Technical Information Report

AAMI TIR17:2008

Compatibility of materials subject to sterilization

Association for the Advancement of Medical Instrumentation

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

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*.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

AAMI Technical Information Report

AAMI TIR17:2008
(Revision of AAMI TIR17:1997)

Compatibility of materials subject to sterilization

Approved 26 August 2008 by
Association for the Advancement of Medical Instrumentation

Abstract: Provide guidance for health care manufacturers in the qualification of polymeric materials, ceramics, and metals in health care products that are sterilized by the following modalities: a) radiation (gamma, electron beam, or x ray); b) ethylene oxide; c) moist heat (steam); d) dry heat; e) hydrogen peroxide; and f) ozone. Annexes address the specific sterilization modality concerns.

Keywords: material qualification, sterilization

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

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 might 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 might 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, 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795.

Published by

Association for the Advancement of Medical Instrumentation
1110 N. Glebe Road, Suite 220
Arlington, VA 22201-4795
www.aami.org

© 2008 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 AAMI at 1110 N. Glebe Road, Suite 220, Arlington, VA 22201-4795. Phone: (703) 525-4890; Fax: (703) 525-1067.

Printed in the United States of America

ISBN 1-57020-321-0

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Contents

Page

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. For each International Standard that has been adopted by AAMI (and ANSI), the table below gives the corresponding U.S. designation and level of equivalency to the International Standard. NOTE: Documents are sorted by international designation.

Other normatively referenced International Standards may be under consideration for U.S. adoption by AAMI; therefore, this list should not be considered exhaustive.

International designation	U.S. designation	Equivalency
IEC 60601-1:2005	ANSI/AAMI ES60601-1:2005	Major technical variations
IEC 60601-1-2:2007	ANSI/AAMI/IEC 60601-1-2:2007	Identical
IEC 60601-2-2:2006	ANSI/AAMI/IEC 60601-2-2:2006	Identical
IEC 60601-2-4:2002	ANSI/AAMI DF80:2003	Major technical variations
IEC 60601-2-19:1990 and A1:1996	ANSI/AAMI II36:2004	Major technical variations
IEC 60601-2-20:1990 and A1:1996	ANSI/AAMI II51:2004	Major technical variations
IEC 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 and Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:2004	Major technical variations
IEC 60601-2-47:2001	ANSI/AAMI EC38:2007	Major technical variations
IEC 60601-2-50:2001	ANSI/AAMI/IEC 60601-2-50:2006	Identical
IEC/TR 60878:2003	ANSI/AAMI/IEC TIR60878:2003	Identical
IEC/TR 62296:2003	ANSI/AAMI/IEC TIR62296:2003	Identical
IEC 62304:2006	ANSI/AAMI/IEC 62304:2006	Identical
IEC/TR 62348:2006	ANSI/AAMI/IEC TIR62348:2006	Identical
ISO 5840:2005	ANSI/AAMI/ISO 5840:2005	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001/(R)2004	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996/(R)2002	Identical
ISO 8637:2004	ANSI/AAMI RD16:2007	Major technical variations
ISO 8638:2004	ANSI/AAMI RD17:2007	Major technical variations
ISO 10993-1:2003	ANSI/AAMI/ISO 10993-1:2003	Identical
ISO 10993-2:2006	ANSI/AAMI/ISO 10993-2:2006	Identical
ISO 10993-3:2003	ANSI/AAMI/ISO 10993-3:2003	Identical
ISO 10993-4:2002 and A1:2006	ANSI/AAMI/ISO 10993-4:2002 and A1:2006	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:2007	ANSI/AAMI/ISO 10993-6:2007	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995/(R)2001	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999/(R)2005	Identical
ISO 10993-10:2002 and Amendment 1:2006	ANSI/AAMI BE78:2002 ANSI/AAMI BE78:2002/A1:2006	Minor technical variations Identical
ISO 10993-11:2006	ANSI/AAMI/ISO 10993-11:2006	Identical
ISO 10993-12:2007	ANSI/AAMI/ISO 10993-12:2007	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999/(R)2004	Identical
ISO 10993-14:2001	ANSI/AAMI/ISO 10993-14:2001/(R)2006	Identical
ISO 10993-15:2000	ANSI/AAMI/ISO 10993-15:2000/(R)2006	Identical
ISO 10993-16:1997	ANSI/AAMI/ISO 10993-16:1997/(R)2003	Identical
ISO 10993-17:2002	ANSI/AAMI/ISO 10993-17:2002	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
ISO/TS 11135-2:2008	ANSI/AAMI/ISO TIR11135-2:2008	Identical

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

International designation	U.S. designation	Equivalency
ISO 11137-1:2006	ANSI/AAMI/ISO 11137-1:2006	Identical
ISO 11137-2:2006 (2006-08-01 corrected version)	ANSI/AAMI/ISO 11137-2:2006	Identical
ISO 11137-3:2006	ANSI/AAMI/ISO 11137-3:2006	Identical
ISO 11138-1: 2006	ANSI/AAMI/ISO 11138-1:2006	Identical
ISO 11138-2: 2006	ANSI/AAMI/ISO 11138-2:2006	Identical
ISO 11138-3: 2006	ANSI/AAMI/ISO 11138-3:2006	Identical
ISO 11138-4: 2006	ANSI/AAMI/ISO 11138-4:2006	Identical
ISO 11138-5: 2006	ANSI/AAMI/ISO 11138-5:2006	Identical
ISO/TS 11139:2006	ANSI/AAMI/ISO 11139:2006	Identical
ISO 11140-1:2005	ANSI/AAMI/ISO 11140-1:2005	Identical
ISO 11140-3:2007	ANSI/AAMI/ISO 11140-3:2007	Identical
ISO 11140-4:2007	ANSI/AAMI/ISO 11140-4:2007	Identical
ISO 11140-5:2007	ANSI/AAMI/ISO 11140-5:2007	Identical
ISO 11607-1:2006	ANSI/AAMI/ISO 11607-1:2006	Identical
ISO 11607-2:2006	ANSI/AAMI/ISO 11607-2:2006	Identical
ISO 11737-1: 2006	ANSI/AAMI/ISO 11737-1:2006	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO 11737-3:2004	ANSI/AAMI/ISO 11737-3:2004	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	Identical
ISO 14155-1:2003	ANSI/AAMI/ISO 14155-1:2003	Identical
ISO 14155-2:2003	ANSI/AAMI/ISO 14155-2:2003	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998	Identical
ISO 14161:2000	ANSI/AAMI/ISO 14161:2000	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO/TR 14969:2004	ANSI/AAMI/ISO TIR14969:2004	Identical
ISO 14971:2007	ANSI/AAMI/ISO 14971:2007	Identical
ISO 15223-1:2007 and A1:2008	ANSI/AAMI/ISO 15223-1:2007 and A1:2008	Identical
ISO 15225:2000 and A1:2004	ANSI/AAMI/ISO 15225:2000/(R)2006 and A1:2004/(R)2006	Identical
ISO 15674:2001	ANSI/AAMI/ISO 15674:2001	Identical
ISO 15675:2001	ANSI/AAMI/ISO 15675:2001	Identical
ISO 15882:2003	ANSI/AAMI/ISO 15882:2003	Identical
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
ISO 18472:2006	ANSI/AAMI/ISO 18472:2006	Identical
ISO/TS 19218:2005	ANSI/AAMI/ISO 19218:2005	Identical
ISO 22442-1:2007	ANSI/AAMI/ISO 22442-1:2007	Identical
ISO 22442-2:2007	ANSI/AAMI/ISO 22442-2:2007	Identical
ISO 22442-3:2007	ANSI/AAMI/ISO 22442-3:2007	Identical
ISO 25539-1:2003 and A1:2005	ANSI/AAMI/ISO 25539-1:2003 and A1:2005	Identical
ISO 25539-2:2008	ANSI/AAMI/ISO 25539-2:2008	Identical
ISO 81060-1:2007	ANSI/AAMI/ISO 81060-1:2007	Identical

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Committee representation

Association for the Advancement of Medical Instrumentation

Compatibility of Materials Subject to Sterilization Working Group

This technical information report (TIR) was developed by the AAMI Compatibility of Materials Subject to 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 Compatibility of Materials Subject to Sterilization Working Group had the following members:

Cochairs	Byron J. Lambert, PhD, Abbott Laboratories
	Jeff Martin, Alcon Research Ltd.
Members	Lloyd Brown, Covidien
	Nancy Chobin, RN CSPDM, St. Barnabas Healthcare System (independent expert)
	Phillip Franciskovich, Steris Corporation
	France Frechette, MSc, TSO3 Inc.
	Joel R. Gorski, PhD, NAMSA
	Arthur C. Harris, Cook Inc.
	Carolyn L. Kinsley, LexaMed
	Roland Kippenhan, Minntech Corporation
	Byron J. Lambert, PhD, Abbott Laboratories
	Colleen Patricia Landers, RN, Canadian Standards Association
	Anne D. Lucas, FDA/CDRH
	Brad Lundahl, Sterigenics International
	Ralph Makinen, Boston Scientific Corporation
	Jeff Martin, Alcon Research Ltd.
	Craig A. Meadows, Medtronic Inc.
	Gerry A. O'Dell, MS, Gerry O'Dell Consulting
	Wayne Jerome Rogers, Wayne J Rogers Consulting
	Dan Smith, Johnson & Johnson
	Paul J. Somodi, PhD, Hospira Inc.
	Larry Talapa, 3M Healthcare
	Donald Tumminelli, SPS Medical Supply Corp
	Wendy Wangsgard, PhD, Nelson Laboratories Inc.
Alternates	Ike Harper, Johnson & Johnson
	Michael O'Hara, FDA/CDRH
	Michael A. Padilla, BSME, Sterigenics International
	Jeff Peltier, Boston Scientific Corporation
	Shaundrea L. Rechsteiner, NAMSA
	Gary J. Socola, SPS Medical Supply Corp
	Martell Kress Winters, BS SM, Nelson Laboratories Inc.
	Kelvin J. Witcher, 3M Healthcare

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

Cochairs	Victoria M. Hitchins, PhD, FDA/CDRH
	William E. Young, Boston Scientific Corporation
Members	Trabue D. Bryans, AppTec
	Peter Burke, Steris Corporation

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Nancy Chobin, RN CSPDM, St. Barnabas Healthcare System (independent expert)
Charles Cogdill, Boston Scientific Corporation
Ramona Conner, RN MSN CNOR, Association of Perioperative Registered Nurses
Jacqueline Daley, Association for Professionals in Infection Control and Epidemiology
Kimbrell Darnell, CR Bard
Lisa Foster, Sterigenics International
James M. Gibson Jr., JM Gibson Associates
Joel R. Gorski, PhD, NAMSA
Deborah A. Havlik, Hospira Worldwide Inc.
Victoria M. Hitchins, PhD, FDA/CDRH
Danny Hutson, Cardinal Health (MP&S)
Lois Atkinson Jones, MS (independent expert)
Susan G. Klacik, CCSMC FCS ACE, IAHCSMM
Byron J. Lambert, PhD, Abbott Laboratories
Colleen Patricia Landers, RN, Canadian Standards Association
David Liu, Johnson & Johnson
Lisa N. Macdonald, Becton Dickinson & Company
Jeff Martin, Alcon Research Ltd.
Patrick J. McCormick, PhD, Bausch & Lomb Inc.
Susie McDonald, American Society for Healthcare Central Service Professionals
Nancy J. Rakiewicz, Ethox International Inc.
Phil M. Schneider, 3M Healthcare
Michael H. Scholla, Dupont Nonwovens
Mark Seybold, Baxter Healthcare Corporation
Andrew Sharavara, Propper Manufacturing Co. Inc.
Mark N. Smith, Getinge USA
William N. Thompson, Covidien
James L. Whitby, MA, MB, FRCP, University of Western Ontario (independent expert)
Martell Kress Winters, BS SM, Nelson Laboratories Inc.

Alternates

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

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

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Foreword

This AAMI Technical Information Report (TIR) was developed to provide additional guidance in order to improve the quality and reduce the costs and time required for performing material qualifications.

One of the activities encompassed within sterilization standards is the evaluation of the effect the mode of sterilization has on product and packaging. This element is mentioned in each of the respective industrial sterilization standards (ANSI/AAMI/ISO 11135 series, ANSI/AAMI/ISO 11137 series, ANSI/AAMI/ISO 17665-1, and ANSI/AAMI/ISO 14937). In summary, the basic requirements for these standards include the implementation of a program to demonstrate the quality, safety, and performance of the product throughout its shelf life or expiration date. Components of such a program are 1) expeditious selection of materials, 2) prudent processing of those materials, 3) testing of any specific properties essential to the intended function of the product, and 4) accelerated aging programs. AAMI TIR17:1997 addressed these four components of a material qualification program for radiation sterilization. There have been many requests from the health care manufacturing industry to expand on the information provided on materials compatibility. Therefore, this current TIR supersedes AAMI TIR17:1997, with an expanded scope that includes the following sterilization modalities:

- radiation,
- ethylene oxide,
- moist heat (steam),
- dry heat,
- hydrogen peroxide, and
- ozone.

These modalities are individually addressed in clause 3 and Annexes A through F of this TIR. Guidance on the processing of materials is carried over from AAMI TIR17:1997 and is provided in clause 4. General guidance on the testing of materials is provided in clause 5. Accelerated aging program information is provided in clause 6. It has been carried over from AAMI TIR17:1997, or if it has been subsequently published elsewhere, references have been provided. To facilitate aging programs with the advent of combination devices, the accelerated aging information is supplemented with a comparison of accelerated aging programs for devices and accelerated stability programs for pharmaceuticals.

The bulk of the guidance on the compatibility of materials subject to sterilization is provided in Annexes A through F. Each sterilization modality is described in enough detail for the reader to understand the parameters of the sterilization process that need to be considered in evaluating the compatibility of materials. One of the most beneficial aspects of the guidance in each annex is a list of compatible materials to aid in the material selection process. Brief reference to the application of each sterilization modality to pharmaceutical and biological agents is also provided.

This TIR contains guidelines that are not intended to be absolute or to be applicable in all circumstances. Judgment should be used in applying the information in this TIR.

NOTE—This document is not an AAMI or an American National Standard and the material contained herein is not normative in nature.

NOTE—This foreword does not contain provisions of the AAMI TIR titled “Compatibility of materials subject to sterilization” (AAMI TIR17:2008), but it does provide important information about the development and intended use of the document.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Compatibility of materials subject to sterilization

1 Scope

The focus of this document is to provide guidance for health care manufacturers in the selection and qualification of polymeric materials, ceramics, and metals in health care products that are sterilized by the following modalities:

- radiation (gamma, electron beam, or x-ray),
- ethylene oxide (EO),
- moist heat (steam),
- dry heat,
- hydrogen peroxide, and

  NOTE—All references to hydrogen peroxide sterilization in this TIR refer to sterilization in the gas phase. Hydrogen peroxide is also used for liquid chemical sterilization, but that application is outside the scope of this TIR.

- ozone.

Guidance in this TIR relates to

- material selection—choosing sterilization-compatible materials (see clause 3 and Annexes A–F);
- material processing—optimizing the functional performance of materials selected, to avoid processing errors that can contribute to negative effects from sterilization (see clause 4);
- material testing—challenging critical aspects of the product for functionality and safety after sterilization and aging (see clause 5); and
- accelerated aging—applying programs that ensure correlation with real-time aging while reducing the cost and amount of time required for material qualifications (see clause 6).

NOTE—Information in this TIR is not intended to provide a rationale for the use of materials without proper qualification of the materials. The information is general in nature and is intended only as a guide to successfully initiating material qualification programs.

2 Definitions, symbols, and abbreviations

For the purposes of this TIR, the following definitions and abbreviations apply.

2.1
absorbed dose:
quantity of ionizing radiation energy imparted per unit mass of a specified material.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

NOTE 1—The unit of absorbed dose is the gray (Gy) where 1 gray is equivalent to absorption of 1 joule per kilogram.

NOTE 2—For purposes of this TIR, the term dose is used to mean, “absorbed dose.”

2.2
accelerated aging (AA):
storage of health care products at elevated temperatures and/or at other intensified environmental conditions in order to simulate real time aging in a shorter amount of time.

2.3
aging factor (AF):
ratio of time between T_{RT} and T_{AA} that is estimated or calculated to achieve the same level of functional degradation of the health care product in real time as that observed under accelerated aging.

2.4
glass transition
reversible change in an amorphous polymer or in amorphous regions of a partially crystalline polymer from (or to) a viscous or rubbery condition to (or from) a hard and relatively brittle one.

2.5
health care product:
medical device(s), including in vitro diagnostic medical device(s), or medicinal product(s), including biopharmaceutical(s).

NOTE—For purposes of this document, the term health care product, or product, refers to the finished medical device and/or additional components within the final package.

2.6
material biocompatibility
lack of an adverse health effect from exposure to materials from which a device is made or in which a device is packaged.

2.7
maximum acceptable dose
dose given in the process specification as the highest dose that can be applied to a defined product without compromising safety, quality or performance.

2.8
Q_{10}
expected or observed change in the rate of a reaction occasioned by a 10° C change in reaction thermal environment.

NOTE—Q_{10} = 2 is a common and conservative estimate for most polymer systems.

2.9
Real time aging (RT):
storage of health care products at ambient conditions in order to evaluate functional properties over time.

2.10
real time equivalent (RTE)
amount of real time to which given accelerated aging conditions are estimated to be equivalent.

NOTE—For example, if AA samples are held at an elevated temperature for 6 months and the AF_0 for the system has been estimated to be 2, then the RTE is 1 year:

$RTE = t_{AA} \times AF_0$

 © 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

= 6 months x 2

= 1 year.

2.11
shelf life
length of time that a product can remain at the typical storage conditions prior to use without having an unacceptable effect on its functionality and biocompatibility or the length of time chosen for its expiration.

2.12
t
time, over which aging studies are conducted.

NOTE—t_{RT} and t_{AA} symbolize the storage time over which real time and accelerated aging studies have been conducted.

2.13
T
temperature, measured in ºC, utilized in aging studies.

NOTE—T_{RT} and T_{AA} symbolize real time and accelerated aging temperatures, respectively.

2.14
T_g
approximate midpoint of the temperature range over which the glass transition takes place.

2.15
Tm
The melt temperature or the temperature of molten plastic.

[ASTM D-883-08]

3 Selection of materials—Guidance

3.1 General

In the design and development of medical products requiring sterilization, consideration should be given to the needs of the customer, the performance requirements for the finished device, the choice of materials of construction, and the sterilization method. The product must meet safety and efficacy requirements while providing a benefit to the patient and user. The product requirements can limit the choices of materials available for construction and can ultimately determine the acceptable mode of sterilization based on compatibility with various sterilization methods. It should be noted that product design characteristics can affect the mode of sterilization; for example, gaseous modalities require that surfaces to be sterilized be accessible to the sterilant.

Materials must be selected so that the final products are compatible with the sterilizing agent. Information about compatibility of specific materials can be obtained from materials manufacturers, published literature, Internet searches, and so forth. In the event that supporting information is not available, the effects of exposure to the sterilizing agent on the physical and chemical properties of materials and on their biological safety should be assessed (see 5.4). The effects of repeated exposure to the sterilizing agent on the properties of materials should be studied, using the process parameters that are likely to maximize material effects. The materials evaluated and the outcomes of all tests should be documented, together with the criteria against which the properties of materials were assessed before and after exposure to the sterilizing agent.

Ultimately, it is the device manufacturer's responsibility to demonstrate that the sterile device meets its intended performance requirements and is safe and effective.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

3.2 Guidance specific to different sterilization modalities

Guidance is provided on the compatibility of medical device materials with each sterilization modality in Annexes A through F. Several material families are addressed within the following classes of materials: thermoplastics, thermosets, adhesives, elastomers, metals, ceramics/glasses, and other materials. Each annex describes its sterilization modality in enough detail for the reader to understand the parameters of the sterilization process that need to be considered in evaluating the compatibility of materials.

The information provided in the annexes is a general guide to the compatibility of materials that are intended to be used to initiate a successful material qualification program. It is unacceptable to use this information as the sole rationale for using a material with a given sterilization modality. For instance, the material compatibility tables in the annexes do not provide a comprehensive list of all materials used in medical products, and they are not indicative of all applications of the materials listed.

Summaries of the sterilization modalities relative to the material compatibility fundamentals of medical devices are provided in the sections that follow. Brief reference to the application of each sterilization modality to pharmaceutical and biological agents, where applicable, is also provided.

3.2.1 Radiation sterilization

Because of its high reliability, safety, relative ease of validation, and strong technical support, ionizing radiation has been used for more than half a century to sterilize medical devices. It is one of the few commercially available sterilization methods that results in high levels of microbial reduction without requiring direct accessibility of all surfaces. Sterilization of any location within a product depends on the dose received at that location. As this will vary based on product thickness and density, refer to ANSI/AAMI/ISO 11137-3 for specific methods for determining dose distribution within a product. Radiation sterilization results in products that have no sterilant residues, are not radioactive, and are available for immediate use by the final user without additional testing. The one limitation to this universal applicability is that a limited number of polymeric materials degrade because of the effect of the radiation on the polymer bonds from which they are composed.

Radiation sterilization uses high-energy radiation to disrupt molecular bonds (i.e, to ionize or excite material bonds). The level of ionizing energy, or dose, received by the product to achieve sterilization is measured in kGy (kilogray) and can be delivered by gamma or x-ray photons or directly by high-energy electrons. It should be noted that the maximum energy received by a product will dictate product functionality and can be 1.1 to 3.0 times the minimum sterilization dose because of the irradiator's design and the product's geometry and density.

During the radiation sterilization process, all environmental conditions such as humidity and pressure remain constant. Products are subjected to an increase in temperature, which depends on the dose, dose rate, and irradiation process. Although temperature, moisture, and pressure changes that typically affect the integrity of the package seal in the application of gas-stain modalities are not of consequence, changes in the material's physical properties might affect the strength of the package seal. Depending on the product design, dose requirements, and product requirements, most materials commonly used for medical device fabrication can be used. The poststerilization changes need to be evaluated. Some materials, such as polyacetal, unstabilized polypropylene, and polytetrafluoroethylene (PTFE), degrade at routine sterilization doses and must be carefully evaluated and, in some cases, avoided, if possible.

Consideration must be given to the potential physical and chemical changes in products and materials because stabilization of the ionized states can take various pathways. These pathways are usually a combination of recombination (no change), chain scission (decrease in molecular weight and strength), and cross-linking (stiffening or increase in strength), although one pathway can dominate and determine the integrity of the post-irradiated product. Materials subjected to radiation sterilization should be evaluated for the following:

- changes in physical properties, such as embrittlement, discoloration, odor generation, stiffening, softening, enhancement or reduction of chemical resistance, and an increase or decrease in melt temperature;

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

- changes in chemical properties, such as decomposition, generation of gases, polymerization, and possible formation of toxic compounds;

- differences in expansion rates, which could affect the bond strengths of mated parts; and

- changes in material or product functionality and performance over the shelf life of the product.

Pharmaceutical applications—Although irradiation is used as a terminal sterilization process for component containers that are normally used in packaging pharmaceutical products, pharmaceuticals and drugs are not commonly sterilized by irradiation. Success has been attained with dry formats (i.e., penicillin, heparin); however, issues related to the production of free radicals can enable the formation of contaminants other than the primary active ingredients. Successful processing of pharmaceuticals has been attained when the immediate processing environment is modified or controlled (e.g., refrigerated or oxygen-free environments).

Biological applications—Although radiation can and is used for many biological applications (e.g., tissue), it can have undesirable effects. Collagen and other biological molecules can be negatively affected by radiation, causing a reduction in the strength or in the incorporation of the biologic into the patient (e.g., bone formation or blood vessel formation). Controlled irradiation conditions can improve the condition of the biologic and negate the negative affects of irradiation (e.g., low temperatures, water or oxygen content, or free radical scavengers and radioprotectants).

See Annex A for more information.

3.2.2 EO sterilization

EO sterilization uses multiple conditions in routine processing (i.e., heat, moisture, pressure changes, and exposure to EO or its nonflammable diluents). Product and packaging should be designed to allow for the removal of air and the penetration of steam and EO. Consideration should be given to the potential physical and chemical effects of these conditions and the formation of residuals. During an EO sterilization process, products can be subjected to environmental stresses such as vacuum and pressure changes, elevated temperature, and changes in humidity. The product can also react with the EO, the diluent gases used, or both. Furthermore, a high moisture content and changes in pressure might affect the strength of package seals with a consequent loss of integrity. The product design should ensure that functionality and safety are not compromised by exposure to the anticipated range of sterilization conditions.

Pharmaceutical applications—EO may be used to sterilize some pharmaceutical active components and/or packaging systems and components before aseptic processing. The use of EO as a terminal sterilization process for pharmaceuticals can be limited because the EO process might alkylate or hydrolyze chemically reactive species, the relatively long times at temperatures of 40 °C to 60 °C might cause some thermal degradation, and the vacuum pulses might evaporate components of the formulation that have low boiling points. EO is used as a terminal sterilization process for some combination products that might also include a coating. In some cases where the pharmaceutical packaging is impermeable to EO and the contents have been aseptically processed, EO can be used as a surface sterilant for the exterior of the pharmaceutical container or the inner packaging.

Biological applications—The complex matrices of many biological products might result in high EO residual levels, and the EO process might alkylate or hydrolyze chemically reactive species.

See Annex B for more information.

