Technical Information Report

AAMI TIR56: 2013/(R)2024

Guidance for the development, validation and routine control of an ethylene oxide sterilization process utilizing flexible bag systems for the sterilization of medical devices

AAMI

Advancing Safety in Health Technology

Guidance for the development, validation and routine control of an ethylene oxide sterilization process utilizing flexible bag systems for the sterilization of medical devices

Approved 27 December 2013 and reaffirmed 18 October 2016 and 11 September 2020 and 26 March 2024 by **AAMI**

Abstract: This AAMI Technical Information Report (TIR) provides information to be considered during the development, validation, and routine control of EO sterilization processes that are performed using gas diffusion within individually sealed flexible sterilization bags.

Keywords: sterilization, flexible bag systems, diffusion, EO, ethylene oxide

AAMI Technical Information Report

A technical information report (TIR) is a publication of the Association for the Advancement of Medical Instrumentation (AAMI) Standards Board that addresses a particular aspect of medical technology.

Although the material presented in a TIR may need further evaluation by experts, releasing the information is valuable because the industry and the professions have an immediate need for it.

A TIR differs markedly from a standard or recommended practice, and readers should understand the differences between these documents.

Standards and recommended practices are subject to a formal process of committee approval, public review, and resolution of all comments. This process of consensus is supervised by the AAMI Standards Board and in the case of American National Standards by the American National Standards Institute.

A TIR is not subject to the same formal approval process as a standard. However, a TIR is approved for distribution by a technical committee and the AAMI Standards Board.

Another difference is that, although both standards and TIRs are periodically reviewed, a standard must be acted on—reaffirmed, revised, or withdrawn—and the action formally approved usually every five years but at least every 10 years. For a TIR, AAMI consults with a technical committee about five years after the publication date (and periodically thereafter) for guidance on whether the document is still useful—that is, to check that the information is relevant or of historical value. If the information is not useful, the TIR is removed from circulation.

A TIR may be developed because it is more responsive to underlying safety or performance issues than a standard or recommended practice, or because achieving consensus is extremely difficult or unlikely. Unlike a standard, a TIR permits the inclusion of differing viewpoints on technical issues.

CAUTION NOTICE: This AAMI TIR may be revised or withdrawn at any time. Because it addresses a rapidly evolving field or technology, readers are cautioned to ensure that they have also considered information that may be more recent than this document.

All 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.

Comments on this technical information report are invited and should be sent to AAMI, Attn: Standards Department, 901 N. Glebe Road, Suite 300, Arlington, VA 22203.

Published by

AAMI
901 N. Glebe Road, Suite 300
Arlington, VA 22203
www.aami.org

© 2014 by the Association for the Advancement of Medical Instrumentation

All Rights Reserved

Publication, reproduction, photocopying, storage, or transmission, electronically or otherwise, of all or any part of this document without the prior written permission of the Association for the Advancement of Medical Instrumentation is strictly prohibited by law. 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 the Copyright Clearance Center.

Printed in the United States of America

ISBN 978-1-57020-519-4

Contents

Page

Glossary of equivalent standards v

Committee representation vi

Foreword x

Introduction xi

1 Scope 1

2 Terms and definitions 1

3 Process descriptions 3
3.1 Type 1 - Gas injection systems 3
3.2 Type 2 – EO cartridge based systems utilizing permeable flexible sterilization bags 4
3.3 Type 3 - EO cartridge based systems utilizing effectively impermeable flexible sterilization bags 5

4 Quality management systems 6

5 Sterilizing agent characterization 6
5.1 General 6
5.2 Sterilizing agent 6
5.3 Microbicidal effectiveness 6
5.4 Material effects 6
5.5 Safety and the environment 6

6 Process and Equipment Characterization 7
6.1 Process characterization 7
6.2 Equipment characterization 8

7 Product definition 9

8 Process definition 12

9 Validation 13
9.1 Installation qualification 13
9.2 Operational qualification 13
9.3 Performance qualification 15
9.4 Varying load configurations 17
9.5 Review and approval of validation 17

10 Routine Monitoring and Control 19

11 Product Release from Sterilization 20

12 Maintaining Process Effectiveness 20
12.1 General 20
12.2 Calibration 20
12.3 Maintenance of equipment 20
12.4 Requalification 21
12.5 Assessment of change 21
12.6 Assessment of equivalence 22

Annexes

A Microbial Validation Using an Augmented Overkill Approach 24

B Microbial Validation Using Reduced EO Concentration 26

Bibliography 27

Tables and Figures

Table 1 — Flexible bag sterilization system types 3

Figure 1 — Sample PCD styles (A & B) 23

Figure 2 — How the overkill or SAL of 10^{-6} is achieved using the internal PCD (BI in EO cartridge) 24

