American National Standard

ANSI/AAMI ST67:2011

Sterilization of health care products—Requirements and guidance for selecting a sterility assurance level (SAL) for products labeled "sterile"

Association for the Advancement of Medical Instrumentation

Objectives and uses of AAMI standards and recommended practices

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

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

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

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a frame of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards 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 ST67:2011
(Revision of ANSI/AAMI ST67:2003/(R)2008)

Sterilization of health care products—Requirements and guidance for selecting a sterility assurance level (SAL) for products labeled “sterile”

Developed by
Association for the Advancement of Medical Instrumentation

Approved 11 April 2011 by
American National Standards Institute, Inc.

Abstract: This standard establishes requirements and guidance for selection of an appropriate sterility assurance level for terminally sterilized health care products.

Keywords: sterility assurance level (SAL), terminal sterilization

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 N. Fairfax Dr., Suite 301
Arlington, VA 22203-1633
www.aami.org

Printed in the United States of America

ISBN 1–57020–416–0

Contents

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. The code in the US column, "(R)20xx" indicates the year the document was officially reaffirmed by AAMI. E.g., ANSI/AAMI/ISO 10993-4:2002/(R)2009 indicates that 10993-4, originally approved and published in 2002, was reaffirmed without change in 2009.

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 and ANSI/AAMI ES60601-1:2005/A2:2010 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 60601-2-4:2010	ANSI/AAMI/IEC 60601-2-4:2010	Identical
IEC 60601-2-16:2008	ANSI/AAMI/IEC 60601-2-16:2008	Identical
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 60601-2-27:2011	ANSI/AAMI/IEC 60601-2-27:2011	Identical
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 80001-1:2010	ANSI/AAMI/IEC 80001-1:2010	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 62366:2007	ANSI/AAMI/IEC 62366:2007	Identical
IEC/TR 80002-1:2009	ANSI/IEC/TR 80002-1:2009	Identical
ISO 5840:2005	ANSI/AAMI/ISO 5840:2005/(R)2010	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001/(R)2010	Identical
ISO 7199:2009	ANSI/AAMI/ISO 7199:2009	Identical
ISO 8637:2010	ANSI/AAMI/ISO 8637:2010	Identical
ISO 8638:2010	ANSI/AAMI/ISO 8638:2010	Identical
ISO 10993-1:2009	ANSI/AAMI/ISO 10993-1:2009	Identical
ISO 10993-2:2006	ANSI/AAMI/ISO 10993-2:2006/(R)2010	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/(R)2010	Identical
ISO 10993-7:2008	ANSI/AAMI/ISO 10993-7:2008	Identical
ISO 10993-9:2009	ANSI/AAMI/ISO 10993-9:2009	Identical
ISO 10993-10:2010	ANSI/AAMI/ISO 10993-10:2010	Identical
ISO 10993-11:2006	ANSI/AAMI/ISO 10993-11:2006/(R)2010	Identical
ISO 10993-12:2007	ANSI/AAMI/ISO 10993-12:2007	Identical
ISO 10993-13:2010	ANSI/AAMI/ISO 10993-13:2010	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 10993-16:2010	ANSI/AAMI/ISO 10993-16:2010	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
ISO 11135-1:2007	ANSI/AAMI/ISO 11135-1:2007	Identical

International designation	U.S. designation	Equivalency
ISO/TS 11135-2:2008	ANSI/AAMI/ISO TIR11135-2:2008	Identical
ISO 11137-1:2006	ANSI/AAMI/ISO 11137-1:2006/(R)2010	Identical
ISO 11137-2:2006 (2006-08-01 corrected)	ANSI/AAMI/ISO 11137-2:2006	Identical
ISO 11137-3:2006	ANSI/AAMI/ISO 11137-3:2006/(R)2010	Identical
ISO 11138-1:2006	ANSI/AAMI/ISO 11138-1:2006/(R)2010	Identical
ISO 11138-2:2006	ANSI/AAMI/ISO 11138-2:2006/(R)2010	Identical
ISO 11138-3:2006	ANSI/AAMI/ISO 11138-3:2006/(R)2010	Identical
ISO 11138-4:2006	ANSI/AAMI/ISO 11138-4:2006/(R)2010	Identical
ISO 11138-5:2006	ANSI/AAMI/ISO 11138-5:2006/(R)2010	Identical
ISO/TS 11139:2006	ANSI/AAMI/ISO 11139:2006	Identical
ISO 11140-1:2005	ANSI/AAMI/ISO 11140-1:2005/(R)2010	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/(R)2010	Identical
ISO 11607-2:2006	ANSI/AAMI/ISO 11607-2:2006/(R)2010	Identical
ISO 11663:2009	ANSI/AAMI/ISO 11633:2009	Identical
ISO 11737-1:2006	ANSI/AAMI/ISO 11737-1:2006	Identical
ISO 11737-2:2009	ANSI/AAMI/ISO 11737-2:2009	Identical
ISO/TS 12417:2011	ANSI/AAMI/ISO TIR12417:2011	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 13958:2009	ANSI/AAMI/ISO 13958:2009	Identical
ISO 13959:2009	ANSI/AAMI/ISO 13959:2009	Identical
ISO 14155:2011	ANSI/AAMI/ISO 14155:2011	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 14708-5:2010	ANSI/AAMI /ISO 14708-5:2010	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/(R)2010	Identical
ISO 15223-1:2007 and A1:2008	ANSI/AAMI/ISO 15223-1:2007 and A1:2008	Identical
ISO 15223-2:2010	ANSI/AAMI/ISO 15223-2:2010	Identical
ISO 15225:2010	ANSI/AAMI/ISO 15225:2010	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/(R)2010	Identical
ISO/TS 19218:2005	ANSI/AAMI/ISO 19218:2005	Identical
ISO 20857:2010	ANSI/AAMI/ISO 20857:2010	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 23500:2011	ANSI/AAMI/ISO 23500:2011	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 26722:2009	ANSI/AAMI/ISO 26722:2009	Identical
ISO 27186:2010	ANSI/AAMI/ISO 27186:2010	Identical
ISO 80369-1:2010	ANSI/AAMI/ISO 80369-1:2010	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

AAMI Sterility Assurance Level (SAL) Working Group

This standard was developed by the AAMI Sterility Assurance Level (SAL) Working Group under the auspices of the AAMI Sterilization Standards Committee. Approval of this standard does not necessarily mean that all working group members voted for its approval.

