

Technical Information Report

AAMI/ISO TIR16775: 2023

Packaging for terminally
sterilized medical
devices—Guidance on the
application of ISO 11607-1
and ISO 11607-2

Packaging for terminally sterilized medical devices— Guidance on the application of ISO 11607-1 and ISO 11607-2

Approved 14 March 2023 by
AAMI

Registered 4 June 2023 by
American National Standards Institute, Inc.

Abstract: Provides guidance for the application of the requirements contained in ISO 11607-1 and ISO 11607-2.

Keywords: packaging, sterile barrier, terminal sterilization, medical devices

Published by

AAMI

901 N. Glebe Road, Suite 300

Arlington, VA 22203

www.aami.org

© 2023 by the Association for the Advancement of Medical Instrumentation

All Rights Reserved

This publication is subject to copyright claims of ISO and AAMI. No part of this publication may be reproduced or distributed in any form, including an electronic retrieval system, without the prior written permission of AAMI. All requests pertaining to this document should be submitted to AAMI. It is illegal under federal law (17 U.S.C. § 101, et seq.) to make copies of all or any part of this document (whether internally or externally) without the prior written permission of the Association for the Advancement of Medical Instrumentation. Violators risk legal action, including civil and criminal penalties, and damages of \$100,000 per offense. For permission regarding the use of all or any part of this document, contact the Copyright Clearance Center.

Printed in the United States of America

ISBN 978-1-57020-875-1

AAMI Technical Information Report

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

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

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

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

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

Another difference is that, although both standards and TIRs are periodically reviewed, a standard must be acted on—reaffirmed, revised, or withdrawn—and the action formally approved usually every five years but at least every 10 years. A TIR must be acted on and the action formally approved usually every three years.

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

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

All standards, recommended practices, technical information reports, and other types of technical documents developed by AAMI are *voluntary*, and their application is solely within the discretion and professional judgment of the user of the document. Occasionally, voluntary technical documents are adopted by government regulatory agencies or procurement authorities, in which case the adopting agency is responsible for enforcement of its rules and regulations.

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

ANSI Registration

Publication of this Technical Report that has been registered with ANSI has been approved by the Accredited Standards Developer (AAMI, 901 N. Glebe Road, Suite 300, Arlington, VA 22203). This document is registered as a Technical Report according to the Procedures for the Registration of Technical Reports with ANSI. This document is not an American National Standard and the material contained herein is not normative in nature.

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

Contents

Page

Committee representation	v
Background of AAMI adoption of ISO/TS 16775:2021	ix
Foreword	x
Introduction	xi
1 Scope.....	1
2 Normative references.....	1
3 Terms and definitions.....	1
4 Guidance on Clauses 1-4 of ISO 11607-1:2019 and ISO 11607-2:2019	2
5 Guidance on Clauses 5-11 of ISO 11607-1:2019	10
6 Guidance on Clauses 5-8 of ISO 11607-2:2019	41
Annex A (informative) Design and development for packaging systems—Guidance for industry	51
Annex B (informative) Guidance on the application of the ISO 11607 series in healthcare facilities.....	59
Annex C (informative) Risk analysis tools—Guidance for industry and healthcare facilities	90
Annex D (informative) Considerations for sampling plans—Guidance for healthcare facilities	93
Annex E (informative) Guidance on establishing process parameters—Guidance for industry	95
Annex F (informative) Sterilization considerations—Guidance for industry and healthcare facilities	102
Annex G (informative) Use of contract packagers—Guidance for industry and healthcare facilities	110
Annex H (informative) Example of a handling, distribution and storage checklist—Guidance for healthcare facilities for selecting a sterile barrier system.....	111
Annex I (informative) Investigating failure—Guidance for industry and healthcare facilities	114
Annex J (informative) Validation summary—Guidance for healthcare facilities.....	117
Annex K (informative) Validation for wrapping process—Guidance for healthcare facilities	119
Annex L (informative) Validation for reusable container process—Guidance for healthcare facilities	126
Annex M (informative) Validation for heat sealing process for preformed sterile barrier systems (PSBS)—Guidance for healthcare facilities.....	133
Annex N (informative) Evaluation of sterile packaging by end users—Guidance for healthcare facilities	142
Bibliography	143

Committee representation

Association for the Advancement of Medical Instrumentation

Packaging Working Group

The adoption of ISO/TS 16775 as an AAMI Technical Information Report was initiated by the AAMI Packaging Working Group. AAMI ST-WG07 provides input to the AAMI Sterilization Standards Committee which is the responsible group for providing the U.S. input to the relevant group in the International Organization for Standardization (ISO). U.S. representatives from the Packaging Working Group and the TAG played an active part in developing the ISO document.

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

Cochairs: Jennifer Benolken
Jordan Montgomery

Members: Anas Aljabo, SteriLabs Canada Inc.
David Anundson, Smiths Medical
Edward Arscott, NAMS
Jennifer Asleson, Quality, Microbiology & Sterilization Services LLC
Selendra Barefield
Jennifer Benolken, DuPont Tyvek Medical and Pharmaceutical Protection
Damien Berg, HSPA
Jody Birks, Eagle Medical Inc
Henk Blom, PAXXUS, Inc.
Daniel Burgess, Boston Scientific Corporation
Chris Chamberlen, Sterilization Validation Services
Horlando Cintron, Memorial Sloan Kettering Cancer Center - Monmouth
Aerienne Cunningham, Zuno Medical
Jackie Daly Johnson, Flexible Packing Association
Malinda Elammari, Healthmark Industries Company Inc
Gordon Ely, LexaMed Ltd
Manuel Grandy, SteriComp GmbH
Douglas Harbrecht, Sterility Assurance LLC
David Jagrosse, David Jagrosse Consulting LLC
Nyla Skee Japp
Brian Jarvis, 3M Health Care
Britt Jones, WuXi AppTec Inc
Thomas Kent, Bausch & Lomb Inc
Kelley Kuehne, Medline Industries Inc
Austin Liu, Abbott Laboratories
Wendy Mach, Integra LifeSciences Corporation
Tanya Magana, Ecolab
Paul Marshall, Zimmer Biomet
Bob Massaglia
Josha McCarthy, Sierra Nevada Memorial Hospital
Tom McElroy, IUVO BioScience
Ethan Meyers, Quality Tech Services LLC
Emily Mitzel, GE HealthCare
Sunny Modi, Eurofins Medical Device Testing
Jordan Montgomery, Medtronic Inc Campus
Susumu Nozawa, Siemens Healthineers
Cindy O'Leary-Swinson, WL Gore & Associates Inc
Rodney Patch, Johnson & Johnson
Kimberly Patton, Performance Review Institute MedAccred
Michael Piazza, Alcon Laboratories Inc
Anthony Piotrkowski, STERIS Corporation | Healthcare
Vipul Rajpara, Edwards Lifesciences
Deepa Rampura, Intuitive Surgical Inc

Allison Rearick, WL Gore & Associates Inc
 Cristiane Rocha Andrade, BSI Healthcare
 Daniel Schaefer, West Pharmaceutical Services, Inc.
 Richard Schule, Cleveland Clinic
 Andrew Sharavara, Propper Manufacturing Co Inc
 Joan Spear
 Steve Spencer, Owens & Minor
 Julie TerWee, Pfizer Parenteral Center of Excellence
 Donald Tumminelli, HIGHPOWER Validation Testing & Lab Services Inc
 Steven Turtill, FDA/CDRH
 Stephanie Volk, Convatec
 Ariel Wimbush, Emory Healthcare
 Jarl Yeager, Powder River Medical Resources
 Roberto Zumbado, Philips

Alternates: Kristi Bailye, Baxter Healthcare Corporation
 Douglas Davie, Sterilization Validation Services
 Andrea DeVoe, Eurofins Medical Device Testing
 Melissa Duncan, WuXi AppTec Inc
 Shawn Engberg, MD Furniture & Supply
 Pankaj Gaur, Medtronic Inc Campus
 Becky Gilsdorf, Healthmark Industries Company Inc
 Jennifer Gygi, Sotera Health LLC
 Philipp Hoetzel, Johnson & Johnson
 Eric Kao, NAMSA
 Erin Kyle, Association of Perioperative Registered Nurses (AORN)
 Cliff Labbe, Johnson & Johnson
 Hyung-yul Lee, FDA/CDRH
 James Maher, Becton Dickinson & Company
 Leona Manandhar-Sasaki, Propper Manufacturing Co Inc
 Kira Melton, Intuitive Surgical Inc
 Nathan Morris, IUVO BioScience
 Todd Morrisson, Advanced Sterilization Products (ASP)
 Brian Nissen, Quality Tech Services LLC
 Karen Owens, STERIS Corporation | Healthcare
 Dan Penny, Cardinal Health
 LeRonda Perry, Integra LifeSciences Corporation
 Jimmy Quijas, Abbott Laboratories
 Hugo Felix Rodriguez, Pfizer Parenteral Center of Excellence
 Jason Ruff, Boston Scientific Corporation
 Michael Schoene, Bausch & Lomb Inc
 Ram Singhal, Flexible Packing Association
 Clint Stebbins, Zimmer Biomet
 Mark Sundt, DuPont Tyvek Medical and Pharmaceutical Protection
 Brown Zheng, BSI Healthcare

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

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

Cochairs: Janet Prust
Patrick Weixel

Members: Gregory Aldrich, Fairbanks Memorial Hospital
Anas Aljabo, SteriLabs Canada Inc.
Eseosa Amenaghawon, Cincinnati Childrens Hospital Medical Center
Brett Anderson, Cochlear Ltd
Jennifer Asleson, Quality, Microbiology & Sterilization Services LLC
Richard Bancroft, STERIS Corporation | Healthcare
Leigh Bartlett
Marie Brewer, UnityPoint Health - Surgery Center Cedar Rapids
Trabue Daley Bryans, BryKor LLC
Jonathan Burdach, Nanosonics Limited
Emily Craven, Boston Scientific Corporation
Jacqueline Daley, Providence St Joseph Health System
Gordon Ely, LexaMed Ltd
Afif Jhoel Escheik, Crothall Healthcare
Deannard Esnard
Nicole Felderman, CIVCO Medical Solutions
Brian Fortier, Aorta Medical Inc
Daniel Fowler, WuXi AppTec Inc
Diah Ginem, Stryker
Barbara Goodman
Magnus Graham, BSI Healthcare
Alberto Guzman Paret, Cordis US Corp
Shelley Hagan, Henry Ford Health
Ashley Hammer, Washington Regional Medical Center
Douglas Harbrecht, Sterility Assurance LLC
Deborah Havlik, DA Havlik Consulting
Crystal Heishman, U of L Hospital - University of Louisville
Mollie Holter, MicroBio Consulting LLC
Stephanie Jean Homuth, Hennepin County Medical Center Warehouse
Ebow Holdbrook-Smith, WellSpan Health
Clark Houghtling, Cosmed Group Inc
Angela Jensen, Rush Foundation Hospital
Lois Atkinson Jones, Northwell Health
Nicholas Kalanta, McLane Children's Hospital
Susan Klacik, HSPA
Erin Kyle, Association of Perioperative Registered Nurses (AORN)
Byron Lambert, Abbott Laboratories
Marissa Jones Lewis, Veterans Administration (VA) Central Office
Emily Lorchheim, ClorDiSys Solutions, Inc
Kelly Marcum, HCA Healthcare
John Mazzilli, Saddleback Memorial Medical Center
Patrick McCormick, Bausch & Lomb Inc
Gerald McDonnell, Johnson & Johnson
Russell Mills, Zimmer Biomet
Leslie Nichols, Mayo Clinic
Cathy Nutter
Gerry O'Dell, Gerry O'Dell Consulting
James O'Reilly, St Joseph Health System - Trinity Health
Ken Paddock, Baxter Healthcare Corporation
Kia Parker, The Ohio State Wexner Medical Center-University Hospital
Kimberly Patton, Performance Review Institute MedAccred
Nancy Pickens
Karana Pierre
Dawn Pierson, CS Medical LLC
Janet Prust, St. Croix Standards Consulting, LLC
Joan Rickard, Montefiore Medical Center
Angela Salmen
Michael Scholla

Linda Schultz, Northside Hospital Surgical Services Atlanta
Joan Spear
Sopheak Srun, Quality Tech Services LLC
Mark Swanson, Quality and Regulatory Expert Partners
Larry Talapa, 3M Health Care
Julie TerWee, Pfizer Parenteral Center of Excellence
James Treharn, St. Peter's Health
Sara Vinson, University of Florida
Adrienne Watson
Patrick B. Weixel, FDA/CDRH
James Wiggs, Legacy Health System
Ariel Wimbush, Emory Healthcare
Martell Winters, Sotera Health LLC
Roberto Zumbado, Philips

Alternates: Kendall Ashe, CS Medical LLC
Jennifer Benolken, DuPont Tyvek Medical and Pharmaceutical Protection
Damien Berg, HSPA
Stacy Bohl, Boston Scientific Corporation
Richard Burgess, BSI Healthcare
Densley Coke
Kimbrell Darnell, Becton Dickinson & Company
Aaron David DeMent, Sotera Health LLC
April Doering, 3M Health Care
Anna Grayson, Grayson Associates
David Kelman, Sterile Edge
Rhashamekia Law
Cathy Leckwart, WuXi AppTec Inc
Paul Lorchheim, ClorDiSys Solutions, Inc
Michelle Luebke, Baxter Healthcare Corporation
Shaun McGinley, Zimmer Biomet
David McGoldrick, Abbott Laboratories
Shane Pinkston, Getinge USA
Christine Render, Cosmed Group Inc
Petra Richards, Kaiser Foundation Health Plan/Hospitals
Susan Rogers, Veterans Administration (VA) Central Office
Molly Swanson, Quality Tech Services LLC
Lisa Ward, STERIS Corporation | Healthcare

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.

