

This is a preview of "ANSI/AAMI/ISO 13408-...". Click here to purchase the full version from the ANSI store.

American National Standard



ANSI/AAMI/ ISO 13408-2:

PREVIEW COPY

2018

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

Aseptic processing of health
care products—Part 2:
Sterilizing filtration

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 Online monthly newsletter. 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 Standards Monitor Online.

American National Standard

ANSI/AAMI/ISO 13408-2:2018



Aseptic processing of health care products—Part 2: Sterilizing filtration

PREVIEW COPY

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

Approved 17 November 2017 by
AAMI

Approved 1 February 2018 by
American National Standards Institute

Abstract: Specifies requirements for sterilizing filtration as part of aseptic processing of health care products. It also offers guidance to filter users concerning general requirements for selection, set up, validation and routine operation of a sterile-filtration process to be used for aseptic processing of health care products. This document does not apply to removal of mycoplasma or viruses by filtration nor to filtration of whole cell vaccines.

Keywords: sterilizing filtration, filters, aseptic processing

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.



PREVIEW COPY

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

Published by

AAMI
4301 N. Fairfax Dr., Suite 301
Arlington, VA 22203-1633
www.aami.org

For a complete copy of this AAMI document, contact AAMI at
+1-877-249-8226 or visit www.aami.org.

© 2018 by the Association for the Advancement of Medical Instrumentation

All Rights Reserved

This publication is subject to copyright claims of ISO and AAMI. No part of this publication may be reproduced or distributed in any form, including an electronic retrieval system, without the prior written permission of AAMI. All requests pertaining to this document should be submitted to AAMI. It is illegal under federal law (17 U.S.C. § 101, *et seq.*) to make copies of all or any part of this document (whether internally or externally) without the prior written permission of the Association for the Advancement of Medical Instrumentation. Violators risk legal action, including civil and criminal penalties, and damages of \$100,000 per offense. For permission regarding the use of all or any part of this document, complete the reprint request form at www.aami.org or contact AAMI, 4301 N. Fairfax Drive, Suite 301, Arlington, VA 22203-1633. Phone: (703) 525-4890; Fax: (703) 276-0793.

Printed in the United States of America

ISBN 978-1-57020-696-2

Contents

Page

Glossary of equivalent standards.....	iv
Committee representation.....	v
Background of AAMI adoption of ISO 13408-2:2018.....	vii
Foreword.....	viii
Introduction	ix
1 Scope.....	1
2 Normative references	1
3 Terms and definitions.....	2
4 Quality system elements.....	3
5 Sterilizing filter characterization.....	4
6 Process and equipment characterization.....	5
7 Fluid definition	7
8 Process definition.....	8
9 Validation.....	11
10 Routine monitoring and control	15
11 Product release from sterilizing filtration.....	16
12 Maintaining process effectiveness.....	16
Annex A (informative) Guidance on the application of this document	18
Bibliography.....	33

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

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.

www.aami.org/standards/glossary.pdf



PREVIEW COPY

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

Committee representation

Association for the Advancement of Medical Instrumentation

Aseptic Processing Working Group

The adoption of ISO 13408-2 as an American National Standard was initiated by the AAMI Aseptic Processing Working Group (ST/WG 9). AAMI ST/WG 9 functions as a U.S. Technical Advisory Group to the relevant work in the International Organization for Standardization (ISO). U.S. representatives from AAMI ST/WG 9 played an active part in developing the ISO standard.

