazar, Johnson & Johnson
Kathy Hoffman, Sterigenics International
Jim Kaiser, Bausch & Lomb Inc.
Joseph J. Lasich, BS, Alcon Laboratories Inc.
Chiu S. Lin, PhD, FDA/CDRH
Natalie Lind, IAHCSSM
Ralph Makinen, Boston Scientific Corporation
Mary S. Mayo, CR Bard
David Ford McGoldrick, BS, Abbott Laboratories
Jerry R. Nelson, PhD, Nelson Laboratories Inc.
Karen Polkinghorne, Dupont Nonwovens
Mike Sadowski, Baxter Healthcare Corporation
John R. Scoville, Jr., Steris Corporation
Jason Voisinet, Ethox International Inc.
Craig A. Wallace, 3M Healthcare
Valerie Welter, Hospira Worldwide Inc.
William E. Young, Boston Scientific Corporation

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

Foreword

This document is part of a series of technical information reports (TIRs) intended for use in conjunction with ANSI/AAMI/ISO 11135-1:2009. The other reports in the series are listed below:

- AAMI TIR14:2009, *Contract sterilization using ethylene oxide*;
- AAMI TIR15:2009, *Physical aspects of ethylene oxide sterilization*;
- AAMI TIR28:2009, *Product adoption and process equivalence for ethylene oxide sterilization*; and
- ANSI/AAMI/ISO TIR11135-2:2008, *Sterilization of health care products—Ethylene oxide—Part 2: Guidance on the application of ANSI/AAMI/ISO 11135-1*.

The original TIR16, along with other AAMI TIRs, provided additional guidance to the 1994 edition of the industrial EO sterilization standard 11135, which was revised in 2007 under a new designation, ANSI/AAMI/ISO 11135-1:2007, *Sterilization of health care products—Ethylene oxide—Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*. In 2008, ISO published its own guidance document for the 11135 standard, ISO/TR 11135-2:2008, *Sterilization of health care products—Ethylene oxide—Part 2: Guidance on the application of ISO 11135-1*, which was based to a great extent on the earlier AAMI technical information reports. Correspondingly, the AAMI Industrial EO sterilization working group is updating its TIRs to take into account changes to the 11135 standard as well as to avoid redundancy with ANSI/AAMI/ISO TIR11135-2:2008.

This TIR provides guidance related to the microbiological aspects of EO sterilization that is typically not covered in depth, or at all, in the existing guidance documents for EO sterilization. It is designed to provide information that will assist in design, qualification, and routine processing of EO sterilization processes. This TIR condenses pertinent information that may be available in a variety of sources in one location and is based on practices that have been found to be used successfully within the United States. This TIR contains guidelines that are not intended to be absolute or to apply in all circumstances. One should use judgment in applying the information in this TIR.

As used within the context of this document, “should” indicates that among several possibilities one is recommended as particularly suitable without mentioning or excluding others, or 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 should be avoided but not prohibited. “May” is used to indicate that a course of action is permissible within the limits of the TIR. “Can” is used as a statement of possibility and capability. “Must” is used only to describe “unavoidable” situations, including those mandated by government regulations. See also the NOTE on Page 1.

Suggestions for improving this technical information report are invited. Comments and suggested revisions should be sent to AAMI, 4301 Fairfax Drive, Suite 301, Arlington, VA 22203.

NOTE—This foreword does not contain provisions of AAMI TIR16:2009, *Microbiological aspects of ethylene oxide sterilization*, but it does provide important information about the development and intended use of the document.

Microbiological aspects of ethylene oxide sterilization

NOTE—This technical information report is not a standard, and the material contained herein is not normative in nature. The committee has used the term "shall" in a few instances, based on their knowledge of requirements contained in relevant standards and regulatory requirements.

1 Scope

This technical information report (TIR) addresses various microbiological aspects of the development and validation of an ethylene oxide (EO) sterilization process. It does not cover the various factors that can have an effect on the bioburden of the product and on the sterilization process. This TIR provides additional guidance to ANSI/AAMI/ISO 11135-1:2007 and ANSI/AAMI/ISO TIR11135-2:2008 for medical device manufacturers, including those that use contract sterilization facilities or contract sterilization operations.

Although the information presented was developed for application to medical devices, the content of this guideline may also be applied to other relevant products or materials.

2 Terms and definitions

For the purposes of this TIR, the terms and definitions in ANSI/AAMI/ISO 11135–1 and ANSI/AAMI/ISO TIR11135–2 and the following apply.

- 2.1 **compromised tissue:** Skin or mucous membrane that has been intentionally or accidentally opened, exposed, or breached.
- 2.2 **inoculated carrier:** Supporting material on or in which a defined number of test organisms has been deposited.

3 Process and equipment characterization

3.1 Sterilization equipment

Guidelines for equipment selection can be found in AAMI TIR15:2009 and EN 1422. Careful selection of the sterilizing equipment and development of the facility design will enable a manufacturer to process a product safely and effectively.

3.2 Process characterization — Physical parameters

3.2.1 Introduction

The variables that have a significant effect on the lethality of an ethylene oxide (EO) sterilization process are ethylene oxide (EO) concentration, relative humidity (RH), temperature, and EO exposure time.

EO concentration and RH may be calculated as prescribed in AAMI TIR15:2009, or they may be directly measured. It is recommended that evacuation and injection rates be established to define their effect on the cycle lethality throughout the program. The use of controlled evacuation and injection rates minimizes the potential for package and product damage. These rates should be incorporated in the final process specifications as appropriate for chamber parameters. It is also important to remember that the actual depth and rate of evacuations might be different for the air-removal versus the sterilant-removal phases, because the product and packaging have been exposed to increased temperature, humidity, and sterilant levels prior to the sterilant-removal phase.

3.2.2 EO concentration

Common practice is to develop and validate cycles using an EO concentration ranging from 400 to 650 milligrams per liter (mg/L), because concentrations in this range have been found to achieve microbiological lethality for most products within a reasonable and practical exposure time. When lower EO concentrations are necessary due to product or process considerations, the exposure time may need to be increased to achieve the same lethality; however, the time increase may be mitigated if the temperature of the process can be increased sufficiently.