At the time this document was published, the **AAMI Sterility Assurance Level (SAL) Working Group** had the following members:

Cochairs:
Trabue D. Bryans, WuXi AppTec Inc.
Victoria M. Hitchins, PhD, FDA/CDRH

Members:
Christopher Anderson, Boston Scientific Corporation
Thomas J. Berger, PhD, Hospira Worldwide Inc.
David J. Brodersen, Covidien
Trabue D. Bryans, WuXi AppTec Inc.
Brian R. Drumheller, CR Bard
Sylvie Dufresne, PhD, TSO3 Inc.
Niki Fidopiastis, Sterigenics International
Naomi Gamm, St Jude Medical Inc.
Zory R. Glaser, PhD MPH CSPDM
Joyce M. Hansen, JM Hansen & Associates
Victoria M. Hitchins, PhD, FDA/CDRH
Robert Dennis Houlsby, Abbott Laboratories
Jim Kaiser, Bausch & Lomb Inc.
Carolyn L. Kinsley, LexaMed
Roland C. Kippenhan, Minntech Corporation
David Liu, Johnson & Johnson
Ronald G. Lulich, 3M Healthcare
Lisa N. Macdonald, Becton Dickinson & Company
Gerald E. McDonnell, PhD, Steris Corporation
Joseph M. Mello, Ethide Laboratories Inc.
Gerry A. O'Dell, MS, Gerry O'Dell Consulting
Dave Parente, NAMSA
Manuel Saavedra, Jr., Kimberly-Clark Corporation
Mark Seybold, Baxter Healthcare Corporation
Ian Shorr, CareFusion
Sopheak Srun, MPH, Quality Tech Services Inc.
Donald Tumminelli, SPS Medical Supply Corp
Jason Voisinet, Moog Medical Devices
Martell Kress Winters, BS SM, Nelson Laboratories Inc.

Alternates:
Diane Battisti, Johnson & Johnson
Nancy Blaszko, Sterigenics International
Kimbrell Darnell, CR Bard
April J. Doering, St Jude Medical Inc.
Steven J. Elliott, WuXi AppTec Inc.
Joel R. Gorski, PhD, NAMSA
John Grillo, PhD, Hospira Worldwide Inc.
Sean Hanley, Boston Scientific Corporation
Katherine E. Hill, 3M Healthcare
John T. Ice, Covidien
Maggie Ladd, BA BS, Kimberly-Clark Corporation
Sharon K. Lappalainen, FDA/CDRH
Chris Lau, LexaMed
Antonio F Lopez, CareFusion
John Masefield, Steris Corporation
Jonathan Karl Olson, MA, Minntech Corporation
Leslie A. Phillips, Bausch & Lomb Inc.
Nancy Rakiewicz, Moog Medical Devices

Mike Sadowski, Baxter Healthcare Corporation
Michael G. Sprague, Ethide Laboratories Inc.
Wendy Wangsgard, PhD, Nelson Laboratories Inc.
Cheryl Work, Becton Dickinson & Company
Christine H. Yunker, Abbott Laboratories

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.

AAMI Sterilization Standards Committee

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

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

Members:
Christopher Anderson, Boston Scientific Corporation
Trabue D. Bryans, WuXi AppTec Inc.
Peter A. Burke, PhD, Steris Corporation
Nancy Chobin, RN CSPDM, St Barnabas Healthcare System
Ramona Conner, RN MSN CNOR, Association of Perioperative Registered Nurses
Jacqueline Daley, Association for Professionals in Infection Control
Kimbrell Darnell, CR Bar
Dave Dion, Cardinal Health (MP&S)
Lisa Foster, Sterigenics Internationa
Joel R. Gorski, PhD, NAMSA
Deborah A. Havlik, Hospira Worldwide Inc.
Victoria M. Hitchins, PhD, FDA/CDRH
Lois Atkinson Jones, MS
Susan G. Klacik, CCSMC FCS ACE, IAHCSMM
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, Moog Medical Devices
Michael H. Scholla, Dupont Protection Technologies
Mark Seybold, Baxter Healthcare Corporation
Andrew Sharavara, PhD, Propper Manufacturing Co Inc.
Mark N. Smith, Getinge USA
William N. Thompson, Covidien
Martell Kress Winters, BS SM, Nelson Laboratories Inc.
William E. Young, (Independent Expert)

Alternates:
Lloyd Brown, Covidien
Glenn W. Calvert, Becton Dickinson & Company
Steven J. Elliott, WuXi AppTec Inc.
Thomas J. Frazar, Johnson & Johnson
Kathy Hoffman, Sterigenics International
Jim Kaiser, Bausch & Lomb Inc.
Natalie Lind, IAHCSMM
Reynaldo Lopez, Cardinal Health (MP&S)
Ralph Makinen, Boston Scientific Corporation
Mary S. Mayo, CR Bard
David Ford McGoldrick, BS, Abbott Laboratories
James B. Neher, MS RAC, NAMSA
Jerry R. Nelson, PhD, Nelson Laboratories Inc.
Karen Polkinghorne, Dupont Protection Technologies
Wallace E. Puckett, PhD, Steris Corporation

Mike Sadowski, Baxter Healthcare Corporation
Jason Voisinet, Moog Medical Devices
Craig A. Wallace, 3M Healthcare
Valerie Welter, Hospira Worldwide Inc.

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 standard was developed by the AAMI Sterility Assurance Level (SAL) Working Group (formerly the Microbiological Quality [SALs] of Processed Medical Devices Working Group) under the auspices of the AAMI Sterilization Standards Committee.