Background of AAMI adoption of ISO/TS 16775:2021

As indicated in the foreword to the main body of this document (page x), the International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of this standard, which was developed by ISO/TC 198, *Sterilization of health care products* to provide additional guidance to the ISO 11607 series.

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

AAMI/ISO TIR16775 was registered by the American National Standards Institute (ANSI) on 4 June 2023.

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

AAMI (and ANSI) have adopted other ISO standards and technical reports.

As used within the context of this document, “shall” indicates requirements strictly to be followed to conform to the recommended practice. “Should” indicates that among several possibilities, one is recommended as particularly suitable, without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action should be avoided but is not prohibited.

“May” is used to indicate that a course of action is permissible within the limits of the recommended practice. “Can” is used as a statement of possibility and capability. Finally, “must” is used only to describe “unavoidable” situations, including those mandated by government regulation.

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

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

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

Suggestions for improving this standard are invited. Comments and suggested revisions should be sent to Standards Department, AAMI, 901 N. Glebe Road, Suite 300, Arlington, VA 22203.

NOTE—Beginning with the ISO foreword on page x AAMI/ISO TIR16775:2023, *Packaging for terminally sterilized medical devices—Guidance on the application of ISO 11607-1 and ISO 11607-2* is identical to ISO/TS 16775:2021.

Foreword

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

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

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

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

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

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 102, *Sterilizers and associated equipment for processing of medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO/TS 16775:2014), which has been technically revised.

The main changes compared to the previous edition are as follows:

- updates to reflect ISO 11607-1:2019 and ISO 11607-2:2019 editions;
- intent and guidance is provided for each clause of the standard to improve usability of this document.
- new annexes have been added;
- some annexes have been removed.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Sterile barrier systems are intended to allow for sterilization, provide physical protection, maintain the sterility of their contents until the point of use and ensure aseptic presentation. The sterile barrier system, depending on conditions of handling, distribution or storage, can be combined with additional protective packaging to create a packaging system.

ISO 11607-1 specifies the requirements for materials, sterile barrier systems, and packaging systems, including the validation of the packaging system design while ISO 11607-2 specifies the requirements for packaging process validation. The requirements outlined in these standards are generic and are applicable to healthcare facilities and wherever medical devices are packaged and sterilized. It is recognized that the circumstances of the application of these standards will be different when they are used in a healthcare facility, by a medical device manufacturer or reprocessor.

This document provides guidance on the application of ISO 11607-1 and ISO 11607-2. This latest revision has been completely reorganised following the structure of ISO 11607-1 and ISO 11607-2 and referring to individual or groups of clauses or subclauses while indicating the intent of the requirements followed by relevant guidance. It can be used for the systematic application of ISO 11607-1 and ISO 11607-2 or as a reference when questions come up about specific requirements. Clause 4 covers the general requirements that are identical in ISO 11607-1 and ISO 11607-2, while Clause 5 applies to ISO 11607-1:2019 and Clause 6 to ISO 11607-2:2019. Guidance on the application of risk management over the packaging life cycle has been added in anticipation of the upcoming amendments to ISO 11607 (all parts).

This guidance document is applicable to healthcare facilities and to industry while differences for the two environments are addressed as necessary. Although healthcare facilities are usually not involved in sterile barrier system design tasks, their part in the sterile barrier system and packaging system design process consists of carefully selecting an appropriate sterile barrier system and protective packaging based on the identified risks related to the content, sterilization method, transport, storage and aseptic presentation. Sterile barrier and packaging systems and the related processes must then be properly validated, and sealing, closure and assembly processes must be controlled and monitored. To ensure patient safety, healthcare facilities should develop written procedures to be implemented by adequately trained personnel. Guidance given in the annexes of this document is applicable to healthcare facilities and/or industry, as indicated.

The conditions of use of this guidance can vary widely around the world and can be subject to interpretation by circumstances and regulatory environments.

Packaging for terminally sterilized medical devices— Guidance on the application of ISO 11607-1 and ISO 11607-2

1 Scope

This document provides guidance for the application of the requirements contained in ISO 11607-1 and ISO 11607-2. It does not add to, or otherwise change, the requirements of ISO 11607-1 and ISO 11607-2. This is an informative document, not normative. It does not include requirements to be used as basis of regulatory inspection or certification assessment activities.

The guidance can be used to better understand the requirements of ISO 11607-1 and ISO 11607-2 and illustrates the variety of methods and approaches available for meeting the requirements of those International Standards. It is not required that this document be used to demonstrate conformity with them.

Guidance is given for evaluation, selection and use of packaging materials, preformed sterile barrier systems, sterile barrier systems and packaging systems. Guidance on validation requirements for forming, sealing and assembly processes is also given.

This document provides information for both healthcare facilities and the medical devices industry for terminally sterilized medical devices.

This document does not provide guidance for applications of packaging materials and systems after their opening. In the use of packaging for other purposes such as a “sterile field” or transport of contaminated items, other regulatory standards will apply.

2 Normative references

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

ISO 11607-1:2019, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 11607-2:2019, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11607-1:2019 and ISO 11607-2:2019 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at <https://www.iso.org/obp>
- IEC Electropedia: available at <http://www.electropedia.org/>

3.1

process

set of interrelated or interacting activities that use inputs to deliver an intended result

Note 1 to entry: Whether the “intended result” of a process is called output, product or service depends on the context of the reference.

Note 2 to entry: Inputs to a process are generally the outputs of other processes and outputs of a process are generally the inputs to other processes.

Note 3 to entry: Two or more interrelated and interacting processes in series can also be referred to as a process.

[SOURCE: ISO 9000:2015, 3.4.1, modified — Notes to entry 4, 5 and 6 are deleted.]

3.2

risk

combination of the probability of occurrence of harm and the severity of that harm

[SOURCE: ISO/IEC Guide 63: 2019, 3.10, modified — Note 1 to entry deleted.]

3.3

risk control

process (3.1) in which decisions are made and measures implemented by which *risks* (3.2) are reduced to, or maintained within, specified levels

[SOURCE: ISO/IEC Guide 63: 2019, 3.12]

3.4

risk estimation

process (3.1) used to assign values to the probability of occurrence of harm and the severity of that harm

[SOURCE: ISO/IEC Guide 63: 2019, 3.13]

3.5

risk evaluation

process (3.1) of comparing the estimated *risk* (3.2) against given risk criteria to determine the acceptability of the risk

[SOURCE: ISO/IEC Guide 63: 2019, 3.14]

4 Guidance on Clauses 1-4 of ISO 11607-1:2019 and ISO 11607-2:2019

4.1 Scope (ISO 11607-1:2019, Clause 1 and ISO 11607-2:2019, Clause 1)

4.1.1 Intent

The objective of the scope is to outline the purpose of the standard, its applicability, as well as any exclusions or limitations.

4.1.2 Guidance

ISO 11607-1:2019 and ISO 11607-2:2019 are “group standards” as defined in ISO 16142-1^[1] as it applies to a wide range of packaging types that are intended to maintain sterility of terminally sterilized medical devices until the point of use. Group standards are horizontal in nature within the medical device sector and are developed to address the essential principles that are applicable to a wide range of medical devices. Furthermore, as defined by ISO 16142-1,

ISO 11607-1:2019 and ISO 11607-2:2019 are also process standards. Process standards provide the requirements for manufacturers to develop, implement, and maintain processes applicable to all stages of the lifecycle of a medical device. These processes are typically established in the frame of a quality management system like ISO 13485^[2] or ISO 9001^[3], although these standards are not a normative requirement as outlined in Clause 4 of this document.

The scopes of ISO 11607-1 and ISO 11607-2 apply to healthcare facilities, medical device manufacturers and wherever medical devices are placed in sterile barrier systems (SBSs), packaged and sterilized. It is recognized that the circumstances of the application of these documents will be different when they are used in a healthcare facility compared with when they are used by a medical device manufacturer or reprocessor.

ISO 11607-1:2019 and ISO 11607-2:2019 can also be applied by any suppliers of packaging materials or preformed SBSs. In this case the conformity statements will be limited to what the manufacturer can claim since full conformance is only possible for the completely sealed or closed SBS validated for a specific device or family of devices. Manufacturers of materials and preformed SBSs should clearly indicate what is covered and not covered in their conformity statements.

As a summary, ISO 11607-1:2019 and ISO 11607-2:2019 are horizontal group standards and process standards applicable to several stages of the lifecycle of sterile medical packaging providing the requirements for:

- a) packaging materials, preformed SBSs and SBSs (ISO 11607-1:2019, Clause 5);
- b) the development process of the SBSs and the packaging system including:
 - the required forming, sealing and assembly processes;
 - the design validations;
 - the process validations;
 - revalidations, periodic, if applicable, and in case of changes;
 - change controls;
 - the controls during routine operations.

It addresses materials, packaging, and also combination of packaging and device. It covers also sterile fluid path packaging where the SBS functionality is integrated with the construction of the device. ISO 11607-2 is applicable wherever a seal or closure is formed and was never intended to cover manufacturing of materials like sheets of sterilization wrap or rigid trays that are manufactured outside of a form-fill-seal process.

4.2 Normative references (ISO 11607-1:2019, Clause 2 and ISO 11607-2:2019, Clause 2)

4.2.1 Intent

Normative references list standards which are required to understand and to apply the standard.

This clause provides the normative references to other standards that apply as well to conform with the requirements of ISO 11607-1:2019 and ISO 11607-2:2019.

4.2.2 Guidance

Normative references are referred to in the text of a standard in such a way, that some or all of the cited content constitutes requirements for the document. In order to be able to apply the standard, all normatively cited references should be available to the user.

4.3 Terms and definitions (ISO 11607-1:2019, Clause 3 and ISO 11607-2:2019, Clause 3)

4.3.1 Intent

Many terms used in a standard document can, depending on the context in which they are used, have a slightly different meaning. This clause refers to the definitions of key terms in order to clarify their intent and meaning for the purpose of this document.

4.3.2 Guidance

The definitions of ISO 11607-1:2019 and ISO 11607-2:2019 apply and it is recommended to review those along with this document. Definitions in the current editions of these documents align with the definitions in ISO 11139:2018^[4].

4.4 Quality and risk management (ISO 11607-1:2019, 4.1, 4.2 and ISO 11607-2:2019, 4.1, 4.2)

4.4.1 Intent

This subclause introduces the need to have formal systems for quality and risk management to support appropriate execution and documentation of the activities described to conform with ISO 11607-1:2019 and ISO 11607-2:2019.