3.2.3 Moist heat (steam) sterilization

The material effects from moist heat sterilization are caused by (a) exposure to heat or moisture for the required time, (b) repeated exposures to the conditions of sterilization, or (c) both. Materials subjected to moist heat processes can incur, and should be evaluated for, the following changes:

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

- changes in physical properties, such as hydration, softening, cracking, dulling, discoloration, deformation, or shape alterations;

- changes in chemical properties, such as decomposition, elution and extraction of additives and ingredients, generation of gases, polymerization, formation of toxic compounds, or corrosion;

- differences in expansion rates, which could cause damage to mated parts; and

- material functionality or product performance.

Metals can be subjected to steam corrosion, material fibers can be damaged, and rubbers and plastics can be altered as temperatures reach or exceed glass transition temperatures and/or melting points. It should be noted that oxidative processes occur in this sterilization process and there is a potential for corrosion attributable to water hydrolysis, pH change, and contaminants carried in the steam.

Pharmaceutical applications—Moist heat is a popular method in the pharmaceutical industry and in hospital health care facilities. Large- and small-volume parenteral solutions are terminally sterilized using moist heat processes. The major concern with sterilization by heat is the rate of material degradation relative to the rate of biological inactivation.

Biological applications—In most situations, moist heat applies temperatures that are too high to allow the biological materials to function properly after sterilization. In some circumstances, moist heat may prove to be a valid method for lyophilized biological products (e.g., cortical bone).

See Annex C for more information.

3.2.4 Dry heat sterilization

The material effects from dry heat sterilization are caused by exposure to elevated temperatures that are generally greater than those seen in a moist heat process. Dry heat processes typically use longer exposure times, repeated exposures, or both. Materials processed in dry heat sterilization might exhibit the following changes and differences:

- changes in physical properties, such as softening, melting, charring, cracking, dulling, discoloration, deformation, or shape alterations;

- changes in chemical properties, such as decomposition, generation of gases, polymerization, formation of toxic compounds, or corrosion;

- differences in expansion rates, which could cause damage to mated parts; and

- material functionality or product performance.

Metals can be subjected to dry heat sterilization. However, material fibers can be damaged and rubbers and plastics altered as temperatures reach or exceed glass transition temperatures and melting points. It should be noted that oxidative processes occur in this sterilization process.

Pharmaceutical applications—Dry heat sterilization is generally used in the preparation of component materials. There is extensive use of dry heat for the sterilization and depyrogenation of glass vials and ampoules and for the sterilization of heat-stable ingredient powders or raw materials. Dry heat has been used in the sterilization of liquids in sealed containers and syringes.

Biological applications—Generally, dry heat uses temperatures that are too high to allow the biological materials to function properly after sterilization.

See Annex D for more information.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

3.2.5 Hydrogen peroxide sterilization

Materials that are good candidates for low-temperature hydrogen peroxide sterilization are hydrophobic and chemically stable, and they resist oxidation and moisture. In the design of devices with these qualities, it is best to avoid decomposers (such as silver, copper, and copper alloys) and absorbers (such as polyurethane, nylon, and cellulosic materials). Noncatalytic, nonabsorbent materials such as PTFE, polyethylene, stainless steel, or low-copper-aluminum alloys are recommended. Adhesives that use large proportions of amines as curing or cross-linking agents tend to be incompatible.

In general, all materials that are commonly used for medical instrument fabrication do not retain enough sterilant residuals to affect biocompatibility, and poststerilization aeration usually is not required. In addition, the hydrogen peroxide gas plasma method uses the plasma phase to further eliminate residuals. It is important to discuss the specific concerns of sterilant residuals with the equipment manufacturer. As with EO sterilization, the residual level of hydrogen peroxide depends on the material family, grade, load density in the chamber, loading weight, specific cycle parameter, and packaging used.

Implantable and ophthalmic devices might require special processing. Contact the equipment manufacturer for specific applications. Biocompatibility according to the appropriate standard should be established for devices.

Pharmaceutical applications—Neither hydrogen peroxide gas plasma nor hydrogen peroxide vapor sterilization is commonly used to sterilize pharmaceuticals. Some success has been achieved using hydrogen peroxide gas plasma to sterilize combination devices (e.g., drug coatings on medical devices) and terminal sterilization of the exterior of filled drug containers (e.g., prefilled syringes).

See Annex E for more information.

3.2.6 Ozone sterilization

Materials that are good candidates for low-temperature ozone sterilization should be resistant to oxidation and moisture. This method of sterilization cannot be used for fluids or woven textiles. Ozone sterilization is a process that produces surface oxidation. Therefore, the shape of the materials as well as the design of a device is closely related to the longevity and resistance of the device to sterilization. For example, polymeric components with large surface-to-mass ratios (e.g., fibrous material) will undergo fast oxidative degradation. Although such materials can be satisfactorily used in the manufacture of a device that has limited reuse, they might not be satisfactorily used for a device with a longer lifespan.

Pharmaceutical applications—Ozone sterilization is not known to be in use in pharmaceutical applications.

See Annex F for more information.

3.3 Comparison of materials compatibility

Table 1 provides a general overview of material compatibility and product functionality (exclusive of residuals and biocompatibility) for different classes of materials and polymers processed by each of the sterilization modalities. The material compatibility indicates the level of compatibility with a standard single-use sterilization using standard process conditions, dose requirements, or both. It should be noted that there is variability within a class of material, polymer type, or grade of material. The conditions under which the materials are processed or exposed during the sterilization process will also have some effect on the materials compatibility. Materials and products composed of the materials must be qualified through a formal material-product qualification program.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table 1—Material compatibility table, given a single processing

Key: (●) = poor; (● ●) = fair; (● ● ●) = good; (● ● ● ●) = excellent; (U) = unknown

Material	Radiation	EO	Moist heat	Dry heat	Hydrogen peroxide	Ozone
Thermoplastics						
Acrylonitrile butadiene styrene (ABS)	● ● ●	● ● ● ●	● to ● ●	● to ● ●	● ● ● ●	● ●
Fluoropolymers						
Polytetrafluoroethylene (PTFE)	●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Perfluoro alkoxy (PFA)	●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Perchlorotrifluoroethylene (PCTFE)	● ● ● to ● ● ● ●	● ● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ● ●
Polyvinyl fluoride (PVF)	● ● ●	● ● ● ●	● ● to ● ● ●	● ● to ● ● ●	● ● ● ●	U
Polyvinylidene fluoride (PVDF)	● ● ● to ● ● ● ●	● ● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ● ●
Ethylenetetrafluoroethylene (ETFE)	● ● ● to ● ● ● ●	● ● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ● ●
Fluorinated ethylene propylene (FEP)	● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Polyacetals (e.g., polyoxymethylene)	●	● ● ● ●	● ● to ● ● ●	● ● to ● ● ●	● ● ● ●	● ● ●
Polyacrylates (e.g., polymethylmethacrylate)	● ● to ● ● ●	● ●	● to ● ●	● to ● ●	● ●	● ● ●
Polyamides (e.g., nylon)	● ● to ● ● ●	● ● ● ●	● to ● ● ● ●	● to ● ● ● ●	● ● ●	● ● ●
Polycarbonate (PC)	● ● ● to ● ● ● ●	● ● ● ●	● to ● ● ●	● ●	● ● ● ●	● ● ● ●
Polyesters, saturated	● ● to ● ● ●	● ● ● ●	● to ● ● ●	● to ● ●	● ● ● ●	● ● ● ●
Polyethylene (PE), various densities	● ● ● to ● ● ● ●	● ● ● ●	● to ● ● ●	● to ● ●	● ● ● ●	● ● ● ●
Polyimides (e.g., polyetherimide)	● ● ● ●	● ● ● ●	● ● to ● ● ● ●	● ● ● to ● ● ● ●	● ● ● ●	● ● ● ●
Polyketones (e.g., polyetheretherketone)	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Polypropylene (PP)						
Natural	● to ● ●	● ● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ● ●
Stabilized	● ● to ● ● ●	● ● ● ●	● ● to ● ● ●	● to ● ● ●	● ● ● ●	● ● ● ●
Polystyrene (PS)	● ● ● ●	● to ● ● ●	● to ● ● ● ●	● to ● ● ● ●	● ● ● ●	● ●

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table 1—Material compatibility table, given a single processing (continued)

Key: (●) = poor; (● ●) = fair; (● ● ●) = good; (● ● ● ●) = excellent; (U) = unknown						
Material	Radiation	EO	Moist heat	Dry heat	Hydrogen peroxide	Ozone
Polysulfones	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●	● ● ● ●	● ● ●
Polyurethane (PU)	● ● to ● ● ● ●	● to ● ● ●	● to ● ●	● to ● ●	● ● ●	●
Polyvinylacetates (PVA)	● ● ●	●	● to ● ●	● to ● ●	● ● ● ●	U
Polyvinylchloride (PVC)	● ● ●	● ● ● ●	● to ● ●	● to ● ●	● ● ● ●	● ● ● ●
PVC, plasticized	● ● ●	● ● ● ●	● to ● ●	● to ● ●	● ● ● ●	● ● ●
Styrene acrylonitrile (SAN)	● ● ● to ● ● ● ●	● to ● ● ●	● to ● ●	● to ● ●	● ● ● ●	U
Thermosets						
Epoxy	● ● ● ●	● ● ● to ● ● ● ●	● ● to ● ● ● ●	● ● to ● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●
Phenolics	● ● ● ●	● ● ●	● ● to ● ● ●	● ● to ● ● ●	● ● ●	● ● ● ●
Polyester, unsaturated	● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●	● ● ● to ● ● ● ●	U	● ● ● ●
Polyimides	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●	● ● ● ●	U
Polyurethanes						
Aliphatic	● ● ● ●	● to ● ● ●	● to ● ●	● to ● ●	● ● ●	●
Aromatic	● ● ● to ● ● ● ●	● to ● ● ●	● to ● ●	● to ● ●	● ● ●	●
Adhesives						
Acrylic	● ● to ● ● ●	● ●	● to ● ●	● to ● ●	● ●	● ● ●
Epoxy	● ● ● ●	● ● ● to ● ● ● ●	● ● to ● ● ● ●	● ● to ● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●
Fluoroepoxy	● ● ● ●	U	● ● ● to ● ● ● ●	● ● to ● ● ●	● ●	● ● ●
Silicone	● ● to ● ● ●	● ● ● ●	● to ● ● ●	● ● to ● ● ● ●	● ●	● ● ●
Elastomers						
Butyl	●	● ● ● ●	● ● to ● ● ● ●	● to ● ● ●	● ● ●	●
Ethylene propylene diene monomer (EPDM)	● ● ● to ● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●	● ● to ● ● ●	● ● to ● ● ●	● ●
Natural rubber	● ● ● to ● ● ● ●	● ● ●	● to ● ●	● to ● ●	● ● ●	●

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table 1—Material compatibility table, given a single processing (continued)

Key: (●) = poor; (● ●) = fair; (● ● ●) = good; (● ● ● ●) = excellent; (U) = unknown						
Material	Radiation	EO	Moist heat	Dry heat	Hydrogen peroxide	Ozone
Nitrile	● ● ● to ● ● ● ●	● ● ● ●	● ● to ● ● ●	● to ● ●	● ● ●	U
Polyacrylic	● ● to ● ● ●	● ●	●	●	● ●	● ● ●
Polychloroprene	● ● ●	● ● ●	● ● to ● ● ●	● to ● ●	● ● ● ●	●
Silicone	● ● to ● ● ●	● ● ● ●	● to ● ● ● ●	● ● to ● ● ● ●	● ● ● ●	● ● ● ●
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	● ● to ● ● ●	● ● ● to ● ● ● ●	● to ● ●	● to ● ●	● ● ● ●	●
Urethane	● ● ● to ● ● ● ●	● to ● ● ●	● to ● ●	● to ● ●	● ● ●	●
Metals						
Aluminum	● ● ● ●	● ● ● ●	● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Brass	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ●
Copper	● ● ● ●	● ● ●	● ● ●	● ● ● ●	● ● ●	● ● ●
Gold	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Magnesium	● ● ● ●	U	● ● ●	● ●	● ● ●	U
Nickel	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ●	●
Silver	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● to ● ● ●	●
Stainless steel	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Titanium	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Ceramics/glasses						
Aluminum oxides	● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●	● ● ●	● ● ● ●	● ● ● ●
Silica	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●	● ● ● ●
Zirconium oxides	● ● ● ●	● ● ● ●	● ● to ● ● ●	● ● to ● ● ●	● ● ● ●	● ● ● ●
Other materials						
Bioabsorbables						
Polyglycolides	● to ● ● ●	●	● to ● ●	● to ● ●	● to ● ● ●	U
Polylactides	● to ● ● ●	●	● to ● ●	● to ● ●	● to ● ● ●	U
Cellulosics						
Cellulose ester	● ●	● ● ● ●	● to ● ●	● to ● ● ●	●	● to ● ● ●

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table 1—Material compatibility table, given a single processing (continued)

Key: (●) = poor; (● ●) = fair; (● ● ●) = good; (● ● ● ●) = excellent; (U) = unknown						
Material	Radiation	EO	Moist heat	Dry heat	Hydrogen peroxide	Ozone
Cellulose acetate propionate	● ● to ● ● ●	● ● ● ●	● to ● ●	● to ● ●	●	● to ● ● ●
Cellulose acetate butyrate	● ● to ● ● ●	● ● ● ●	● to ● ●	● to ● ●	●	● to ● ● ●
Cellulose, paper, cardboard	● ● to ● ● ●	● ● ● ●	● to ● ●	● to ● ●	●	● to ● ● ●
Liquid crystal polymer (LCP)	● to ● ● ● ●	U	● ● ● ●	● ● ● to ● ● ● ●	● ● ● ●	● ● ● to ● ● ● ●

4 Manufacturing process and design considerations

4.1 General

The functional performance of many polymeric materials can be affected more by processing variables than by the method of sterilization chosen. Reviewing processing issues related to health care product materials will help prevent problems and increase the probability of designing and implementing sterilization-compatible health care products.

Process variables such as molding, extrusion, film calender, subassembly, and product assembly can profoundly affect the subsequent physical performance of a polymer. Like other engineered systems, polymeric molecules tend to fail at the point of greatest cumulative stress. Polymers respond to the combined effect of stresses and environmental exposures. Hence, for success in material qualification, it is important to understand and control all of the variables affecting the polymers, such as

- shrinkage stress,
- residual molding stress,
- processed-in stress,
- applied stress,
- sonic welding,
- rapid crystallization,
- designed-in-loading,
- solvent or chemical attack,
- hydrolysis or inadequate drying,
- ultraviolet radiation,
- temperature,
- regrind, and
- oxidation.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

These effects are even more noteworthy in conjunction with sterilization processing because molecules that are already stressed can be more susceptible to sterilization degradation. Guidance in Annexes A through F is, in general, applicable to materials processed at optimum conditions.

4.2 Impact of processing versus impact of sterilization

In selecting a sterilization method, it is important to consider the tradeoff between material stresses and the economics of processing. This tradeoff is especially important for molding, extrusion, and calender processes. For example, unless other directions are provided in order to comply with component specifications, an injection molding cycle will usually be optimized for maximum output of parts rather than optimization of physical properties. Because the overall cost of a molding cycle is predominantly dictated by the time required for heat removal and for the molten polymer to become a solid, running a cycle with mold and melt temperatures that are lower than the ideal is attractive. Doing so, however, ensures that the quality of the part will be compromised. Such a compromise can be critical in the case of health care products intended for sterilization. Poor processing of materials, with residual stresses, can potentially reduce material performance—regardless of the sterilization method employed.

"Quality" optimized processing parameters, based on quality improvements, often result in reduced overall costs, despite output reduction. Increasing mold temperature, for example, has been shown to improve physical properties, such as impact strength, by a factor of 10 or more (which is significantly greater than any effect on impact strength that results from sterilization processing). The substantial and dominating effects of other material processing variables could explain the inconsistencies in the literature on the sterilization compatibility of some materials. See Figure 1.

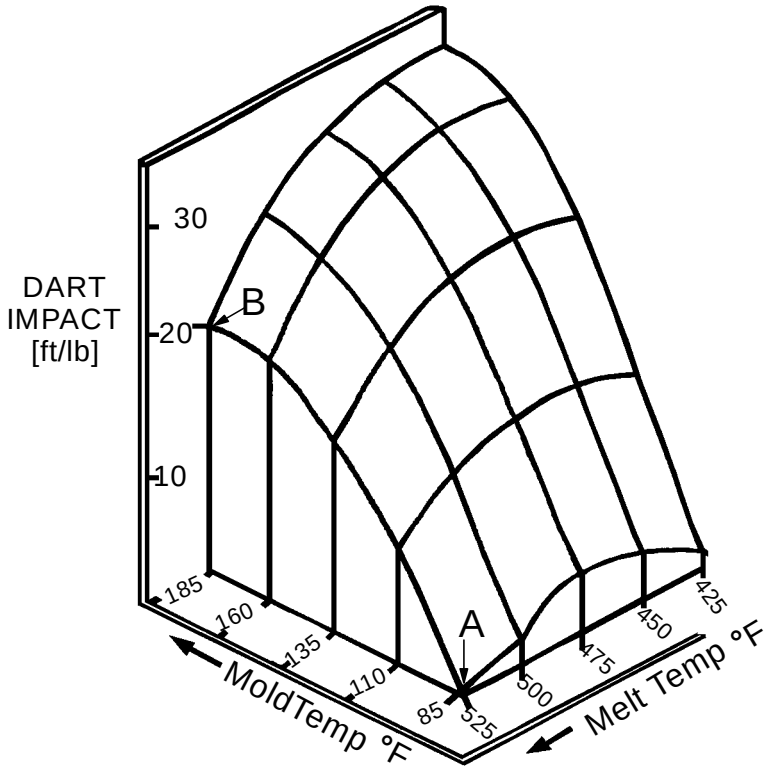


Figure demonstrates that impact strength increases by 20 times in ABS material simply by raising the mold temperature from 85 °F to 185 °F.

Condition A:

Melt 525 °F, mold 85 °F, impact 1 ft-lb

Condition B:

Melt 525 °F, mold 185 °F, impact 20 ft-lb

Figure 1—Impact of process variables on physical properties—Acrylonitrile butadiene styrene (ABS)

 © 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

4.2.1 Processing considerations for injection molding

Mold temperature, melt temperature, and mold filling rate can affect the polymer physical properties (e.g., elongation, impact, and tensile strength) for injection molding much more than sterilization processing will. Therefore, it is important to monitor the control samples carefully, even noting the mold cavity number, which often affects performance. Warm molds and easy filling rates produce ductile parts. Brittle parts are produced in cold molds with tortuous filling and poor venting. Table 2 lists 14 ways to recognize cold-molded parts that are likely to reduce product performance capabilities.

Table 2—How to recognize cold-molded parts

1	Part has no flash.
2	Part has poor gloss or dull finish.
3	Part has no shrink marks.
4	Dimensions are high tolerance or oversized.
5	There are packing rings (blush) at gate.
6	Warping is reduced.
7	Part is cloudy or shows loss of transparency.
8	Part is crazed when contacting solvent.
9	There is a visible weld line opposite gate.
10	Part cracks when bent or flexed.
11	Part is heavier than standard.
12	Part sticks in cavity but is free on cores.
13	Part distorts when heated.
14	Durometer readings are higher than standard (harder).

4.3 Product design considerations

Product design can have a significant influence on the long-term performance and reliability of a product or component. The mode of sterilization for poorly designed products can lead to premature part failure caused by increased sensitivity to processing conditions and environmental attack. To compensate for the effects of all the stresses that lead to losses in physical properties, incorporate appropriate design guidelines, as indicated in the following paragraphs. For each polymer, follow material suppliers' design guidelines that might be specific to the polymer's unique morphology and chemistry. Such guidelines can make the polymer less susceptible to various processing and environmental stresses.

Products intended to be sterilized by gas or vapor should be designed so that the vapor or heated water can access the areas to be sterilized. In some cases, as in the case of steam sterilization of stoppered bottles or vials, the closures must be prewetted or treated to contain a minimum moisture content, to facilitate sterilization (e.g., the moisture content of bottle stoppers must be controlled to facilitate heat transfer and to avoid dry heat conditions). Likewise, the packaging must be designed to facilitate the transfer of sterilant and conditions to the product.

In terms of device construction compatibility, wrapped items, products of large mass, and large load sizes require longer times for adequate heating, moisture penetration, and heat diffusion. These conditions can negatively affect the materials and device performance.

For injection molding, the following guidelines should be used:

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

(a) Avoid thick to thin transitions.

(b) Incorporate generous radii everywhere.

(c) Avoid interference fits and long-term creep loading exceeding 20 % of yield strength.

(d) Design molds for fast and easy filling, with gates sized and located to minimize material flow pressures and paths. Also, design the part for easy ejection, to minimize ejection forces and molded-in stresses.

Figure 2 illustrates guidelines for molding design.

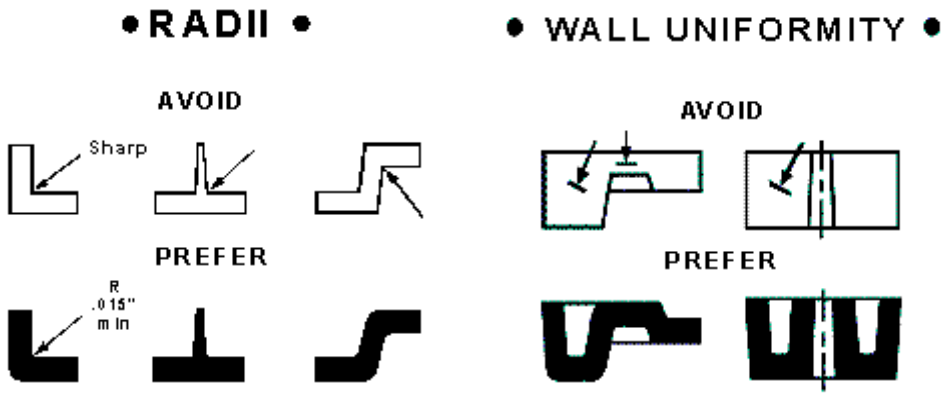


Figure 2—Molding design guidelines

Follow material suppliers' design guidelines for each polymer that might be specific to the polymer's unique morphology and chemistry. Doing so can make the polymer less susceptible to various processing and environmental stresses.

Perform an appropriate failure or reliability analysis to ensure that critical failure modes are understood and addressed appropriately. For critical components, consider establishing functional safety factors (Stubstad and Hemmerich, 1994) to apply after all manufacturing, environmental, and sterilization processing is complete and the components have been aged.

5 Material testing

The second stage of the qualification process is the testing of sterilization materials for product functionality and biocompatibility. Tests included should evaluate specific properties essential to the intended function of the product. Material compatibility derived from reference information alone is inadequate for determining the proper function and performance requirements for the material or product.

5.1 Definition of requirements for product functionality

Before testing is initiated, the functional product requirements should be determined and specified. Material qualification tests should challenge the effect of sterilization on the functional requirements of the product and also

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

challenge the dominant or critical failure modes or both. During testing and as part of the design process, the potential failure modes should be identified, through a documented risk analysis or reliability plan (e.g., ANSI/AAMI/ISO 14971), failure mode and effects analysis (FMEA), or another tool. This plan should take into consideration field experience and complaint files on related products, product design specifications, and common product use. Another valuable method for identifying potential failure modes is to challenge samples to failure. For example, with radiation sterilization, a product is exposed to radiation overdosing (e.g., 100 kGy), and then the product's failure modes are investigated. It is important to identify critical failure modes before beginning shelf-life testing. Without this knowledge, aging studies might not be meaningful or efficient.

5.2 Definition of worst case sterilization processing conditions

5.2.1 General

Worst case sterilization processing conditions should be established and used to qualify materials and products for function and safety. Worst case conditions are ones that are not expected to be exceeded during routine sterilization processing. Such conditions are different for each sterilization process but are those that are determined to have an effect on the material or product. These conditions are

- dose,
- temperature,
- humidity,
- pressure (change rate and/or level),
- time, and
- sterilant concentration.

Other factors that need to be considered are processing variability and the number of times the product might be sterilized.