At the time this document was published, the **AAMI Aseptic Processing Working Group** had the following members:

Cochairs: Gordon Ely
Robert Tomaselli

Members: Cara Beougher, Medtronic Inc Campus
Beth Brusdal, Bausch & Lomb Inc
Trabue Bryans, BryKor LLC
Robb Calabro, AbbVie
Tim Carlson, Becton Dickinson & Company
Sean Colwell, WuXi AppTec Inc
Kim Darnell, CR Bard
Steven Elliott, NAMSA
Gordon Ely, MiMedx Group
Brent Geiger, Cantel Inc
Doug Harbrecht, Sterility Assurance LLC
Deborah Havlik, Hospira, a Pfizer company
Brent Huberty, Boston Scientific Corporation
Jim Kulla, LexaMed Ltd
Alison Laughlin, Baxter Healthcare Corporation
Christine Loshbaugh, Edwards Lifesciences
Tonya Morris, Nelson Laboratories LLC
Rod Parker, Stryker Instruments Division
Janet Prust, 3M Healthcare
Manny Saavedra, Halyard Health
Jennifer Schmidt, FDA/CDRH
Myra Smith, FDA/CDRH
Ronald Smith, Johnson & Johnson
Robert Tomaselli, Robert P. Tomaselli Consulting
Dennis Wildes, St Jude Medical Inc
Roberto Zumbado, Philips

Alternates: Stacy Bohl, Boston Scientific Corporation
Phil Cogdill, Medtronic Inc Campus
Alyce Dobie, Bausch & Lomb Inc
David Dominguez, Becton Dickinson & Company
Wade Johnston, Halyard Health
Jeff Martin, Sterilization and Quality System Consulting LLC
Elaine Mayhall, FDA/CDRH
Emily Mitzel, Nelson Laboratories LLC
Robert Reich, LexaMed Ltd
Leslie Tavares, WuXi AppTec Inc
Sean Toler, Baxter Healthcare Corporation
Robert White, Johnson & Johnson

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



PREVIEW COPY

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

Background of AAMI adoption of ISO 13408-2:2018

As indicated in the foreword to the main body of this document (page viii), the International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of this standard, which was developed by ISO Technical Committee 198, *Sterilization of health care products*, to fill a need for guidance regarding processes, programmes and procedures for development, validation and routine control of the manufacturing process for aseptically processed health care products.

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

ANSI/AAMI/ISO 13408-2 was approved by the American National Standards Institute (ANSI) on 1 February 2018.

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.

AAMI (and ANSI) have adopted other ISO standards. See the Glossary of Equivalent Standards for a list of ISO standards adopted by AAMI, which gives the corresponding U.S. designation and the level of equivalency with the ISO standard.

As used within the context of this document, "shall" indicates requirements strictly to be followed to conform to the recommended practice. "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 recommended practice. "Can" is used as a statement of possibility and capability. Finally, "must" is used only to describe "unavoidable" situations, including those mandated by government regulation.

NOTE Users of this standard are advised that this document is an AAMI identical adoption of an ISO document and that the following international conventions have been carried over to the AAMI publication:

- British English spelling (e.g. colour instead of color)
- Use of SI units (e.g. metres instead of feet, Celsius instead of Fahrenheit, etc.)
- Decimal comma instead of a decimal point (e.g. 1 000,15 instead of 1,000.15)

The concepts incorporated in this standard should not be considered inflexible or static. This standard, like any other, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as technological advances are made and as new data come to light.

Suggestions for improving this standard are invited. Comments and suggested revisions should be sent to Standards Department, AAMI, 4301 N. Fairfax Dr, Suite 301, Arlington, VA 22203-1633.

NOTE Beginning with the ISO foreword on page viii, this American National Standard is identical to ISO 13408-2:2018.

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This second edition cancels and replaces the first edition (ISO 13408-2:2003), which has been technically revised.

A list of all parts in the ISO 13408 series can be found on the ISO website. This is a preview edition of an AAMI guidance document and is intended for informational purposes only. Do not evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

Introduction

ISO 13408 1 covers general aspects of aseptic processing. Several processes including sterilizing filtration, lyophilization, clean and sterilization in place, isolator systems, and alternative processes for medical devices and combination products were found to be in need of supplementary information, which was too extensive to be included in the corresponding annexes to ISO 13408 1. This information is presented in ISO 13408 2 to ISO 13408 7.