4.4.2 Guidance

4.4.2.1 Guidance on quality system requirements (4.1)

A quality management system is a formalized system that documents processes, procedures, and responsibilities for achieving quality policies and objectives.

Such a formal quality management system helps to coordinate and direct activities to meet customer and regulatory requirements and improve the effectiveness and efficiency on a continuous basis.

Examples of standards describing such quality management systems include but are not limited to ISO 9001^[3], ISO 13485^[2], US FDA Quality System regulation^[5,6] and ANSI/AAMI ST90^[7]. Implementing a third-party audited quality management system is a good practice, but not a requirement of ISO 11607 (all parts).

ISO 11607-1:2019 and ISO 11607-2:2019 emphasise the need to formalize quality system elements to have appropriate control of records, design and development, product realization, measurements, calibration, data analysis and decisions taken to improve outcomes or to correct non-conformities. The quality system should also consider training of personnel, change management and revalidations as well as supplier controls.

4.4.2.2 Guidance on risk management requirements (4.2)

Risks to the user and patient, defined as the combination of the probability of occurrence of harm and the severity of that harm, are by nature inherent to medical devices and related activities and need to be minimized.

Risk management requirements are applicable to all stages of the life cycle of a terminally sterilized medical device, its accessories, and packaging related activities. ISO 11607-1:2019 and ISO 11607-2:2019 cover specifically the packaging life cycle phases of packaging design and development, validation and production.

An ongoing risk management process should be established, implemented, documented and maintained to minimize the risk for the user and the patient. This process should include:

- 1) identification of hazards and hazardous situations associated with the packaging system,
- 2) risk estimation and risk evaluation against defined criteria for risk acceptability,
- 3) risk control,
- 4) monitoring the effectiveness of the risk control measures.

NOTE 1 Local regulatory requirements can provide mandatory criteria for risk acceptability or these criteria can be based on the generally accepted state of the art.

NOTE 2 PFMEA (Process Failure Mode and Effect Analysis) is an example of a risk analysis tool that is used widely in the industry.

This process should apply throughout the phases of design and development, validation and production of the packaging system. The following life cycle phases should be included:

a) Design and development phase

- Packaging system design (see ISO 11607-1:2019, Clause 6)
- Sealing and assembly process development (see ISO 11607-2:2019, 5.1)

b) Validation phase

- Performance and stability testing (see ISO 11607-1:2019, Clause 8)
- Usability evaluation (see ISO 11607-1:2019, 7)
- Process validation (see ISO 11607-2:2019, 5.2, 5.3, 5.4 and 5.5)

c) Production phase

- Process control and monitoring (see ISO 11607-2: 2019, 5.6)
- Assembly (see ISO 11607-2: 2019, Clause 6)
- Use of reusable SBSs (see ISO 11607-2: 2019, Clause 7)
- Process changes and revalidation (see ISO 11607-2: 2019, 5.7)
- Packaging system changes (see ISO 11607-1: 2019, Clause 9)

NOTE 3 ISO 14971^[8] provides requirements for application of risk management to medical devices.

A risk management plan should be documented in accordance with the risk management process for each packaging system including as minimum

- scope of the planned risk management activities
- criteria for risk acceptability,
- activities for verification of the implementation and effectiveness of risk control measures.

Risk management plans for similar packaging systems can be combined, in such case the rationale for these similarities should be documented. Risk management plans and related documentation for packaging systems can be combined with those for the medical device.

Packaging related risk management is understood as a continuous iterative process throughout the phases of design and development, validation and production of the product, requiring regular system evaluation and updating. Risk management and risk-based decision making are elements of state-of-the-art quality management.

For further guidance on risk management and risk analysis tools during design and development, users should refer to the following annexes of this document:

- Annex A Design and development for packaging systems – guidance for industry
- Annex B Guidance on the application of the ISO 11607 series in healthcare facilities
- Annex C Risk analysis tools – Guidance for industry and healthcare facilities

4.5 Sampling (ISO 11607-1:2019, 4.3 and ISO 11607-2:2019, 4.3)

4.5.1 Intent

The purpose of this subclause is to make sure that the science of statistics is the basis of sampling plans so that results have acceptable confidence and are sufficiently reliable.

4.5.2 Guidance

Sampling plans should be risk based (considering the safety of patient and healthcare user) and suitable for the intended use, in other words depending on the device or the process (healthcare users should see also Annex D of this document).

The key elements of sampling plans reflecting the risk are the following:

a. Quality level

It is important to define what quality level is required and should be proven. This can be expressed in an AQL (acceptance quality limit)^[9,10], a percentage of conforming products, a C_{PK} value (minimum process capability index)^[11] and many other performance metrics.

b. Confidence level

Unless a 100 % inspection is performed, there is always an uncertainty in the outcome of test results based on sampling. Without having an 100 % inspection there are always situations where a good batch will be rejected, or a bad batch will be accepted based on the coincidence of the samples taken. The level of certainty is expressed in the confidence level.

NOTE 1 A 100 % inspection without uncertainty assumes that the inspection is based on a fail-safe non-destructive test method. A 100 % inspection does not ensure that 100 % of errors will be caught.

Other factors that influence the choice for a sampling system and related sample size:

c. Type of test data / test data format

Depending on the product characteristic measured and the chosen test method, the test will generate either discrete or continuous data. These data types are also sometimes referred to as attribute or variable data.

Discrete data can only take particular values. The number of those values can be infinite, but each is distinct and there is no grey area in between. Discrete data can be numeric, for example numbers of particles, but it can also be categorical, for example red or blue, or good or bad, or pass or fail.

Continuous data are not restricted to defined separate values but can take any value over a continuous range. Continuous data are numeric. Examples are seal strength, seal width, etc.

Each data type requires different suitable sampling plans. Because continuous data contains much more information than discrete data, the required sample size for continuous data is smaller than for discrete data if the

same quality level and reliability level are required. To reduce the required sample size for pass/fail data it can be possible to use a grading scale to produce data with greater resolution (e.g. scoring of visual inspection of seals and ranking the results with a numeric value).

d. Available process / product performance information

Information available from engineering studies, similar processes, similar products or other sources can provide an indication for the process capability or product variability to be validated. This initial estimation can be used for sample size calculations.

NOTE 2 For example, if a process capability with a C_{PK} of 3 is expected, the sample size can be lower than for a process with an expected C_{PK} of 1,33.

e. Population composition and available samples

It is important to understand the difference between situations where the number of samples is taken from a larger batch and situations where the required number of pieces are built or manufactured for evaluation or validation purposes. The latter case could be for devices that are only built in small quantities. In both cases it is essential that samples represent the final process or the process settings that are being evaluated.

f. Packaging configuration

The packaging configuration (i.e. unit packages, number of SBSs and the protective packaging, shipper box, etc.) needs to be considered depending on the type of test and purpose of the test. For example, distribution simulation for performance testing (see 5.26 of this document) needs to include the entire packaging system while sealing process validation (see 6.2 through 6.9 of this document) may focus only on the SBS.

4.6 Test methods (ISO 11607-1:2019, 4.4 and ISO 11607-2:2019, 4.4)

4.6.1 Intent

The purpose of this subclause is to provide the necessary requirements for test methods to demonstrate conformity so that they produce meaningful and reliable data and that appropriate decisions can be taken based on the data generated.

4.6.2 Guidance

Test methods exist to provide measures of SBSs and/or packaging systems and packaging materials, both to assess suitability for use and as a means of monitoring the manufacturing process. Test methods that have statements of precision and bias are preferred, see Annex B of ISO 11607-1:2019. Not all test methods are appropriate all of the time; some test methods are most appropriate for research and development and others for conformity monitoring. The choice of which test method to employ is driven by the requirements of and applicability to the product (device and package) through its life cycle and should be chosen such that the parameters probed are closely related to medical device SBS and/or packaging system attributes.

NOTE 1 For a guide to available tests, see Annex B of ISO 11607-1:2019.

When evaluating the choice of materials for preformed SBSs or SBSs and for all validation activities, ISO 11607-1:2019 4.4.1 requires the rationale for the selection of an appropriate test to be established and recorded. It is recommended to document this in a formal test plan, which will then also include the respective acceptance criteria for the selected methods. Annex B of ISO 11607-1:2019 includes a selection of test methods, but it is perfectly acceptable to include other test methods, if conformity with ISO 11607-1:2019, 4.4, is demonstrated. For more information on generating a final packaging system validation protocol for healthcare facilities, see Annex B of this document.

A critical component of the packaging validation is to define what constitutes a positive outcome for the validation. The acceptance criteria (ISO 11607-1:2019 4.4.2) should be established prior to beginning the validation and should be centred on delivery of the medical device to the end user in an undamaged and sterile condition. Detailed acceptance criteria can allow for accepting specified damage to a medical device or its packaging system. The form and content of acceptance criteria can vary widely, in accordance with the particular situation. Methods can range from simple pass-fail judgments to highly quantitative scoring or analysis systems. Protocol acceptance criteria and packaging system specifications are closely linked, though a protocol will probe more aspects of a packaging system than are typically monitored during routine production.

NOTE 2 When providing test results to users of materials and preformed SBS in a healthcare facility, it can be helpful to fully explain rationale for acceptance criteria thresholds.

Subclause 4.4.3 of ISO 11607-1:2019 and ISO 11607-2:2019 requires that all test methods used to show conformity with this standard are validated. Test method validation has been interpreted in many ways. Validation confirms, through objective evidence, that requirements for a specific intended use or application have been fulfilled.

NOTE 3 For more information on validation of test methods, see ASTM F3263 Standard Guide for Packaging Test Method Validation^[12] and the SBA guidance for test method validation^[13].

Test methods that have been subjected to formal/systematic inter-laboratory studies (ILS, also known as round-robin studies) are beneficial because the ILS will provide the user with a statement which in turn provides some sense of the repeatability, reproducibility and in some cases the sensitivity of the test method.

Repeatability is a measure of the variation within a laboratory and can be due to several variables including operators, test apparatus, variation over time, etc.

Reproducibility is a measure of the variation between laboratories.

Sensitivity of the test method is a measure of the limits of the test method.

The precision and bias statement contained in an ASTM standard indicates that the test method can be validated; however, it is important to note that it is not validated in a new laboratory without additional steps. When adopting an ILS test method into the laboratory, steps need to be taken to demonstrate that the test method performs in a comparable way to the performance in the ILS. Typically, an ILS test report will use samples of different materials that produce measurements over the range of the test method results. While these samples are typically not identified in the ILS, frequently, those in the trade can determine the source of these samples. It is therefore possible to perform a limited internal study to determine the repeatability within your laboratory. This study might take into consideration factors such as multiple operators or apparatus, etc. The results of this validation study need to be documented (ISO 11607-1:2019, 4.4.3). An appropriate acceptance criterion is that the internal repeatability should be equal to or better than the ILS reproducibility (ISO 11607-1:2019, 4.4.2).

It is not necessary to demonstrate that an integrity test method sensitivity is the same as determined in the ILS. This can be accomplished by documenting in the rationale that the sensitivity limits in your laboratory are a subset within the range of the ILS. For example, if the laboratory only performs hydrostatic head testing on materials within the range of 20 to 50 units, there is no need to validate the test method for values below 15 and above 60 units. However, this limitation needs to be noted and if a sample is tested above or below the specified limits the test method would have to be validated within this new range.

Integrity test methods are key methods to be included into every validation protocol and they need to be validated considering the expected sensitivity, i.e. the smallest hole or leak rate that can be detected by the method or often referred to also as the precision of the test method. This is typically conducted by producing packages with a seal channel using a wire of a known size corresponding to the targeted sensitivity. If the method is capable to detect the simulated channel, then it is considered validated for this established sensitivity. A rationale needs to be established for the selection of a given sensitivity.

NOTE 4 ASTM test methods include a precision and bias section providing information on sensitivity of integrity test methods

There are many acceptable test methods that have not been subjected to an ILS. These can be from the scientific literature, national standard methods, or developed by the laboratory. The most important issues with these tests are: demonstrating that the test is actually measuring the property intended to be measured; determining the sensitivity and accuracy are sufficient to measure the intended property over the specified range of values and determining the repeatability of the test method. These can be determined by application of the scientific process through carefully designed experiments. Again, the results of this experimentation need to be documented (ISO 11607-1:2019, 4.4.3).