The purpose of this standard is to codify current North American sterilization practices and provide a standardized framework for determining appropriate SALs.

While the 2003 edition of ANSI/AAMI ST67 was very restrictive in what was required for supporting the use of SALs other than 10^{-6}, this updated version allows manufacturers to select an alternate SAL, such as 10^{-5} or 10^{-4}, for those types of products that are sensitive to 10^{-6} sterilization processes. The revised standard requires the use of the most rigorous SAL that the product can withstand, as well as a risk assessment in order to select an alternate SAL. This focus on risk assessment aligns with other regulatory documents.

As used within the context of this standard, “shall” indicates requirements strictly to be followed in order to conform to the standard; “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 is not prohibited; “may” is used to indicate that a course of action is permissible within the limits of the standard; and “can” is used as a statement of possibility and capability. “Must” is used only to describe “unavoidable” situations, including those mandated by government regulation.

AAMI and ANSI procedures require that standards be reviewed every five years and, if necessary, revised to reflect technological advances that may have occurred since publication.

The concepts incorporated in this standard should be considered flexible and dynamic. AAMI policies and procedures require that AAMI standards and recommended practices be reviewed and, if necessary, revised at least once every five years. 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 and suggested revisions should be sent to Technical Programs, AAMI, 4301 N. Fairfax Drive, Suite 301, Arlington, VA 22203-1633.

NOTE—This foreword does not contain provisions of the AAMI standard *Sterilization of medical devices—Requirements for products labeled “sterile”* (ANSI/AAMI ST67:2011), but it does provide important information about the development and intended use of the document.

Introduction

A sterile medical device is one that is free of viable microorganisms. Sterility of a medical device can be achieved through:

a) a terminal sterilization process;

b) sterilization of components, followed by sterile filtration of the final liquid formulation and aseptic filling into sterilized containers; or

c) a combination of chemical/physical sterilization and aseptic processing.

Products produced in accordance with manufacturing quality system requirements for medical devices typically have microorganisms on them before sterilization. Such products are nonsterile. The purpose of sterilization processing is to inactivate the microbiological contaminants and thereby transform the nonsterile products into sterile products.

The inactivation of a pure culture of microorganisms by a sterilizing agent (e.g., dry heat, moist heat, ethylene oxide, or radiation) approximates an exponential rate of kill. Thus, there is always a finite probability that a microorganism might survive, regardless of the extent of treatment applied. For a given extent of treatment, the probability of survival is influenced by the number and resistance of microorganisms and the environment in which the organisms exist during treatment. The sterility of any one product is defined in terms of the probability of a viable microorganism on the product following sterilization. This probability is typically referred to as a sterility assurance level (SAL).

Requirements for quality systems for the design, development, production, supply, installation, and servicing of medical devices are given in the U.S. Food and Drug Administration's (FDA's) Quality System Regulation (21 CFR 820) and the International Organization for Standardization's (ISO's) ISO 13485, adopted in the U.S. by AAMI (current edition ANSI/AAMI/ISO 13485:2003/(R)2009). ANSI/AAMI/ISO 13485 is an application of the ISO 9000 series of quality management system standards. The ISO 9000 series of standards recognizes that there are certain processes used in manufacturing for which the results cannot be fully verified by subsequent inspection and testing of the product. Terminal sterilization, sterile filtration, and aseptic processing are examples of such processes. For this reason, terminal sterilization, sterile filtration, and aseptic processing must be validated before commercial release of product, and these processes must be monitored routinely. The manufacture of a sterile medical device also requires attention to product and package or container characteristics, facilities, controls, and other aspects of a quality system.

The purpose of this standard is to codify current North American sterilization practices and provide a standardized framework for determining appropriate SALs. The following guidance is provided in the annexes:

a) the background and history of sterility assurance,

b) examples of terminally sterilized products and sterility assurance levels that have historically been selected, and

c) risk assessment.

Sterilization of health care products— Requirements and guidance for selecting a sterility assurance level (SAL) for products labeled “sterile”

1 Scope

1.1 Inclusions

This standard specifies requirements and provides guidance for selecting an appropriate SAL for a terminally sterilized health care product that is labeled “sterile.” The requirements and guidance provided in this standard also apply to the selection of an appropriate SAL for a terminally sterilized health care product that is labeled “Sterile Fluid Path.”

1.2 Exclusions

This standard does not address health care products that are not labeled “sterile.” For example, nonsterile health care products that possess antimicrobial properties or contain preservatives for the control of microbial levels are not addressed.

This standard does not address the sterility of aseptically processed products.

2 Normative references

The following normative references contains provisions that, through reference in the text, constitute provisions of this standard. For any dated reference, subsequent amendments to or revisions of the reference do not apply. However, parties to agreements based on this standard are encouraged to investigate the possibility of applying the most recent editions of the normative references indicated below.

U.S. FOOD AND DRUG ADMINISTRATION. Quality system regulation. *Code of Federal Regulations*, Title 21, Part 820.

U.S. FOOD AND DRUG ADMINISTRATION. Human cells, Tissues, and Cellular and Tissue-based products. *Code of Federal Regulations,* Title 21, Part 1271 (Revised April 1, 2010).

3 Definitions

For the purposes of this standard, the following definitions apply.

3.1 bioburden: Population of viable microorganisms on or in the product and/or sterile barrier system.

[ANSI/AAMI/ISO TIR11139:2006, 2.2]

3.2 Combination product: Any product comprised of any combination of a drug and a device; a device and a biological product; a biological product and a drug; or a drug, a device, and a biological product.

3.3 D value, D_{10} value: Time or dose required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions.

[ANSI/AAMI/ISO TIR11139:2006, 2.11]

3.4 medical device: Any instrument, apparatus, appliance, material, or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

— diagnosis, prevention, monitoring, treatment, or alleviation of disease;

— diagnosis, monitoring, treatment, alleviation of, or compensation for an injury or handicap;

— investigation, replacement, or modification of the anatomy or a physiological process; or

— control of conception;

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.