Figure 3 — Comparison of theoretical EO concentration (lethality) profiles for full production cycle and validation cycle using half the production EO concentration. Validation lethality is equal to ½ the exposure and ¼ the lethality obtained during EO injection and removal, based on using the same injection and evacuation rates 25

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

Industrial EO Sterilization Working Group

This Technical Information Report (TIR) was developed by the AAMI Industrial EO 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 EO Sterilization Working Group** had the following members:

Chairs:
Jeff Martin, Alcon Laboratories Inc
Gerry A. O'Dell, MS, Gerry O'Dell Consulting

Members:
Edward Arscott, NAMSA
Anne F. Booth, MS, Booth Scientific Inc
Lloyd Brown, Covidien
Tim Carlson, Becton Dickinson & Company
Dennis E. Christensen, BS, Process Challenge Devices LLC
Gary N. Cranston, Consulting & Technical Services/PCS
Elaine Daniell, CR Bard
Douglas D. Davie, Sterilization Validation Services
Darci Diage, Direct Flow Medical Inc
Mary Ann Drosnock, MS, Olympus America Inc
William F. FitzGerald, PE, FitzGerald & Associates Ltd
Dan B. Floyd, Nelson Laboratories Inc
Sarah Gagnon, Microtest Laboratories Inc
Naomi Gamm, St Jude Medical Inc
Zory R. Glaser, PhD MPH CSPDM, Johns Hopkins University-School of Public Health
Michael Groendyk, Javelin Medical
Thomas Hansen, Terumo Americas Corporate
Douglas F. Harbrecht, Sterility Assurance LLC
Arthur C. Harris, Cook Inc
Deborah A. Havlik, Hospira Worldwide Inc
Jason Hedrick, Medtronic Inc WHQ Campus
Danny Hutson, CareFusion
Nupur Jain, Intuitive Surgical Inc
Jim Kaiser, Bausch & Lomb Inc
David King, Tandem Diabetes Care Inc
Carolyn L. Kinsley, LexaMed Ltd
Mindy Kobus, Mesa Laboratories Biological Indicator Division- Bozeman Facility
Karen A. Kowalczyk, Centurion Sterilization Services
Reynaldo Lopez, Cardinal Health (MP&S)
Christine Loshbaugh, Edwards LifeSciences
Ralph Makinen, Boston Scientific Corporation
Jeff Martin, Alcon Laboratories Inc
Albert E. May, Andersen Products Inc
David Ford McGoldrick, BS, Abbott Laboratories
Russell D. Mills, GE Healthcare
Gary Mitchel, PE, Johnson & Johnson
Sarah A. Mowitt
Dave Parente, Ecolab
Michelle Peterson, Stryker Instruments Division

© 2014 Association for the Advancement of Medical Instrumentation

Nancy Rakiewicz, Moog Medical Devices
Manuel Saavedra, Jr., Kimberly-Clark Corporation
Steven Seamons, WL Gore & Associates Inc
Jon Seulean, Terumo BCT
Mark Seybold, Baxter Healthcare Corporation
Harry L. Shaffer, Sterilization Consulting Services
David Silor, Zimmer Inc
Bill South, Steris Corporation
Michael Sprague, Ethide Laboratories Inc
Sopheak Srun, MPH SM(NRCM), Quality Tech Services Inc
Ralph Stick, WuXi AppTec Inc
Fenil Sutaria, Medline Industries Inc
Radhakrishna S. Tirumalai, US Pharmacopeia Convention Inc
Steven E. Turtil, FDA/CDRH
Craig A. Wallace, 3M Healthcare
P. Richard Warburton, ChemDAQ Inc
Richard L. Weisman, Fresenius Medical Care Renal Therapies Group
Beverly G. Whitaker, CQA RAB MBA, Indigo Consulting Group Inc
William T. Young, Sterigenics International

Alternates:
David E. Barlow, PhD, Olympus America Inc
August Baur, Centurion Sterilization Services
Marjean Boyter, Fresenius Medical Care Renal Therapies Group
Robert H. Bradley, Mesa Laboratories Biological Indicator Division-Bozeman Facility
Carolyn Braithwaite-Nelson, Spectranetics Corporation
Trabue D. Bryans, BryKor LLC
Susan Bullis, Johnson & Johnson
Greg Bush, Alcon Laboratories Inc
Claudia Camp, Stryker Instruments Division
Phil Cogdill, Covidien
Greg Crego, Moog Medical Devices
Jessica Desmond, Microtest Laboratories Inc
John DiCaro, Covidien
Dave Dion, Cardinal Health (MP&S)
David A. Dominguez, CareFusion
Brian R. Drumheller, CR Bard
Steven Elliott, FDA/CDRH
Scott A. Giraud, Medtronic Inc WHQ Campus
William K. Gordon, Steris Corporation
Matthew Hart, Boston Scientific Corporation
Sharon Higgins, GE Healthcare
David M. Hilliker, ChemDAQ Inc
Ezra Koski, A, Terumo BCT
James P. Kulla, BS MS, LexaMed Ltd
Wesley Lantz, Zimmer Inc
John Lindley, Andersen Products Inc
Paul Littley, Nelson Laboratories Inc
Ronald G. Lulich, 3M Healthcare
Jody L. Markling, St Jude Medical Inc
Janette Martinez, BS, Edwards Lifesciences (PR)
Patrick J. McCormick, PhD, Bausch & Lomb Inc
Joseph Mello, Ethide Laboratories Inc
Laurie Nawrocki, NAMSA
Koyejo Obadina, Abbott Laboratories
Mike Padilla, Sterigenics International
Andrew Porteous, Baxter Healthcare Corporation