Sterilizing filtration is a critical step in an aseptic manufacturing process. Validation of sterilizing filtration processes can be complex and is generally conducted in both a process and product specific manner. This document describes requirements that, if met, will provide a sterilizing filtration process that consistently removes microorganisms from a fluid (liquid or gas) without negatively affecting the quality of the filtrate. Furthermore, conformity with the requirements ensures that a sterilizing filtration process is both reliable and reproducible so that a determination can be made, with reasonable confidence, that the sterilizing grade filter/s will provide a sterile filtrate under specified operational conditions. This (the reliability and reproducibility of the filtration process) is essential, as unlike a micro-biocidal sterilization process where process variables can be monitored continuously, microbial retention and physical integrity of a sterilising grade filter cannot be monitored on a continuous basis throughout a filtration process.

Where validation establishes a reproducible relationship between the product-specific bacterial retention capability of a sterilizing grade filter and the physical integrity of that filter, then suitable non-destructive pre-use and post-use filter integrity tests are used to determine whether a full-scale sterilizing filtration process has been conducted successfully. During terminal sterilization the kinetics of inactivation follows a mathematical order and allow calculation of a sterility assurance level (SAL). Removal of organisms from a fluid by filtration does not follow such mathematical order and so the use of the term "sterility assurance level" is not appropriate for product sterilized by filtration.

Advancing Safety in Health Technology

There has been a significant increase in the development and availability of biopharmaceuticals, biologic-based medical devices and cell-based health care products since publication of the initial 2003 edition of this document. This second edition emphasizes the importance of a thorough understanding of the nature of the indigenous bioburden of a fluid that is to be sterilized by filtration, including its relationship to the test microorganism used to determine microbial retention capability of the sterilizing grade filter. For example, Mycoplasma can cause serious contamination problems during the manufacturing of biopharmaceutical, biotechnological and cell-based health care products. A thorough understanding of the indigenous bioburden enables suitable safeguards to be implemented during development, validation and control of a sterilizing filtration process to ensure the safety and quality of the filtered fluid.

While the activities required by this document have been grouped together and are presented in a particular order, this document does not require that the activities be performed in the order that they are presented. The activities required are not necessarily sequential, as the programme of development and validation may be iterative. It is possible that performing these different activities will involve a number of separate individuals and/or organizations, each of whom undertake one or more of these activities. This document does not specify the particular individuals or organizations to carry out the activities.

Guidance on the application of this document is given in Annex A.



PREVIEW COPY

This is a preview edition of an AAMI guidance document and is intended to allow potential purchasers to evaluate the content of the document before making a purchasing decision.

For a complete copy of this AAMI document, contact AAMI at +1-877-249-8226 or visit www.aami.org.

Aseptic processing of health care products—Part 2: Sterilizing filtration

1 Scope

This document specifies requirements for sterilizing filtration as part of aseptic processing of health care products conducted in accordance with ISO 13408-1. It also offers guidance to filter users concerning general requirements for set-up, validation and routine operation of a sterilizing filtration process.

This document is not applicable to removal of viruses.

Sterilizing filtration is not applicable to fluids that intentionally contain particles larger than the pore size of the filter (e.g. bacterial whole-cell vaccines).

This document is not applicable to high efficiency particulate air (HEPA) filters.

This document does not specify requirements for the development, validation and routine control of a process for removing the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeldt-Jakob disease. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11135, *Sterilization of health-care products—Ethylene oxide—Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 11137-1, *Sterilization of health-care products—Radiation—Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11139,¹ *Sterilization of health care products—Vocabulary—Terms used in sterilization and related equipment and process standards*

ISO 13408-1:2008, *Aseptic processing of health care products—Part 1: General requirements*

ISO 13408-1:2008/Amd. 1:2013, *Aseptic processing of health care products—Part 1: General requirements—Amendment 1*

ISO 13408-5, *Aseptic processing of health care products—Part 5: Sterilization in place*

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

¹ Under preparation. Stage at the time of publication: ISO/DIS 11139:2017(E).