5.2.2 Considerations for processing conditions unique to radiation sterilization

The major concern for radiation processing is the maximum acceptable dose. Figure 3 displays the concept of a qualification dose equal to or exceeding the product's maximum dose specification.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

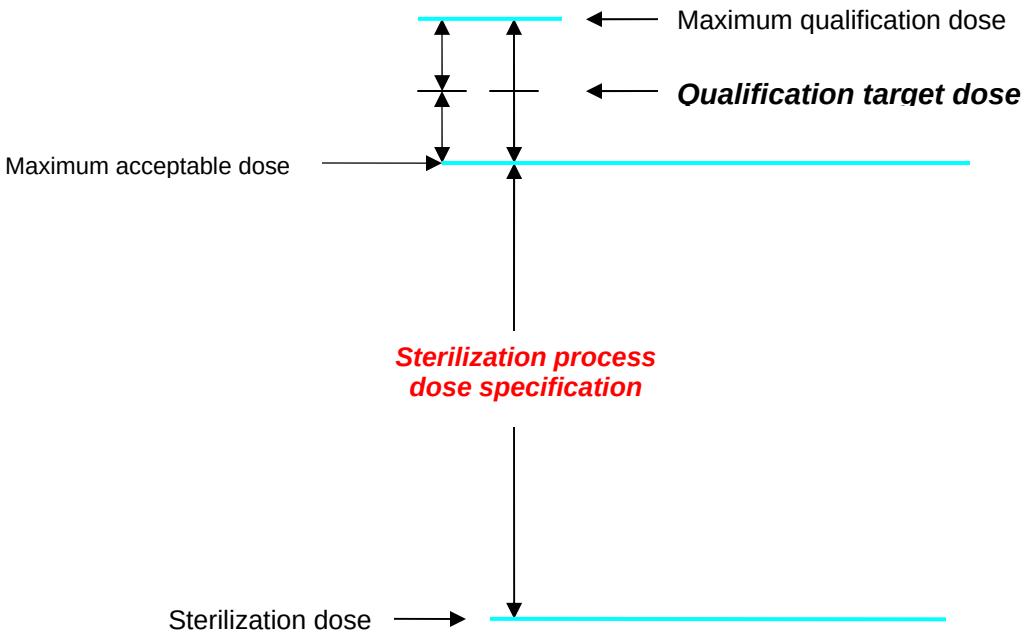


Figure 3—Concept of a qualification dose

Material qualification performed at a low dose rate can reveal greater degradation (e.g., embrittlement) than a high dose rate irradiation, as a result of enhanced oxidative effects (Cleland et al., 1993; Ishigaki and Yoshii, 1992; Williams, 1995; Farrell and Hemmerich, 1995). Consequently, a material that formerly qualified at a low dose rate (gamma) will typically require minimal qualification to demonstrate material compatibility at a higher dose rate (E-beam). Conversely, a material formerly qualified at a high dose rate can require more substantial qualification in the low dose rate application. This consideration is important to keep in mind for materials that degrade oxidatively (e.g., polypropylene and aliphatic nylon) or for materials used in applications that have large surface-to-mass ratios (e.g., films, fibers, adhesives).

5.3 Product functionality testing

The factors listed below relate to device and package integrity testing and should be considered when defining challenge tests and acceptable criteria for a given sterilization method:

(a) Use tests that specifically challenge the dominant or critical failure modes that have been identified (see 5.1). See the ANSI/AAMI/ISO 11607 series for package integrity challenge tests and validation guidance. See Table 3 for a list of selected standard test methods that can apply to product functionality testing.

NOTE—It is necessary to design tests to challenge the specific failure mode of the product in a given application.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table 3—Physical and functional test methods for plastic material evaluation

Test method	Test reference
Tests for embrittlement:	
1. Tensile properties	
a) Tensile strength	o ASTM D638-03 o ISO 527 series o ASTM D88-02 o ASTM D412-06A
b) Ultimate elongation	
c) Modulus of elasticity	
d) Work	ISO 527 series
e) Package seal strength	ASTM F88-07A
2. Flexural properties	
a) Flange bending test	Williams, Dunn, Sugg, and Stannet.
b) Flexbar test	ISO 178:2001
3. Impact resistance	ASTM D1822-06
4. Hardness	
a) Shore	ISO 868:2003
b) Rockwell	ASTM D785-08
5. Compressive strength	ISO 604:2002
6. Burst strength	ASTM F-2054-07
a) For package seal strength	ASTM F-2054
7. Tear strength	ASTM D-1004-03 ISO 6383-1:1983
Tests for discoloration:	
1. Yellowness index	ASTM E-313-05
2. Optical spectrometry	ASTM D-1746-03

(b) Whenever possible, tests should be designed to yield variable data rather than attribute data. Variable data are required to iterate an aging factor (AF) or to use most advanced methods for estimating shelf life. Zero-failure

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

test results should be avoided when possible because they diminish understanding of ultimate product performance and failure modes.

(c) Test units should consist of products constructed of the same or equivalent components or subassemblies and manufactured by the same or equivalent manufacturing processes as those used for routine production. Variability in raw materials, manufacturing processes, and storage conditions should be addressed during qualification. The test units should be finished devices in the final package. Subassemblies and even specially prepared test samples are satisfactory in certain cases; however, justification for their use should be documented.

(d) Acceptance criteria should be defined for all tests. The criteria chosen should reflect customers' essential functional requirements or safety requirements according to design specifications rather than arbitrary levels that restrain the validation process unnecessarily. The criteria should also be a function of the variability and criticality of the parameter being tested. For devices that can be reprocessed, acceptable limits of reuse should be defined setting the maximum number of reuses.

(e) A sufficient number of product samples should be selected so that the acceptance criteria can be met in a statistically valid manner. (See ISO/TR 8550:1994.)

(f) A written test protocol should be developed, specifying the accelerated aging conditions (e.g., temperature, humidity, heat cycling); transportation simulation considerations; time intervals; sample sizes; and specific tests and acceptance criteria to be undertaken at each test time interval. Thermal cycling is particularly valuable in assessing designs that involve differentials in expansion coefficients, especially with adhesive bonding. Relatively large samples might be required, and proper resource planning must be executed to ensure adequate accelerated aging oven space, ambient storage, human resources, and test equipment. Adequate controls should be designed into the protocol (e.g., using one batch for all samples or randomizing samples) so that appropriate comparisons can be made between time intervals.

(g) Samples should be manufactured and processed as specified in the protocol.

(h) Aging should be initiated after the majority of sterilization byproducts and residuals have decayed or dissipated. Depending on the sterilization process, this can take hours in the case of vaporized hydrogen peroxide (VHP), to 48 hours in the case of radiation processing. Zero-time samples and controls are then tested, with samples from the aged and control groups removed and tested at the appropriate times in accordance with the protocol.

NOTE—Degradation reaction rates during the first 48 hours after sterilization are typically much higher than rates following this initial period. Indeed, for many materials, degradation induced by sterilization processing is largely complete during this initial period. The time frame for the high reaction rates depends on the characteristics of the material under investigation and the sterilization process.

(i) Product test results should be evaluated with appropriate statistical methods to determine whether the product meets the acceptance criteria for each test interval.

5.4 Material biocompatibility

5.4.1 General

The evaluation of materials and products for biocompatibility is accomplished by material toxicity testing in conjunction with material characterization (see the ANSI/AAMI/ISO 10993 series for detailed information on evaluation of biocompatibility). Material characterization and screening tests for candidate materials can be accomplished early in the design process and might identify potential biosafety issues that could lead to unnecessary redesign expense later in the process. Physiochemical reactions, cytotoxicity, and hemolysis are examples of screening tests that are sensitive, inexpensive, and rapid. Biocompatibility and environmental data from material suppliers are good sources of information for use in evaluating candidate component materials. In addition, many

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

useful databases are available for evaluating candidate materials. See the informative references in the bibliography (MEDLINE, RTECS, and TOXLINE and TXLIT).

In addition, chemical characterization of the materials involved plays an important role in attempts to screen materials by identifying and quantifying the bioavailability and physiochemical constituents of the device. This process includes characterization of the following:

- the base material (e.g., molecular weight, polydispersity, linear or branched, cross-linked, composition);
- additives such as colors, antioxidants, and plasticizers;
- processing aids that remain as part of the device and are potentially leachable (e.g., internal lubricants);
- trace components of toxicological concerns (e.g., monomers of known toxicity, heavy metals, transition metal catalysts); and
- any other questionable biological or toxicological components (e.g., particulates, pyrogens).

5.4.2 Biocompatibility concerns regarding sterilant residuals

Under certain conditions, products sterilized with EO, hydrogen peroxide, and ozone can retain residual sterilant. These residuals must be removed to levels required in other standards or in demonstration of biocompatibility. ANSI/AAMI/ISO 10993-7 presents the allowable limits for EO and ethylene chlorohydrin residuals in medical devices. ANSI/AAMI/ISO 10993-7 is accepted by most countries, but some have added their own constraints on top of the international requirements.

In EO sterilization, EO and ethylene chlorohydrin are the primary residuals of concern. However, other residual chemicals can form. Ethylene chlorohydrin is formed when the EO reacts with chloride ions or active chlorine-containing chemicals in the load. Thus, if a device contains no chlorine atoms and was not cleaned with a chlorine-containing compound before sterilization, no ethylene chlorohydrin will be formed. If a device was treated with a chlorine-containing cleaning agent to lower the bioburden before sterilization, very large quantities of chlorohydrin can be formed. In general, ethylene chlorohydrin is not removed by aeration.

Polymers that are processed using hydrogen peroxide sterilization might retain small amounts of hydrogen peroxide but are generally aerated in a chamber under vacuum. The use of gas plasma facilitates the conversion of residual hydrogen peroxide into water and oxygen. Metals and many polymers do not retain measurable residual peroxide. Biocompatibility with the appropriate standard should be established for devices, especially implants and ophthalmic devices. It is important to discuss the specific concerns of sterilant residuals with the equipment manufacturer. As with EO sterilization, residual levels of hydrogen peroxide depend on the material family, grade, load density in the chamber, loading weight, specific cycle parameter, and packaging used.

The ozone molecule is very unstable and rapidly decomposes into the reactive species of hydroxyl radicals and atomic oxygen. Processing with ozone will not form residual chemicals; however, the biocompatibility of processed devices must be demonstrated.

See the ANSI/AAMI/ISO 10993 series of documents for detailed information on evaluation of biocompatibility.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

6 Accelerated aging programs

6.1 Background

ANSI/AAMI/ISO 11137-1:2006 requires that the "product shall meet its specified functional requirements throughout its defined lifetime" (8.1.1). Similar requirements apply to all sterilization modalities and, in fact, to all health care products. One method used to assess shelf life is to age the product under real-time storage conditions for the product's intended shelf life. Real-time aging is the most reliable means of validating the safe and effective performance of a medical device throughout its shelf life and remains the benchmark by which an AA program is evaluated. However, since product testing should be completed before product release, real-time aging delays the introduction of potentially valuable technology to the market, with a concurrent loss of benefit to the patient. AA programs avoid these delays.

AA programs systematically addressed in the 1997 version of AAMI TIR17 have been published in conference proceedings (G.4.3, G.4.4, G.4.5), including background information, application boundaries, and methodical AA protocols (Fixed AF method and Iterative AF method). The methods ranged from conservative, relatively inexpensive protocols to more complex, more aggressive, and more expensive protocols. AA program concepts have also been applied to medical device packaging (sterile barrier) materials and published (G.4.1, G.4.2).

In addition, a rigorous delineation of the rationale for responsibly applying the AA methods in the medical device industry has been published (G.4.7). Empirical data from several industries with aging conditions more severe than those of the medical device industry were explored and the theoretical foundations for the Q_{10} methodology were fully developed.

6.2 New guidance

The AA programs referred to above, initially developed for radiation sterilization or packaging, apply to all sterilization modalities. The principles are completely transferable across sterilization modalities, although there are, naturally, individual points of guidance specific to either radiation sterilization or packaging materials. Detailed guidance on these programs is readily available to users of all sterilization modalities in the documents referenced in subclause G.4.

Annex G provides a brief summary of the framework, theoretical foundations, and methods for AA programs that apply to all sterilization modalities. Annex G also provides an example of a creative application of an AA program method (the Iterative AF method) to enable a device material technology to get to market and benefit patients by avoiding inappropriate AA program constraints that use a more conservative AA method (the Q_{10} = 2, Fixed AF method). It is important to note that the foundational reason it is appropriate to iterate AFs with real-time data is that real-time data are the most clinically relevant data; it is appropriate that they be used to inform the choice of AFs. Annex G also provides a comparison of AA programs for medical devices with accelerated stability programs for pharmaceuticals. This comparison is provided in light of the rapid growth of the combination-device market (medical devices incorporating pharmaceutical or biologic materials) and the resulting need for clarity at regulatory points of intersection as these markets grow together.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex A

Radiation sterilization—Material compatibility fundamentals

A.1 Background

High-energy ionizing radiation produces excitations of orbital electrons that cause cleavage of bonds resulting in ionization of molecules. The resultant energy-rich radicals initiate a series of dissociation, abstraction, and addition reactions that ultimately lead to chemical stability or instability.

Inactivation of microorganisms via ionizing radiation occurs by both direct and indirect effects of ionizations resulting from excitations of orbital electrons and cleavage of bonds. Direct ionization of DNA, key enzymes, and other essential cell components results in microorganisms' direct death and inability to reproduce. The reaction of free radicals produced in cellular fluid and the environment in which the organism resides creates a hostile environment and, indirectly, microorganism death.

A.2 Sterilization process variations and parameters

The rate of energy deposition and penetrability will vary depending on the type of radiation processing. Gamma (^{60}Co) processing takes hours but has greater penetrability, whereas electron beam processes would be significantly shorter (i.e., measured in seconds), but have substantially less penetrability. These fundamental process differences in energy deposition can lead to differences in processing temperature, oxidative effects, and dose uniformity ratio (DUR). A typical DUR in a gamma process is approximately 1.6 or less, while the DUR in an electron beam process can often exceed twice the minimum dose (DUR ≥ 2.0), depending on the material density and depth of path.

A.3 Material compatibility

A.3.1 General

The loss of functional properties is often the most important characteristic effect of polymer irradiation. Properties that are affected can include tensile strength, impact strength, shear strength, elongation, and color, among others. The influence of radiation on these properties and the general performance of a polymer (including physical properties, odor, and color) differ depending on whether a polymer scissions (causing reduced toughness and elongation) or cross-links (causing increased strength and stiffness). All materials lose physical properties at very high radiation doses; however, below the destructive level of exposure, radiation treatment can enhance properties and impart benefits of commercial value. The dose range in which a given plastic maintains its valuable properties depends greatly on the chemical structure of the polymer. Thus, the dose necessary to produce similar significant physical property changes in two different polymers could vary from as low as a few kilograys to as high as hundreds of kilograys (see Figure A.1).

Databases, literature sources, and manufacturers' information can be used to identify radiation-stable materials that tolerate the doses required for the particular product design and function. The majority of polymers are radiation stable at the doses typically used in the radiation sterilization of health care products. However, radiation stability of any polymer can vary significantly depending on

- the radiation dose absorbed;

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

- the residual or functional stress (processing, part design and function);
- the molecular weight;
- the product cross-section thickness (films, coatings, and fibers);
- the morphology (e.g., percent crystalline);
- the environment during irradiation, storage, and use (e.g., oxygen, temperature, and moisture); and
- the dose rate (i.e., gamma, x-ray, or electron beam).

Therefore, all polymer selections should be thoroughly challenge tested in the specific application and processing conditions under consideration.

Figure A.1 summarizes a substantial amount of the information available from government, industrial, and scientific studies and publications concerning the effects of radiation on polymer properties after exposure to various doses. Figure A.1 graphically displays the dose ranges at which a number of common thermoplastics and thermosets show significant change in properties (i.e., a 25 % loss in elongation). Loss of elongation is a commonly used measure of the effect of irradiation because it equates to a brittleness failure; however, a similar figure could be developed on the basis of an alternate physical property (i.e., tensile). Figure A.1 provides a visual means of making an initial estimate of a polymer's ability to withstand a particular radiation sterilization process.

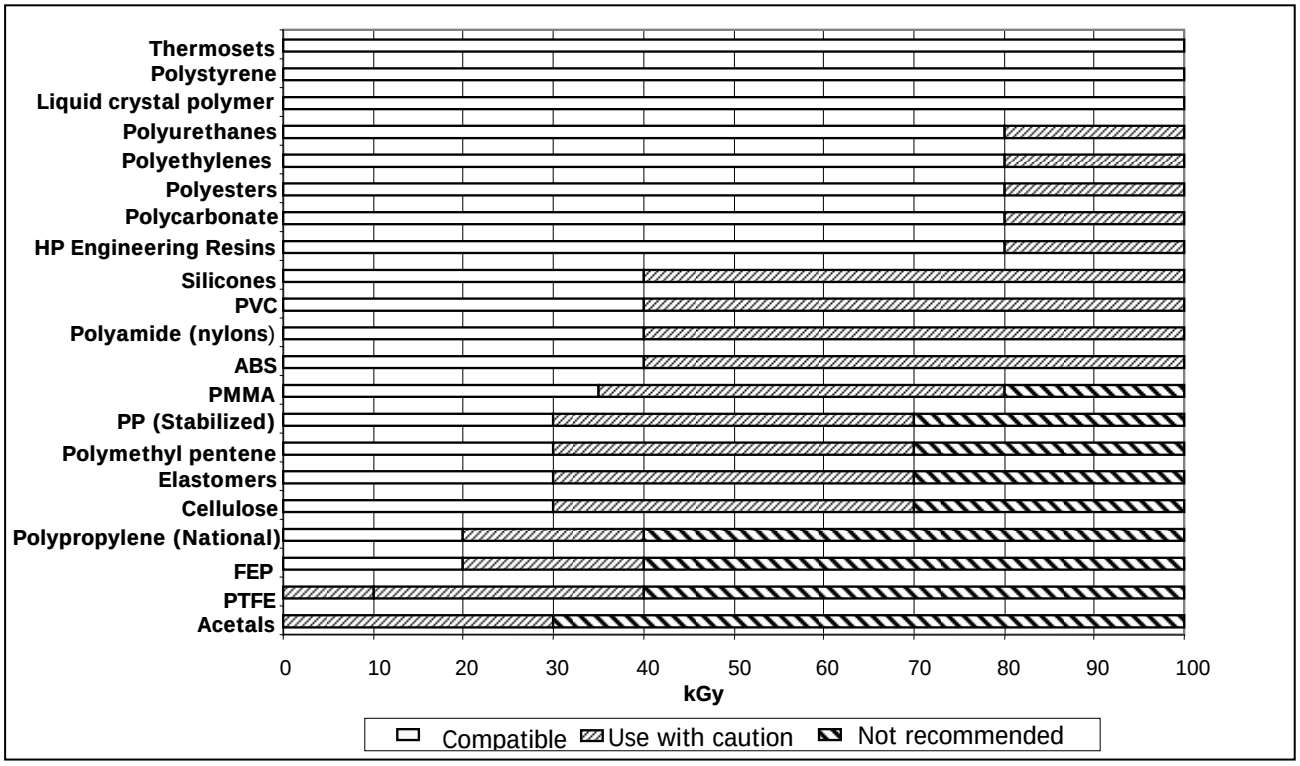


Figure A.1—Relative radiation stability of medical polymer "families"

NOTE—HP = high performance; PVC = polyvinylchloride; ABS = acrylonitrile butadiene styrene; PMMA = polymethylmethacrylate; PP = polypropylene; FEP = Fluorinated ethylene propylene; PTFE = polytetrafluoroethylene.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

A.3.1.1 Compatibility guidelines

Selection of materials should start with the following basic radiation application guidelines:

(a) Most polymers are durable at the radiation doses typically employed for sterilization of health care products (i.e., ≤ 50 kGy). However, a few polymers (e.g., polyacetal, unstabilized polypropylene, and polytetrafluoroethylene; see Table A.1) are significantly degraded at these doses.

(b) Those polymers that cross-link more than they scission generally perform better in the radiation environment.

(c) Aromatic materials are more radiation resistant than aliphatic materials. The benzene ring structure present in aromatic polymers acts as a stabilizer, rearranging itself to accept or donate an electron as needed. Examples of aromatic polymers are styrene, polyester, polycarbonate, and polysulfone.

(d) Antioxidants and ultraviolet stabilizers improve radiation resistance; the impact of these additives on biocompatibility should be considered.

(e) The material with the highest molecular weight possible for the application (with the narrowest molecular weight distribution) should be used.

(f) Amorphous materials provide better radiation enhancement when compared with semi-crystalline materials. Likewise, for semi-crystalline materials, higher amorphous content provides better radiation resistance.

NOTE—The exception to this guideline is highly crystalline (> 95 % crystalline) materials, which generally have high radiation resistance owing to the dominance of their strong, nested, compact, and mutually reinforced polymer chains.

(g) Materials with low O_2 permeability are more radiation resistant.

(h) Materials used in thin films and fibers should be selected with caution because of the enhanced effect of oxidation resulting from the large surface-to-mass relationship.

(i) Effects of radiation on polymers generally are cumulative with each subsequent exposure of a product. Therefore, the effects from a total dose from one continuous irradiation would be equivalent to the same total dose from multiple irradiations. This cumulative effect relates to total absorbed dose and not to the number of exposures.

The exceptions to this rule are materials that are prone to radiation-induced oxidative scissioning, for which large surface-to-mass designs or irradiation at high dose rates can bias the expected final outcome, and high dose-rate applications (i.e., e-beam), for which temperature effects can be offset through incremental dosing.

(j) Another effect of radiation processing is discoloration (usually yellowing) from the development of specific radical chromophores in the polymer. Color development, which occurs at widely differing doses in different polymers, usually diminishes to some extent with storage time after irradiation. Discoloration usually appears before any measurable loss in physical properties. This is the case with polyvinylchloride (PVC) and polycarbonate (PC), in which radiation-induced yellowing from conjugated double bonds develops at a dose much lower than is necessary to cause any reduction in its physical properties; however, the color that is developed can be undesirable.

(k) Odors can develop from irradiated polymers as a result of specific radio-stabilizing chemistries and the formation of free radicals. The polymers that most often exhibit postirradiation odors are polyethylene, polyvinylchloride, and polyurethane. If the reaction chemistries of the odors are understood, they can often be mitigated through the use of antioxidants, use of reduced processing temperatures, or use of a polymer with higher molecular weight. Odor reduction can also be accomplished through the use of gas-permeable packaging or elevated temperature conditioning.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

A.3.1.2 Compatibility fundamentals—Radiation chemistry

High-energy radiation produces excitations of orbital electrons, which cause cleavage of polymer bonds, resulting in ionization of polymer molecules, thus creating active species (radicals). These energy-rich polymer radicals initiate a series of dissociation, abstraction, and addition reactions that ultimately lead to chemical stability or instability. This stabilization process, which in a rare number of polymers can continue for weeks after irradiation, often results in physical and chemical changes in the polymers. The resultant changes can include embrittlement induced by chain scissioning, as well as odor; softening and toxicological response; or discoloration induced by cross-linking, stiffening, curing, grafting, chemical resistance, and increase in melt temperature.

Molecular weight, chain length, entanglement, polydispersity, branching, and pendant and terminal chain functionality contribute to the polymer's structure-property relationship, and each of these characteristics can be modified with radiation. Understanding the direction and magnitude of these changes in characteristics, as a function of radiation exposure (dose), is crucial to predicting the performance and utility of the postirradiated plastics.

The influence of radiation-induced active species on the properties and performance of a polymer can vary by location within the part. During irradiation, radicals are formed in the polymer, proportional to the local dose. However, the associated chemical reactions that follow are also determined by the local concentration of reactants (e.g., oxygen concentration is higher near the exterior surfaces) and tensile stresses that can vary sharply throughout the part. In addition, the orientation of molecular chains during processing (e.g., extrusion) can have a profound effect on radiation damage. Molecular structures that most commonly fail during irradiation are those under the greatest combined stress from their environment (e.g., load, solvent, and residual molding stress).

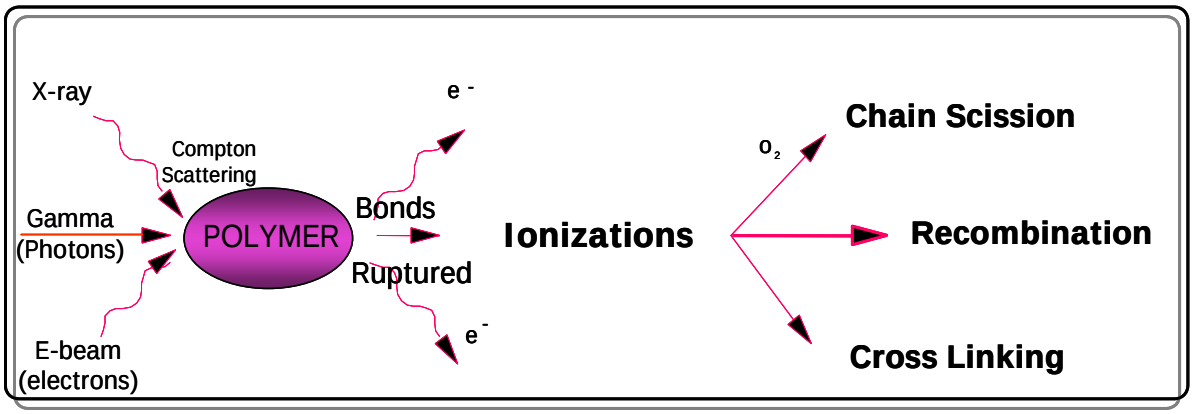


Figure A.2—Molecular structures—Ionizations

Irradiation-induced stabilizing reactions can be grouped into three classes:

(a) Recombination—Polymer chains are joined to re-form their original configuration, resulting in no change of properties.

(b) Cross-linking—Polymer chains are joined and grafted and a network is formed, resulting in an increase in strength and decrease in elongation.

(c) Chain scission—polymer chains terminate in shorter sections, resulting in reduced molecular weight and resultant loss of strength and elongation (embrittlement).

The physical changes in material as a result of these stabilizing reactions can include one or more of the following:

- brittleness;

 © 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

- color (i.e., of glass, PVC);
- odor;
- stiffness or softness;
- toxicity;
- chemical inertness;
- melt temperature; and
- pH (wet or buffered).

Usually, all these processes take place simultaneously during and after irradiation. The different responses to radiation for different polymers are intrinsically related to the chemical structure of the polymer. However, the final balance of the process depends on the chemical composition and morphology of the polymer and its surrounding environment. Often the most significant mode of radiation-induced degradation is the embrittling chain scission reactions that result from interaction with oxygen. Free radicals oxidize easily, especially at the surface of the polymers where oxygen is readily available. In some cases, inert gas (e.g., nitrogen and argon) or vacuum can be used to eliminate oxidation; antioxidants (free radical scavengers) such as hindered amines are also useful in limiting oxidation.