[ANSI/AAMI/ISO TIR11139:2006, 2.24]

NOTE—For purposes of this standard, "medical device" includes *in vitro* diagnostic and combination products that have been determined by the FDA to be medical devices.

3.5 product: Result of a process.

NOTE—For purposes of sterilization standards, product is tangible and can be raw material(s), intermediate(s), subassembly(ies), and health care products.

[ANSI/AAMI/ISO TIR11139:2006, 2.36]

3.6 sterile: Free from viable microorganisms.

[ANSI/AAMI/ISO TIR11139:2006, 2.43]

3.7 sterile fluid path: Interior surfaces of a medical device that come into contact with a fluid during use of the device and are free from viable microorganisms.

3.8 sterility assurance level (SAL): Probability of a single viable microorganism occurring on an item after sterilization.

NOTE—SAL is normally expressed as 10^{-n}. The term SAL has a quantitative value, and 10^{-6} is lower than 10^{-3}.

[ANSI/AAMI/ISO TIR11139:2006, 2.46]

3.9 sterilization: Validated process used to render a product free from viable microorganisms.

NOTE—In a sterilization process, the nature of microbial inactivation is described by an exponential function. Therefore, the presence of a viable microorganism on any individual item can be expressed in terms of probability. While this probability may be reduced to a very low number, it can never be reduced to zero. (cf. sterility assurance level (3.8).)

[ANSI/AAMI/ISO TIR11139:2006, 2.47]

3.10 terminal sterilization: Validated process whereby product within its primary package is sterilized.

4 Determination of an appropriate SAL for a health care product to be labeled "STERILE"

4.1 General

4.1.1 Generally an SAL value of 10^{-6} has been used for terminal sterilization of health care products. An SAL of 10^{-3} has been used for certain health care products, depending on their intended use or their inability to withstand a terminal sterilization process that provides an SAL of 10^{-6} (see Annex A).

4.1.2 A terminally sterilized product with an SAL of greater than 10^{-3}, e.g., 10^{-2}, 10^{-1}, etc., shall not be labeled as sterile.

4.1.3 The choice of a sterilization process and SAL shall be addressed during the development of the product and process design requirements in conformance with a quality system (e.g., see 21 CFR 820.30 Design Controls).

4.1.4 The appropriate validation method shall be selected in order to demonstrate that the sterilization process will routinely achieve the chosen SAL (see 4.2.3).

4.2 Selection of an SAL for a terminal sterilization process

4.2.1 General

For health care products to be terminally sterilized, the SAL shall be selected on the basis of the criteria given in 4.2.2, 4.2.3, and/or 4.2.4 (see Figure 1). If the health care product is intended to come into contact with breached skin or compromised tissue, and an SAL higher than 10^{-6} (e.g. $10^{-5,}$ 10^{-4}) is selected, a risk analysis shall be performed as part of a risk assessment process to support the chosen SAL. See Annex C for guidance on performing a risk analysis.

NOTE—Clause 4.2.4 describes instances in which SALs other than 10^{-6} may be acceptable.

4.2.2 Selection based on intended use of the health care product

NOTE—Examples of products that historically have been terminally sterilized and the SALs that historically have been selected for the products are provided in Annex B.

The SAL selected for a terminally sterilized device is related to the risk of patient infection associated with the intended use of the device:

a) a 10^{-6} SAL shall be used for:

   — products intended to come into contact with breached skin or compromised tissue (i.e., tissue that has lost its natural barrier integrity or is damaged or injured);

   — invasive products that enter normally sterile tissue;

   — products with claims of sterile fluid pathways; and

   — surgically implanted devices.

   NOTE—4.2.4 describes instances in which other SALs may be acceptable.

b) a 10^{-3} SAL, or an SAL providing a greater assurance of sterility (i.e., 10^{-4}, 10^{-5}, etc.), shall be used for:

   — products not intended to come into contact with breached skin or compromised tissue,

   — topical products that contact intact skin or mucous membranes, or

   — products that meet the criteria specified in 4.2.4.

4.2.3 Selection based on sterilization process and/or validation method

NOTE—Examples of products that historically have been terminally sterilized and the SALs that historically have been selected for the products are provided in Annex B.

The extent of treatment with a sterilizing agent that is determined as being required to achieve a particular SAL may be related to the validation method used. For example, in general, a bioburden-based validation method will give a shorter extent of treatment to achieve a particular SAL than a biological indicator–bioburden or "overkill" method. Validation methods for specified sterilization processes are detailed in ANSI/AAMI/ISO 17665-1, ANSI/AAMI/ISO 11135, ANSI/AAMI/ISO 11137, ANSI/AAMI/ISO 14161, ANSI/AAMI/ISO 14937, and ANSI/AAMI ST63.

For those products that require a 10^{-6} SAL and are incapable of withstanding the sterilization process chosen, alternative sterilization processes and/or validation methods should be investigated before selecting an alternative SAL (e.g., 10^{-5}, 10^{-4}, or 10^{-3}) (see also 4.2.4). For example, if the manufacturer has chosen to validate a moist heat sterilization process using an overkill method and the product cannot withstand the process, alternative sterilization processes (e.g., ethylene oxide or radiation) or validation methods (e.g., biological indicator–bioburden or bioburden) should be investigated.

4.2.4 Selection based upon the product's inability to withstand a terminal sterilization process that achieves a 10^{-6} SAL

NOTE—Examples of products that historically have been terminally sterilized and the SALs that historically have been selected for the products are provided in Annex B.