Tyrone S. Rouse, Kimberly-Clark Corporation
Matthew Russell, Cook Inc
Arnold Shechtman, BS, Medline Industries Inc
Brian Wallace, Intuitive Surgical Inc
Daryl Woodman, Andersen Products Inc
Casimir John Woss, PhD, FitzGerald & Associates Ltd

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

Chairs:
Victoria M. Hitchins, PhD, FDA/CDRH
Michael H. Scholla, PhD, Dupont Protection Technologies

Members:
Christopher Anderson, Boston Scientific Corporation
Trabue D. Bryans, BryKor LLC
Nancy Chobin, RN CSPDM, St Barnabas Healthcare System
Charles Cogdill, Covidien
Ramona Conner, RN MSN CNOR, Association of Perioperative Registered Nurses
Jacqueline Daley, Sinai Hospital of Baltimore
Kimbrell Darnell, CR Bard
Lisa Foster, Medpoint LLC
Joel R. Gorski, PhD, NAMSA
Joyce M. Hansen, Johnson & Johnson
Douglas F. Harbrecht, Sterility Assurance LLC
Deborah A. Havlik, Hospira Worldwide Inc
Susan G. Klacik, CCSMC FCS ACE, IAHCSMM
Byron J. Lambert, PhD, Abbott Laboratories
Colleen Patricia Landers, RN, Timmins & District Hospital
Reynaldo Lopez, Cardinal Health (MP&S)
Jeff Martin, Alcon Laboratories Inc
Patrick J. McCormick, PhD, Bausch & Lomb Inc
Gerald E. McDonnell, PhD, Steris Corporation
Janet M. Prust, 3M Healthcare
Nancy Rakiewicz, Moog Medical Devices
Mark Seybold, Baxter Healthcare Corporation
Andrew Sharavara, PhD, Propper Manufacturing Co Inc
Mark N. Smith, Getinge USA
James Sidney Wiggs, BSN CRCST, Legacy Health System
Martell Kress Winters, BS SM, Nelson Laboratories Inc
William T. Young, Sterigenics International

Alternates:
Lloyd Brown, Covidien
Peter A. Burke, PhD, Steris Corporation
Dave Dion, Cardinal Health (MP&S)
Ken Eddington, NAMSA
Gordon M. Ely, WuXi AppTec Inc
Thomas J. Frazar, Johnson & Johnson
Martha M. Kadas, Sterigenics International
Jim Kaiser, Bausch & Lomb Inc
Natalie Lind, IAHCSMM
Ralph Makinen, Boston Scientific Corporation
Mary S. Mayo, CR Bard
David Ford McGoldrick, BS, Abbott Laboratories

© 2014 Association for the Advancement of Medical Instrumentation

Jerry R. Nelson, PhD, Nelson Laboratories Inc
Patrick Polito, Moog Medical Devices
Karen Polkinghorne, Dupont Protection Technologies
Mike Sadowski, Baxter Healthcare Corporation
Craig A. Wallace, 3M Healthcare

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

Foreword

The processes, methods, and equipment described in this TIR vary significantly from those described in ANSI/AAMI/ISO 11135-1:2007. These differences include but are not limited to the following:

- The body of information provided in ANSI/AAMI/ISO 11135-1:2007 is complemented by supporting documentation found in ANSI/AAMI/ISO 11135-2:2008, as well as a number of related AAMI TIR documents, significant parts of which may not apply to methods and materials that are the subject of this TIR.
- The 11135 series includes 100 % verification of chamber installation and the associated performance qualification (physical and microbiological) of fixed equipment; the methods described in this document rely upon the validation of an integrated, flexible bag/chamber design and a high degree of quality assurance during the manufacturing process of the flexible bag/chamber (and other accessories).
- Methods included in this document identify processes based solely on gas injection by weight, variable, or diminishing (i.e., decreasing by diffusion through the flexible bag) ethylene oxide (EO) concentrations in the atmosphere external to the package but internal to the “flexible bag sterilization systems” per the design of the method.
- Approaches to validation, routine monitoring, and control of cycles may differ significantly from those indicated in 11135.
- For some process designs, the lethality of the process relies completely on storage conditions and time (post introduction of EO) to effectively provide the requisite sterility assurance level. In addition, the lethality provided during the storage period within the sterilization/aeration cabinets may also act simultaneously in providing the aeration method. There are also a number of specialized and novel equipment designs necessary to remove EO from a flexible sterilization bag that vary considerably from the methods described in 11135. New considerations may arise regarding the identification of worst-case aeration processes, as well as subsequent validation.