In summary, validation of test methods in a laboratory requires the demonstration through experimentation that the test method performs as intended and is shown to be repeatable within that laboratory. Without this validation step, the user cannot determine if the data they gather is appropriate or not.

4.7 Documentation (ISO 11607-1:2019, 4.5 and ISO 11607-2:2019, 4.5)

4.7.1 Intent

This subclause defines the documentation requirements of all records that demonstrate conformity to ISO 11607-1:2019 and ISO 11607-2:2019.

4.7.2 Guidance

Records demonstrating the conformity to ISO 11607-1:2019 and ISO 11607-2:2019 are required.

ISO 11607-1 requires a specified retention period for all records which are used to demonstrate conformity. The retention period should be defined based on all applicable requirements such as customer and regulatory requirements, expiry date, traceability, period of time expected to be in the marketplace for example.

Some records can have different retention periods than others dependant on whether a record is related to a particular batch (e.g. seal strength of preformed SBS) or the lifetime of the material/SBS (e.g. training documentation and calibration certificates).

Records and documents to be retained include but are not limited to:

- a) performance data (methods used, values, etc.);
- b) specifications (drawings, composition, etc.);
- c) evidence of test method validations;
- d) validation protocols and conclusions.

Also, other data, such as production data and conditions, can be considered.

Modification of materials, SBSs, production methods (sealing equipment) or the intended use require a record of the decision and new documentation about the materials and production methods, or revision of the current documentation (see also ISO 11607-2:2019, 5.7).

Documentation and records can be in any format or type (e.g. hard copy or electronic media). Good recording practices should be followed. Documents and records should be easily identifiable concerning the product/product family in question, so considerations should be given to title, date of issue, author, etc.

When electronic records are used, degradation of storage media and availability of the software should be considered for the specified retention time. The method of storing the records should also be considered to allow access as and if needed (e.g. audits, customer complaints or post-market follow up).

5 Guidance on Clauses 5-11 of ISO 11607-1:2019

5.1 General requirements for materials, preformed sterile barrier systems and sterile barrier systems (ISO 11607-1:2019, 5.1.1 and 5.1.2)

5.1.1 Intent

These subclauses introduce requirements to qualify materials, preformed SBS and SBS.

5.1.2 Guidance

Choosing appropriate packaging materials for a sterilizable medical device requires careful consideration (ISO 11607-1:2019, 5 and 6). Aspects of the SBS to be considered include but are not limited to:

- compatibility with sterilization;
- robustness with respect to processing;
- storage;
- handling, and distribution;
- microbial barrier properties;
- ease of opening for aseptic presentation;
- a number of considerations regarding end use of the medical device.

It is advised to include packaging system material selection early in the design process of the medical device. Leaving this important consideration until the end of the design process can result in delays in a medical device being introduced into the marketplace or impose limitations on shelf life or other end use considerations. Manufacturers of packaging materials or medical packaging can be a significant asset in determining suitable options.

Note 1 and 2 of ISO 11607-1:2019, 5.1.1 discusses use of the EN 868 series, however there is no prerequisite to conform with the EN 868 series in order to conform with ISO 11607-1:2019.

Consider the environmental impact of disposal of preformed SBS and SBS (see Annex D in ISO 11607-1:2019) which can include recycling. When selecting materials, consider the objective to enable recycling.

5.2 Conditions for production and handling (ISO 11607-1:2019, 5.1.3 and 5.1.4)

5.2.1 Intent

This subclause provides basic requirements to be put in place in order not to degrade or damage materials and/or preformed SBSs during processing.

5.2.2 Guidance

As packaging materials are evaluated for compatibility with equipment and processing conditions, consideration needs to be given to predetermined requirements which ensure consistent and reliable production of SBSs. Depending on the properties of the material, the equipment should be designed or adapted accordingly.

Manufacturers of materials or preformed SBSs can provide guidance based on the requirements of these subclauses and other known issues regarding the conditions of use. For example forming and sealing parameters (as temperature, pressure, dwell time), storage conditions (humidity, temperature), etc. under which the material and/or preformed SBS shall be produced and handled.

Materials typically have temperature range limits that have to be considered during processing. For example, medical paper can be compatible with laser printing while nonwoven materials often are not, as the temperature exceeds the limits for these materials.

The pressure range can be important: e.g. for sealing processes, there could be limits regarding the maximum pressure that can be applied to the materials (concerning ISO 11607-1 5.1.4 b), downstream use conditions such as during sterilisation and shipping can also include environmental pressure ranges/changes that can influence SBS and material selections. See also 5.9.2 of this document (in particular the note) regarding compatibility with sterilisation methods and the rate of pressure change that can be applied.

Some materials are hygroscopic and humidity outside manufacturers' recommendations can affect some physical properties and cause issues with material properties during processing, for example sealing, printing or lamination. Recommendations issued by material or SBS manufacturers should be followed.

Some polymer materials are sensitive to exposure to UV light from sunlight or other sources. If UV stabilizers are required, care should be taken to ensure biocompatibility requirements can be met.

Consideration should be given to appropriately control the level of cleanliness and bioburden during storage, processing, and handling operations.

Electrostatic charging of some materials needs to be considered as it can lead to attraction of particles and/or sudden discharges of electrostatic charges via an operator. Electrostatic charges can be controlled by installing electrostatic bars (or other static dissipative technologies) to remove static electricity into strategic locations of a packaging process.

5.3 Source, history and traceability of materials (ISO 11607-1:2019, 5.1.5)

5.3.1 Intent

This section outlines the importance of controlling materials used as input to a process to manufacture SBSs and the need to maintain traceability information for follow up in case of issues.

5.3.2 Guidance

Complete traceability of an SBS and/or packaging system and its components is maintained, primarily as an aid in determining the root cause of any non-conformances. This is a requirement when conformity with 5.1.5 of ISO 11607-1:2019 is claimed or when a quality management system like ISO 9001^[3] or ISO 13485^[2] is implemented. In some jurisdictions, it can be a regulatory requirement as well.

Knowing the source and controlling materials is essential for producing a reliable preformed SBS and/or SBS. In this context, it is essential to deal with any deviations or changes that can have an impact on the output of the process by implementing corrective actions and/or performing change assessments. (For more information about change control, see 5.29.)

Material verification is a key procedural traceability element to avoid material mix ups, like combining incorrect top web and bottom web materials or using an incorrect polymer material for the manufacturing of a film.

5.4 Properties to be evaluated (ISO 11607-1:2019, 5.1.6)

5.4.1 Intent

The intent of this subclause is to be a general introduction to the key goals to be fulfilled by materials and/or preformed SBSs to secure the appropriate functionalities expected from a terminally sterilized medical device packaging system.

5.4.2 Guidance

The following list of general properties can be considered as a checklist of the items to be addressed in a packaging solution selection and/or validation to ensure the intended requirements are achieved. Documenting the review and assessment of each of these properties is the expected good practice to demonstrate conformity with applicable requirements of ISO 11607-1:2019:

- Microbial barrier evaluation can be addressed through guidance in this document related to 5.1.7 h), 5.2.1, 5.2.2 and 5.2.3 of ISO 11607-1:2019. Some standardized test methods, guides and procedures that may be used to support this evaluation are listed in ISO 11607-1:2019, Annex B (under microbial barrier and microbial barrier surrogate).
- Biocompatibility and toxicological evaluation can be addressed through guidance in this document related to subclauses 5.1.7 a), 5.1.7 g), 5.1.9 b), 5.4 c), 6.1.1 and 6.2.3 l) of ISO 11607-1:2019. Some standardized test methods, guides and procedures that may be used to support this evaluation are listed in ISO 11607-1:2019 Annex B (under biocompatibility).
- Physical and chemical properties evaluation can be addressed through guidance in this document related to subclauses 5.1.7 b), 5.1.7 c), 5.1.7 d), 5.1.7 e), 5.1.7 f), 5.1.9 b), 6.1.3, 6.1.4, 6.2.3 b), 6.2.3 c), 6.2.3 d) and 8.2.1 of ISO 11607-1:2019. Some standardized test methods, guides and procedures that may be used to support this evaluation are listed in ISO 11607-1:2019 Annex B (under basis weight, burst, chloride, cleanliness, conditioning, pH, printing & coating, sulphate, tear resistance, tensile properties, thickness).
- Compatibility with forming, sealing and assembly processes can be demonstrated through guidance in this document related to subclauses 5.1.11 c), 5.1.8 a), 5.1.8 b), 5.1.8 c), 5.1.9 c), 5.1.9 e), 5.1.9 f) and 8.1 of ISO 11607-1:2019. Some standardized test methods, guides and procedures that may be used to support this evaluation are listed in ISO 11607-1:2019 Annex B (under coat weight, peel-open characteristic, seal strength, sterile barrier seal integrity).
- Compatibility with intended sterilization process(es) can be demonstrated through guidance in this document related to subclauses 5.1.7 f), 5.1.7 g), 5.1.9 b), 5.1.10 b), 5.1.12 a), 5.3.1, 5.3.2, 5.3.3, 5.4 b), 6.1.5, 6.2.3 l) and 11 of ISO 11607-1:2019. Some standardized test methods, guides and procedures that may be used to support this evaluation are listed in ISO 11607-1:2019 Annex B (under air permeance, biocompatibility, peel-open characteristic, pH, pore size, seal strength, sterile barrier integrity, wet burst in wet conditions, wet tensile properties).
- Potential use-by-date limitations for pre-sterilization storage and shelf-life limitations for post-sterilization storage can be addressed through guidance in this document related to subclauses 4.5.2, 6.1.6, 6.2.3, 8.3.1, 8.3.2, 8.3.3, 8.3.4, 8.3.5, 8.3.6 and 11 of ISO 11607-1:2019. Some standardized test methods, guides and procedures that may be used to support this evaluation are listed in ISO 11607-1:2019 Annex B (under accelerated ageing, conditioning, performance testing).

5.5 General performance requirements for materials (ISO 11607-1:2019, 5.1.7 and 5.1.8)

5.5.1 Intent

The purpose of these subclauses is to define general performance requirements on materials for preformed SBSs, SBSs and packaging systems.

5.1.7 outlines basic considerations with respect to the material's sterility maintenance and medical device protection functionalities, covering barrier and integrity performances, consistent physical properties, non-detrimental chemical properties, as well as material safety considerations.

5.1.8 covers additional requirements related to the eventual addition of an adhesive layer on one surface of the material.

5.5.2 Guidance

5.5.2.1 Regarding requirements for leachables and odours [ISO 11607-1:2019, 5.1.7 a)]

Packaging material components could migrate into the medical device (i.e. leachables) and interact with its contents, which could lead to adverse effects. In the same way, medical device material components could migrate into the packaging system materials resulting in adverse effects. The risk needs to be assessed (see 4.4.2.2 for guidance on

risk management) and appropriate compatibility studies should be performed, as chemical leaching can cause reactions or changes of a molecular nature — such as oxidation or crystallization of materials. Material additives (e.g. heat-seal coating components, film or paper additives, plasticizers, slip agents, anti-blocking agents, processing aids, polymer by-products) should be checked to confirm they have not changed (sterilization, aging, etc.) or are not interacting with the packaging system or medical device to create the opportunity for a defect. Potential chemical interaction between the protective packaging and SBS (e.g. yellowing of the SBS due to transfer of antioxidants from corrugated materials or poly-liners) also should be considered.

NOTE ASTM D4754^[14] deals with extractables testing. ISO 10993-13^[15] deals with degradation products from polymers.

Material's odours are usually readily evident, but it should be noted that if packs are gamma sterilized, odours related to the content which might develop, can abate when a porous SBS is used.

5.5.2.2 Regarding requirements for visible material defects (5.1.7 b) of ISO 11607-1:2019)

Visual inspection is a valuable means of monitoring material integrity to ensure that the integrity is consistent with the specified acceptance criteria. Localized thickening and/or thinning can be assessed by ensuring compliance with thickness variation specification.