If, based on its intended use, a product would be required to possess a 10^{-6} SAL, but the product is incapable of withstanding the sterilization process, the selection of an SAL other than 10^{-6} may be necessary. A risk assessment may be used as an indication of risk and as a rationale for selecting a different SAL when the following conditions apply:

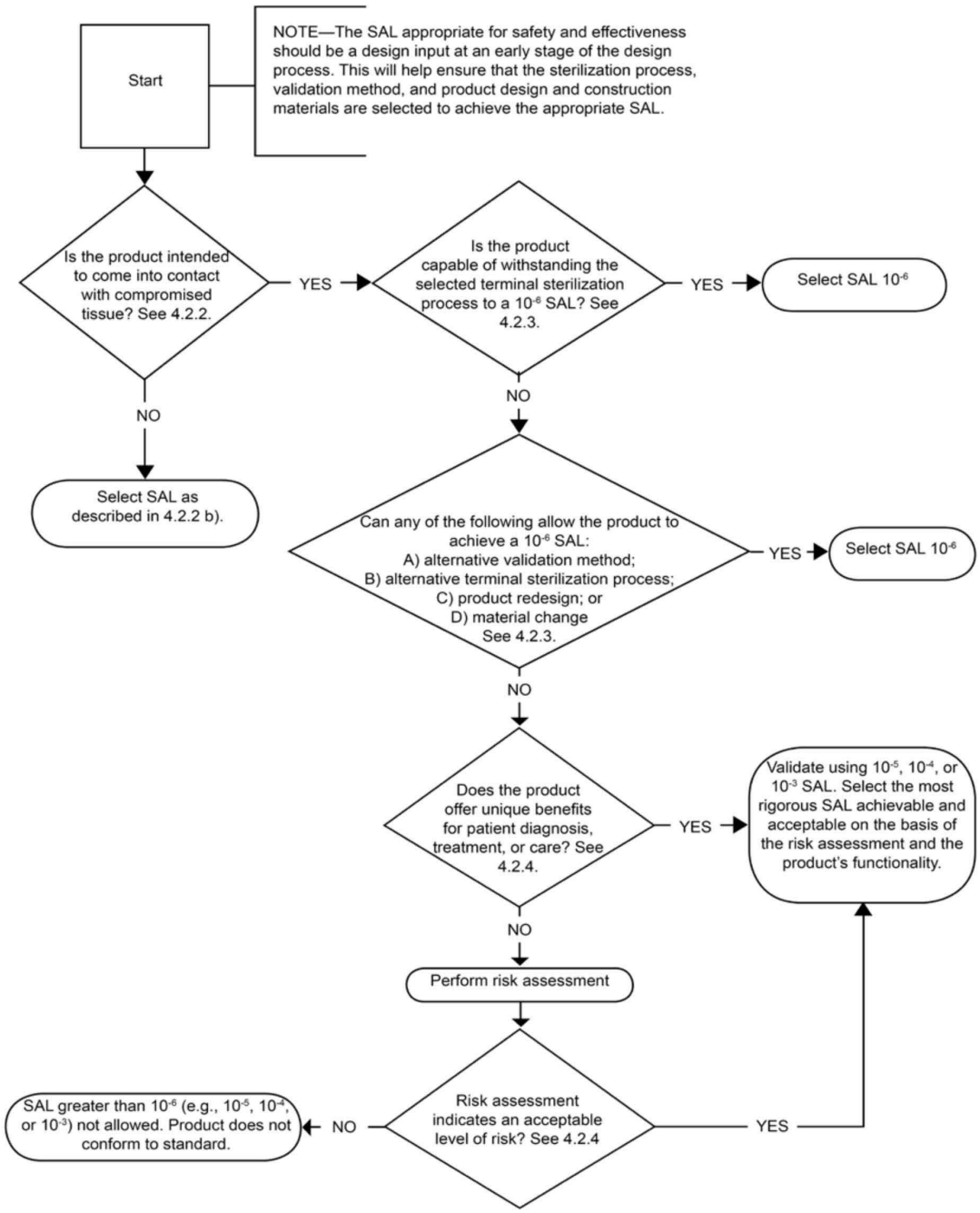
a) the product cannot be designed to allow a sterilization process that achieves an SAL of 10^{-6} without adversely affecting its essential safety and function; and

b) the product offers unique or superior benefits for patient diagnosis, treatment, or care.

In these instances, the product is sterilized by means of a validated sterilization process in which the theoretical probability of a viable microorganism being present on the product after sterilization is an SAL of 10^{-5}, 10^{-4}, or 10^{-3}. The most rigorous SAL shall be selected (i.e., a 10^{-5} SAL shall be chosen before a 10^{-4} SAL, and a 10^{-4} SAL shall be chosen before a 10^{-3} SAL), based upon the safety and effectiveness of the product after sterilization.

Figure 1—Decision tree for selection of SAL for medical devices to be terminally sterilized (section 4.2)

NOTE—This figure is intended to be used in conjunction with sections 4.2.2., 4.2.3, and 4.2.4.



Annex A
(informative)

Background and historical application of sterility assurance

A.1 Sterility assurance levels (SALs)

The effectiveness of a validated sterilization process can be determined by measuring the kinetics of microbial inactivation. The concept of SAL is derived from the exponential value of inactivation kinetics. The value of SAL is expressed as a negative power to the base 10. Historically, there have been several definitions of SAL. The definition chosen for this standard is that used by the International Organization for Standardization (ISO).

SALs were first developed by the food canning industry. Since it was impossible to establish sterility by sampling cans of product after moist heat sterilization, a safety factor was established that incorporated the kinetics of inactivation of *Clostridium botulinum* spores so that the moist heat cycle would have the equivalent of a 12-log spore reduction (i.e., 12 D value).

In the mid-1960s, the National Aeronautics and Space Administration (NASA) used the dry heat sterilization process for the Viking Planetary Space Probe. For this process, NASA specified that the probability of landing a microorganism on Mars would be 10^{-4} or less. Also in the 1960s, the Swedish public health authorities selected an SAL of 10^{-6} (or an SAL providing a greater assurance of sterility) for medical devices labeled "STERILE."