© 2014 Association for the Advancement of Medical Instrumentation ▪ AAMI TIR56:2013

Introduction

As a result of a revision to ANSI/AAMI/ISO 11135-1, the exclusion in the document stating “This part of ISO 11135 does not cover sterilization by injecting ethylene oxide or mixtures containing ethylene oxide directly into individual product packages,” was revised to state, “This International Standard does not cover sterilization by injecting EO or mixtures containing EO directly into packages **or a flexible chamber**.” The addition of the flexible chamber to the international standard clarified the intent that ANSI/AAMI/ISO 11135 should only be applied to traditional fixed sterilization chambers, and that ANSI/AAMI/ISO 14937:2009/(R)2013 should be used for the requirements and guidance related to these types of EO processes. Ethylene oxide sterilization is a long-standing sterilization process, and EO sterilization within flexible sterilization bags has been used commercially since the 1960s. However, little published information was available to provide guidance on adequately addressing development, validation, and routine control of these EO systems. Therefore, the Industrial EO Sterilization Working Group chose to develop a technical information report (TIR) that addresses these aspects as a prelude to the eventual development of an international standard.

During the development of the TIR, there was strong objection by some to the use of EO sterilization within a flexible sterilization bag; therefore, this document does *not* represent a committee or national consensus. Most of this objection centered around two specific areas of concern. The first objection was the lack of workplace safety information that is provided in this TIR. The decision not to include safety related details within this TIR is consistent with the position that has been taken in other industrial sterilization standards or guidance documents. Information related to the safe use of EO in the workplace is readily available (see https://www.osha.gov/SLTC/ethyleneoxide/) and its use falls under the regulatory auspices of OSHA (29 CFR 1910.1047) (2005). Additional information related to the carcinogenic properties of EO can be found in World Health Organization, 2008.

The second objection was related to the dearth of published information related to EO sterilization in flexible sterilization bags that documented its efficacy or repeatability. The biggest differences between traditional EO sterilization and this non-traditional method are the use of the flexible sterilization bag with a very low concentration of EO and the absence of significant air removal during the process. While there is not significant literature related to this process in particular, there is considerable literature on the efficacy and repeatability of EO sterilization in general, even under conditions that are somewhat similar to those used during EO sterilization in a flexible sterilization bag ([1] and [2]). During the development of this TIR, two articles were published ([5] [6]) that have particular relevance to this process. The expectation is that as the TIR is used, additional information will be made public to further substantiate its efficacy and repeatability, as well as to refine how the processes are developed, validated and routinely controlled.

Guidance for the development, validation, and routine control of an ethylene oxide sterilization process utilizing flexible bag systems for the sterilization of medical devices

1 Scope

This TIR includes information to be considered during the development, validation, and routine control of EO sterilization processes that are performed using gas diffusion within individually sealed flexible sterilization bags.

2 Terms and definitions

2.1
abatement system
device that is attached to the exhaust from the sterilization/aeration cabinet and connected to the outside atmosphere. It is designed to absorb and/or react with the EO gas exhausted from the cabinet and reduce the amount of EO exhausted to the external atmosphere

2.2
aeration cycle
part of the sterilization process, after the sterilization portion of the cycle, during which EO and/or its reaction products dissipate from the device(s)

2.3
chemical integrator
demonstrates that the sterilization parameters over a specified range of sterilization cycles have been met in a specified sterilization wrap, container, cassette, or pouch

2.4
dunnage
material that duplicates the weight, volume, thermal characteristics, EO absorption characteristics, surface geometry and tortuosity, and other critical properties of the devices being tested

2.5
effectively impermeable
term used to describe a bag material that does not allow for diffusion of EO during the sterilization cycle

2.6
EO cartridge
single use, hermetically sealed container that holds a predetermined weight of EO. The EO cartridge is designed to be manually activated through the flexible material of the flexible sterilization bag, releasing 100 % EO

2.7
exposure time
period for which the process parameters (temperature, relative humidity, and EO concentration) are maintained within specified tolerances

© 2014 Association for the Advancement of Medical Instrumentation ▪ AAMI TIR56:2013