5.5.2.3 Regarding material basis weight (5.1.7 c) of ISO 11607-1:2019)

The basis weight of a material is its mass per unit area. Test methods to determine basis weight include ISO 536^[16], JIS P-8124^[17], ASTM D4321^[18], ASTM D3776-6M^[19] and TAPPI T410^[20]. EN 868^[21-26] series specify an acceptable range of variations per major type of packaging materials.

5.5.2.4 Regarding material cleanliness (5.1.7 d) of ISO 11607-1:2019)

Regarding cleanliness, the expectation is that packaging materials should be adequately free of dirt, dust, grease, and other forms of contamination (hairs, insects, etc.). Particulates can be embedded or loose, foreign or bits of parent material. The level of particulate present can be controlled in a manufacturing process by implementing appropriate contamination and cross-contamination risk control measures at the source of the problem. Overall performance can be assessed based on specified acceptance criteria. As applicable, specific acceptance criteria should be established by categories of particulates or foreign materials.

Three main categories can be specified:

- a) Loose particulates on the surface of the material of the SBS and/or packaging system that can be brushed or rubbed off.
- b) Foreign material resulting from the manufacturing process and embedded between layers of a laminate or within a film, non-woven, or paper.
- c) Particulates or visually displeasing items inherent to manufacturing raw materials such as, but not limited to, pulp shives, small particles of resins/polymers with higher-than-average molecular weight, gels or carbon particles resulting from localized excessive heat in processing. All these derive from parents' materials and should therefore be considered separately from process related embedded foreign material particulates.

NOTE TAPPI Dirt Estimation Chart provides a means of measurement which can be utilized for specifying product cleanliness levels and contamination control requirements. EN 13795^[27] or IEST-STD-CC1246E^[28] provide methods for specifying product cleanliness levels and contamination control requirements.

5.5.2.5 Regarding material physical properties (5.1.7 e) of ISO 11607-1:2019)

The SBS should be capable of protecting the medical device's sterility, efficacy, and/or functionality until time of use. Physical property requirements of the SBS or preformed SBS will depend on the mass and the profile of the contents, the type of protective packaging (if applicable), storage conditions and the distribution system.

There are several factors that affect material performance. Physical properties referred to in ISO 11607-1 5.1.7 e) are the following:

- a) *Tensile strength*: The tensile strength of a material is the maximum force (tension) required to break or fracture the material and is expressed as force per unit area. ISO 1924-2^[29] and ASTM D882^[30] are normally used to provide guidance on testing tensile strength. Associated to tensile strength is elongation, defined as being the difference in length, expressed as a percentage of the original length, when a material is subjected to a tensile load. Typically, elongation at break is reported.
- b) *Thickness variation*: Thickness is the determination of a single layer of the material using a caliper and soft rubber platens. This soft platen method eliminates the surface roughness effect and, because the platen closing pressure is more uniformly distributed over the test area, partially eliminates the compressibility effect. Hence, the soft platen method is preferred when the measured thickness is used to calculate the material thickness variation, for instance expressed as “coefficient of variation” or “relative standard deviation” (ratio of the standard deviation σ to the mean μ). Test methods to determine thickness include but are not limited to ISO 534^[31] and ASTM F2251^[32].
- c) *Tear resistance*: Tear resistance is the ability of a material to resist tearing and for the material to continue to propagate an initiated tear. Test methods to determine tear resistance include but are not limited to ISO 1974^[33], ASTM D1922^[34] and ASTM D1424^[35].
- d) *Air permeance*: Air permeance is the degree to which a material admits a flow of air through a sample. It can be measured using a range of air leakage instruments of different types such as the Bendtsen air permeance tester (this tool measures the flow of air through a fixed area in ml/min) or the Gurley tester (this tool measures the time for 100ml of air to flow through a set area). Other appropriate test methods can be found in Annex B of ISO 11607-1: 2019. This property is considered as key to monitor material breathability and is expressed in $\mu\text{m}/\text{Pa}\cdot\text{s}$ as being the volume of air passing through a surface area of 1m^2 under a pressure of 1Pascal during 1 second.
- e) *Bursting strength*: This test method is designed to measure the maximum bursting strength defined as the pressure at which a sheet (e.g. paper or non-woven) will burst. The maximum pressure reading up to the rupture point is recorded as the bursting strength. Used as a measure of resistance to rupture, bursting strength is determined by procedures such as ISO 2758^[36], JIS P-8112^[37], TAPPI T403^[38] and ASTM D3786^[39].

For selected properties, EN 868 series^[21-26] specify acceptance limits per major type of packaging materials. It is to be noted that these test methods to assess physical properties will characterize the material but are not directly predictive of the performance of the completed SBS performance. Further evaluation, such as laboratory simulated packaging system performance tests, frequently needs to be performed to assess material performance of the SBS for a specific medical device.

Some other properties can be relevant and therefore should be evaluated. ISO 11607-1:2019 Annex B and EN 868 series provide some additional properties to be specified, as appropriate.

5.5.2.6 Regarding material chemical and toxicological characteristics (5.1.7 f) and 5.1.7 g) of ISO 11607-1:2019)

When choosing a material for a sterile barrier or packaging system there are basic safety requirements that should be met. The source, history and traceability of manufacturing of the used raw materials should be known and controlled. Chemical properties should be evaluated. This will typically include toxicity tests and the evaluation of possible chemical interactions between material and medical device (through check of material neutral pH, low contents of sulfate or chloride. EN 868 series^[21-26] specify an acceptable range of variations per major type of packaging material).

The following should be considered and/or evaluated for packaging materials:

- Presence of toxic heavy metals.
- Presence of natural rubber latex.

- Compliance with food packaging regulations (although not required by medical packaging regulations, this is commonly used as the first point of reference when evaluating the toxicological properties of packaging materials),

NOTE 1 Examples of regulations are FDA Code 21 CFR 170 –189^[40], BFR 36 XXXVI^[41] and the European Commission Regulation No 10/2011^[42] on plastic materials and articles intended to come into contact with food.

- Biocompatibility (testing is subsequently carried out depending on the specific application).

NOTE 2 Guidance to assess biocompatibility can be found in ISO 10993-1^[43] and ASTM F2475^[44].

5.5.2.7 Regarding microbial barrier properties (ISO 11607-1:2019, 5.1.7 h))

In non-porous materials, the microbial barrier requirement is met by demonstrating that the material does not permit the passage of air, as detailed in ISO 11607-1:2019, Annex C. In porous packaging materials, the microbial barrier can be assessed using test methods as listed in ISO 11607-1:2019, Annex B.

See also 5.8 of this document on microbial barrier properties.

5.5.2.8 Regarding materials with adhesive coatings (ISO 11607-1:2019, 5.1.8)

As the seal integrity depends on the coating pattern continuity and uniformity, attention is to be drawn on ensuring non-occurrence of any defects such as skips, voids or breaks in the pattern of the layer of adhesive added on one side of the material.

NOTE For information, EN 868-7^[24] Annex E proposes a method for the determination of regularity of seal adhesive coatings on paper, which could not be applicable to other porous webs.

The coat weight of an adhesive coated substrate can affect its sealability, seal strength, and adhesive transfer (if required). Depending on the adhesive and substrate, coat weight can influence the cohesive or adhesive failure modes of the seal during peeling, which affect the consistency of seal strength and coating transfer appearance between two substrates. For consistent results in sealing and peeling, the coat weight needs to be within the specified acceptance criteria. EN 868 series^[21-26] specify an acceptable range of variations of coating mass depending on coated substrates with associated test methods. Alternatively, ASTM F2217^[45] provides a standard practice for coating/adhesive weight determination.

5.6 Additional requirements for sterile barrier systems and preformed sterile barrier systems (ISO 11607-1:2019, 5.1.9)

5.6.1 Intent

The purpose of this subclause is to provide guidance on additional requirements for preformed SBSs and SBSs, in order to minimize contamination and to ensure that specified seal and peel requirements are fulfilled. The examination of the seal performance contributes to demonstrating that the seal integrity and/or closure is effective, and that sterility is maintained until the point of use or expiry date.

5.6.2 Guidance

5.6.2.1 General

Conformity with ISO 11607-2 is required.

If multiple types of packaging components are to be used it is important to verify that components are compatible with other components as well as the sterile contents contained inside and the intended sterilization process.

SBS chemical constituents could migrate into the medical device (leachables) and interact with its contents, which could lead to adverse effects. In the same way medical device materials could migrate into the packaging system

materials resulting in adverse effects. The risk needs to be assessed and compatibility studies should be performed as appropriate.

NOTE 1 Not all SBSs or preformed SBSs are intended to be peelable.

A SBS should be opened according to the manufacturing instructions. If there is a specific orientation needed to prevent delamination when opening, that orientation should be followed. The formed package should show by design which direction the packaging has to be opened (e.g. arrow sign, shape of seal).

Seals should be tested for strength and reviewed to determine if the results meet the desired seal strength for the SBS. Other criteria include peelability, seal visual attributes, and failure of material(s) during opening, e.g. delamination. For guidance on how to establish sealing windows, users should refer to Annex E of this document.

NOTE 2 For aseptic presentation see ISO 11607-1:2019, Clause 7.

5.6.2.2 Seal strength

The primary means of characterizing package seal strength is to measure the force required to separate two packaging components. Such a separation can be part of the SBS and/or packaging system design, in order to facilitate aseptic presentation, or it can represent the force required to rupture a permanent (or “weld”) seal. Seal strength measurements are key indicators of the sealing process. Measured seal strength values are dependent on but not limited to:

- the nature of packaging material(s) used;
- the set-up of the sealing equipment (e.g. sealing temperature, dwell time and sealing pressure);
- the materials and conditions of the sealing tool in the sealing equipment;
- the parameters of the method used to test the seal.

When determining specified seal strength values the characteristics of the materials and ability of sealing process should be considered.

The sealability of the material combinations under evaluation should be tested in the laboratory using a range of conditions designed to demonstrate extremes in seal strength and quality. These seals should be tested for seal strength and reviewed to determine if the results meet the specified seal strength for the SBS and/or packaging system. This process is typically used as a screening tool for selection of material combinations and can be used to evaluate pre- and post-sterilization seal strength and for determining specified seal strength values. Thereafter, seal strength measurements can be used to monitor manufacturing and to ensure a process output is within specification limits as long as seal strength data has been demonstrated to be a suitable monitor of the process.

ASTM F88/F88M^[46] is the definitive test method for characterizing seal strength. ASTM F88/F88M provides information on differences in technique. Seal strength assessed by different techniques (e.g. F88/F88M technique A, B and C) are likely to give different results so that consistency and specification of used technique is important when evaluating seal strength. EN 868-5^[47] defines specific testing conditions based on ASTM F88/F88M, in order to align testing and make the results comparable. See Annex B of ISO 11607-1:2019.

5.6.2.3 Bursting strength

A means by which an entire SBS is tested, burst testing involves internally pressurizing a package and noting the impact of that pressure on the package seals. The degradation of seals (creep), the time to package failure (creep to burst), and the ultimate bursting strength are measurements obtained by ASTM F1140^[48] (unrestrained) and ASTM F2054^[49] (restrained) test methods. While bursting strength testing probes the entire SBS at once, it does not apply the force equally to all parts of the package, and necessarily carries more variability in the observed results than seal strength testing. Burst testing is more typically used for in-process control and is not considered to be a whole package integrity test. When it will be used as such a control, then concurrent seal strength and burst testing should be performed at the time of validation.

5.7 Reusable sterile barrier systems (ISO 11607-1:2019, 5.1.10, 5.1.11 and 5.1.12)

5.7.1 Intent

These subclauses list additional requirements for reusable SBSs like reusable rigid containers or reusable woven wrap materials in order to ensure that these reusable components comply to minimum performance requirements during each use of their serviceable life.

5.7.2 Guidance

ISO 11607-1:2019, 5.1.10 requires that for a reusable preformed SBS, the manufacturer recommends reprocessing steps and demonstrate, that when so reprocessed, the SBS will maintain the minimum performance characteristics, or the end of serviceable life shall be detectable.