High dose rates available from electron beam irradiation systems can also limit the oxidative degradation of polymers by minimizing the time for oxygen replenishment required for radical-oxygen reactions. The application of these techniques is particularly important for oxidation-sensitive materials—especially those formed into thin profiles, such as coatings, films, and fibers.

The rupturing of bonds that reduce the molecular weight and strength of the polymer (chain scission) and the linking of molecules that results in the formation of large three-dimensional networks (cross-linking) occur simultaneously, with one mechanism usually dominating. If chain scission dominates, polymers lose mechanical strength and low-molecular-weight fragments, gas, and unsaturated bonds often result. If cross-linking dominates, the polymer increases in tensile strength, rigidity, and toughness, and it decreases in elongation. Cross-linking and chain scissioning (degradation) are two competing processes that always coexist under radiation. Typically, the change in the polymer's properties depends on which of the two is predominant at a certain time under the conditions present. For a given polymer, both chain scission and cross-linking change with radiation conditions such as absorbed dose and temperature.

The balance of these competing reactions is critical and will vary from polymer to polymer and part to part, depending on the chemical composition (e.g., aromatic); the morphology of the polymer (e.g., percent crystalline, molecular weight, density); the design of the part (thick versus thin sections); the total radiation dose absorbed; the rate at which the dose is deposited; and, to some degree, the postirradiation storage environment (temperature and oxygen). This balance can also be affected by process-induced stresses and the environment during irradiation (especially the presence or absence of oxygen).

A.3.2 Specific materials

A.3.2.1 General

Table A.1 lists various materials and their general compatibility with radiation sterilization. The information in the table and in the subclauses that follow is not exhaustive, and device manufacturers should use it as a general guideline for the selection of materials. Before a material is selected, the vendor or manufacturer should always be consulted for more information.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

A.3.2.2 Summary of material compatibility

A.3.2.2.1 Thermoplastics

By far the majority of polymers used in the manufacture of medical products are thermoplastics. Thermoplastics are long-chain polymers that can be softened upon heating and are formed into their desired shape upon cooling. Because of the frequent use of thermoplastics in medical product design, most radiation-induced changes have been studied and are noted in Figure A.1 and Table A.1.

A.3.2.2.2 Thermosets

The chemical reactions of formation for thermosets are terminal, and thus minimal ionizations occur upon irradiation. High heat stability is typical. Because of the lack of ionization potential, all thermosets are stable at radiation doses that are typical of medical product sterilization. Postirradiation stability for a limited number of thermosets is listed in Table A.1.

A.3.2.2.3 Elastomers

Elastomers can be thermosets or thermoplastics, manmade or natural, and their response to irradiation is just as diverse. Elastomers containing butyl or butadiene sectional groups typically are not highly stable to radiation. Silicone elastomers are very stable. However, it should be noted that silicone-based elastomers are created by cross-linking reactions that are promoted by either peroxide or platinum catalysts. Because of their higher final cross-link density, platinum-cured systems tend to display less postirradiation cross-link enhancement than do peroxide-based systems. Postirradiation stability for a number of elastomers is listed in Table A.1.

A.3.2.2.4 Adhesives

With consideration to their greater surface-to-mass ratios, adhesives will be stable to irradiation on the basis of their base compositional polymer, as displayed in Figure A.1 and Table A.1; however, adhesives based on cross-linking (i.e., initiated by ultraviolet) for their final properties should be anticipated to have enhanced bond characteristics after irradiation because of enhanced postirradiation cross-link densities. This enhanced postirradiation bond strength or cross-link should also be anticipated for bonds formed from any similar or compatible materials (i.e., polyethylene or polyethylene heat seal).

A.3.2.2.5 Metals

Metals are very stable under the influence of irradiation. Metallic bonds are unique, resulting in minimal ionizations and thus no significant change in properties. Because of their unique and very mobile electron structures, they do not ionize as a result of the low-energy radiation used in medical product sterilization, and thus no change in properties should be anticipated. Electrical systems can undergo significant changes in resistance owing to changes in the electrical potential of the circuit. The electrons in the valance band might shift to the conductive band and lower the resistance of the circuit, a condition that is not reversible. However, caution should be used in high dose applications (i.e., e-beam) because of metal's low specific heats; localized severely elevated temperature rises might result. Also, in systems that use high-energy e-beam accelerators, neutron displacements and creation of measurable radioactive subspecies have been reported in some metals (see 5.1.2 of ANSI/AAMI/ISO 11137-1). Because of the very high rate of energy deposition in electron beam, care should be taken when product designs incorporate metals, as very large temperature gradients can develop. It is generally the case that metals are not negatively affected by radiation.

A.3.2.2.6 Glass and ceramics

Silicon-based materials, such as glass and ceramics are very stable under the influence of irradiation. They tend not to ionize. However, glass severely discolors (i.e., yellows) because of the processing aids it contains for their enhanced formability. Should the color development be objectionable, the addition of cerium in the glass formulation

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

might negate the color change. Also, heat, time, or both will reduce or eliminate the radiation-induced color. Other physical properties are not affected.

A.3.2.2.7 Liquids

Because of the plethora of ionization formed during irradiation of liquid (H_2O-based) systems, stabilization is difficult to predict or maintain. In many cases, a buffering agent (radical scavenger) can negate the formation of numerous hydrogen-based radicals to help maintain the liquid systems' preirradiation properties.

A.3.2.2.8 Contact surfaces and antiblocking

Product designs using polymers that tend to cross-link (i.e., PVC, silicone) should avoid placing surfaces in intimate contact with each other, because cross-link bonds can develop and act to tack the surfaces together. Antiblocking agents can be used if surface contact cannot be avoided. Also, some flexible materials such as PVCs can leach out plasticizers, and this leakage can transfer to other surfaces.

A.3.2.2.9 Biological materials

Biological materials (tissue, bone, serum, proteins) are typically irradiated while in a frozen or dry protective state. The lower temperature state "locks" the structure so that recombination is the most probable outcome and thus no change in final properties occurs. In addition, select additives (radical scavengers) have been purported to promote recombination as the most likely postirradiation reaction for many biological products.

A.3.2.2.10 Packaging

Radiation sterilization offers complete freedom in package design because permeation to gas and moisture is not a requirement. Sealed packaging containing inert gases can be used to reduce the effects of oxidation. Massive package sizes or high-density products surrounded by low-density wraps and foams should be avoided because their use can result in large variances in the maximum to minimum dose delivered to a product. Packaging materials should be selected in accord with the guidelines in Table A.1 to avoid undesirable discoloration or increases in seal strength.

Table A.1—General guide to radiation stability of materials

Table A.1 shows typical radiation resistances of medical polymers in stress-free parts measured at the point where 25 % of the polymer's elongation is lost because of radiation. This circumstance might well be the "best case." If the part being considered has a significant degree of residual stress as a result of manufacture, the dose at which the 25 % loss of elongation occurs can be considerably lower.

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		**(NL) = not likely (L) = likely**	
Material	**Single use (< 50 kGy)**	**Comments**	**Resterilization (< 100 kGy)**	**Comments**
Thermoplastics				
Acrylonitrile butadiene styrene (ABS)	● ● ●	High-impact grades are not as radiation resistant as standard impact grades because of the higher butadiene content.	L	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table A.1—General guide to radiation stability of materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely	
Material	**Single use (< 50 kGy)**	**Comments**	**Resterilization (< 100 kGy)**	**Comments**
Fluoropolymers				
Polytetrafluoroethylene (PTFE)	●	When irradiated, PTFE and PFA are significantly damaged. The other fluoropolymers show significantly greater stability. Some (for example, PVDF) are excellent.	NL	
Perfluoro alkoxy (PFA)	●		NL	
Perchlorotrifluoroethylene (PCTFE)	● ● ● to ● ● ● ●		L	
Polyvinyl fluoride (PVF)	● ● ●		L	
Polyvinylidene fluoride (PVDF)	● ● ● to ● ● ● ●		L	
Ethylenetetrafluoro-ethylene (ETFE)	● ● ● to ● ● ● ●		L	
Fluorinated ethylene propylene (FEP)	● ●		NL	
Polyacetals (e.g., polyoxymethylene)	●	Irradiation causes significant chain scission (i.e., embrittlement). Color changes have been noted (yellow to green).	NL	
Polyacrylates (e.g., polymethylmethacrylate)	● ● to ● ● ●		NL	
Polyamides (e.g., nylon)	● ● to ● ● ●	Nylon 10, 11, 12, and 6-6 are more stable than 6. Nylon film and fiber are less resistant.	L	Very dependent on design and use requirements.
Polycarbonate (PC)	● ● ● to ● ● ● ●	Yellows—mechanical properties are not greatly affected; color-corrected radiation formulations are available.	L	
Polyesters, saturated	● ● to ● ● ●	Polybutylene terephthalate is not as radiation stable as polyethylene terephthalate resins.	L	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table A.1—General guide to radiation stability of materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely	
Material	**Single use (< 50 kGy)**	**Comments**	**Resterilization (< 100 kGy)**	**Comments**
Polyethylene (PE), various densities	● ● ● to ● ● ● ●	High-density polyethylene is not as stable as medium-density polyethylene and low-density polyethylene, linear low-density polyethylene.	L	
Polyimides (e.g., polyetherimide)	● ● ● ●		L	
Polyketones (e.g., polyetheretherketone)	● ● ● ●		L	
Polypropylene (PP)				
Natural	● to ● ●	Physical properties are greatly reduced when irradiated (for example, chain scissioning). Radiation-stabilized grades, using high molecular weight, copolymerized and alloyed with polyethylene, with additional stabilizers should be used in most radiation applications. Use of electron beam at high dose rate may reduce oxidative degradation.	NL	
Stabilized	● ● to ● ● ●		NL	
Polystyrene (PS)	● ● ● ●	Will begin to yellow at > 50 kGy.	L	
Polysulfones	● ● ● ●	Natural material is yellowish.	L	
Polyurethane (PU)	● ● to ● ● ● ●	Aromatic discolors; polyesters are more stable than esters. Retains physical properties.	L	
Polyvinylacetates (PVA)	● ● ●		NL	
Polyvinylchloride (PVC)	● ● ●	Cross-linking dominates and significant yellow color development occurs at doses > 30 kGy). Addition of antioxidants and heat	NL	Significant discoloration likely.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table A.1—General guide to radiation stability of materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely	
Material	**Single use (< 50 kGy)**	**Comments**	**Resterilization (< 100 kGy)**	**Comments**
		stabilizers to formulations will retard color development. High-molecular-weight organotin stabilizers improve radiation stability: color-corrected radiation formulations are available.		
PVC, plasticized	● ● ●	Cross-linking (stiffening) dominates.	L	Discoloration likely.
Styrene acrylonitrile (SAN)	● ● ● to ● ● ● ●		L	
Thermosets				
Epoxy	● ● ● ●		L	
Phenolics	● ● ● ●	Includes the addition of mineral fillers.	L	
Polyester, unsaturated	● ● ● ●	Includes the addition of mineral or glass fibers.	L	
Polyimides	● ● ● ●		L	
Polyurethanes				
Aliphatic	● ● ● ●		L	
Aromatic	● ● ● to ● ● ● ●	Darkening can occur. Possible breakdown products could be derived.	L	
Adhesives				
Acrylic	● ● to ● ● ●		L	Embrittlement possible.
Epoxy	● ● ● ●		L	
Fluoroepoxy	● ● ● ●		L	
Silicone	● ● to ● ● ●		L	
Elastomers				
Butyl	●	Friable, sheds particulate, chain scission.	NL	
Ethylene propylene diene monomer (EPDM)	● ● ● to ● ● ● ●		L	
Natural rubber	● ● ● to ● ● ● ●		L	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table A.1—General guide to radiation stability of materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		**(NL) = not likely (L) = likely**	
Material	**Single use (< 50 kGy)**	**Comments**	**Resterilization (< 100 kGy)**	**Comments**
Nitrile	● ● ● to ● ● ● ●	Discolors.	L	
Polyacrylic	● ● to ● ● ●		NL	
Polychloroprene	● ● ●	Discolors; the addition of aromatic plasticizers renders the material more stable to irradiation.	L	
Silicone	● ● to ● ● ●	Cross-linking dominates. Platinum-cured silicones are superior to peroxide-cured silicones because their preirradiation cross-link density is greater. Full cure during manufacture can reduce postirradiation cross-link effects. Phenyl-methyl silicones are more stable than are methyl silicones.	L	Stiffening due to cross-linking likely.
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	● ● to ● ● ●	Butadiene scissions.	L	
Urethane	● ● ● to ● ● ● ●		L	
Metals				
Aluminum	● ● ● ●		L	
Brass	● ● ● ●		L	
Copper	● ● ● ●		L	
Gold	● ● ● ●		L	
Magnesium	● ● ● ●		L	
Nickel	● ● ● ●		L	
Silver	● ● ● ●		L	
Stainless steel	● ● ● ●		L	
Titanium	● ● ● ●		L	
Ceramics/glasses				
Aluminum oxides	● ● ● ●		L	
Silica	● ● ● ●		L	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table A.1—General guide to radiation stability of materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely	
Material	**Single use (< 50 kGy)**	**Comments**	**Resterilization (< 100 kGy)**	**Comments**
Zirconium oxides	● ● ● ●		L	
Other materials				
Bioabsorbables				
Polyglycolides	● to ● ● ●		NL	
Polylactides	● to ● ● ●		NL	
Cellulosics				
Cellulose ester	● ●	Esters degrade less than other cellulosics.	NL	
Cellulose acetate propionate	● ● to ● ● ●		L	
Cellulose acetate butyrate	● ● to ● ● ●		L	
Cellulose, paper, cardboard	● ● to ● ● ●		L	
Liquid crystal polymer (LCP)	● to ● ● ● ●	Commercial LCPs; natural LCPs are not stable.	L	

Primary sources: International Atomic Energy Agency; NASA/Jet Propulsion Laboratory; and polymer manufacturers' literature.

A.4 References

[A.4.1] Cleland, M.R., O'Neil, M.T., and Thompson, C.C. In Sterilization Technology: A Practical Guide for Manufacturers and Users of Healthcare Products. Morrissey, R.F., and Phillips, G.B.,(eds.) New York: Van Nostrand Reinhold, 1993, p. 218.

[A.4.2] Croonenborghs B, Smith MA, and Strain P. X-ray versus gamma irradiation effects on polymers. *Radiation Physics and Chemistry*, 76:1676–1678, 2007.

[A.4.3] Farrell, Paul J., and Hemmerich, Karl J., *Selecting a Radiation Sterilization Method, Medical Device and Diagnostic Industry*, 17(8):82-90, 1995.

[A.4.4] Hemmerich KJ. Polymer materials selection for radiation-sterilized products. *Medical Device & Diagnostic Industry*, February 2000.

[A.4.5] Ishigaki, J, and Yoshii, F. Radiation Effects on Polymer Materials in Radiation Sterilization of Medical Supplies, *Radiation Physics & Chemistry*. 39(6):527-533, 1992.

[A.4.6] International Atomic Energy Agency, *Guidelines for industrial radiation sterilization of disposable medical products, Co 60 gamma irradiation.*,TEC DOC-539. Vienna: IAEA, 1990.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[A.4.7] Kiang PH. *Effect of gamma irradiation on elastomeric closures*. Report 16. Bethesda (MD): Parenteral Drug Association, 1992.

[A.4.8] Ley FF. The effect of irradiation on packaging materials. *J Soc Cos Chem*, 27:715, 1976.

[A.4.9] Morrissey CJ. Degradation of dielectrics in space. *NASA Tech Brief*, 9(2):Item 111, June 1985a.

[A.4.10] Morrissey CJ. Synthetic organic materials in nuclear powerplants. *NASA Tech Brief*, 9(2):Item 107, June 1985b.

[A.4.11] Reichmanis E, et al. Radiation effects on polymeric materials: A brief overview. In: Reichmanis E, et al., (eds.), *Irradiation of polymeric materials*. Symposium Series 527, Washington (DC), American Chemical Society, 1993.

[A.4.12] Skeins WE and Williams JL. Ionising radiation's effects on selected biomedical polymers. In M Szycher (ed.), *Conference proceedings: Biocompatible polymers, metals, and composites*. Lancaster (PA): Technomic Publishing, 1983, p. 1001.

[A.4.13] Smith MA, Lundahl B, and Strain P. Effects of x-ray irradiation on material properties. *Medical Device & Technology*, April 2005.

[A.4.14] Williams, J., In Weighing the Choices in Radiation Sterilization: Electron-Beam and Gamma, *Medical Device and Diagnostic Industry*, 17(3):69, 1995.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex B

EO sterilization—Material compatibility fundamentals

B.1 Background

EO is an effective sterilant for most medical devices. It is relatively low cost per device sterilized. Its properties are well understood, and skilled users can rapidly develop and validate effective sterilization cycles. A typical EO sterilization cycle is executed at relatively low temperatures, which makes the process ideal for most polymeric materials that would be destroyed by higher temperatures. In addition, there are no free radicals that can significantly degrade materials. Furthermore, most electronic devices can be successfully processed in EO, whereas they could be destroyed by other processes.

B.2 Sterilization process variations and parameters

B.2.1 General

Most materials are compatible with 100 % EO and with the nonflammable blends. Even though a general material class might be listed as compatible, it is the designer's responsibility to ensure that the specific formulation used, as produced with the final processing conditions, is compatible with the sterilants being used and with the physical parameters of the specific cycle being used.

B.2.2 Process variations

The configuration of the sterilant used can vary. The commonly used configurations are explained in the following subclauses.

B.2.2.1 Pure EO

Pure EO is the most commonly used gas sterilant. It is used in many small chambers in hospitals and industry and in almost all large chambers greater than 2.8 m^3 (100 ft^3). The reasons for its use are mainly economic. It is much cheaper than the nonflammable blends and generally does not require chamber pressures above atmospheric. If necessary, the potential flammability and explosivity issues can be addressed by adding an inert gas such as nitrogen to the chamber atmosphere.

B.2.2.2 Nonflammable blends

The most common nonflammable blend in current use is a mixture of approximately 8.6 weight percent EO and 91.4 % HFC 124 (chlorotetrafluoroethane). This blend corresponds to approximately 22.6 % volume percent EO when it is vaporized. To achieve an effective killing concentration, the sterilant pressure rise is generally in the range of 16 to 27 PSI (110 to 186 kilopascal [kPa] rise). Since the HCFC-124 component of this blend causes some depletion of the earth's ozone layer, international agreements call for it to be phased out of production starting around 2010. It is to be phased out completely by 2015.

This blend causes very few materials compatibility problems.

 © 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

The likely replacement for the current HFC-124 blend is a mixture of approximately 81.9 % HFC 125 (pentafluoroethane), 7.7 % HFC 227 (heptafluoropropane), and 10.4 % EO. The pressure increases needed to achieve effective killing concentrations of EO are about the same as those used for the HFC-124 blend. The volume percent EO when the blend is vaporized is approximately 22 %. Based on its physical properties, this blend can be even less damaging to sensitive materials than are previously available blends of EO. This blend should begin to phase into commercial use around 2009.

The so-called 10/90 blend is a mixture of CO_2 and EO. This blend is not in common use. The current formulation is approximately 9 % EO and 91 % CO_2. The volume percentage for this blend when the gas is vaporized is 9 % (the molecular weights of CO_2 and EO are about the same, so the weight and volume percentages are about the same). To achieve an effective killing concentration, the sterilant pressure rise is generally in the range of 30 to 45 PSI (207 to 310 kPa).

B.2.3 Process parameters

In the EO sterilization process, there are process variations or parameters that need to be taken into consideration:

- temperature,
- humidity, and
- pressure (change rate and/or level).

Typical sterilization temperatures range from 30 °C to 60 °C, with humidity levels usually greater than 30 %. However, the sterilization process can be modified to accommodate materials that can be moisture or temperature sensitive, although these modifications will affect the lethality of the process and they do have a limit. Materials or products can also be affected by the pressure rate changes or levels that are typically used in the cycle, but as with the temperature and humidity cycle, modifications are often possible.

B.3 Material compatibility

B.3.1 General

It should be noted that, for some materials, physical properties determined within 24 hours of removal from the chamber can be different than those seen at two or three months. Some materials show little change in properties within a day or two of sterilization, but then show significant changes at two or three months. Other materials show significant changes upon removal from the sterilizer, but the properties revert to the original values after an extended time at room temperature (weeks to months). The analysis of the effect of EO on a material or device should include a shelf-life test to detect these effects.

It is possible that some polymers, when exposed to EO, will react to a slight extent, causing either an increase or a decrease in mechanical properties. Some materials are known to increase tensile properties, while simultaneously decreasing the elastic modulus. These effects can vary depending on whether the part has significant thickness or is a thin tube or film. Changes in material properties can occur within a very short period of time or can take several months.

The presence of additives or plasticizers can significantly affect the properties of some materials, including their suitability for EO sterilization. Additionally, under some conditions a material that is generally thought to be compatible with EO will not be compatible when tested. This incompatibility is often due to formulation changes in the material.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

The anticipated number of sterilization cycles must be considered when designing a device. Materials can retain adequate properties after one sterilization cycle but lose significant properties following additional sterilization processing. The analysis of the effect of EO on a material or device should include a shelf-life test to detect these effects.

B.3.2 Specific materials

Table B.1 lists various materials and their general compatibility with EO sterilization. The information in this table is not exhaustive, and device manufacturers should use it only as a general guideline for the selection of materials. Before material is selected, the vendor or manufacturer should always be consulted for more information.

Table B.1—Compatibility of selected polymeric materials with EO sterilization

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		**(NL) = not likely (L) = likely (U) = unknown**	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Thermoplastics				
Acrylonitrile butadiene styrene (ABS)	● ● ● ●		L	May be some materials property loss on multiple cycles.
Fluoropolymers			L	
Polytetrafluoroethylene (PTFE)	● ● ● ●		L	Excellent.
Perfluoro alkoxy (PFA)	● ● ● ●		L	
Perchlorotrifluoroethylene (PCTFE)	● ● ● ●		L	
Polyvinyl fluoride (PVF)	● ● ● ●		L	
Polyvinylidene fluoride (PVDF)	● ● ● ●		L	
Ethylenetetrafluoro-ethylene (ETFE)	● ● ● ●		L	
Fluorinated ethylene propylene (FEP)	● ● ● ●		L	
Polyacetals (e.g., polyoxymethylene)	● ● ● ●		L	
Polyacrylates (e.g., polymethylmethacrylate)	● ●		NL	Some loss in tensile properties on multiple cycles.
Polyamides (e.g., nylon)	● ● ● ●		L	
Polycarbonate (PC)	● ● ● ●	Some formulations may be subject to	L	Some formulations may be subject to

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table B.1—Compatibility of selected polymeric materials with EO sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
		stress cracking and some loss of tensile properties after multiple cycles and an extended time after processing.		embrittlement, stress cracking, and some loss of tensile properties after multiple cycles.
Polyesters, saturated	● ● ● ●	Compatible.	L	
Polyethylene (PE), various densities	● ● ● ●	Generally compatible. High-density polyethylene may lose some tensile properties.	L	Generally compatible. High-density polyethylene may lose some tensile properties.
Polyimides (e.g., polyetherimide)	● ● ● ●	Depending on formulation and application. Very thin tubing may present compatibility issues. Bulk structural materials are generally compatible.	L	
Polyketones (e.g., polyetheretherketone)	● ● ● ●	Compatible.	L	
Polypropylene (PP)				
Natural	● ● ● ●	May be some long-term effect on tensile modulus.	L	Vendor information varies on multiple cycle compatibility. Tensile losses up to 20 % reported.
Stabilized	● ● ● ●		L	
Polystyrene (PS)	● to ● ● ●	Some embrittlement and loss of tensile strength for some formulations has been reported.	NL	Generally not recommended for large number of cycles.
Polysulfones	● ● ● ●		L	
Polyurethane (PU)	● to ● ● ●	Performance depends on formulation, cure conditions, material thickness, and end-use stresses.	L	Performance depends on formulation, cure conditions, material thickness, and end-use stresses.
Polyvinylacetates (PVA)	●		NL	
Polyvinylchloride (PVC)	● ● ● ●	Rigid PVC may decrease impact	L	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table B.1—Compatibility of selected polymeric materials with EO sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
		resistance after exposure.		
PVC, plasticized	● ● ● ●	Medical-grade plasticized tubing may contain significant residual levels until aerated.	L	
Styrene acrylonitrile (SAN)	● to ● ● ●	Generally acceptable for one cycle, but may embrittle and lose tensile properties on multiple cycles. Might exhibit surface cracking and stress cracking on multiple cycles.	NL	Might embrittle and lose tensile properties on multiple cycles. May exhibit surface cracking and stress cracking on multiple cycles.
Thermosets				
Epoxy	● ● ● to ● ● ● ●		L	
Phenolics	● ● ●		L	
Polyester, unsaturated	● ● ● ●		L	
Polyimides	● ● ● ●		L	
Polyurethanes				
Aliphatic	● to ● ● ●		L	
Aromatic	● to ● ● ●		L	
Adhesives				
Acrylic	● ●	Some loss in tensile properties reported on multiple cycles with HCFC-124/EO blends. Some crazing could occur.	L	Some loss in tensile properties reported on multiple cycles with HCFC-124/EO blends. Some crazing could occur.
Epoxy	● ● ● to ● ● ● ●		L	
Fluoroepoxy	U		U	
Silicone	● ● ● ●		L	
Elastomers				
Butyl	● ● ● ●	Butyl is even stable in liquid EO.	L	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table B.1—Compatibility of selected polymeric materials with EO sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Ethylene propylene diene monomer (EPDM)	● ● ● ●	Generally compatible, but changing curing method from peroxide cure to sulfur cure may result in formation of small amounts of polyethylene oxide inside the matrix of the material.	L	
Natural rubber	● ● ●		L	Can be limited number of cycles.
Nitrile	● ● ● ●		L	
Polyacrylic	● ●		NL	
Polychloroprene	● ● ●		L	
Silicone	● ● ● ●		L	
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	● ● ● to ● ● ● ●		L	
Urethane	● to ● ● ●		L	
Metals		Most metals are compatible with multiple sterilization cycles. In the presence of some metals, EO may react with water vapor to form glycols on the surface of the metal.		
Aluminum	● ● ● ●		L	
Brass	● ● ● ●		L	
Copper	● ● ●		L	
Gold	● ● ● ●		L	
Magnesium	U		U	
Nickel	● ● ● ●		L	
Silver	● ● ● ●		L	
Stainless steel	● ● ● ●		L	
Titanium	● ● ● ●		L	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table B.1—Compatibility of selected polymeric materials with EO sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Ceramics/glasses				
Aluminum oxides	● ● ● ●		L	
Silica	● ● ● ●		L	
Zirconium oxides	● ● ● ●		L	
Other materials				
Bioabsorbables				
Polyglycolides	●		NL	
Polylactides	●		NL	
Cellulosics				
Cellulose ester	● ● ● ●		L	
Cellulose acetate propionate	● ● ● ●		L	
Cellulose acetate butyrate	● ● ● ●		L	
Cellulose, paper, cardboard	● ● ● ●		L	
Liquid crystal polymer (LCP)	U		U	

B.4 References

[B.4.1] Anand VP, et al. Re-evaluation of ethylene oxide hemolysis and irritation potential. *J Biomed Mater Res*, 64A:648–654, 2003.