In 1979, the Canadian Health Protection Branch proposed a Microbiological Survival Index (MSI), which was defined as the reciprocal of the logarithm for the probability of a survivor from a sterilization process. The Canadian Health Protection Branch proposed labeling sterile medical products with the MSI numbers corresponding to SALs of 10^{-3} (MSI-3) and 10^{-6} (MSI-6). Such labeling met with strong opposition from both industry and medical care professionals because of the perceived inferiority of 10^{-3} versus 10^{-6} and an anticipated market battle over labeling claims that had no corresponding clinical benefit to the patient. However, the North American medical device industry and the Bureau of Medical Devices of the U.S. Food and Drug Administration (FDA) supported the use of two SALs which would be based on the assessment of the capabilities of the microbial inactivation potential of a sterilization process and on the intended use of the medical device (Bruch, 1981). Implicit in the meaning of SAL is not just the concept of sterility and the probability of an item being contaminated, but also the elements of good manufacturing practices (GMPs) and process validation. An SAL is a measurement or estimate of lethality of the entire sterilization process (Favero, 1993).

Research has shown that factors other than SAL influence the outcome of patient infection and the use of sterile medical devices. These factors include (a) device material, (b) improper handling of the device once sterile packaging is opened, (c) extent of patient and device exposure time during surgery or other procedures, (d) number and types of microorganisms contacted, and (e) immune status of the patient. So far, there has never been a relationship established between the particular SAL of a medical device and hospital-acquired (nosocomial) infections. Factors associated with nosocomial infections have been studied, and it has been documented that the microorganisms associated with those infections may originate from (a) microbial flora of the patients themselves, (b) other patients, visitors, and health care personnel, or (c) the hospital environment (Elek and Conen, 1957; Ritter et al., 1976; Moylan et al., 1987; Greene, 1993; Merritt et al., 1999).

SAL is the probability of a survivor per item determined from first-order death rate kinetics data after exposure to the sterilant used for the sterilization process. The required SAL is assured by such factors as the sterilization cycle development, calibration of equipment, validation of the sterilization process, standard loads with known zones of minimum lethality, process monitoring and control, product and process change control, and GMPs such as control of microbial contamination on products before the sterilization process. Implicit in an SAL, then, is not just the probability of an item being nonsterile, but also all of the elements of GMPs and process validation.

In the 1990s, the European Committee for Standardization (CEN) established the standard *Sterilization of medical devices—Requirements for medical devices to be labeled sterile* (EN 556). CEN determined that it would not be acceptable to ascribe two different interpretations (i.e., 10^{-3} and 10^{-6} SALs) to the term "STERILE." An SAL of 10^{-6} was chosen for EN 556, with the provision that a greater probability of non-sterility could be permitted under special circumstances.

Annex B
(informative)

Examples of terminally sterilized products and sterility assurance levels that have historically been selected

Table B.1—Examples of historical sterility assurance levels for terminally sterilized products*

10^{-3}	10^{-6}
a) Products not intended to come into contact with breached skin or compromised tissue, such as: 1) Collection or transfer devices: — Blood collection tubes for *in vitro* diagnostic tests — Culture media devices — Serological pipettes — Specimen containers 2) Topical devices: — ECG electrodes — Drainage bags — Grounding pads — Equipment drapes 3) Mucosal contacting devices: — Tongue depressors — Examination gloves — Urinary catheters b) Products that might not withstand a 10^{-6} SAL process: 1) Porcine heart valves 2) Wound dressings of a biological nature 3) Cell therapy products[1] 4) Tissue based products[1]	a) Products intended to come into contact with breached skin or compromised tissue, such as: 1) Wound dressings 2) Cardiac catheters 3) Cauterizing devices 4) Scalpels and other surgical instruments 5) Surgeons' gloves 6) Syringes 7) Hypodermic needles 8) Parenteral solutions 9) Peritoneal dialysis solutions 10) Prefilled syringes 11) Laparotomy sponges 12) Incise drapes b) Invasive products that enter normally sterile tissue c) Products with claims of sterile fluid pathways: 1) Fluid pathways of IV sets 2) Fluid pathways of syringes 3) Blood collection containers or bags d) Surgically implanted devices: 1) Reconstructive devices (e.g., hip, knee, elbow) 2) Implantable devices (e.g., pacemakers) 3) Trauma devices (e.g., nails, screws, plates, pins, wires) 4) Sutures 5) Intraocular lenses e) Components used in aseptic processing

* Depending on its intended use and material composition, the same product may be listed in both columns and require different SALs.

[1] U.S. Food and Drug Administration. Human cells, Tissues, and Cellular and Tissue-based products. *Code of Federal Regulations,* Title 21, Part 1271 (Revised April 1, 2010).

Annex C
(informative)

Guidance on performing a risk analysis for selecting an SAL for a product that cannot be sterilized to a 10^{-6} SAL

C.1 In considering a risk analysis for selecting an SAL for a product, first follow the decision tree in Figure 1 to demonstrate that the device cannot withstand a 10^{-6} SAL and cannot be redesigned in order to attain a 10^{-6} SAL.

C.2 ISO 14971 provides guidance on application of risk management to medical devices. Additionally, refer to the quality systems regulations for requirements pertaining to validation and verification of the product, including its total product life cycle. Specific to this document (ST67), a risk analysis can be performed using the criteria in 4.2, along with other pertinent criteria specific to the product. The results of this risk analysis can provide a rationale for the selection of an SAL for a specific product based on an overall risk assessment.

C.3 In performing a risk analysis to evaluate an SAL other than 10^{-6}, there are many associated factors that may impact the safety of the device. When performing a risk analysis, start with such elements as the nature of the device itself, the patient population in whom the device will be used, and the procedures associated with the use of the device. Some examples of additional factors to consider in the analysis may include the following (the list presented is not exhaustive):

a) the type of contact the product has with the patient (e.g., intact skin, mucous membranes, circulating blood)

b) the types of organisms associated with the manufacture of the device and their resistance to sterilization (e.g., source of raw materials, personnel, manufacturing processes, environmental isolates, pathogenic organisms, ability of certain types of microorganisms to withstand certain sterilization processes)

c) the material(s) that make up the device and the device construction (e.g., some materials/types of construction are more prone to contamination than others)

d) the number and types of organisms (i.e., bioburden) that might be present on the device following manufacturing (for comparison to the number of organisms required for infection and/or “objectionable” organisms from a contamination standpoint)

e) potential for shift in bioburden over time

f) the length and type of storage conditions following manufacturing and prior to sterilization (for assessment of the potential for bioburden survival/die-off), and

g) the intended use of the device (for assessment of the mechanism for potential patient infection).