ISO 11607-1:2019, 5.1.11 details specific requirements for rigid reusable containers. For healthcare facilities, guidance on application of ISO 11607-1:2019 and ISO 11607-2:2019 is given in Annex B.

Annex B also provides guidance on the use of sterilization wrap, as well as guidance on the specific additional requirements for reusable woven wrap as given in ISO 11607-1:2019, 5.1.12.

Information on further requirements on reusable sterilization containers can be found in ANSI/AAMI ST77:2013/(R)2018^[50] and EN 868-8:2018^[51].

5.8 Microbial barrier properties (ISO 11607-1:2019, 5.2)

5.8.1 Intent

This subclause provides the basic requirements for microbial barrier properties for impermeable and porous materials.

5.8.2 Guidance

All sterilizable medical packaging materials for SBSs need to provide an adequate microbial barrier.

The selection of appropriate materials will be influenced by the design decision taken under Clause 6 of ISO 11607-1:2019.

The NOTE under ISO 11607-1:2019, 5.2.3 refers to two types of tests, those based on microbiological methods and physical test methods based on challenging materials with particulates, also labelled as microbial surrogate methods in Annex B of ISO 11607-1:2019.

NOTE Whole package (SBS) microbial challenge testing is currently not standardized in any consensus standard. In these tests typically the SBS is exposed to an aerosol challenge of a known concentration of a known microorganism. The outside of the system is then decontaminated, aseptically opened, and a sterility test is performed on the medical device. While proposed as an alternative to physical integrity testing, these methods are not particularly reliable and are technically challenging to execute and validate. When validated, these methods can be appropriate if they are the only possibility when physical testing is not achievable, e.g. for evaluating the integrity of tortuous path closure SBSs^[52].

5.9 Compatibility with the sterilization process (ISO 11607-1:2019, 5.3)

5.9.1 Intent

Sterilization processes can interact with packaging to affect its properties, and therefore its suitability for an application. This subclause ensures this effect is properly evaluated.

5.9.2 Guidance

The ability of SBSs to withstand sterilization processes and maintain their structural integrity as well as other material characteristics and properties is a critically important requirement (ISO 11607-1:2019, 5.3 and 6.1.5). As a result, the

method(s) of sterilization should be identified early so packaging materials, preformed SBSs or SBSs that are compatible with the sterilization method(s) can be selected.

Gaseous sterilization methods such as moist heat, ethylene oxide (EO), vaporized hydrogen peroxide (VH₂O₂) or others, require pressure driven gas exchange through the SBS and/or packaging system which can induce significant mechanical stress on the pack. This depends on a packaging design that is sufficiently porous, and with the porous areas located in an unhindered position in the packaging system. It can also be necessary to provide suitable room in all additional layers of packaging to accommodate SBS expansion during the sterilization cycle. These sterilization methods also require elevated temperature and humidity conditions, with which the materials chosen need to be compatible.

ISO 11607-1 requires assessment of the compatibility with sterilization processes. For sterilization methods like moist heat, EO, VH₂O₂ or others that can create rapid pressure changes, this includes an evaluation that the SBS is not adversely affected by the rate of change in pressure. This should be done on the actual process taking into account material variability (see ISO 11607-1:2019, 5.3.2).

NOTE ISO/TS 22421 includes a requirement that the technical description for a sterilizer includes a statement of the maximum rate of pressure change in an operating cycle. The rate of pressure change in ISO/TS 22421 is expressed as the pressure gradient calculated as a rolling average using a rate of measurement of 1 s and time interval for calculation of the rolling average of 3 s. The maximum calculated rolling average from at least three replicated operating cycles is to be given. This provides some information on the rate of pressure change that the SBS is likely to experience in an operating cycle but that assessment of compatibility of the SBS with the sterilization process should be done on the actual process taking into account material variability (see ISO 11607-1:2019, 5.3.2).

While the impact on material properties due to EO are often negligible, other methods, such as radiation or VH₂O₂, can induce significant changes in material properties, potentially impacting packaging stability and performance (ISO 11607-1:2019), see AAMI TIR17^[53].

Initial selection of packaging materials or preformed SBSs can be made on the data and recommendations available from manufacturers and in the public domain which approximates to the anticipated conditions of use. However, it is imperative that the type and number of anticipated sterilization cycles are evaluated at some point, preferably on the final SBS, including the medical device or equivalent proxy, as part of the selection process. Evaluations of sterilization compatibility may be leveraged between sterile product families and packaging families based on worst case considerations or other valid rationales (see ISO 11607-1:2019, 6.1.9). This can be the case, for example, where many similar but not identical medical devices or combinations of medical devices are packaged in the same or similar packaging. Evaluation of the effects of sterilization on the closure/seal integrity and opening features of the SBS should be included. Annex F offers a more detailed review of sterilization methods and their effects to assist with material selection.

5.10 Labelling system (ISO 11607-1:2019, 5.4)

5.10.1 Intent

This section governs the labelling of the SBS so that the product identification and instructions for use are clearly visible and readable by the end user, and that such labelling does not introduce unacceptable risk to the SBS or its contents or potential interference with the sterilization process.

NOTE ISO 11607-1 only addresses the presence of labelling, not the specific information to be printed on the label. Specific expectations for labelling content will vary by region and regulatory framework and specific regulations on label content (e.g. US FDA, European medical device regulation (MDR), ISO) apply.

5.10.2 Guidance

5.10.2.1 Type of labelling

Labelling can either be printed directly on the packaging materials or on label stock which is then affixed to the packaging materials. If using separate labels, specifications for label stock should be established, considering similar requirements to those for SBS materials, e.g. nontoxic, abrasion resistant, clean. Ink used should not bleed or leach onto contents.

5.10.2.2 Placement of labelling

Visual device recognition at point of use is critical. Therefore, it is important to place labelling in a position where it does not hinder device identification. For instance, many SBSs have a clear side to facilitate device identification. If this is the case, any labelling placed on that side should not impede that ability.

5.10.2.3 Ability to remain attached and intact

Labelling should remain adhered to the substrate complete and undamaged such that labelling content is not compromised following sterilization, and subsequent handling, distribution and storage. Labelling should be evaluated as part of performance testing/studies on the SBSs. Label printing and adhesion can also be evaluated during an aging study.

5.10.2.4 Legibility

In order to satisfy legibility requirements, the printing process should be designed properly, with consideration given to adhesion to the substrate and potential of damage to the print or label.

- a) Print design: It is important to keep in mind the attributes of the packaging materials when designing the print. Printing in the seal area is discouraged, as it can affect the sealability of a material, as well as the sealing process can affect the ink and/or print legibility. Labelling should also not be placed in the seal area prior to sealing as it can impact the ability to seal consistently.
- b) Print (or label) adhesion to substrate: New packaging materials to be printed should be subject to an evaluation for printability. The printability of a material is related to its wettability or surface tension. Surface tension measurement, whether utilizing contact angle equipment, or dyne solutions, can be used to determine the level of surface treatment and/or the printable side of a substrate. Some treated surfaces can degrade, which can affect their printability over time. Poor ink or anchorage/adhesion to material can affect the appearance and legibility of print or the functionality of coatings on packaging materials. Since the acceptability of the degree of anchorage is specific to each application, an acceptability criterion should to be agreed upon by user and producer of packaging material. See ASTM F2252^[54]. The amount of ink coverage, top coating or label on a porous material can also affect material porosity and sterilization effectiveness which should be considered when designing print or label.
- c) Potential for damage to print/label: In order to remain legible until the point of use through the hazards of sterilization, handling, distribution, storage and conditions of use labels should be designed to be indelible which is also a regulatory requirement in some jurisdictions (i.e. in Europe under the MDR). The ability to survive these hazards should be evaluated. These hazards can typically be divided into two categories, those posed by physical abrasion or rubbing and those posed by exposure to an agent that can smear or remove the ink.

Abrasion of printed packaging material in the distribution environment can change the graphic appearance of an SBS and/or packaging system by scuffing, removing, or rendering print unreadable. In laboratory conditions, comparing abrasion resistance of surface printed materials against established standards can approximate the effects during shipping and handling and distribution. For further guidance see ASTM D5264^[55].

The printed surface of SBS and/or packaging system materials can be exposed to chemicals during its life cycle. In thinking about “chemicals” it is important to consider environments of use where wet hands are anticipated as well as environments where fluids can be present. Exposure to chemicals can degrade, soften, smear, and remove printing, which affects its appearance and legibility. The relative resistance to known or expected chemicals should be evaluated. For further guidance see ASTM F2250^[56].

5.10.2.5 Compatibility of labelling with sterilization process

- a) Sterilization parameters: Sterilization process conditions such as temperature, humidity, chemicals used should not affect the legibility of print or adherence of labels.

- b) Sterilization effectiveness: Labels should not be placed in an area where they will impact the sterilization process, without evaluating the impact. For instance, labels placed on the breathable area of an SBS when using a gas-based sterilization process can impede the flow of that sterilant. The effectiveness of the sterilization process should be evaluated to confirm this is acceptable.

5.10.2.6 Protection of sterile barrier system and contents

- a) Application to SBS: When placing print or labelling on package care should be taken that this process does not damage the materials. This is especially important when this step occurs after inserting the content, as the shape or composition of components can affect the ability to apply the label consistently and without damage.
- b) Hand-writing process: Ballpoint pens or any writing instrument or printing system with the potential for creating a hole or puncture in the SBS should not be used. Any handwriting on the package should be outside the area enclosed by the outside dimensions of the seals, not inside the seals where the sterile contents will be contained. Writing on SBSs known as wrappers should be on the closure tape, not on the wrapper itself. Writing on closure tapes or adhesive labels should be done before applying them. Only pens with non-toxic ink that is suitable for use with the chosen sterilization process should be used.

For further information on the process of labelling, see 6.11 of this document.

5.11 Storage and transport of materials and preformed sterile barrier systems (ISO 11607-1:2019, 5.5)

5.11.1 Intent

The intent of this subclause is to create requirements that materials and preformed SBSs are to be transported and stored so that there is no degradation of those attributes that allow sterile contents protection and preservation of sterility when formed into the fully assembled SBS.

5.11.2 Guidance

Considerations should be given to the various types of delivery and storage, and variations in environmental conditions which might be encountered when transporting and storing materials and preformed SBSs.

Manufacturers of materials and preformed SBSs should ensure their outer transport packaging provide adequate protection for storage and transport and advise purchasers on appropriate storage and transport conditions and of any known risks and ways to mitigate them. Environmental conditions (e.g. temperature variation, relative humidity, direct sunlight or ultraviolet light) or any other conditions occurring during storing and transportation can affect the properties and functionality of the materials and/or preformed SBSs.

Materials and preformed SBSs, for example, need to be protected against dust and any foreign matter that would alter their cleanliness levels, increase bioburden potentially leading to a compromise of the materials usability for an SBS application.

Materials may be sensitive to aspects of the storage use condition and should be stored or conditioned following the manufacturer's recommendations.

Protection will typically be accomplished by overwrapping/encasing in poly wrap, light-blocking or metallized wrap if light exposure is a potential risk, and /or cartons suitable for protecting the materials.

Suggested storage cautions to mitigate specific risks will typically be provided by the manufacturer. These can include statements such as do not store in direct sun light, keep dry, no excessive heat, do not stack, etc. Additionally, it can be required, depending on the conversion processes to condition materials or move them into the area in which they will be processed for at least 24 hours to allow them to reach equilibrium if they are being moved in from a less controlled environment.

During storage and transportation, it is recommended to keep original wrapping in place and minimize handling of materials (e.g. reels, trays, die cut lids, wrapping sheets) and preformed SBSs to protect them from contamination as

well as from the effect of environmental conditions (e.g. relative humidity, direct sunlight or fluorescent light, temperature).

When selecting suitable storage facilities, one should consider not only environmental conditions (e.g. temperature and humidity) but also ways to minimize the risk of possible physical damage. It can be appropriate to check the product periodically in storage to detect possible deterioration. Consideration should be given to administrative procedures for use-by-dates, stock rotation and lot segregation.