[B.4.2] Buben I, et al. Problems with sterilization using ethylene oxide: Residues in treated materials. *Centr Eur J Public Health*, 7(4):197–202, 1999.

[B.4.3] *Ethylene Oxide Users Guide*, 2nd ed. 1999. http://www.ethyleneoxide.com.

[B.4.4] Gilding DK, et al. Ethylene oxide sterilization: Effect of polymer structure and sterilization conditions on residue levels. *Biomaterials*, 1:145–148, 1980.

[B.4.5] Guess WL. Residual ethylene oxide and reaction products in polymers. *Bull Parenter Drug Assoc*; 24:68–75, 1970.

[B.4.6] Hermanson N. Effects of alternate carriers of ethylene oxide sterilant on thermoplastics. Presented at Society of Plastics Engineers, October 1, 1991.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[B.4.7] Hermanson N, et al. The effects of high energy and EtO sterilization on thermoplastics. *Medical Device & Diagnostic Industry*, pp. 101–106, August 1997.

[B.4.8] Hermanson N, and Navarrete L. The changes in ethylene oxide sterilization and their effects on thermoplastics. Presented at ANTEC 1996, Indianapolis, IN, 1996.

[B.4.9] Lerouge S et al. Reuse of catheters: Surface modification induced by gas plasma and pure ethylene oxide sterilization. Presented at the 24th Annual Meeting of the Society for Biomaterials, San Diego (CA), 1998.

[B.4.10] Nair P. Currently practiced sterilization methods—Some inadvertent consequences. *J Biomater Appl*, 10:121–135, 1995.

[B.4.11] Plastics Design Library. *The effect of sterilization methods on plastics and elastomers*. Morris (NY): Plastics Design Laboratory, 1994.

[B.4.12] Rogers W. Steam: Uses and challenges for device sterilization. *Medical Device & Diagnostic Industry*, pp. 80–87, March 2006.

[B.4.13] Sturdevant M. *Sterilization compatibility of rigid thermoplastic materials*. Dow Chemical Company report, 1988.

[B.4.14] Vink P, and Pleijsier K. Aeration of ethylene oxide sterilized polymers. *Biomaterials*, 7:225–230, 1986.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex C

Moist heat sterilization—Material compatibility fundamentals

C.1 Background

Heat is the oldest and possibly the most recognized agent of microbial destruction. It is a popular method used in the pharmaceutical industry, in hospital health care facilities, and to a lesser degree for the terminal sterilization of distributed medical devices. Moist heat is inexpensive, environmentally friendly, and widely available.

The major concern with moist heat sterilization is the degradation or destruction of materials by heat or moisture. Moist heat, however, can sterilize acetal, glass, liquids, polypropylene, polytetrafluoroethylene (PTFE), fibers, or celluloses (papers) that can be damaged or be rendered impractical by other methods. If prudently applied and controlled, moist heat does not corrode metals.

In some cases, high temperature and short times have shown less deleterious effects or chemical degradation of heat-sensitive fluids than reduced temperatures and longer times. This finding is generally accepted in the case of nutritional degradation of foods and parenteral compounds.

C.2 Sterilization process variations and parameters

Moist heat sterilization can occur in the form of saturated steam, water spray, steam-air mixture, super-heated steam, or water immersion. The major sources of process variations follow:

- temperature;
- pressure, vacuum, or both;
- time; and
- presence of water or water vapor.

Moist heat sterilization is often performed at temperatures of 121 °C to 134 °C. However, processing temperatures of moist heat sterilizers may range from 105 °C to 150 °C. In saturated steam processes, the processing temperature corresponds to a saturated steam pressure significantly above atmospheric pressure.

Process pressures used in moist heat applications cover a wide range, depending on the type of process required. Processes might use deep vacuum levels for the elimination of air, while exposure pressures range from a low of 3 psig or 17.9 psia or 123.4 kPa for a low temperature process to as high as 70 psig or almost 90 psia or 620.2 kPa for air overpressure, water spray, and water immersion processes. The latter processes are generally used to maintain the integrity of the container and compensate for the pressure created by the increase in temperature.

Exposure time can vary with the temperature equilibrium and the heat-up and cool-down times. The rate of product heating should be controlled to minimize the possibility of differential expansion. The cool-down phase can be a period in which packaging or containers burst or distort with change in internal pressure versus external pressure and can require a positive pressure overlay. A longer heat-up and cool-down phase typically reduces the exposure time required. Heat-up time enhances the heating of material. Cooling time reduces heat and eliminates moisture from the sterilizer.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Drying removes residual moisture and polymer hydration. Post-heated drying can provide additional inactivation by not allowing damaged microbes to repair themselves through nucleic acid annealing that might otherwise be observed as a phenomenon of slow growth during sterility incubation. Drying with circulation and heat can help eliminate or remove visible water marks and restore material distortion. Poststerilization heat drying can complete inactivation of microbes that did not get enough moisture for inactivation. Sterilized material left in a wet state can become susceptible to recontamination if not protected by a proper barrier.

C.3 Material compatibility

C.3.1 General

A variety of factors must be considered when a material compatible with moist heat sterilization is selected. It is important to recognize the influence that load, mass, or stress might have on a material during moist heat sterilization. Generally, the lower the temperature of the moist heat sterilization process, the more materials are compatible.

The glass transition temperature (T_g) of many polymers is typically a good indication of material rigidity and compatibility to heat. For example, processing below a glass transition temperature typically maintains the optimal rigid compatibility of the polymer to moist heat. As the temperature of the polymer drops below the T_g, the polymer typically becomes more hardened or brittle. As the temperature rises above the T_g, the polymer becomes more rubber-like and capable of elastic or plastic deformation without fracture. Elastomers, in general, have a T_g below room temperature but are moist heat compatible above their T_g. In addition, reaching the melting temperature of the polymer must be avoided. Knowledge of the maximum operating temperature, upper service temperature, or heat deflection temperature of the material under consideration is necessary to ensure that the parameters for moist heat sterilization cycle are suitable. Polymer heat stability will also depend on molecular orientation. A high degree of crystallinity will enhance thermal stability.

C.3.2 Specific materials

Table C.1 lists various materials and their general compatibility with moist heat sterilization. The information in this table is not exhaustive, and device manufacturers should use it only as a general guideline for the selection of materials. Before a material is selected, the vendor or manufacturer should be consulted for more information.

Table C.1—Materials compatibility with moist heat sterilization

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		**(NL) = not likely (L) = likely (U) = unknown**	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Thermoplastics		(C.4.9 to C.4.13, C.4.14, C.4.16)		
Acrylonitrile butadiene styrene (ABS)	● to ● ●	Poor to possible (C.4.14) depending on grade, filler. Run heat-resistant grade at low temperature process.	NL	Possibly compatible with very low temperature cycles.
Fluoropolymers		(C.4.10).		(C.4.1).
Polytetrafluoroethylene (PTFE)	● ● ● ●	(C.4.14). Compatible up to 170 °C or higher.	L	degrades with long-term service

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table C.1—Materials compatibility with moist heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Perfluoro alkoxy (PFA)	● ● ● ●	Working temperatures up to 204 °C or higher.	L	(C.4.10, C.4.14), up to 170 °C.
Perchlorotrifluoroethylene (PCTFE)	● ● ●	(C.4.2, C.4.14). Up to 150 °C; in packaging, a moisture barrier.	L	Continuous temperature, 150 °C.
Polyvinyl fluoride (PVF)	● ● to ● ● ●	Heat deflection temperature up to 125 °C (C.4.14), 134 °C.	NL	Limited use; requires low temperatures.
Polyvinylidene fluoride (PVDF)	● ● ●	U for use temperature of 150 °C (302 °F); however, some grades may only go to 125 °C.	L	Multiple, maximum operating temperature 130 °C (275 °F).
Ethylene tetrafluoro-ethylene (ETFE)	● ● ●	(C.4.14). Up to 150 °C.	L	
Fluorinated ethylene propylene (FEP)	● ● ● ●	(C.4.14). Up to 170 °C or 200 °C (392 °F).	L	(C.4.10). Repeatable.
Polyacetals (e.g., polyoxymethylene)	● ● to ● ● ●	(C.4.10). Up to 121 °C (C.4.14), or higher; may degas.	L	Used up to 100 cycles at 121 °C.
Polyacrylates (e.g., polymethylmethacrylate)	● to ● ●	Poor to fair; some high-resistant grades. Modified (C.4.1).	NL	
Polyamides (e.g., nylon)	● to ● ● ● ●	(C.4.2, C.4.8). Poor to excellent. (C.4.12, C.4.14) Depends on grade, form, formula, and function or fit). Biaxially oriented and cast nylon autoclavable/retortable. (C.4.2).	NL	Possible in some conditions to resterilize. (C.4.12).
Polycarbonate (PC)	● to ● ● ●	(C.4.10). Typically 121 °C (C.4.6), but some grades can be sterilized at 134 °C (C.4.12, C.4.14). Some have heat deflection up to 145 °C.	L	(C.4.10). Some only compatible with a few cycles; (C.4.6, C.4.12) others compatible to 200 cycles.
Polyesters, saturated	● to ● ● ●	(C.4.4). Possible (C.4.12) to excellent; depends on type grade, form, function. Some polyethylene terephthalate (PET) attacked by moisture; polybutylene terephthalate PBT is another form. Copolyester. (C.4.4).	L	PET can be sterilized up to 240 °F; polyethylene naphthalate (PEN) is compatible with moist heat.

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table C.1—Materials compatibility with moist heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
		Oriented PET more autoclavable. (C.4.2).		
Polyethylene (PE), various densities	● to ● ● ●	Poor to fair. High-density polyethylene, (HDPE), fair. (C.4.22). Polyolefin spun, good. (C.4.12).	NL	Reinforcement of HDPE required to improve its temperature compatibility.
Polyimides (e.g., polyetherimide)	● ● to ● ● ● ●	(C.4.12, C.4.14). Possible to excellent, depending on grade, form, and function.	L	Polyetherimide withstands up to 4,000 (C.4.12) cycles (e.g., 1,000–2,500 at 5 min at 134 °C). (C.4.6).
Polyketones (e.g., polyetheretherketone)	● ● ● ●	High temperature resistance. (C.4.12, C.4.14).	L	Polyetheretherketone has great heat resistance. Good up to 2,000 hours of steam. Typically long service.
Polypropylene (PP)		Depends on grade, form, formula, and function or fit. (C.4.1, C.4.2,C.4.7, C.4.12, C.4.13, C.4.14, C.4.22).	L	Heat resistant grades are required. (C.4.13).
Natural	● ● ●			
Stabilized	● ● to ● ● ●	Copolymer more resistant. (C.4.1).		(C.4.10).
Polystyrene (PS)	● to ● ● ● ●	Standard NL; but syndiotatic polystyrene (SPS), (C.4.7), and styrene/polyphenyoxides (PPO) good to excellent.	L	SPS is compatible. (C.4.7).
Polysulfones	● ● ● ●	(C.4.10, C.4.12, C.4.14). Polyether sulfone (PES) is less resistant. (C.4.12).	L	(C.4.1, C.4.10, C.4.14) up to 1,500 autoclave cycles, but not PES. (C.4.12).
Polyurethane (PU)	● to ● ●	Poor/possible (C.4.14), but some grades may be fair; caution: aromatic PU resin may form toxic 4,4 - methylenedianiline (MDA).	NL	
Polyvinylacetates (PVA)	● to ● ●	Depends on form, function, formulation, and copolymerization. Heat-stable PVA hot-melt adhesives used.	U	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table C.1—Materials compatibility with moist heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polyvinylchloride (PVC)	● to ● ●	Rigid PVC NL, but possible with some modifiers; heat stabilizers and formulation.	NL	
PVC, plasticized	● to ● ●	(C.4.9, C.4.10, C.4.14, C.4.21, C.4.22). Plasticized PVC fair depending on form, formulation and function.	NL	
Styrene acrylonitrile (SAN)	● to ● ●	Poor (C.4.12) to fair depending on grade.	NL	
Thermosets		(C.4.9 to C.4.13, C.4.16).		
Epoxy	● ● to ● ● ● ●	Numerous types of reinforced epoxies. Physical properties can vary. Heat distortion temperatures up to 470 °F.	L	
Phenolics	● ● to ● ● ●	Autoclaving can lead to phenolic degradation and extractables into fluids.	NL	
Polyester, unsaturated	● ● ● to ● ● ● ●	There are a variety of unsaturated polyesters (e.g., vinyl esters). Stability is better when cross-linked.	L	Isophthalic acid–based polyester. High temperature resistance, possibly excellent.
Polyimides	● ● ● ●	Bis maleimides (BMI) and acetylene-terminated polyimide (ACTP) have use-service temperatures of 127–232 °C and 316 °C.)	L	
Polyurethanes		Typically possible, depending on grade, formulation, function. There are heat-resistant cross-linked polyurethanes.	NL	
Aliphatic	● to ● ●	Radiation cross-linked increases its resistance.	NL	
Aromatic	● to ● ●	Thermoset PU resins do not form DMA in polyurethane (aromatic).	NL	
Adhesives		(C.4.2 to C.4.9).		
Acrylic	● to ● ●	Some can tolerate autoclaving, depending on grade, formulation—fair. There is an acrylic adhesive film in a tape up to 280 °F.	NL	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table C.1—Materials compatibility with moist heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Epoxy	● ● to ● ● ● ●	Depending on grade and formulation, deflection temperature from 200 °F to 500 °F.	L	Some can lose retention of initial strength after only 5 cycles.
Fluoroepoxy	● ● ● to ● ● ● ●	Epoxy adhesives depend on cure and formulation.	L	Epoxy adhesives cured with heat are more resistant than those cured at room temperatures.
Silicone	● to ● ● ●	Typically good, depending on form, formulation, function. Good to excellent.	L	Some may be good for only up to 6–8 cycles.
Elastomers		(C.4.3, C.4.8, C.4.12, C.4.14, C.4.22).		
Butyl	● ● to ● ● ● ●	(C.4.8). Good, depending on type, grade. Resistant to water and up to 120 °C.	L	Halobutyl (halogenated polyisobutylene).
Ethylene propylene diene monomer (EPDM)	● ● ● to ● ● ● ●	(C.4.8). Good up to 125 °C in water, up to 134–150 °C in air.	NL	Requires temperatures near 105 °C.
Natural rubber	● to ● ●	(C.4.8). Possible to fair (C.4.8, C.4.14); there are autoclavable grades; plastomers enhance thermal stability. Possible to fair.	L	Hardens with use; withstands repeated autoclaving at 250 °F for 20 min.
Nitrile	● ● to ● ● ●	(C.4.8). Good resistance to moisture and water; tolerates temperatures up to 120 °C.	L	Requires lower processing conditions, below 230 °F.
Polyacrylic	●	(C.4.22, C.4.3). Polyacrylate is a heat resistant rubber; water resistance can be improved but with decrease in heat.	NL	Resistance to water is poor.
Polychloroprene	● ● to ● ● ●	(C.4.8). Fair resistance to moisture, up to 230 °F; intermittent to 250 °F. Fair to very good.	L	Requires lower processing conditions, below 230 °F.
Silicone	● to ● ● ● ●	Excellent (C.4.12) resistance to water, but poor barrier to moisture vapor resistance. Some finished devices may do better at lower temperatures.	L	Silicone rubber may become soft and sticky (tacky); up to 25 times (C.4.12).

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table C.1—Materials compatibility with moist heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	● to ● ●	Depends on grade, type, form, and formulation. Possible to fair.	NL	Possible with temperatures up to 210 °F.
Urethane	● to ● ●	There are some heat-resistant grades. Depends on type, form, and formulation. Aliphatic versions are typically compatible, some up to 135 °C. Aromatic versions can form MDA (C.4.12).	NL	
Metals		(C.4.11, C.4.22, C.4.2, C.4.17).		
Aluminum	● ● ●	(C.4.2). Aluminum foil; typically single use with inhibitors.	NL	Corrosion may be limited if anodized.
Brass	● ● ● ●	(C.4.11). Used in steam traps.	L	
Copper	● ● ●	No reaction when heated in steam, but surface blackens when heated strongly in air.	L	Copper and brass corrosion inhibitor includes triazole.
Gold	● ● ● ●	No reaction when heated in air and no reaction when heated in steam.	L	
Magnesium	● ● ●	Magnesium metal is autoclavable, as titanium, but not magnesium powder per se.	L	
Nickel	● ● ● ●	Used in autoclaves.	L	
Silver	● ● ● ●	Virtually no reaction when heated in air and no reaction when heated in steam. Autoclaving does not remove activity.	L	
Stainless steel	● ● ● ●	Varies with grade, content of other inhibitors.	L	Chrome: stainless steel pitting and dulling of cutting edges after sterilization cycles.
Titanium	● ● ● ●	Resists corrosion.	L	Nickel-titanium alloy improved. Titanium molybdenum is nickel free and has good corrosion resistance.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table C.1—Materials compatibility with moist heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Ceramics/glasses				
Aluminum oxides	● ● ● to ● ● ● ●	(C.4.2). Withstands corrosion more than aluminum.	U	
Silica	● ● ● ●	Withstands extreme temperatures and is relatively inert; (C.4.2) silicon oxide.	L	
Zirconium oxides	● ● to ● ● ●	Depends on the quality of zirconium. Quality of zirconium is regularly tested in an autoclave for 5 hours at 134 °C.	NL	Steam roughs zirconium ceramic; recommend no resterilization.
Other materials				
Bioabsorbables		Heat and hydrolysis attack. A case where autoclaving typically cannot sterilize biologic material.		
Polyglycolides (PGA)	● to ● ●	Cross-linked PGA may be compatible.	NL	
Polylactides (PLA)	● to ● ●	Compatible PLAs have been developed.	NL	
Cellulosics		Poor to excellent, depending on grade, form, function, formulation.		
Cellulose ester	● to ● ●		L	
- Cellulose acetate propionate	● to ● ●		L	
- Cellulose acetate butyrate	● to ● ●	Typically melts below 100 °C, but heat-stable grade exists for low steam processing.	NL	
- Cellulose, paper, cardboard	● to ● ●	(C.4.2). Some papers go up to 134 °C. A variety of materials have been autoclaved (e.g., Kraft, glassine, paper crepe, cellophane, parchment). (C.4.11).	NL	Wetness can cause contamination, weakness.
Liquid crystal polymer (LCP)	● ● ● ●	(C.4.2). Autoclavable/retortable; parts can withstand autoclaving temperatures of 135 ºC. May be limited to 1 or 2 runs at 134 °C. More tolerant at 121 °C. (C.4.12).	L	Resterilizable at lower temperatures. (C.4.12).

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

C.4 References

[C.4.1] Anes J, et al. Use of plastics for parenteral packaging. In: Avis KE, Lieberman HA, and Lachman L (eds.), *Pharmaceutical dosage forms: Parenteral medication*, Vol. 1, 2nd ed.. Munich: Marcel Dekker, pp. 387–444, 1992.

[C.4.2] Berger K, and Doriff D. Achieving efficacy and sterility in flexbile packaging. *Medical Device & Diagnostic Industry*, pp. 1–8, August 2001.

[C.4.3] Canon Communications. *Modern plastics worldwide world encyclopedia: The global plastics magazine*., 2004, http://www.modplas.com/worldencyclopedia/search, various pages of manufacturer Information.

[C.4.4] Czuba L. Medical plastics for PVC replacement in medical solution containers. *Medical Device & Diagnostic Industry*, pp.1–5, April 1999.

[C.4.5] Czuba L. Polymers: Paving the road of medical device progress. *Medical Device & Diagnostic Industry*, pp. 1–4, August 2004.

[C.4.6] Frissora C. Trends in device design: Implications for materials selection. *Medical Device & Diagnostic Industry*, pp. 80–90, May, 2007.

[C.4.7] Hermanson N, and Wessel T. Syndiotactic polystyrene: A new polymer for high performance. *Medical Applications*, pp. 1–4, July, 1998.

[C.4.8] Marino F, Floyd B, and Rogers W. Industrial sterilization: A review of current principles and practices. 1992. In: Avis KE, Lieberman HA, and Lachman L (eds.), *Pharmaceutical dosage forms: Parenteral medication*, Vol. 2. New York: Marcel Dekker, pp. 1–54, 142, 155–215, 378, 1984.

[C.4.9] Modern Plastics, Modern Plastics World Encyclopedia, yearly, Modern Plastics, New York.

[C.4.10] Perkins JJ. *Principles and methods of sterilization in health sciences*. Springfield (IL): Charles C. Thomas , pp. 54, 204, 261–262, 296–299, 301, 1970.

[C.4.11] Plastics Design Library. *The effect of sterilization methods on plastics and elastomers*. Morris (NY): Plastics Design Laboratory, 1994.

[C.4.12] Portnoy R. Clear radiation, autoclavable polyproylene. *Medical Plastics and Biomaterials*, pp. 1–9, January, 1997.

[C.4.13] Rogers W. *Sterilisation of polymer healthcare products*. Shawbury (UK): Rapra Technology, pp. 11–12, 88, 90, 99, 247–254, 282, 298-302, 2005.

[C.4.14] Rogers W. Steam: Uses and challenges for device sterilization. *Medical Device & Diagnostic Industry*, pp. 80–87, March 2006.

[C.4.15] Rubin I. *Handbook of plastic materials and technology*. New York: John Wiley & Sons, 1990.

[C.4.16] Skeins WE, and Williams JL. Biocompatible polymers, metals, and composites. In: Szycher M, ed. Society of Plastics Engineers, 1978.

[C.4.17] Smith E. Elastomeric closures for parenterals. In: Avis KE, Lieberman HA, and Lachman L (eds.) *Pharmaceutical Dosage Forms: Parenteral Medication*, Vol. 1, 2nd ed. Munich: Marcel Dekker, pp. 445–512, 1992.

[C.4.18] Steward R. New polymers offer advantages for medical devices and packaging. *Plastics Engineering*, pp. 20–27, October, 2005.

[C.4.19] Sturdevant M. Sterilization compatibility of rigid thermoplastic materials. Dow Chemical Company report, 1988.

[C.4.20] Szycher M. *High performance biomaterials*. Lancaster (PA): Technomic Publishing, 1991.

[C.4.21] Tang FW, Lambert BJ, and Rogers WJ. *Polymers in Medical Applications*. Shrewsbury (UK): Rapra Technology, pp. 12–15, 2001.

[C.4.22] Thermo Fisher Scientific. NALGENE labware technical data—autoclaving. 2007.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex D

Dry heat sterilization—Material compatibility fundamentals

D.1 Background

Dry heat is an ancient form of preservation and inactivation. Dry heat sterilization can be delivered through convection, conduction, thermal irradiation, infrared, or incineration. Dry heat has been used in the spacecraft, pharmaceutical, health care, and medical device industries and can sterilize many materials that other methods cannot. These materials include glass, powders, oils, pastes, most metals, many heat-stable polymers, and electrical components. Dry heat sterilization is simpler, involves fewer processing parameters, and requires less sophisticated equipment and facilities than many other methods. The process is inexpensive and uses no toxic chemicals, consumables, or isotopes. It is environmentally friendly and reliable and generates no residues.

D.2 Sterilization process variations and parameters

The dry heat sterilization process can be performed in a convection oven, with infrared radiation, through rapid heat transfer by forced air, or through continuous belt sterilizers in a radiant heat tunnel. No matter the equipment used, two process variables and parameters must be considered:

- temperature and
- time.