C.4 The manufacturer is responsible for obtaining and interpreting product-specific data for a risk analysis. Each factor associated with a risk analysis must be based on valid clinical and/or scientific data and be well rationalized. As a result, each risk analysis performed for selecting an SAL will be different.

NOTE—The SAL risk analysis should be submitted to the FDA as part of the premarket submission process for any new device requiring an SAL of 10^{-6} (see 4.2.2 a) but claiming an alternate SAL. The FDA will consider alternate SALs on a case-by-case basis.

C.5 The following shows examples of factors that could be evaluated for performing a risk analysis associated with a particular SAL. These are intended to only be examples for providing information about possible factors that might be used in an SAL risk analysis as part of an overall risk assessment. The factors selected, the rationales provided, the probabilities shown, and the data described will not necessarily apply to a particular device or given situation. These examples do not take into account the use of multiple devices, immuno-compromised patients, and many other risk factors. In addition, only summaries of the rationale and data are provided in these examples. The full rationale and supporting data are not included, but would be expected to be documented.

Examples of factors that might be associated with a risk analysis for sterility assurance

1. Probability of an organism surviving sterilization:

The SAL chosen should be based on experimental data of the effects of terminal sterilization on the device materials. The most rigorous SAL is to be chosen based on the device's functionality.

Examples of probabilities corresponding to SALs:

10^{-3} = 1 in 1,000 probability

10^{-4} = 1 in 10,000 probability

10^{-5} = 1 in 100,000 probability

2. Probability of an organism being viable at the time of use:

Many organisms die off after a period of time in a hostile environment, such as in storage with no source of nutrients. This probability of viability might be determined based on an experiment showing the percent of a product's bioburden surviving after the minimum time that could elapse between sterilization and use of the device.

Examples of probabilities corresponding to data obtained for organism viability:

20% of the bioburden survives in the time period = 1 in 5 probability

50% of the bioburden survives in the time period = 1 in 2 probability

3. Probability of an organism getting into patient's tissue:

Some products may only have a portion of the device that comes into contact with the patient's compromised tissue. The probability of an organism getting into a patient's tissue might be determined based on this information. To address the issue of bioburden distribution on a device, a worse-case assumption could be made that 100% the product's bioburden is located on the patient-contacting portion of the device.

Examples of probabilities corresponding to a device's patient-contacting portion:

10% of the device contacts patient tissue = 1 in 10 probability

40% of the device contacts patient tissue = 1 in 2.5 probability

100% of the device contacts patient tissue = 1 in 1 probability

4. Probability of an organism being pathogenic:

Not all organisms comprising the product's bioburden are considered pathogenic. The probability of an organism being pathogenic can be determined based on the types of organisms found in the bioburden and an understanding of their clinical infectivity (e.g., pathogenic nature, number required to cause an infection, etc.).

Examples of probabilities corresponding to the pathogenicity of bioburden organisms:

25% of the bioburden organisms are considered pathogenic = 1 in 4 probability

100% of the bioburden organisms are considered pathogenic = 1 in 1 probability

Overall probability:

For the above factors, the overall probability can be calculated that an organism that survived the sterilization process could be viable at the time of use, could get into the patient's tissue, and could be pathogenic.

Overall probability = (probability of # 1) X (probability of # 2) X (probability of # 3) X (probability of # 4)

Annex D
(informative)

Bibliography

[1] AKERS J and AGALLOCO J. Sterility and sterility assurance. *PDA J Pharm Sci Technol*, March/April 1997, vol. 51, no. 2, pp. 72–77.

[2] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—Ethylene oxide—Part 1 Requirements for the development, validation, and routine control of a sterilization process for medical devices*. ANSI/AAMI/ISO 11135-1:2007. Arlington (VA): AAMI, 2007.

[3] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—Ethylene oxide—Part 2: Guidance on the application of AAMI/ISO 11135-1*. ANSI/AAMI/ISO 11135-2:2008. Arlington (VA): AAMI, 2008.

[4] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—Radiation—Part 1: Requirements for the development, validation, and routine control of a sterilization process for medical devices*. ANSI/AAMI/ISO 11137-1:2006/(R)2010. Arlington (VA): AAMI, 2006.

[5] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—Radiation—Part 2: Establishing the sterilization dose*. ANSI/AAMI/ISO 11137-2:2006. Arlington (VA): AAMI, 2006.

[6] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—Radiation—Part 3: Guidance on dosimetric aspects*. ANSI/AAMI/ISO 11137-3:2006/(R)2010. Arlington (VA): AAMI, 2006.

[7] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Packaging for terminally sterilized medical devices—Part 1: Requirements for materials, sterile barrier systems, and packaging*. ANSI/AAMI/ISO 11607-1:2006. Arlington (VA): AAMI, 2006.

[8] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Packaging for terminally sterilized medical devices—Part 2: Validation requirements for forming, sealing, and assembly processes*. ANSI/AAMI/ISO 11607-2:2006. Arlington (VA): AAMI, 2006.

[9] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products - Biological indicators - Guidance for the selection, use, and interpretation of results.* ANSI/AAMI/ISO 14161:2009. Arlington (VA): AAMI, 2009.

[10] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—General requirements for characterization of a sterilizing agent and the development, validation, and routine control of a sterilization process for medical devices.* ANSI/AAMI/ISO 14937:2009. Arlington (VA): AAMI, 2009.

[11] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Medical devices—Application of risk management to medical devices*. ANSI/AAMI/ISO 14971:2007. Arlington (VA): AAMI, 2007.