Manufacturers of materials and preformed SBSs can provide data as part of their supplier documentation on retention of product attributes such as seal strength if applicable, material strength (e.g. tensile, tear, puncture), or performance characteristics (e.g. barrier properties, optical properties, sealing performance) for real time aged materials and preformed SBSs stored in specific storage conditions or after accelerated aging.

While the user of materials or preformed SBSs should consider this data in determining their own required storage conditions, it is important to realize that the conditions in these studies do not always exactly mirror the storage and transport conditions at the medical device manufacturer or in the healthcare facility. Deviations from the conditions utilized by the manufacturer should be evaluated by the user to determine that they will not cause degradation of the materials or SBSs.

The requirements of 5.5 of ISO 11607-1:2019 apply to materials and preformed SBSs. Once the SBS is filled and fully formed/sealed and placed into a packaging system, the storage and transport conditions are evaluated by the user (medical device manufacturer or healthcare facility) in accordance with Clause 8 of ISO 11607-1:2019 on packaging system performance and stability.

5.12 Design and development (ISO 11607-1:2019, 6.1.1)

5.12.1 Intent

The highest priority of the development of a medical device packaging system is to systematically minimize the risk to the healthcare user/patient.

5.12.2 Guidance

The intent of this subclause is to minimize the risk through appropriate design and development covering the fundamental functions of an SBS, i.e. allow for sterilization, protect the contents, maintain microbial barrier and allow for aseptic presentation.

Different jurisdictions can define the need to minimize risk slightly differently for example requiring minimizing the risk as far as possible or as low as reasonably possible which obviously changes the requirement. In some jurisdictions like the EU, it is required to minimize the risk for the specified intended use and/or the reasonably foreseeable misuse.

Guidance on risk management is provided in 4.4.2.2 and Annex C of this document.

As a minimum the following aspects that apply to all packaging systems, components and materials should be considered when assessing risks:

- a) they should be made of known and traceable materials with processes capable of meeting the requirements of ISO 11607-1:2019 (see requirements in ISO 11607-1:2019, 5.1.3, 5.1.4 and 5.1.5);
- b) they should be non-toxic (see requirements in ISO 11607-1:2019, 5.1.6; for guidance see 5.5.2.6);

NOTE If the SBS or associated components contain natural rubber latex, the SBS should be labelled indicating natural rubber latex is present.

- c) there should be documented evidence that the ingress of microorganisms can be prevented when demonstrated under test conditions which consider sterilization process, handling, distribution, and storage for sterility maintenance up to the point of use (see requirement in ISO 11607-1:2019, 5.1.6 and 5.2, 8);

- d) they should have a demonstrated ability to meet the required physical properties for materials and closures (such as weight or grade, seal width and seal strength), resist tearing or puncture, be capable of opening or peeling in a continuous and homogenous manner, without delamination tearing (see requirements in ISO 11607-1:2019, 5.1.7 and 5.1.9);
- e) they should be compatible with the intended sterilization process and parameters capable of producing a sterile medical device (see requirement in ISO 11607-1:2019, 5.3);
- f) they should be compatible with the labelling system; if present, have colour fast printing inks that do not degrade, fade or become illegible after exposure to the intended sterilization process (see requirement in ISO 11607-1:2019, 5.4);
- g) they should be protected from the effects of environmental conditions (e.g. relative humidity, direct sunlight or fluorescent light, temperature) during storage and distribution (see requirements in ISO 11607-1:2019, 5.5 and Clause 8);
- h) they should allow aseptic presentation (see requirement of ISO 11607-1:2019, Clause 7).

5.13 Aseptic presentation (ISO 11607-1:2019, 6.1.2)

5.13.1 Intent

The contents of the SBS are to be dispensed without compromising sterility of the device.

5.13.2 Guidance

At the point of use, the user needs to be able to remove the contents from the SBS without compromising sterility.

Aseptic presentation is the transfer of sterile contents from its SBS using conditions and procedures that minimize the risk of microbial contamination.

To adequately minimize the risk of microbial contamination during aseptic presentation, the packaging system designer needs to focus on the opening features of the packaging system considering the specific application in the healthcare environment. Hence, it is essential to understand as much about the customer and the environment of the customer as possible in order to design an effective packaging system.

An assessment of customer requirements should at a minimum include the following:

- a) Customer: It is important to understand who will be using the packaging system. For a terminally sterilized implantable medical device, this is often an operating room technician, however, it could also be a variety of personnel in a number of circumstances. Understanding as much about the customer as possible will help the design decision-making process.
- b) Customer environment: Determine the use environment where the SBS will be opened. For a terminally sterilized medical device this is usually an operating room or healthcare environment but can be a home care environment as well. This can often be a high stress environment; steps should be taken to ensure that using the packaging system does not add to the stress level in the use environment.

NOTE The number of 'sterile barrier layers' can affect the ability to present a medical device aseptically. The selection of a single sterile barrier or a double sterile barrier can be based on the end user needs or the risk of the device. See 5.22 of this document. In some healthcare facilities, sterile goods are stored in location where SBSs and packaging systems can be exposed to dust. In such case, packaging systems should be designed to allow end users to remove the protective packaging before entering the sterile environment (i.e. operating room) to reduce risk of contamination at point of use (see also 5.17.2 in this document for additional guidance).

- c) Ease of opening: The SBS should be easy to open in order to allow for the medical device to be dispensed aseptically. This is fundamental for sterile medical device packaging. If the SBS is difficult to open, the likelihood

of contamination increases. If applicable to the packaging design or type, the following hazardous situation should be considered:

- opening at the wrong end or taking the device from the wrong end;
- not having enough room to grab the opening notch for the lid;
- peel force too high or too low;
- tearing of top or bottom web;
- handling difficulties with large or small size packaging as well as large and/or heavy device;
- handling sharp devices;
- top or bottom web curling inwards so that the device is contaminated;
- opening too small;
- particulate or fiber release during opening;
- device not being secured and moving during opening so that the unsterile edge of the packaging is touched;
- difficulties of pulling device from its snap-fit feature of the packaging;
- not having enough room for the gloved fingers to grab the device;
- difficulties of holding the packaging during opening;
- not being able to recognize the sterile layer in case of multi-layer packaging (see also 5.17 of this document).

Depending on the packaging design or device, additional hazard or hazardous situation could be identified during the risk assessment.

- d) Medical device identification: Consider any medical device identification requirements specific to the customer needs, or that will help the customer in the use environment.

Clause 7 of ISO 11607-1:2019 provides step by step guidance on performing usability evaluation for aseptic presentation.

5.14 Physical protection (ISO 11607-1:2019, 6.1.3 and 6.1.4)

5.14.1 Intent

The intent of 6.1.3 and 6.1.4 of ISO 11607-1:2019 is to describe the main design input requirements for the packaging system and the protective packaging in order to protect the sterility of the contents inside the SBS until point of use.

5.14.2 Guidance

This standard uses three terms:

1. Sterile barrier system (SBS) — minimum package that minimizes the risk of ingress of microorganisms and allows aseptic presentation of the sterile contents at the point of use;

2. Protective packaging — configuration of materials designed to prevent damage to the SBS and its contents from the time of their assembly until the point of use;
3. Packaging system — combination of a SBS and protective packaging.

The packaging system is to be considered the combination of the SBS and the minimum necessary protective packaging for the product to be distributed safely to the end user until point of use. For example, cargo containers and pallets, or, transfer cabinet used in healthcare facilities (even though they can be considered protective packaging) are generally not to be regarded as part of this minimum level of protective packaging. They are considered transport accessories. The packaging system can have one, two or more layers of unit or user packaging.

The protective packaging is usually additional layers of packaging outside the SBS. Protective packaging can also be protective components or materials inside the SBS. For example, if the medical device is sharp or has sharp points or edges, these can be shielded with protective materials to keep them from puncturing or interfering directly with the SBS or help keep the device in a fixed safe location inside the SBS.

When designing the different components in the packaging system, consideration should be given to the conditions and environment throughout the packaging lifecycle (sterilization, thermal and mechanical hazards from handling, distribution, storage, etc.).

For detailed inputs to the design phase, see Annexes A and B of this document.

5.15 Sterilization compatibility (ISO 11607-1:2019, 6.1.5)

5.15.1 Intent

The SBS must be compatible with and allow for product sterilization. This encompasses the entire packaging system that is processed through sterilization.

5.15.2 Guidance

Annex F of this document discusses the details of selecting materials for compatibility with the sterilization process.

The sterilization process for the medical device should be understood prior to designing the packaging system. Knowing the sterilization process will help guide key decisions regarding the materials of construction for the SBS. Additional information on sterilization process requirements and references can be found in Annex F of this document.

Subclause 5.9 of this document includes guidance on sterilization compatibility and contains more detail on material compatibility requirements detailed in ISO 11607-1:2019, 5.3.

5.16 Maintenance of Sterility (ISO 11607-1:2019, 6.1.6 and 6.1.7)

5.16.1 Intent

ISO 11607-1 requires the SBS to maintain sterility until the point of use or expiry.

5.16.2 Guidance

5.16.2.1 Handling, distribution, and storage guidance

The packaging system designer should understand the stresses imposed upon the packaging system through its total life cycle. These stresses include all factors of handling, distribution and storage. The requirements for these environments are determined largely by the type of medical device, type of packaging system, sterilization process and the type of distribution. A thorough understanding of these factors will help to address all pertinent medical device protection requirements. The sterility maintenance will help to define the appropriate sterile barrier and packaging system materials. Evidence that the ingress of microorganisms can be prevented is demonstrated under test conditions which consider sterilization process, handling, distribution and storage.

An assessment of handling, distribution and storage requirements should at a minimum include the following:

- a) **Storage:** A thorough assessment of storage environments should be conducted. This assessment should include the storage environments at the manufacturing facilities, the distribution centres and of the end users. The key factors are space limitations, stacking or shelving issues and the temperature/humidity exposures. The storage environment of the end users can be difficult to quantify. However, at a minimum there should be an understanding of any variability of how the end user will be storing the medical device. This could include storage at a healthcare facility, at a regional centre, or medical devices being carried between clinical sites by sales force personnel.
- b) **Distribution/transportation:** An assessment of the distribution environment should be conducted. A complete evaluation of a distribution environment can be time consuming and costly, however, there should be a basic understanding of the factors involved in distribution in order to design a cost-effective packaging system. Determine basic factors such as the transportation means used to move medical devices between: the manufacturing facility; the remote or contract sterilization facility (if applicable); the distribution centre; and the customer. Distribution assessment should also consider any distribution by the customer. The methods of accomplishing these medical device movements are critical design inputs. Product distribution could include multiple transportation episodes, such as the return of a partially utilized kit of devices to the manufacturer.
- c) **Handling:** An assessment of medical device handling should be completed. This assessment includes several factors from the manufacturing, distribution and customer environments. Medical device protection requirements are often directly related to how the medical device is handled, whether it is manual handling or machine handling. The means by which the medical device is handled is often determined by the packaging configuration, whether it is a single unit or a palletized unit, and how it arrives at the point of use.

When the use conditions are properly defined for the packaging system, these conditions should then be accurately accounted for in the performance and stability testing. Contents will be sterile as long as sterile barrier integrity is maintained. Clause 8 of ISO 11607-1:2019 (specifically, 8.2 and 8.3) contains requirements on the validation of packaging systems with consideration to the conditions of use.

5.17 Requirements for multi-layer packaging (ISO 11607-1:2019, 6.1.8)

5.17.1 Intent

The end user needs to be able to recognize the layer of packaging that is the sterile barrier in order to apply proper handling techniques when using the packaging system in particular during aseptic presentation.

5.17.2 Guidance

There can be circumstances where it is difficult to differentiate between a validated SBS (see ISO 11607-1:2019, 9.1) and protective packaging that looks like an SBS. In these circumstances the labelling should include an indication to identify the SBS(s). In instances where two layers of packaging appear similar, an indication to the end user if layers are an SBS can assist in determining the proper handling/dispensing techniques.