Dry heat sterilization is typically performed at temperatures of 160 °C to 190 °C but can be performed in the range of 105 °C to 135 °C. The lower temperatures can sterilize as many materials as moist heat sterilization. However, the extended heating time for dry heat sterilization may cause a gradual softening or distortion of the outer layers of certain materials., A longer cycle, lower temperature, and integration of heat lethality during the heating and cooling steps can be used to avoid polymer or product degradation. Knowledge of the rate of polymer degradation or decomposition and the kinetics of death rate bioburden at different temperatures can make it possible to optimize cycle parameters.

Exposure times can vary with the temperature. The higher the temperature is, the shorter the exposure time will be (e.g., 330 °C for 1.15 sec, 190 °C for 6 min, 180 °C for 30 min, 160 °C for 2 hours, 121 °C for overnight, 105 °C to 112 °C for 30 hours or longer). Increasing temperature can dehydrate microbes faster, resulting in shorter inactivation times. Exposure time depends on load, time to penetrate, and the validation approach used.

It is also important to recognize the influence that load, mass, or stress can have on a material during dry heat sterilization, because some materials may soften and flatten as a result of direct contact with other items in the load.

D.3 Material compatibility

D.3.1 General

When choosing a material, start by selecting a polymer and material that best fits the dry heat process and temperature of choice. The number of materials that can be dry heat sterilized increases as the sterilization

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

temperature decreases. Selection begins with consideration of the material's heat deflection, glass transition, melting, and optimum operating temperatures. Material heat stability can be enhanced by the addition of heat stabilizers or glass fibers. Dry heat sterilization is especially advantageous when used for materials that are adversely affected by moisture, hydration, or corrosion. Some transparent plastics that might absorb extremely small amounts of water vapor and appear cloudy after autoclaving can be ideal candidates for dry heat sterilization. Conversely, acrylonitrile butadiene styrene, acrylics, polystyrene, and low-density polyethylene can be damaged by exposure to high temperatures.

D.3.2 Specific materials

Table D.1 lists various materials and their general compatibility with dry heat sterilization. The information in the table is not exhaustive, and device manufacturers should use it only as a general guideline for the selection of materials. Before a material is selected, the vendor or manufacturer should always be consulted for more information.

Table D.1—Materials compatibility with dry heat sterilization

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		**(NL) = not likely (L) = likely (U) = unknown**	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Thermoplastics		(D.4.3 to D.4.11, D.4.12)		
Acrylonitrile butadiene styrene (ABS)	● to ● ●	(D.4.10). Possible/poor; depending on grade, filler, function and formulation, heat-resistant grade at low temperature process.	NL	With low temperature.
Fluoropolymers				
Polytetrafluoroethylene (PTFE)	● ● ● ●	(D.4.10, D.4.11). Compatible up to 170 °C or higher.	L	Grades with long-term service.
Perfluoro alkoxy (PFA)	● ● ● ●	(D.4.10, D.4.11). Working temperatures up to 204 °C.	L	Up to 170 °C.
Perchlorotrifluoroethylene (PCTFE)	● ● ●	(D.4.10, D.4.11). Up to 150 °C.	L	Up to 150 °C.
Polyvinyl fluoride (PVF)	● ● to ● ● ●	(D.4.11). Heat deflection temperature up to 125 °C (D.4.10),134 °C.	NL	Limited use
Polyvinylidene fluoride (PVDF)	● ● ●	(D.4.11).	L	Maximum operating temperature is 130 ºC (275 ºF).
Ethylene tetrafluoro-ethylene (ETFE)	● ● ●	(D.4.10, D.4.11). Up to 150 °C.	L	
Fluorinated ethylene propylene (FEP)	● ● ● ●	(D.4.11). Up to 170 °C (D.4.10) or 200 °C (392 °F).	L	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table D.1—Materials compatibility with dry heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		**(NL) = not likely (L) = likely (U) = unknown**	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polyacetals (e.g., polyoxymethylene)	● ● to ● ● ●	Up to 121 °C (D.4.10, D.4.11) or higher; may degas.	L	Used up to 100 cycles at 121 ºC.
Polyacrylates (e.g., polymethylmethacrylate)	● to ● ●	Possible to poor; some high resistant grades.	NL	
Polyamides (e.g., nylon)	● to ● ● ● ●	(D.4.10, D.4.11). Depends on type, form, function, and formulation.	NL	Possible to resterilize some heat-resistant forms.
Polycarbonate (PC)	● ●	(D.4.2, D.4.10, D.4.11). Some grades can be sterilized at 134 °C.	L	Some only compatible for a few cycles; others to 200 cycles.
Polyesters, saturated	● to ● ●	(D.4.10). Depends on type grade, form, function. Some good polyethylene terephthalate (PET) films; low temperatures required.	NL	Polyethylene naphthalate (PEN) is better than PET.
Polyethylene (PE), various densities	● to ● ●	(D.4.2). Poor to possible/poor; (D.4.10, D.4.11) high-density polyethylene (HDPE), fair. Polyolefin, possibly fair.	NL	Reinforcement of HDPE required to improve its temperature compatibility.
Polyimides (e.g., polyetherimide)	● ● ● to ● ● ● ●	Excellent (D.4.10, D.4.11), depending on grade, form, and function.	L	Polyetherimide withstands up to 4,000 cycles (e.g., 1000–2500 cycles at 5 min at 134 °C).
Polyketones (e.g., polyetheretherketone)	● ● ● ●	High temperature resistance (D.4.7, D.4.10, D.4.11).	L	Polyetheretherketone has great heat resistance (up to 20,000 hours of dry heat.)
Polypropylene (PP)		(D.4.2, D.4.10, D.4.11). Depends on grade, form, formula, function, and fit.	NL	
Natural	● ● ●			
Stabilized	● to ● ● ●			
Polystyrene (PS)	● to ● ● ● ●	Standard poor; syndiotatic polystyrene (SPS) is excellent and styrene/polyphenyoxides (PPO) good.	L	Use SPS.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table D.1—Materials compatibility with dry heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polysulfones	● ● ● to ● ● ● ●	(D.4.10). Typically all types excellent (D.4.11); however, polyether sulfone (PES) less resistant.	L	
Polyurethane (PU)	● to ● ●	(D.4.10). Poor, but some grades possible. (D.4.11).	NL	
Polyvinylacetates (PVA)	● to ● ●	Heat-stable PVA with hot melt adhesives required; depends on form, formulation, function.	NL	
Polyvinylchloride (PVC)	● to ● ●	Rigid PVC is poor, but possible with modifiers, heat stablilizers.	NL	
PVC, plasticized	● to ● ●	(D.4.11). Depends on form, formulation, and function.	NL	
Styrene acrylonitrile (SAN)	● to ● ●	Possible/poor; depends on grade.	NL	
Thermosets		(D.4.1, D.4.3, D.4.12)		
Epoxy	● ● to ● ● ● ●	Good heat-resistant types of epoxies required, but physical properties can vary. Heat distortion temperatures up to 470 °F.	L	Some with mechanical strength stable to 400 °F. Properties decrease with increased exposure at about 100 hours.
Phenolics	● ● to ● ● ●	Some compatible up to 150 °C.	L	
Polyester, unsaturated	● ● ● to ● ● ● ●	There are a variety of unsaturated polyesters. Better cross-linked. Some have maximum working temperatures up to 170 °C.	L	Isophthalic acid–based polyester has high temperature resistance.
Polyimides	● ● ● to ● ● ● ●	Bis maleimides (BMI) and acetylene-terminated polyimide (ACTP) have use-service temperatures of 127–232° C and 316 °C.	L	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table D.1—Materials compatibility with dry heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polyurethanes		Typically poor, depending on grade, form, function. There are heat-resistant cross-linked polyurethanes.	NL	
Aliphatic	● to ● ●	Crosslinking by radiation increases its resistance.	NL	
Aromatic	● to ● ●	No MDA, aromatic.	NL	
Adhesives				
Acrylic	● to ● ●	Depends on grade, formulation. Acrylic adhesive film in a tape up to 280 °F.	NL	
Epoxy	● ● to ● ● ● ●	Depending on grade and formulation, deflection temperature from 200 °F to 500 °F.	L	Some can lose retention of initial strength after only five cycles.
Fluoroepoxy	● ● to ● ● ●	Epoxy adhesives depend on cure and formulation.	L	Epoxy adhesives cured with heat are more heat resistant than those cured at room temperatures.
Silicone	● ● to ● ● ● ●	Typically excellent (D.4.11); depends on form, formulation, function—good to excellent.	L	
Elastomers				
Butyl	● to ● ● ●	(D.4.2). Resistance to water and up to 120 °C.	L	
Ethylene propylene diene monomer (EPDM)	● ● to ● ● ●	(D.4.2). Up to 134–150 °C in air; others only up to 120 °C.	L	Continuous use operation temperature of 105 °C.
Natural rubber	● to ● ●	Poor; some autoclavable grades; plastomer enhances thermal resistance. To 230 °F.	NL	Hardens with use; some discoloration over time.
Nitrile	● to ● ●	(D.4.2). Tolerates temperatures up to 120 °C.	NL	Lower conditions required, below 230 °F.
Polyacrylic	●	Polyacrylate is a heat-resistant rubber; up to 125 °C.	Possible	

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table D.1—Materials compatibility with dry heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polychloroprene	● to ● ●	(D.4.2). Fair resistance to moisture, up to 230 °F; intermittent to 250 °F possible.	NL	Resterilization is possible at processing below 110 °C.
Silicone	● ● to ● ● ● ●	(D.4.2). Excellent resistance (D.4.11). Some parts, finished devices may do better at lower temperatures.	L	Silicone rubber may become soft and sticky (tacky).
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	● to ● ●	Depends on grade, type, form, and formulation. Possible/poor to fair.	NL	Possibly compatible at temperatures up to 100 °C.
Urethane	● to ● ●	Some heat-resistant grades. Depends on type, form, and formulation. Some compatible up to 135 °C.	NL	Compatibility improved with silicone.
Metals		(D.4.2)		
Aluminum	● ● ● ●	(D.4.11).	L	
Brass	● ● ● ●	Used in steam traps.	L	
Copper	● ● ● ●	No reaction when heated in steam; but surface blackens when heated strongly in air.	L	Copper and brass corrosion inhibitor includes triazole.
Gold	● ● ● ●	No reaction when heated in air, and no reaction when heated in steam.	L	
Magnesium	● ●	Magnesium metal.	U	
Nickel	● ● ● ●	Used in autoclaves.	L	
Silver	● ● ● ●	Virtually no reaction when heated in air, and no reaction when heated in steam. Autoclaving does not remove activity.	U	There may be some changes.
Stainless steel	● ● ● ●	(D.4.2, D.4.11). Varies with grade, content of other inhibitors.	L	Chrome:stainless steel pitting and dulling of cutting edges after sterilization cycles.
Titanium	● ● ● ●	(D.4.11). Resists corrosion.	L	Nickel-titanium alloy improved; titanium molybdenum is nickel free and has good corrosion resistance.

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table D.1—Materials compatibility with dry heat sterilization (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Ceramics/glasses				
Aluminum oxides	● ● ●	Withstands corrosion more than aluminum.	U	
Silica	● ● ● ●	(D.4.2). Withstands extreme temperatures and is relatively inert.	L	
Zirconium oxides	● ● to ● ● ●	Depends on the quality of zirconium. Quality is regularly tested in an autoclave for 5 hours at 134 °C.	L	
Other materials				
Bioabsorbables		Heat and hydrolysis attack. A case where normal dry heat cannot sterilize biologic material; however, unusually low vacuum-processing dry heat temperature process may do so.		
Polyglycolides (PGA)	● to ● ●	Cross-linked PGA is resistant.	NL	
Polylactides (PLA)	● to ● ●	PLA has improved grades.	NL	
Cellulosics				
Cellulose ester	● to ● ● ●			
Cellulose acetate propionate	● to ● ●	Possible.	NL	
Cellulose acetate butyrate	● to ● ●	Typically melts below 100 °C, but heat stable. Grades exist for low processing.	NL	
Cellulose, paper, cardboard	● to ● ●	(D.4.11). Some papers go up to 134 °C. A variety of items have been autoclaved (for example, Kraft, glassine, paper, crepe cellophane parchment, filters).	NL	Wetness could cause contamination, weakness.
Liquid crystal polymer (LCP)	● ● ● to ● ● ● ●	Parts withstand 135 °C, but depending on form up to 340 °C. Good to excellent.	L	Some grades continuous service temperatures to 240 °C.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

D.4 References

[D.4.1] Canon Communications. *Modern plastics worldwide world encyclopedia: The global plastics magazine*, 2004. http://www.modplas.com/worldencyclopedia/search.

[D.4.2] Marino F, Floyd B, and Rogers W. Industrial sterilization: A review of current principles and practices. 1992: In: Avis KE, Lieberman HA, and Lachman L (eds.). *Pharmaceutical dosage forms: Parenteral Medication*, Volume w**.** Munich: Marcel Dekker, pp. 1–54, 142, 155–215, 378, 1992.

[D.4.3] Modern Plastics. Modern Plastics World Encyclopedia, yearly, Modern Plastics;, New York.

[D.4.4] Nighswonger G (with Rogers W). Dry-heat sterilization methods focus of draft standard. *Medical Device & Diagnostic Industry*, p. 19, August 2002.

[D.4.5] Perkins JJ. *Principles and methods of sterilization in health sciences*. Springfield (IL): Charles C Thomas, pp. 54, 204, 261–262, 296–299, 301, 1970.

[D.4.6] Plastics Design Library. *The effect of sterilization methods on plastics and elastomers*. Morris (NY): Plastics Design Laboratory, 1994.

[D.4.7] Pflug E, et al. Principles of the thermal destruction of microorganisms. In: Block SS (ed.), *Disinfection, sterilization, and preservation* , 5th ed. Philadelphia (PA): Lippincott, Williams & Wilkins, pp. 97–98, 99, 101, and other information within Chapter 6, 2001.

[D.4.8] Rhodes A, and Fletcher D. Principles of sterilization, sterility tests, and asepsis." In: *Principles of industrial microbiology*. Oxford (UK): Pergamon, pp. 50–51, 1966.

[D.4.9] Rogers W. *Sterilisation of polymer healthcare products*. Shawbury (UK): Rapra Technology, pp. 11–12, 74–75, 88– 90 , 247–254, 277–283, 298–302, 2005.

[D.4.10] Rogers W. Steam: Uses and challenges for device sterilization. *Medical Device & Diagnostic Industry*, pp. 80–87, March 2006.

[D.4.11] Rubin I. *Handbook of plastic materials and technology*. New York: John Wiley & Sons, 1990.

[D.4.12] Sturdevant M. Sterilization compatibility of rigid thermoplastic materials. Dow Chemical Company report, 1988.

[D.4.13] Szycher M. *High-performance biomaterials*. Lancaster (PA): Technomic Publishing, 1991.

[D.4.14] Thermo Fisher Scientific. NALGENE labware technical data, 2007.

 © 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex E

Hydrogen peroxide sterilization—Material qualification fundamentals

E.1 Background

Hydrogen peroxide (H_2O_2) is an oxidizing agent that can be used for sterilization either as a liquid or as a gas. It is also known as hydrogen dioxide. The information presented here applies only to sterilization with hydrogen peroxide in the gas phase. When in the gas phase, hydrogen peroxide generally follows the ideal gas law. Hydrogen peroxide has excellent antimicrobial properties against a wide range of microorganisms, including bacterial endospores. Under carefully controlled process conditions, hydrogen peroxide is also safe for use with many materials. Hydrogen peroxide can be decomposed into water and oxygen, rendering it environmentally safe.

E.2 Sterilization process variations and parameters

E.2.1 Process variations

There are two general terminal sterilization methods available using hydrogen peroxide as the sterilant—hydrogen peroxide gas plasma and hydrogen peroxide vapor.

In sterilization with hydrogen peroxide, process variations or parameters need to be taken into consideration, such as

- temperature;
- presence of plasma; and
- pressure (change rate and/or level).

NOTE 1—It is important to note that material compatibility information and considerations for one type of sterilization system do not necessarily apply to the other system or any other oxidative-based systems.

NOTE 2—Plasma is a state of matter distinguishable from a solid, liquid, or gas. Gas plasmas are highly ionized gases composed of ions, electrons, and neutral atomic particles that produce a visible glow. For more information see Annex H of ANSI/AAMI ST58:2005.

Table E.1 presents the typical phases of the hydrogen peroxide sterilization cycle.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table E.1—Hydrogen peroxide sterilization process phases

Evacuation and conditioning	The sterilization chamber is evacuated to remove air from the chamber and packaging; the chamber is conditioned to achieve conditions for sterilization.
Hydrogen peroxide exposure	A solution of hydrogen peroxide and water is vaporized and allowed to surround and interact with the devices to be sterilized. NOTE 1—For gas plasma systems, typical hydrogen peroxide concentrations are 6–18 mg/L, cycle times range from 15 minutes to 4 hours, and temperatures range from 40 ºC to 60 ºC (104 ºF to 140 ºF). NOTE 2—For hydrogen peroxide vapor systems, typical hydrogen peroxide concentrations are 0.5–9 mg/L, cycle times range from 45 min to 8 hours and temperatures range from 25 ºC to 55 ºC (77 ºF to 122 ºF).
Gas plasma, if applicable	Hydrogen peroxide gas plasma processes use a strong electrical field to create plasma. The plasma breaks down the peroxide into a cloud of highly energized species that recombine, turning the hydrogen peroxide into water and oxygen.
Evacuation and, if applicable, aeration	Systems without gas plasma require aeration.
Final vent	The chamber is returned to atmospheric pressure.

E.2.2 Parameters

E.2.2.1 Temperature

Typical product temperatures do not exceed 55 °C. Cycles can be developed with other load temperatures, depending on application.

E.2.2.2 Pressure

Because of the deep vacuum required for sterilization, the items to be sterilized must be able to withstand the pressure changes. Some devices use special venting caps to allow pressure equalization between external and internal spaces. Physical damage to the device might occur if it is not capable of withstanding both deep vacuums and the rate of pressure change from a given cycle.

E.2.2.3 Plasma (hydrogen peroxide gas plasma sterilization)

Plasma will affect some materials by surface modification. In some instances, the effect is temporary. Devices to be processed should be evaluated for surface modifications and effects on functionality.

E.3 Material compatibility

E.3.1 General

Because of the oxidative nature of the hydrogen peroxide sterilization environment, some materials are not recommended for use. The durability depends on the specific molding conditions (i.e., a component of medical devices with high residual stress could be less durable than a component that has been properly stress relieved). It is

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

also important to note that material compatibility information for sterilization by hydrogen peroxide vapor may not apply to sterilization by hydrogen peroxide gas plasma.

E.3.2 Specific materials

Table E.2 lists materials and their general compatibility with hydrogen peroxide sterilization. The information in this table is not exhaustive, and device manufacturers should use it only as a general guideline for the selection of materials. Before a material is selected, the vendor or manufacturer should always be consulted for more information.

Table E.2—Material compatibility guidance—Specific materials

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		**(NL) = not likely (L) = likely (U) = unknown**	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Thermoplastics				
Acrylonitrile butadiene styrene (ABS)	● ● ● ●		L	No change after > 100 cycles.
Fluoropolymers				
Polytetrafluoroethylene (PTFE)	● ● ● ●		L	No change after > 100 cycles.
Perfluoro alkoxy (PFA)	● ● ● ●		U	
Perchlorotrifluoroethylene (PCTFE)	● ● ● ●		U	
Polyvinyl fluoride (PVF)	● ● ● ●		U	
Polyvinylidene fluoride (PVDF)	● ● ● ●		U	
Ethylenetetrafluoro-ethylene (ETFE)	● ● ● ●		U	
Fluorinated ethylene propylene (FEP)	● ● ● ●		U	
Polyacetals (e.g., polyoxymethylene)	● ● ● ●		L	Significant color changes or slight material changes after 10–100 cycles. Grade dependent.
Polyacrylates (e.g., polymethylmethacrylate)	● ●	Grade dependent.	NL	Significant material changes or crazing after 10–50 cycles.
Polyamides (e.g., nylon)	● ● ●		L	Severe material degradation after 10–100 cycles. Grade dependent.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table E.2—Material compatibility guidance—Specific materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polycarbonate (PC)	● ● ● ●		L	No change after > 100 cycles.
Polyesters, saturated	● ● ● ●		L	
Polyethylene (PE), various densities	● ● ● ●		L	No change after > 100 cycles.
Polyimides (e.g., polyetherimide)	● ● ● ●		L	No change after > 100 cycles.
Polyketones (e.g., polyetheretherketone)	● ● ● ●		L	No change after > 100 cycles.
Polypropylene (PP)			L	No change after > 100 cycles.
Natural	● ● ● ●			
Stabilized	● ● ● ●			
Polystyrene (PS)	● ● ● ●		L	No change after > 100 cycles.
Polysulfones	● ● ● ●		U	Grade dependent.
Polyurethane (PU)	● ● ●		L	Some color change or loss of gloss after 100 cycles.
Polyvinylacetates (PVA)	● ● ● ●		L	No change after > 100 cycles.
Polyvinylchloride (PVC)	● ● ● ●		L	Some color change or surface changes after 50 cycles.
PVC, plasticized	● ● ● ●		U	
Styrene acrylonitrile (SAN)	● ● ● ●		U	
Thermosets				
Epoxy	● ● ● ●	Grade dependent.	U	Grade dependent.
Phenolics	● ● ●	Grade dependent.	U	Grade dependent.
Polyester, unsaturated	U		NL	
Polyimides	● ● ● ●	Grade dependent.	U	Grade dependent.
Polyurethanes		Grade dependent.	U	Grade dependent.
Aliphatic	● ● ●			
Aromatic	● ● ●			
Adhesives		(E..4.1)		
Acrylic	● ●		NL	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table E.2—Material compatibility guidance—Specific materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Epoxy	● ● ● ●		U	Grade dependent.
Fluoroepoxy	● ●		U	
Silicone	● ●		U	
Elastomers				
Butyl	● ● ●		NL	
Ethylene propylene diene monomer (EPDM)	● ● to ● ● ●		L	
Natural rubber	● ● ●		NL	May degrade after three cycles.
Nitrile	● ● ●		L	Grade dependent.
Polyacrylic	● ●		L	Grade dependent.
Polychloroprene	● ● ● ●		L	Severe material degradation after 100 cycles.
Silicone	● ● ● ●		L	No change after >100 cycles.
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	● ● ● ●		L	Some color change or surface changes after 50 cycles.
Urethane	● ● ●		L	Grade dependent.
Metals		(E..4.3)		
Aluminum	● ● ● ●		L	No change after > 100 cycles.
Brass	● ● ● ●		L	No change after > 100 cycles.
Copper	● ● ●		L	Limited to small amounts.
Gold	● ● ● ●		L	Limited to small amounts.
Magnesium	● ● ●		L	Limited to small amounts.
Nickel	● ● ●		L	Limited to small amounts.
Silver	● to ● ● ●		L	Limited to small amounts.
Stainless steel	● ● ● ●		L	No change after > 100 cycles.
Titanium	● ● ● ●		L	No change after > 100 cycles.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table E.2—Material compatibility guidance—Specific materials (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Ceramics/glasses				
Aluminum oxides	● ● ● ●		L	Limited to small amounts.
Silica	● ● ● ●		L	No change after > 100 cycles.
Zirconium oxides	● ● ● ●		L	Limited to small amounts.
Other materials				
Bioabsorbables				
Polyglycolides	● to ● ● ●		NL	
Polylactides	● to ● ● ●		NL	
Cellulosics				
Cellulose ester	●		NL	Do not process.
Cellulose acetate propionate	●		NL	Do not process.
Cellulose acetate butyrate	●		NL	Do not process.
Cellulose, paper, cardboard	●		NL	Do not process.
Liquid crystal polymer (LCP)	● ● ● ●		L	No change after > 100 cycles.

NOTE—Advanced Sterilization Products provided the information in this table based on published (Feldman and Hui, 1997, and Hui et al, 1999), and unpublished studies conducted in STERRAD® Sterilization Systems.

E.4 References:

[E.4.1] Association for the Advancement of Medical Instrumentation, *Chemical sterilization and high-level disinfection in health care facilities*. AAMI ST58:2005. Arlington, (VA): AAMI, 2005.

[E.4.2] Feldman LA, and Hui HK. Compatibility of medical devices and materials with low-temperature hydrogen peroxide gas plasma. *Medical Device & Diagnostic Industry*, December 1997.

[E.4.3] Hawkins CL, and Davies MJ. Generation and propagation of radical reactions on proteins. *Biochimica et Biophysica acta*, 1504:196–219, 2001.

[E.4.4] Hui HK, Feldman LA, Timm D, and Wu S. Materials compatibility of materials with low-temperature hydrogen peroxide gas plasma. *Infection Control Today*, May 1999.

[E.4.5] Imlay JA. Pathways of oxidative damage. *Annual Reviews in Microbiology*, 57:395–418, 2003.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex F

Ozone sterilization—Material compatibility fundamentals

F.1 Background

Historically, ozone has been used in the treatment of water and wastewater and for the disinfection and preservation of food. However, ozone is a strong oxidizer, which makes it an efficient sterilizing agent. In a gaseous or vapor form, ozone can be used to sterilize medical products and other materials in the ozone sterilizer or chamber. Because ozone is a metastable product, it cannot be stored and is therefore produced in situ, so the operator does not handle the sterilant in any form. Ozone is typically generated within a sterilizer's self-contained ozone generator from USP (United States Pharmacopeia) grade oxygen. Ozone sterilization processes are particularly suited for sterilizing heat-sensitive materials. During sterilization, ozone breaks down into reactive species, including hydroxyl radicals and atomic oxygen.