[12] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. *Sterilization of health care products—Moist heat—Part 1 Requirements for the development, validation and routine control of a sterilization process for medical devices*. ANSI/AAMI/ISO 17665-1:2006. Arlington (VA): AAMI, 2006.

[13] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. Medical devices—Quality management systems—System requirements for regulatory purposes. ANSI/AAMI/ISO 13485:2003/(R)2009. Arlington (VA): AAMI, 2003.

[14] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION. Sterilization of health care products—Requirements for the development, validation, and routine control of an industrial sterilization process for medical devices—Dry heat. ANSI/AAMI ST63:2002. Arlington (VA): AAMI, 2002.

[15] BRUCH CW. Process control release of terminally sterilized medical devices. In: Proceedings of the Second International Kilmer Memorial Conference on the Sterilization of Medical Products, October 16–17, 1980, pp. 103–117. Montreal: Multiscience Publications Limited, 1981.

[16] BRUCH CW. The philosophy of sterilization validation. In: MORRISSEY RF and PHILLIPS GB, eds. *Sterilization technology: A practical guide for manufacturers and users of health care products.* New York: Van Nostrand Reinhold, 1993, pp. 17–35.

[17] CHRISTENSEN E and MILLER A. A European view of sterile. Letter to the editor. *Med Device & Diag Ind*, August 1992, pp. 22–23.

[18] ELEK SD and CONEN PD. The virulence of *Staphylococcus pyogenes* for man: A study of the problem of wound infections. *Brit J Exp Pathol*, 1957, vol. 38, pp. 573–576.

[19] ENZINGER RM. Sterility assurance from post-filling heat treatment. *J Parenteral Science & Technol*, December 1990, vol. 44, no. 6, pp. 294–295.

[20] FAVERO MS. Patient infections: The relevance of sterility assurance levels. In: *Proceedings of the International Kilmer Memorial Conference on the Sterilization of Medical Products*, Brussels, June 13–15, 1993, pp. 156–163. Morin Heights (Canada): Polyscience Publications, 1993.

[21] GRAHAM GS and BORIS CA. Chemical and biological indicators. In: MORRISSEY RF and PHILLIPS GB, eds. *Sterilization technology: A practical guide for manufacturers and users of health care products.* New York: Van Nostrand Reinhold, 1993, pp. 36–69.

[22] GREENE V. Surgery, sterilization, and sterility. *J Healthc Mater Mgmt*, March 1993, pp. 48–52.

[23] HALLS N. Achieving sterility in medical and pharmaceutical products. New York: Marcel Dekker, 1994.

[24] HITCHINS VM. Medical device-associated infections in immunocompromised patients. In: *Infection Control Symposium: Influence of Medical Device Design.* HHS Publication FDA 95-4260, 1995.

[25] INTERNATIONAL ORGANIZATION FOR STANDARDIZATION. Cleanrooms and associated controlled environments—Part 1: Classification of air cleanliness. ISO 14644-1:1999. Geneva: ISO, 1999.

[26] INTERNATIONAL ORGANIZATION FOR STANDARDIZATION. Cleanrooms and associated controlled environments. Cleanroom technology—Biocontamination control—Part 1: General principles and methods. ISO 14698-1:2003. Geneva: ISO, 2003.

[27] INTERNATIONAL ORGANIZATION FOR STANDARDIZATION. Cleanrooms and associated controlled environments. Cleanroom technology—Biocontamination control—Part 2: Evaluation and interpretation of biocontamination data. ISO 14698-2:2003. Geneva: ISO, 2003.

[28] MERRITT K, HITCHINS VM, and NEALE AR. Tissue colonization from implantable biomaterials with low numbers of bacteria. *J Biomed Mater Res*, 1999, vol. 44, pp. 261–265.

[29] MORRISSEY RF, BRUCH CW, SHARBAUGH RJ, FAVERO MS, JARVIS WR, and MASEFIELD J. Sterility and safety assurance of medical devices. *Med Dev & Diag Ind*, April 1992, vol. 115, pp. 78–81.

[30] MORRISSEY RF and PHILLIPS GB. *Sterilization technology—A practical guide for manufacturers and users of health care products.* New York: Van Nostrand Reinhold, 1993.

[31] MOYLAN JA, FITZPATRICK KT, and DAVENPORT KE. Reducing wound infections, improved gown and drape barrier performance. *Arch Surg*, February 1987, vol. 122, pp. 152–156.

[32] NATIONAL AERONAUTICS AND SPACE ADMINISTRATION. *Spacecraft sterilization technology.* Washington (DC): NASA, 1966.

[33] PFLUG IJ. *Introductory course in the microbiology and engineering of sterilization processes.* 4ed. Syllabus. St. Paul: Environmental Sterilization Sciences, May 1980.

[34] RITTER M, EITZEN H, FRENCH M, and HART J. The effect that time, touch and environment have upon bacterial contamination of instruments during surgery. *Ann Surg*, November 1976, vol. 184, no. 5, pp. 642–644.

[35] U.S. FOOD AND DRUG ADMINISTRATION. *Sterile medical devices: A GMP workshop manual.* HHS Publication FDA 84-4174. 4ed. Rockville (MD): Center for Devices and Radiological Health, FDA, March 1984.

[36] U.S. FOOD AND DRUG ADMINISTRATION. Guidance for industry for the submission of documentation for sterilization process validation in applications for human and veterinary drug products. Rockville (MD): Center for Drug Evaluation and Research, and Center for Veterinary Medicine, FDA, November 1994.

[37] WARTENBERG D. Risk assessment: The inexact art of hazard evaluation. In: Proceedings of the International Kilmer Memorial Conference on the Sterilization of Medical Products, Belgium, June 13–15, 1993, pp. 156–163. Morin Heights (Canada): Polyscience Publications, 1993.

[38] WINCKELS HW and DORPEMA JW. Risk assessment, a basis for the definition of sterility. *Med Dev Techn*, November 1994, pp. 38–43.