The sterilant must be able to penetrate all portions of the load and contact all surfaces intended to be sterilized.

F.2 Sterilization process variations and parameters

F.2.1 Process variation

At this time, there are very limited variations in the ozone sterilization process. Items are conditioned to a predetermined state and then ozone is injected. Ozone is generated within the sterilizer. During the sterilization cycle, items are exposed to ozone at typical concentrations of 85 mg/L for 15 min at a temperature of 30 °C to 36 °C. The ozone is allowed to dwell for a fixed time and is then exhausted. During the dwell period, the ozone breaks down in the chamber into reactive species, including free radicals. The breakdown residues of ozone are oxygen and water vapor.

Table F.1 presents typical processing phases and parameters for ozone sterilization.

F.2.2 Process parameters

In ozone sterilization, process variations or parameters need to be taken into consideration, such as

- time,
- temperature,
- humidity, and
- pressure (change rate and/or level).

Because of the strong oxidizing nature of ozone, materials must be resistant to oxidation. The ozone concentration is typically at 85 mg/L for 15 min at a temperature of 30 °C to 36 °C. The process temperatures are generally low, making it suitable for temperature sensitive materials.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table F.1—Typical ozone sterilization cycle

Phase	Description
1) Vacuum and conditioning	A vacuum is drawn to approximately 1 Torr (133 Pa) to remove air from the sterilizer chamber and the load. The load is then conditioned to attain the sterilization conditions.
2) Humidification	Water vapor is pulled inside the chamber for an effective sterilization. The pressure increases consequently.
3) Ozone injection and exposure	Ozone is generated immediately before its gradual injection inside the chamber. Once the ozone concentration has reached its predetermined dose, the load is exposed for a fixed period of time for a successful sterilization
4–6) Repeat phases 1–3 (i.e, vacuum and conditioning, humidification, and ozone injection and exposure)	Phases 4–6 replicate the same conditions as in phases 1–3.
7) Evacuation and ventilation	Ozone is drawn through a catalytic converter where it reverts back to oxygen and water vapor. The sterilizer chamber is returned to atmospheric pressure.

F.2.2.1 Ozone

Ozone is a strong oxidizing agent. Materials must be resistant to oxidation. Lethality is a direct function of the ozone concentration injected into the sterilization chamber. As with other sterilization processes, sterility cannot be ensured unless the product is cleaned and dried before the sterilization cycle. The sterilant must be able to penetrate all portions of the load intended to be sterilized. Thus, device construction and packaging might be more important to achieving sterility than are the materials used to construct the product.

F.2.2.2 Temperature

Materials and medical devices should be resistant to temperature ranges of 30 °C to 36 °C for short periods of time.

F.2.2.3 Humidity

Materials and medical devices should be resistant to high relative humidity levels (> 80 %), which are required for ozone to be effective as a sterilant. Even with a relatively low humidity level, it is possible for humidity to condense into liquid water on the surfaces of a device. Such condensation is most likely to occur during the load conditioning portion of the cycle, when a cold load is placed in the chamber.

F.2.2.4 Pressure excursions

Materials and medical devices should be resistant to vacuum (1 Torr). As such, the process is not recommended for the sterilization of glass ampoules or liquids.

F.3 Material compatibility

F.3.1 General

Materials should be resistant to oxidation and moisture. This method of sterilization cannot be used for fluids or woven textiles. Ozone sterilization is a surface-oxidative process. Therefore, the shape of the materials as well as the

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

design of a device is closely related to the resistance of the device to sterilization and the amount of degradation caused by the sterilization process. For example, polymeric components with large surface-to-mass ratio (e.g., fibers) will undergo fast oxidative degradation. Although such materials can be satisfactorily used in the manufacture of a device intended for single use, they might not be effective for use with a reusable device.

F.3.2 Specific materials

Table F.2 lists materials and their general compatibility with ozone sterilization. The information in this table is not exhaustive, and device manufacturers should use it only as a general guideline for the selection of materials. Further information can be obtained from ozone sterilizer manufacturers.

Table F.2—Ozone material compatibility

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		**(NL) = not likely (L) = likely (U) = unknown**	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Thermoplastics		(F.4.8)		
Acrylonitrile butadiene styrene (ABS)	● ●		U	
Fluoropolymers				
Polytetrafluoroethylene (PTFE)	● ● ● ●		L	No change after > 100 cycles.
Perfluoro alkoxy (PFA)	● ● ● ●		L	No change after > 100 cycles.
Perchlorotrifluoroethylene (PCTFE)	● ● ● ●		L	No change after > 100 cycles.
Polyvinyl fluoride (PVF)	U			
Polyvinylidene fluoride (PVDF)	● ● ● ●		L	No change after > 100 cycles.
Ethylenetetrafluoro-ethylene (ETFE)	● ● ● ●		L	No change after > 100 cycles.
Fluorinated ethylene propylene (FEP)	● ● ● ●		L	No change after > 100 cycles.
Polyacetals (e.g., polyoxymethylene)	● ● ●		L	Color change and loss of gloss. Slight to significant change may occur after > 100 cycles.
Polyacrylates (e.g., polymethylmethacrylate)	● ● ●		L	Slight to significant material change may occur after 10–100 cycles.
Polyamides (e.g., nylon)	● ● ●		L	Color change and loss of gloss. Significant material

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table F.2—Ozone material compatibility (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
				change after 10–100 cycles.
Polycarbonate (PC)	● ● ● ●		L	Slight surface change and loss of gloss. No significant change after > 100 cycles.
Polyesters, saturated	● ● ● ●		U	
Polyethylene (PE), various densities	● ● ● ●		L	Color change and loss of gloss. Significant material change may occur after 10–100 cycles.
Polyimides (e.g., polyetherimide)	● ● ● ●		L	Slight surface change. No significant change after > 100 cycles.
Polyketones (e.g., polyetheretherketone)	● ● ● ●		L	Unfilled polyetheretherketone only—avoid sharp edges. Color change and loss of gloss. No significant change after > 100 cycles.
Polypropylene (PP)				
Natural	● ● ● ●		L	Color change and loss of gloss. Significant material change may occur after 10–100 cycles.
Stabilized	● ● ● ●		L	Color change and loss of gloss. Significant material change may occur after 10–100 cycles.
Polystyrene (PS)	● ●		NL	Significant material or surface change with < 3 cycles.
Polysulfones	● ● ●		L	Slight surface change and loss of gloss.
Polyurethane (PU)	●		NL	Significant material or surface change with < 3 cycles.
Polyvinylacetates (PVA)	U		U	

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table F.2—Ozone material compatibility (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Polyvinylchloride (PVC)	● ● ● ●		L	Color change and loss of gloss. No significant change after > 100 cycles.
PVC, plasticized	● ● ●		NL	Surface change may occur after 5–25 cycles.
Styrene acrylonitrile (SAN)	U		U	
Thermosets		(F.4.8)		
Epoxy	● ● ● to ● ● ● ●		L	Significant material change may occur after 10–100 cycles.
Phenolics	● ● ● ●		L	Loss of gloss. No significant change after > 100 cycles.
Polyester, unsaturated	● ● ● ●		U	
Polyimides	U		U	
Polyurethanes				
Aliphatic	●		NL	Significant material or surface change with < 3 cycles.
Aromatic	●		NL	Significant material or surface change with < 3 cycles.
Adhesives		(F.4.8)		
Acrylic	● ● ●		L	Application specific.
Epoxy	● ● ● to ● ● ● ●		L	Application specific.
Fluoroepoxy	● ● ●		L	Application specific.
Silicone	● ● ●		L	Application specific.
Elastomers		(F.4.8)		
Butyl	●		NL	(F.4.4).
Ethylene propylene diene monomer (EPDM)	● ●		NL	(F.4.4). Significant material or surface change with < 3 cycles.
Natural rubber	●		NL	(F.4.4). Significant material or surface change with < 3 cycles.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table F.2—Ozone material compatibility (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Nitrile	U		U	
Polyacrylic	● ● ●		U	
Polychloroprene	●		NL	Significant material or surface change with < 3 cycles.
Silicone	● ● ● ●		L	Slight material change after > 100 cycles.
Styrenic block copolymers (e.g., styrene-butadiene-styrene, styrene-ethylene-butylene-styrene)	●		NL	Significant material or surface change with < 3 cycles.
Urethane	●		NL	Significant material or surface change with < 3 cycles.
Metals		(F.4.8)		
Aluminum	● ● ● ●		L	No change after > 100 cycles.
Brass	● ● ●		L	
Copper	● ● ●		L	
Gold	● ● ● ●		L	No change after > 100 cycles.
Magnesium	U		U	
Nickel	●		NL	Significant material or surface change with < 3 cycles.
Silver	●		NL	Significant material or surface change with < 3 cycles.
Stainless steel	● ● ● ●		L	No change after > 100 cycles.
Titanium	● ● ● ●		L	No change after > 100 cycles.
Ceramics/glasses		(F.4.8)		
Aluminum oxides	● ● ● ●		L	No change after > 100 cycles.
Silica	● ● ● ●		L	No change after > 100 cycles.
Zirconium oxides	● ● ● ●		L	No change after > 100 cycles.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Table F.2—Ozone material compatibility (continued)

	(●) = poor (● ●) = fair (● ● ●) = good (● ● ● ●) = excellent (U) = unknown		(NL) = not likely (L) = likely (U) = unknown	
Material	**Single use (1 or 2 cycles)**	**Comments**	**Resterilization (> 10 cycles)**	**Comments**
Other materials		(F.4.8)		
Bioabsorbables				
- Polyglycolides	U		U	
- Polylactides	U		U	Significant material or surface change with < 3 cycles.
Cellulosics				
Cellulose ester	● to ● ● ●		NL	
Cellulose acetate propionate	● to ● ● ●		NL	
Cellulose acetate butyrate	● to ● ● ●		NL	
Cellulose, paper, cardboard	● to ● ● ●		NL	
Liquid crystal polymer (LCP)	● ● ● to ● ● ● ●		L	Loss of gloss.

F.4 References

[F.4.1] Association for the Advancement of Medical Instrumentation. *Chemical sterilization and high-level disinfection in health care facilities*. ANSI/AAMI ST58: 2005. Arlington (VA): AAMI, 2005.

[F.4.2] Chaunet M, Dufresne S, and Robitaille S. *The Sterilization Technology for the 21st Century*. TSO_3 Inc., 2007.

[F.4.3] Dufresne S, Chaunet M, and Robitaille S. Ozone as a sterilant: 125L ozone sterilizer of TSO_3, Part 1 : sterilization and ozone. In: *IOA 17th World Congress & Exhibition: Ozone & related oxidants, innovative & current technologies*. Strasbourg (France), 2005.

[F.4.4] Ege S. *Organic Chemistry, Structure and Reactivity*, 3rd ed. Toronto (ON): D.C. Heath and Company, 1994.

[F.4.5] Greenwood NN, and Earnshaw A. *Chemistry of the Elements*. Pergamon Press, 1994.

[F.4.6] Ishizaki I, Shinriki N, and Matsuyama H. Inactivation of bacillus spores by gaseous ozone. *J Appl Bacteriol*, 60:67–72, 1986.

[F.4.7] Turcot R and Legube B. Ozone as a sterilant: 125L ozone sterilizer of TSO_3, Part 2: Calculation of ozone dose and injection duration. In: *IOA 17th World Congress & Exhibition: Ozone & related oxidants, innovative & current technologies*. Strasbourg (France), 2005.

[F.4.8] TSO_3 Inc. Unpublished data.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Annex G

Accelerated aging programs

G.1 Summary of accelerated aging principles and programs applicable to all sterilization modalities

From the perspective of first principles, the most reliable means of validating the safe and effective performance of a medical device throughout its shelf life is to let the device age on a real-time basis for the duration of its shelf life and then to test its functionality. The downside to this plan is the time required. Life-saving technology might not be brought to market as rapidly as possible because of this constraint. This type of conservative diligence might be necessary if there is no safe alternative. However, for most materials, there are safe and conservative alternatives.

A robust foundation for aging in the medical device industry has been laid through the aging work done to apply polymers in severe environments such as the space, nuclear, and geosynthetic industries. In comparison, typical shelf-life storage conditions in hospitals or device manufacturer warehouses are quite controlled and mild. By far the most common aging tool used in accelerated aging (AA) programs for medical devices is temperature. An aging factor (AF) is defined to correlate the rate of aging at shelf-life conditions to the rate of aging at an elevated temperature. The most critical aspect of applying a temperature-based AA method is the definition of the AF. A common and conservative AF is based on $Q_{10} = 2$. This AF defines the rate of aging at a temperature elevated 10 ºC above shelf-life conditions as two times as fast as aging at shelf-life conditions. The $Q_{10} = 2$ AF is derived from Arrhenius's (G.4.30) description of the rates of chemical reactions. The derivation and the surrounding assumptions have been described to demonstrate the theoretical foundation of the $Q_{10} = 2$ AF. An overview of the empirical evidence from other more severe industries adds to the confidence of using the $Q_{10} = 2$ relation in a safe and conservative manner in the medical device industry (G.4.7).

Along with defining an appropriate AF, responsible application of simple temperature-based AA models requires sufficient characterization of the medical device polymers to ensure that the model is being applied appropriately. For example, it would be inappropriate to age a device at a temperature so close to its melting point that it significantly distorts. Also, aging at elevated temperatures that necessitate extreme extrapolation to elevated temperatures is not appropriate unless clear necessity is demonstrated. Hence, maintaining an aging temperature below 60 ºC is recommended if information is not available to support moving to higher temperatures. Finally, the need to characterize materials is evident if AF approximations from the literature more aggressive than $Q_{10} = 2$ are being used. To see if the information from the literature applies, it is important to understand how the materials of the device in question compare with the material being reported in the literature in terms of chemical composition, molecular weight, additive loading, and processing history.

A foundational AA model is called the Fixed AF method. This model applies the $Q_{10} = 2$ AF and is both simple and conservative. For example, suppose that a medical device manufacturer uses the $Q_{10} = 2$ model for aging polymeric devices, and the devices are aged at 10 ºC higher than typical storage conditions. The devices will simulate aging to their shelf life in half the time required to age at real-time conditions. Numerically, this can be stated as follows:

$$t_{AA} = \frac{RTE}{AF_0} = \frac{RTE}{2}, \qquad \textbf{Equation G.1}$$

where t_{AA} = time to age the samples at the elevated temperature

RTE = real-time equivalent; the shelf life being simulated

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

AF_0 = original AF; in this example, $AF_0 = Q_{10} = 2$

For other aging temperatures, AF can be calculated from the following:

$$AF_0 = Q_{10}^{\frac{T_{AA} - T_{RT}}{10}}, \qquad \textbf{Equation G.2}$$

where T_{AA} = elevated temperature at which devices are aged

T_{RT} = room temperature of device storage conditions

By way of simple illustration, refer back to the previous example. Suppose that the device is aged at 30 ºC above shelf-life conditions (e.g., T_{RT} = 20 ºC and T_{AA} = 50 ºC). In this example, with Q_{10} = 2 still being used, from Equation G.2.

$$AF_0 = 2^{\frac{50-20}{10}} = 2^3 = 8.$$

From Equation G.1,

$$t_{AA} = \frac{RTE}{8}.$$

Hence, aging at the elevated temperature will take one-eighth the time required for real time aging.

As in all AA programs, the model must be validated with real-time data. Using the guidelines above, the manufacturer must demonstrate that the device functions acceptably after real-time aging as well as after real-time equivalent (RTE) aging.

The Fixed AF method, with a Q_{10} = 2 value, is most often quite conservative. Often, a device can be aged more aggressively; that is, the time to age the device to verify a given shelf life might be reduced or the shelf life might be extended for a given elevated temperature aging time. However, it is the burden of the device manufacturer to validate a more aggressive AF. A method for doing so is the Iterative AF method. In this method, real-time and AA data are collected simultaneously. The data are correlated to gain feedback on the relative rates of aging. If indeed the Q_{10} = 2 is overly conservative, the required data can be collected with this method to iterate the AF to a more realistic value. Subclause G.2 contains an example of creative application of the Iterative AF method to allow a beneficial device material technology to get to market and benefit patients by avoiding inappropriate AA program constraints that use the more conservative Q_{10} = 2 AA method (i.e., the Fixed AF method).

With even greater expenditure of resources, a manufacturer can use more advanced methods to define an even better estimate of the real AF for a medical device system. One approach is to age the device at multiple elevated temperatures. The benefit of such an investment is the most reliable and aggressive AF possible, which translates to speed to market, extended shelf life, or both. References to several such methods are provided in the reference list at the end of this annex.

Humidity, ultraviolet light, ozone, or other gases can also be used to validate the shelf life of a medical device if the aging process of the materials can be shown to correlate with these environmental factors. It should be noted that aging can be accelerated when multiple aging processes are involved. One should carefully define the combined effect of the accelerating aging in establishing the protocol for these aging process validations. For example, if the aging process is first order relative to the concentration of ozone, the combined AF can be as high as 4 when doubling the ozone concentration and elevating the temperature 10 ºC. Combination device manufacturers should take special note of humidity as an AF because pharmaceuticals can be quite sensitive to this factor. The International Conference on Harmonization (ICH) has developed guidelines on Technical Requirements for

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Registration of Pharmaceuticals for Human Use. These guidelines are recommended for adoption by the regulatory bodies of the European Union, Japan, and the United States. Accelerated aging of medical devices and accelerated stability of pharmaceuticals are compared in G.3. Also, ASTM F1980 provides guidance on understanding water content versus relative humidity in addressing humidity as an AF.

G.2 Example: Getting a product to market by applying the Iterative AF method

A device manufacturer has traditionally used the relatively low-resource Fixed AF method to qualify products using the conservative and responsible $Q_{10} = 2$ assumption to calculate the AF. A 3-year shelf life has been qualified using an aging temperature (T_{AA}) of 55 °C, a room temperature (T_{RT}) of 20 °C, and a resulting AF of 11.3 (i.e., the manufacturer aged the device for 13.8 weeks to qualify a 3-year shelf-life). Real-time aging was run in parallel.

A new coating is to be applied to the device to address a new patient need. The specification is that over the shelf life of the device the coating integrity must stay less than 90 % of the time at zero value. The new coating failed functional testing after 13.8 weeks at 55 °C. The research and development (R&D) team was confident that the bench test used to evaluate the coating was clinically relevant and set at the right level. Several options were available to the manufacturer: for example, reduce the shelf life; see if a reduced $T_{AA,}$ resulting in an extension of the time required for the AA study, would help; redesign the coating; or delay introduction of the coating until real-time data on the coating was available. However, the R&D team had initial real-time data available for the new coating in addition to the aging data at 55 °C. The R&D team's observation was that the real-time degradation of coating integrity was slower than that predicted by the AA model. The team decided to determine the actual AF for the coating (i.e., to challenge the $Q_{10} = 2$ assumption by using the Iterative AF method).

The R&D team began by comparing the rate of coating degradation at room temperature with the degradation rate at AA temperature (55 °C). The team plotted coating degradation versus real time, both at room temperature and at AA conditions (55 °C). See figure G.1.

Next team members evaluated the Fixed AF method (using the $Q_{10} = 2$ assumption). Figure G.2 shows coating degradation versus real-time aging and real-time equivalent aging (using an AF of 11.3) for room temperature and AA data, respectively. Figure G.3 is the same graph, with the scales changed to clarify the slopes of the lines (i.e., so that the degradation rates are easier to see). It is clear that the fixed AF model with the $Q_{10} = 2$ assumption is more conservative than real-time aging. This finding indicates that the Iterative AF method might be appropriate. As already noted, it is appropriate to use real-time data to adjust aging models because real-time data are the most clinically relevant data.

The next step of the analysis is to select an AF that fits the real-time data. Results are shown in Figure G.4. A Q_{10} value of 2.5 appears to be a better fit with the real-time data. A statistical review of the uncertainty of the regression was then completed to ensure that the Q_{10} estimate could be claimed with appropriate confidence, and a report was completed and approved to document the process used and conclusions.

NOTE—If the uncertainty were too large, the team would either reduce the AF estimate or collect more real-time data and continue to iterate the AF estimates with the additional data.

Finally, age estimates (RTE) for coating integrity degradation were recalculated using the updated AF. Again using an aging temperature (T_{AA}) of 55 °C and a room temperature (T_{RT}) of 20 °C, the team found that the resulting AF is 24.7 (i.e., 6.3 week aging data equates to a 3-year shelf life). Degradation data at 6.3 weeks at 55 °C was still above the coating specification (> 90 % of time zero value). The conclusion, therefore, is that the new coating is initially qualified for a 3-year shelf life. Real-time testing of the new coating will continue and the estimates of the actual AF will continue to be updated and confirmed.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

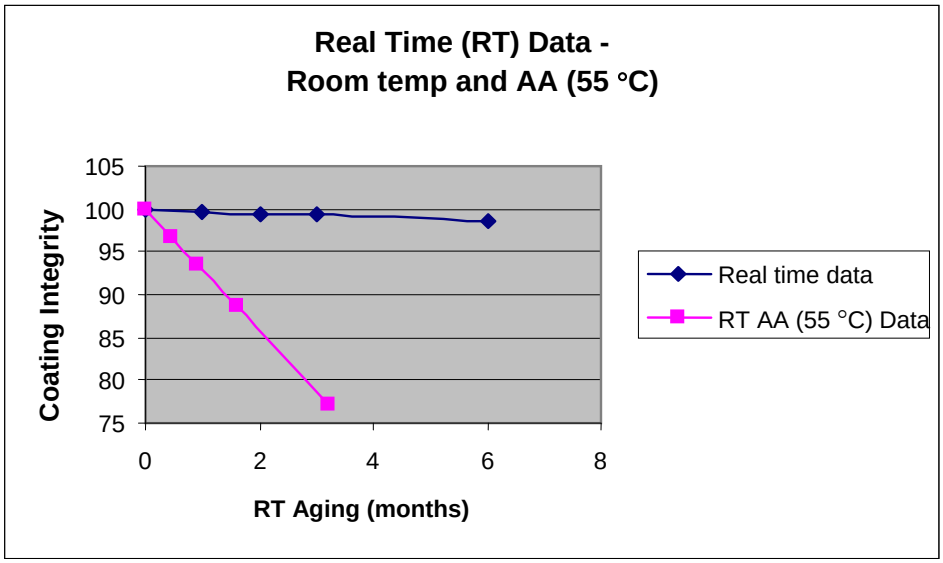


Figure G.1—Comparison of real time data at room temperature and at AA conditions (55 °C)

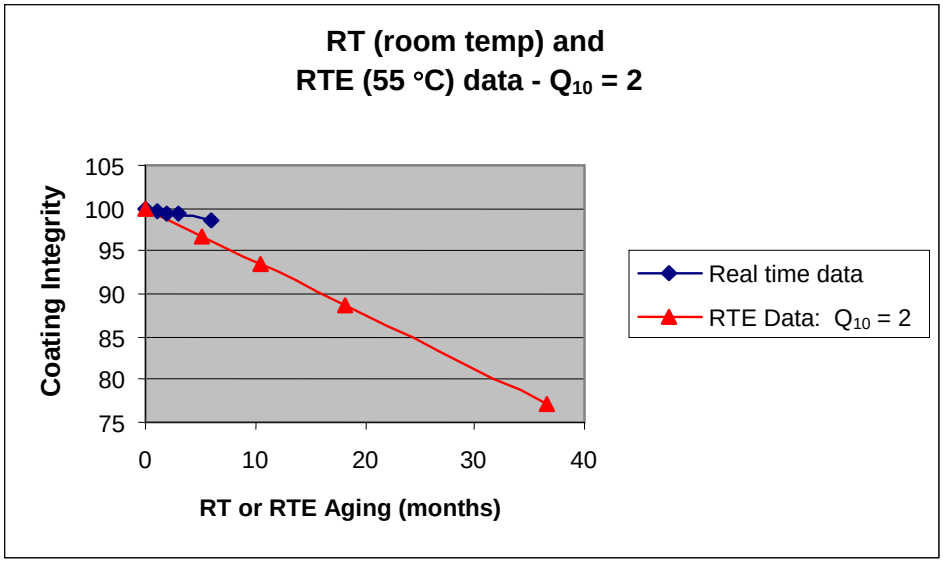
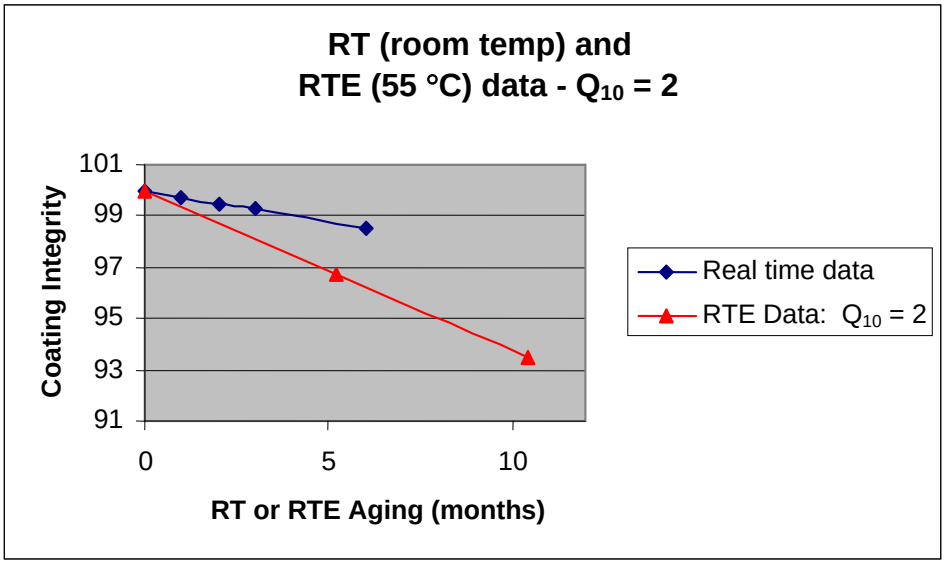


Figure G.2—Comparison of real time data at room temperature with real time equivalent (RTE) data at 55 °C using the $Q_{10} = 2$ assumption

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.



NOTE Scale changed to better visualize slopes (degradation rates).

Figure G.3—Comparison of real time data at room temperature with real time equivalent (RTE) data at 55 °C using the $Q_{10} = 2$ assumption

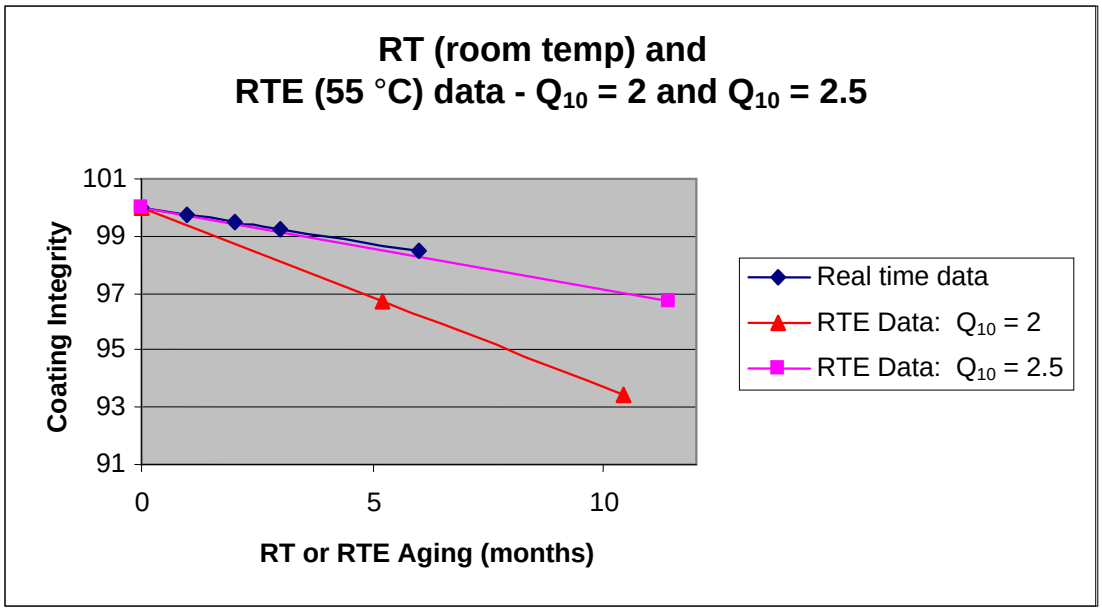


Figure G.4—Comparison of real time data at room temperature with real time equivalent (RTE) data at 55 °C using both the $Q_{10} = 2$ assumption and a Q_{10} value of 2.5.

© 2008 Association for the Advancement of Medical Instrumentation ■ AAMI TIR17:2008

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

G.3 Combination device and drug products

For products that might incorporate a combination of medical devices (such as polymer, metal, glass, and ceramic materials) with bioactive or pharmaceutical drug products or both, the stability of the substance and the device will need to be considered. One must not only consider the functional and safe performance of a device but also demonstrate the stability of active materials. Common practice within the pharmaceutical industry is to apply ICH guidelines for evaluating drug product stability. These guidelines have a conditioning referred to as "accelerated stability." The concept for accelerated stability differs from accelerated aging. To prevent confusion for manufacturers developing combination devices, this clause addresses the differences between accelerated stability for pharmaceuticals and AA for devices.

The stability of a combination device and drug substance or drug product can be evaluated according to the ICH technical requirements for registration of pharmaceuticals for human use. The ICH provides tripartite guidelines for stability testing of new drug substances and products. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and to establish a shelf life for the drug product and recommended storage conditions.

The common international guideline for long-term stability studies specifies 25 ± 2 °C at 60 ± 5 % relative humidity. Accelerated stability studies are specified at 40 ± 2 °C and at 75 ± 5 % relative humidity. Accelerated stability studies also allow the interpretation of data and information on short-term spikes in storage conditions in addition to the excursions allowed by controlled room temperature (see USP).

For medical devices, AA techniques are typically used to predict future performance of critical product materials. Most of these theories are based on the work of Arrhenius, which predicts that the aging rate will double for every 10 °C that the temperature is raised. Although this model is sufficient as an initial approximation for polymer material performance, it is not adequate for predicting the life of a drug product. Drug degradation does not typically correspond to the average Arrhenius model. In addition, Arrhenius does not consider that humidity can have detrimental effects on drug products and excipients independent of temperature.

For pharmaceuticals, product stability is governed by the ICH Q1A(R2), *Stability testing of new drug substances and products*. This guideline is the basis for generating a stability data package for drug products to be registered in the European Union (EC), Japan, and the United States. AA methods for drugs and devices can be run under the same conditions; however, the ICH guidelines must be followed for drug outputs to comply with pharmaceutical standards. Device aging can use these guidelines if they meet the desired shelf-life time. This is a key point of differentiation between device aging and pharmaceutical aging. Device aging can be run at any responsible temperature, but pharmaceutical accelerated stability must be run at 40 °C / 75 % RH.

For drug outputs, the long-term storage condition is used to establish shelf life. Units must not have any significant change after long-term storage to establish an acceptable shelf life. A "significant change" is defined as a 5 % change in assay from the original value or failure to meet any of the predetermined acceptance criteria.

AA testing is conducted to increase the rate of chemical degradation or physical change of the drug substance. Data from these studies will help to predict long-term results on nonaccelerated product and will help to evaluate short-term excursions outside the normal label storage conditions of the product. Device aging criteria should be determined to establish long-term performance safety for the product. Although this typically involves AA to expedite development and time to market, considerations must be given to the established guidelines for pharmaceuticals.

The pharmaceutical guidelines represent a most conservative approach for stability and prediction for long-term performance and safety. It can be desirable for manufacturers to conduct device aging studies in parallel with studies at ICH conditions to gather critical process data and not affect time to market. Manufacturers might also wish to establish equivalence between AA and real-time stability so that future product changes can be evaluated rapidly with high confidence that results will be similar after real-time stability.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

G.4 References

[G.4.1] Association for the Advancement of Medical Instrumentation. *Guidance for ANSI/AAMI/ISO 11607—Packaging for terminally sterilized medical devices—Part 1 and Part 2:2006*. AAMI TIR22:2007. Arlington (VA): AAMI, 2007.

[G.4.2] ASTM International. *Standard guide for accelerated aging of sterile barrier systems for medical devices*. ASTM F1980-2007. Philadelphia (PA): ASTM International, 2007.

[G.4.3] Hemmerich KJ. How to predict shelf life from accelerated aging data: Simplified Q_{10} method. Presented at Session 107, Medtec '97, Amsterdam (Proceedings, pp.1–9. 6S).

[G.4.4] Lambert BJ, and Tang FW. AAMI TIR no. 17 accelerated aging programs. Presented at Session 309, MDM West '98, Anaheim (CA) (Proceedings, pp. 35).

[G.4.5] Lambert BJ, and Tang FW. Overview of ANSI/AAMI Material Qualification Guidance. Presented at Session 108, MDM West '97, Anaheim (CA) (Proceedings, pp. 55).

[G.4.6] Lambert BJ, Tang FW, and Rogers WJ. Polymers in medical applications. *RAPRA Review Reports*, vol. 11 (7), 2001.

[G.4.7] Lambert BJ, and Tang FW. Rationale for practical medical device accelerated aging programs in AAMI TIR17. *Radiation Physics and Chemistry*, 57(3–6):, 349–353, 2000.

Advanced or alternative aging methods

[G.4.8] Carfagno SP, and Gibson RJ. *A review of equipment aging theory and technology*. Palo Alto (CA): Electric Power Research Institute, 1980.

[G.4.9] Donohue J. Radiation-initiated oxidation of HALS stabilized polypropylene. Presented at ANTEC '91, Montreal (ON) (Proceedings, p. 1831).

[G.4.10] Donohue J, and Apostolou S. Predicting post-radiation shelf life from accelerated data: The D&A process. ANTEC '96, Indianapolis (IN) (Proceedings, p. 2819).

[G.4.11] Donohue, J., and Apostolou, S. Shelf-life prediction for radiation-sterilized plastic devices. *Medical Device & Diagnostic Industry*, p. 124, January 1990.

[G.4.12] Fujiyama M, Wakino T, and Kawasaki Y. Structure of skin layer in injection-molded polypropylene. *J Appl Polym Sci*, 35:29–49, 1988.

[G.4.13] Gillen KT, and Clough RL. A kinetic model for predicting oxidating degradation rates in combined radiation—Thermal environments. *J Polym Sci Pol Chem Ed*, 23:2683, 1985.

[G.4.14] Gillen KT, and Clough RL. Accelerated aging methods for predicting long-term mechanical performance of polymers.. In: Clegg DW, and Collyer AA (eds.), *Irradiation effects on polymers*. London: Elsevier Applied Sciences, 1991.

[G.4.15] Gillen KT, and Clough RL. Polymer aging insights available from modulus profiling data. *Pol Eng & Sci*, 29(1):29, 1989.

[G.4.16] Gillen KT, and Clough RL. Predictive aging in radiation environments. *Rad Phys Chem*, 41(6): 803, 1993.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[G.4.17] Gillen KT, Clough RL, and Wise J. Extrapolating accelerated thermal-aging results: A critical look at the Arrhenius method. *Polymer Preprints*, 34(2):185, 1993.

[G.4.18] Gillen KT, et al. Accelerated aging tests for predicting radiation degradation of organic materials. *Nuclear. Safety*, 25(2):238, 1984.

[G.4.19] International Conference on Harmonization. *Harmonised tripartite guideline stability testing of new drug substances and products*, Current Step 4 version, dated 6 February 2003. ICH Q1A (R2).

[G.4.20] International Conference on Harmonization. *Photostability testing of new drug substances and products*. ICH Q1B.

[G.4.21] International Conference on Harmonization. *Stability testing of new dosage forms*. ICH Q1C.

[G.4.22] International Conference on Harmonization. *Impurities in new drug substances*. ICH Q1D.

[G.4.23] International Conference on Harmonization. *Impurities in new drug products*. ICH Q1E.

[G.4.24] International Conference on Harmonization. *Stability testing of biotechnological/biological products*. ICH Q1F.

[G.4.25] International Conference on Harmonization. *Specifications: Test procedures and acceptance criteria for new drug substances and new drug products: Chemical substances*. ICH Q1G.

[G.4.26] International Conference on Harmonization. *Specifications: Test procedures and acceptance criteria for new drug substances and new drug products: Biotechnological/biological products*. ICH Q1H.

[G.4.27] Woo L, and Sanford C. Shelf-life prediction of radiation sterilized medical devices. Presented at ANTEC '87, (Proceedings, *45th Annual Technical Conference & Exhibition (ANTEC),* Brookfield, CT, Society of Plastics Engineers, p 1201, 1987

[G.4.28] Woo L, and Cheung W. Importance of physical aging on medical device design. Presented at ANTEC '88, Proceedings, *46th Annual Technical Conference & Exhibition (ANTEC)*, p. 1352).

[G.4.29] Woo L, et al. Shelf-life prediction methods and applications. *Medical Plastics and Biomaterials*, p. 36, March/April 1996.

Other informative aging references

[G.4.30] Arrhenius SZ. *Physik Chem*. 4:226, 1889.

[G.4.31] Burnay, SE. A practical model for prediction of the lifetime of elastic seals in nuclear environments. In: Clough RL, and Shalaby SW (eds.), *Radiation effects in polymers*, American Chemical Society, Symposium Series 475, p. 524, 1991.

[G.4.32] Clark G. Shelf life of medical devices. Food and Drug Administration, Center for Devices and Radiological Health of Small Manufacturers Assistance, Washington (DC) April 1991.

[G.4.33] Feldman L, and Hui H. Compatibility of medical devices and materials with low-temperature hydrogen peroxide gas plasma. *Medical Device & Diagnostic Industry*, December 1997.

[G.4.34] Hebert G. Effect of molecular orientation on the radiation stability of polypropylene. Presented at SPE ANTEC, May 1992.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[G.4.35] Hill P. Material selection. *Med Dev Tech*, p. 16, January–February 1995.

[G.4.36] Ishigate, I., and Yoshii, F. Radiation effects on polymer materials, in radiation sterilization of medical suppliers, *Radiation Physics and Chemistry*, 39(6): 527, 1992.

[G.4.37] Reich RR, et al. Accelerated aging of packaging: Considerations, suggestions, and use in expiration date verifications. *Medical Device & Diagnostic Industry*, 3:34, 1988.

[G.4.38] Remoldi P, and Montanelli F. Creep and accelerated creep testing for geogreds. Presented at Geosynthetics '93, Vancouver (BC), (Proceedings, p. 773).

[G.4.39] Saunders C, et al. Radiation effects on micro-organisms and polymers for medical products. *Medical Device & Diagnostic Industry*, 5:89, 1993.

[G.4.40] Shelton WS, and Bright DG. Using the Arrhenius equation and rate expressions to predict the long-term behavior of geosynthetic polymers. Presented at Geosynthetics '93. Vancouver (BC), (Proceedings, p. 789).

[G.4.41] Stubstad J. Irradiation of IV sets—A 10-year case study. *Medical Device & Diagnostic Industry*, p. 94, January 1989.

[G.4.42] Stubstad JA, and Hemmerich KJ. Medical plastics: Preventing plastic part failure after radiation sterilization. *Plastics Engineering*, 50(10):29, 1994.

[G.4.43] Sun DC, et al. *Development of an accelerated aging method for evaluation of long-term irradiation effects on ultrahigh-molecular-weight polyethylene implants*. Washington (DC): American Chemical Society, 1996.

[G.4.44] Williams JL. Stability of PP to gamma irradiation. In: Clough RL, and Shalaby SW (eds.), *Radiation effects in polymers,* American Chemical Society, Symposium Series 475, p. 554, 1991.

[G.4.45] Wirrhaus G. Accelerated storage tests: Predictive tests. Pharma Analytical Department, CIBA-GEIGY Ltd., 0-1-4002, Basel (Switzerland).

[G.4.46] Yim G, and Godin M. Long-term HT aging sterilization study of PE and its relationship with oxidative induction OIT Time. Presented at Geosynthetics '93, Vancouver (BC), (Proceedings p. 803).

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

Bibliography

[1] Association for the Advancement of Medical Instrumentation. *Comprehensive guide to steam sterilization and sterility assurance in health care facilities*. AAMI ST79:2006. Arlington (VA): AAMI, 2006.

[2] Association for the Advancement of Medical Instrumentation. Designing, testing, and labeling reusable medical devices for reprocessing in healthcare facilities: A guide for device manufacturers. AAMI TIR12:2004. Arlington (VA): AAMI, 2004.

[3] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 10: Tests for irritation and delayed–type hypersensitivity, and ANSI/AAMI BE78:2002/A1:2006*. ANSI/AAMI BE78:2002. Arlington (VA): AAMI, 2002.

[4] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 18: Chemical characterization of materials*. ANSI/AAMI BE83:2006. Arlington (VA): AAMI, 2006.

[5] Association for the Advancement of Medical Instrumentation. *Sterilization of healthcare products: Requirements for the development, validation, and routine control of a sterilization process for medical devices—Dry heat*. ANSI/AAMI ST63:2002. Arlington (VA): AAMI, 2002.

[6] Association for the Advancement of Medical Instrumentation. *Sterilization of medical devices: Information to be provided by the manufacturer for the processing of resterilizable devices*. ANSI/AAMI ST81:2006. Arlington (VA): AAMI, 2006.

[7] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 1: Evaluation and testing*. ANSI/AAMI/ISO 10993-1, AAMI, 2003.

[8] Association for the Advancement of Medical Instrumentation. Biological *evaluation of medical devices—Part 2: Animal welfare requirements*. ANSI/AAMI/ISO 10993-2:2006. Arlington (VA): AAMI, 2006.

[9] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 3: Tests for genotoxicity, carcinogenicity, and reproductive toxicity*. ANSI/AAMI/ISO 10993-3:2003. Arlington (VA): AAMI, 2003.

[10] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 4: Selection of tests for interactions with blood, and Amendment 1:2006*. ANSI/AAMI/ISO 10993-4:2002. Arlington (VA): AAMI, 2002.

[11] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 5: Tests for* in vitro *cytotoxicity*. ANSI/AAMI/ISO 10993-5. Arlington (VA): AAMI.

[12] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 6: Tests for local effects after implantation*. ANSI/AAMI/ISO 10993-6:2007. Arlington (VA): AAMI, 2007.

[13] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 7: Ethylene oxide sterilization residuals*. ANSI/AAMI/ISO 10993-7, AAMI, 2001.

[14] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 9: Framework for identification and quantification of potential degradation products*. ANSI/AAMI/ISO 10993-9:1999/(R)2005. Arlington (VA): AAMI, 2005.

[15] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 11: Tests for systemic toxicity*. ANSI/AAMI/ISO 10993-11:2006. Arlington (VA): AAMI, 2006.

[16] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 12: Sample preparation and reference materials*. ANSI/AAMI/ISO 10993-12:2007. Arlington (VA): AAMI, 2007.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[17] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 13: Identification and quantification of degradation products from polymeric medical devices*. ANSI/AAMI/ISO 10993-13:1999/(R)2004. Arlington (VA): AAMI, 2004.

[18] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 14: Identification and quantification of degradation products from ceramics*. ANSI/AAMI/ISO 10993-14:2001/(R)2006. Arlington (VA): AAMI, 2006.

[19] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 15: Identification and quantification of degradation products from metals and alloys*. ANSI/AAMI/ISO 10993-15:2000/(R)2006. Arlington (VA): AAMI, 2006.

[20] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 16: Toxicokinetic study design for degradation products and leachables*. ANSI/AAMI/ISO 10993-16:1997/(R)2003. Arlington (VA): AAMI, 2003.

[21] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 17: Establishment of allowable limits for leachable substances*. ANSI/AAMI/ISO 10993-17:2002. Arlington (VA): AAMI, 2002.

[22] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 19: Physico-chemical, morphological and topographical characterization of materials*. ANSI/AAMI/ISO TIR10993-19:2006. Arlington (VA): AAMI, 2006.

[23] Association for the Advancement of Medical Instrumentation. *Biological evaluation of medical devices—Part 20: Principles and methods for immunotoxicology testing of medical devices*. ANSI/AAMI/ISO TIR10993-20:2006. Arlington (VA): AAMI, 2006.

[24] Association for the Advancement of Medical Instrumentation, *Chemical sterilization and high-level disinfection in health care facilities*. AAMI ST58:2005. Arlington, (VA): AAMI, 2005.

[25] Association for the Advancement of Medical Instrumentation. *Guidance for ANSI/AAMI/ISO 11607—Packaging for terminally sterilized medical devices—Part 1 and Part 2:2006*. AAMI TIR22:2007. Arlington (VA): AAMI, 2007.

[26] 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.

[27] 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.

[28] 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. Arlington (VA): AAMI, 2006.

[29] 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.

[30] 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. Arlington (VA): AAMI, 2006.

[31] 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.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[32] 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.

[33] 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 14937:2000. Arlington (VA): AAMI, 2000.

[34] 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.

[35] 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.

[36] ASTM International. *Standard guide for accelerated aging of sterile barrier systems for medical devices*. ASTM F1980-2007. Philadelphia (PA): ASTM International, 2007.

[37] ASTM International. Standard test methods for vulcanized rubber and thermoplastic elastomers-tension. ASTM D412-06A. Philadelphia (PA): ASTM International, 2006.

[38] ASTM International. Standard test method for tensile properties of thin plastic sheeting. ASTM D88-02. Philadelphia (PA): ASTM International, 2002.

[39] ASTM International. Standard test method for tensile properties of plastics. ASTM D638-03. Philadelphia (PA): ASTM International, 2003.

[40] ASTM International. Standard test method for Rockwell hardness of plastics and electrical insulating materials. ASTM D785-08. Philadelphia (PA): ASTM International, 2008.

[41] ASTM International. *Standard terminology relating to plastics*. ASTM D883-08. Philadelphia (PA): ASTM International, 2008.

[42] ASTM International. Standard test method for tear resistance (Graves tear) of plastic film and sheeting. ASTM D1004-03. Philadelphia (PA): ASTM International, 2003.

[43] ASTM International. Standard test method for transparency of plastic sheeting. ASTM D1746-03. Philadelphia (PA): ASTM International, 2003.

[44] ASTM International. Standard test method for tensile-impact energy to break plastics and electrical insulating materials. ASTM D1822-06. Philadelphia (PA): ASTM International, 2006.

[45] ASTM International. Standard practice for calculating yellowness and whiteness Indices from instrumentally measured color coordinates. ASTM E313-05. Philadelphia (PA): ASTM International, 2005.

[46] ASTM International. Standard test method for seal strength of flexible barrier materials. ASTM F88-07A. Philadelphia (PA): ASTM International, 2007.

[47] ASTM International. Standard test method for burst testing of flexible package seals using internal air pressurization within restraining plates. ASTM F2054-07. Philadelphia (PA): ASTM International, 2007.

[48] Cleland M.R., O'Neil M.T., and Thompson C.C. In Sterilization Technology: A Practical Guide for Manufacturers and Users of Healthcare Products. Morrissey R.F., and Phillips G.B.,(eds.) New York: Van Nostrand Reinhold, 1993, p. 218.

[49] Farrell Paul J., and Hemmerich Karl J., *Selecting a Radiation Sterilization Method, Medical Device and Diagnostic Industry*, 17(8):82-90, 1995.

[50] Hong KZ. *Medical Plastics and Biomaterials*, Winter:46, 1995.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.

[51] Ishigaki J, and Yoshii F. Radiation Effects on Polymer Materials in Radiation Sterilization of Medical Supplies, *Radiation Physics & Chemistry*. 39(6):527-533, 1992.

[52] International Organization for Standardization. Plastics—Determination of flexural properties. ISO 178:2001 and A1:2004. Geneva (Switzerland): ISO, 2001 and 2004.

[53] International Organization for Standardization. Plastics—Determination of tensile properties. ISO 527 Series:1993, 1995 and 1997. Geneva (Switzerland): ISO, 1993, 1995 and 1997.

[54] International Organization for Standardization. Plastics—Determination of compressive properties. ISO 604:2002. Geneva (Switzerland): ISO, 2002.

[55] International Organization for Standardization. Determination of indentation hardness by means of a durometer (Shore hardness). ISO 868:2003. Geneva (Switzerland): ISO, 2003.

[56] International Organization for Standardization. Plastics—Film and sheeting—Determination of tear resistance—Part 1: Trouser tear method. ISO 6383-1:1983. Geneva (Switzerland): ISO, 1983.

[57] International Organization for Standardization. *Guide for the selection of an acceptance sampling system, scheme, or plan for inspection of discrete items in lots*. ISO/TR 8550:1994. Geneva (Switzerland): ISO, 1994.

[58] Landfield H. In: Szycher M (ed.), *Biocompatible polymers, metals, and composites*, p.995. Lancaster (PA): Technomic Publishing, 1983.

[59] Lappo VG, et al. In: Morrisey RF and Prokofenko YI (eds). *Sterilization of medical products*, Vol. V., p. 74. Morin Heights (QB): Polyscience Publishing, 1991.

[60] MEDLINE, http://www.nlm.nih.gov/ (U.S. National Library of Medicine).

[61] Rogers W. Qualification of steam sterilization of liquid products. Presented at Seminar Program on Validation of Sterile Manufacturing Processes. In *Proceedings of the Pharmaceutical Manufacturer's Association (PMS)*, Reston, VA: PMS, 1978.

[62] RTECS Registry of Toxic Effects of Chemical Substances (RTECS), http://www.mdl.com) (U.S. Library of Medicine).

[63] Stubstad JA, and Hemmerich KJ. Medical plastics: Preventing plastic part failure after radiation sterilization. *Plastics Engineering*, 50(10):29, 1994.

[64] TOXLINE and TXLIT, http://www.nlm.nih.gov/ (U.S. National Library of Medicine).

[65] *Validation of dry heat processes used for sterilization and depyrogenation*, PDA Technical Report 3, 1981. Bethesda (MD): PDA.

[66] Williams J., In Weighing the Choices in Radiation Sterilization: Electron-Beam and Gamma, *Medical Device and Diagnostic Industry*, 17(3):69, 1995.

[67] Williams, Dunn, Sugg, and Stannet. "Stability of Irradiated polypropylene. 1. Mechanical Properties." *Advances in Chemistry Series*, Stabilization and Degradation of Polymers 169: 142–150, 1978.

[68] Yianni JP. In "Making PVC more biocompatible", *Medical Device Technology* (ENGLAND), Sep. 6(7): 20, 1995.

Ted May / Andersen Products Inc
AAMI Order # 118640 / Order Date: 02/20/2012
Single-user license only. Copying, networking, and distribution prohibited.