NOTE A set of SBS symbols have been validated by the Sterile Barrier Association (SBA). A summary of the validation report is available on the website of the SBA as well as guidance how to use the symbols. The validation demonstrated good comprehension, usability and memory for the symbols which means that healthcare users widely understand the symbols, take the correct actions and memorize the meaning. The symbols are included in ISO 7000^[57] and are available via the ISO Online Browsing Platform. (example: Double SBS: <https://www.iso.org/obp/ui/#iso:grs:7000:3704>). ISO 15223-1^[58] has been revised and published in July 2021 with new symbols that have been developed to deal with the labelling requirements of the medical device regulation (EU) 2017/745^[59] including the new SBS symbols. The plan is that EN ISO 15223-1 will be harmonized with the MDR. Use of an indication to mark the SBS such that it can be recognized as such is now required by the MDR.

The use of symbols to recognize the SBS(s) should be considered when applying risk management for usability. The symbols help the user understand the packaging configuration at the point of use and as such control the risk of

unintentional contamination of the sterile field. Risk management can be the basis to decide which layers are to be labelled and which not. The usability evaluation (see 5.22 of this document) should demonstrate that the labelling system is adequate and correctly interpreted.

For healthcare facilities, attention is drawn to protective packaging called “transportation wrap” only featuring mechanical protection without microbial barrier. To avoid any confusion or misuse, sheet colour coding can be an acceptable practice of recognition indication of a sterile barrier layer. An example of this is when packaging reusable medical devices, a double wrap package made of two layers of breathable webs is used. Each of these sheet layers can be of a different colour. The personnel in the healthcare facility are trained to know that the external one is always of a pre-set colour and is a “dust cover” to be removed prior entering the operating room.

5.18 Packaging families (ISO 11607-1:2019, 6.1.9)

5.18.1 Intent

It can be an efficient and cost-effective way to develop a packaging system family by using the worst-case device/packaging system combination to validate the design.

5.18.2 Guidance

5.18.2.1 General

When determining and assessing the packaging system, thought should be given to other packaging system designs and medical devices that require validation. Many times, similar medical devices, comprising a “product family,” can be validated together, where package materials, packaging machinery, sterilization processes, and other aspects of the medical device use and life cycle are the same or similar. Choosing a device/packaging system combination that represents a “worst-case” example can be advisable, in order to ensure that less demanding variants of the SBS and associated medical device are covered. In all such cases the protocol should include the rationale for this approach. It is also sometimes possible to leverage existing packaging systems for medical devices to reduce the burden associated with the validation protocol, or to validate a worst-case scenario that covers multiple packaging system/medical device combinations. Medical devices with similar physical dimensions and/or packaging system configurations similar to validated structures can provide the basis for a valid rationale to limit the amount of testing required to establish efficacy of an SBS.

5.18.2.2 Packaging family considerations for healthcare facilities

A common SBS can be used to pack and protect a variety of tray families (i.e. trays composed by a set of similar reusable medical devices but not identical) used in the operating room. The worst-case is established by identifying the tray(s) that apply the most stress to the packaging system. The worst-case configuration can be the bulkiest, heaviest, the sharpest or the densest set of reusable items organized in a given size tray. Often, the determination of the worst-case configuration is clear. However, in some cases it can be necessary to test more than one operating room’s tray to ensure that the packaging system has been fully challenged.

The determination of the worst-case scenario can also encompass the review of:

- a) having the reusable medical devices oriented to facilitate aseptic presentation or not;
- b) having the sharp items shielded (so that the healthcare user is protected from injury and the SBS and medical device is protected from damage) or not;
- c) having associated components used inside the SBS in order to ease or facilitate the organization, drying or aseptic presentation (e.g. inner wrap, instrument organizer tray, absorbent tray liners or a containment device around the medical device) or not.

Properly characterizing and evaluating the worst-case configuration will ensure that the other trays in the same category will be appropriately protected by the packaging system. Often historical data exists for already selected material

combinations. Therefore, capitalizing on this available information can be supportive of determining if it is an appropriate solution to be also used on additional configurations / sets of reusable medical devices of the same family.

ISO 11607-1:2019 addresses “worst-case” in three areas and in each case, it means something slightly different. In order to correctly interpret and apply these subclauses dealing with worst-case, it is important to understand the terms that are used.

5.18.2.3 Worst-case configuration — Medical devices

Within medical device product families (i.e. medical devices that are similar but not identical), a common SBS can be used to protect a variety of medical devices. The worst-case is established by identifying the medical device(s) that apply the most stress to the packaging system. The worst-case configuration can be the bulkiest or heaviest item in an otherwise common group of medical devices or an item with the greatest number of fitments or other medical device features. Often, the determination of the worst-case configuration is clear. However, in some cases it can be necessary to test more than one medical device (e.g. the heaviest medical device as well as the medical device with the most fitments) to ensure that the packaging system has been fully challenged. This is especially important when device functionality is also tested with the packaging system. Properly characterizing and evaluating the worst-case configuration will ensure that the other medical devices in the product family will be appropriately protected by the packaging system. Alternatively, a worst-case device which is not a commercial configuration but a combination of other worst-case device features, intended to present the maximum challenge to the packaging system, can be used.

Packaging systems can be designed to contain a range of product, SBS, and product literature configurations. Often this leads to dramatic differences in the weight, or the headspace present within a packaging family. For example, a lighter mass configuration can have more headspace present in the protective packaging, leading to damage to the SBS. Or, a heavy mass configuration can minimize headspace limiting movement but create different opportunities for SBS damage. In some cases, the idea of bracketing can be employed to test extreme ranges within a packaging system, such that all configurations that fit within that range can be included by equivalence.

Alternatively, for performance testing, a worst-case device which is not a sellable configuration but a combination of other worst-case device features, intended to present the maximum challenge to the packaging system, can be used.

5.18.2.4 Worst-case — Sterile barrier system

Additional direction regarding worst-case testing is provided in ISO 11607-1:2019, 8.2.2 on packaging system performance testing, “Performance testing shall be conducted on packaging systems comprised of the worst-case SBS as well as the worst-case protective packaging.” Nominal sealing parameter settings are acceptable but should be justified for package performance testing. There are two predominant approaches to addressing the key issues of this subclause.

The first and most common approach utilizes sourcing preformed SBSs manufactured using a fully validated process. SBSs that have been produced as lots run at typical operating conditions within the validated window are tested and evaluated. By choosing an appropriate sample size from multiple lots (typically three), one can normally be assured, at a given confidence level, that the full range of package characteristics (e.g. seal strength) have been represented. Hence, sample size selection (see 4.5 of this document) and number of lots to be evaluated are important components of the documented rationale. Numerous reference materials exist to assist in sample size determination.

The second approach involves producing SBSs at the worst-case conditions of manufacture, generally the extremes of the validated window. In some cases, SBSs can be produced at the lowest validated temperature, the lowest validated pressure, and the shortest validated dwell to yield SBSs with the low-end worst-case seal quality. Typically, the parameters used to establish the Operational Qualification (OQ) are used to produce the SBSs needed to assess the packaging system performance. This approach should be used when there is documented data that supports the seals are a lower strength than the nominal condition.

The approach to achieving conformity to ISO 11607-1:2019 will vary between medical device manufacturers, but in each case the approach chosen should be supported by an appropriate rationale, to be included in the documented package validation protocol. The choice will be dependent on corporate risk policy and economic considerations.

5.19 Design process (ISO 11607-1:2019, 6.2.1)

5.19.1 Intent

Following a documented design process is intended to be part of the systematic approach to ensuring the safety of the packaging system.

5.19.2 Guidance

The procedures for the design and development process of packaging systems should consider the aspects described in 5.20 of this document.

NOTE This is applicable to medical device manufacturers, manufacturers of medical packaging and healthcare facilities.

Choosing an appropriate packaging material for a sterilizable medical device requires careful consideration. It is desirable to include packaging system development early in the design process of the medical device. Leaving this important consideration until the end of the design process can result in delays in a medical device being introduced into the marketplace or impose limitations on shelf life or other end use considerations. Manufacturers of medical packaging can be a significant resource in determining suitable options.

Medical device manufacturers are directed to Annex A of this document, which provides information on relevant processes and practices.

Healthcare users are directed to Annex B of this document, which provides information on relevant processes and practices.

The use of contract packagers if applicable should also be considered during design. More guidance is available in Annex G of this document.

5.20 Design inputs (ISO 11607-1:2019, 6.2.2 and 6.2.3)

5.20.1 Intent

These subclauses require the design owner to consider the physical characteristics of the product, design inputs related to the end user needs, the use conditions, and the use of materials meeting the prerequisites of ISO 11607-1:2019, Clause 5.

5.20.2 Guidance

5.20.2.1 General

A set of design inputs should be developed prior to considering materials and/or packaging system design. These will be used in assessing the materials and/or design. Design inputs are developed from end user needs and intended uses. This information will come from end users, engineering, manufacturing, marketing, regulatory, etc. Some examples of design inputs are medical device physical attributes, medical device protection requirements (e.g. barrier to light, oxygen, and contamination), sales unit configuration, sterilization process, distribution, handling, and use environment.

Healthcare users are directed to guidance provided in Annex B of this document.

5.20.2.2 Design inputs — medical device attributes

Before the design of a packaging system for a terminally sterilized medical device can begin, it is critical to examine all attributes and requirements of the medical device, which could affect the design of the packaging system. The best way to accomplish this is for those responsible for the design of the packaging system to be involved in the overall product development at an early stage. Obtaining the pertinent information required to begin the design process should be a cross-functional activity requiring input from a number of organizations. These organizations include but are not limited to engineering, manufacturing, marketing, and regulatory.

At a high level, design inputs can be thought of as product attributes and product specific requirements. Product attributes are generally the physical characteristics of the medical device, which will need to be contained. They can be divided into several categories, like product protection requirements, manufacturing requirements, sterilization process requirements, handling, distribution and storage requirements, marketing requirements, budget requirements, customer requirements and regulatory requirements.

Each of these categories are addressed in Annex A of this document to provide baseline guidance for gathering design inputs prior to designing a packaging system for a terminally sterilized medical device product.

5.20.2.3 Product attributes

The first phase of gathering design inputs should involve analysing medical device attributes. These are the physical characteristics of the medical device that will help guide some basic decisions regarding what type of packaging system is necessary for containing the medical device.

Physical characteristics include but are not limited to:

- a) **Size:** The dimensions of the medical device should be understood, including length, width and diameter of the medical device and all accessories that will be part of the total medical device.
- b) **Weight:** Determine the total weight of the medical device and all accessories to be packaged.
- c) **Centre of gravity:** Determine whether the medical device is balanced or offset; this will help determine the orientation of the medical device in the packaging system.
- d) **Profile:** Determine the profile of the medical device and all accessories.
- e) **Sharp edges/points:** Determine whether there are any sharp edges or points on the medical device and accessories that could damage the SBS. Also, determine if the end user, or person opening the packaging system, needs to be protected from any sharp edges or points on the medical device and accessories.
- f) **Surface characteristics:** Determine if the surface of the medical device or accessories have any special protection requirements. For example, it is possible to have a medical device that is coated, a medical device with a rough surface that could abrade sterile barrier materials, or a polished medical device that could be scuffed by the sterile barrier materials.
- g) **Shelf life:** It is important to understand if the medical device has an expiration date. This will guide the development in the planning/execution of stability testing of the packaging.
- h) **Ability to reconfigure:** Determine whether or not the medical device can be manipulated in order to fit in the packaging system. Some packaging systems require the medical device to be placed in the packaging system in a specific orientation. The ability to reconfigure the medical device is often an opportunity to decrease the size of the packaging system.

5.20.2.4 Medical device protection guidance

One of the main functions of a packaging system is to protect the medical device up to the point of use. In order to design a cost-effective packaging system, an assessment of the medical device sensitivities should be conducted. These sensitivities, along with factors such as the processing in manufacturing, sterilization, and handling in distribution and at the point of use will aid in determining the overall medical device protection requirements. Understanding these requirements will help to make decisions regarding material selection for both the SBS and the protective packaging.

An assessment of medical device protection requirements should at minimum include the following:

- a) Temperature sensitivities: Determine if there are any limitations on the exposure of the medical device to temperature extremes. This could determine whether or not the medical device will require a controlled environment during distribution.
- b) Humidity/moisture: Determine if there are any limitations on the exposure of the medical device to humidity extremes or moisture. If a device is sensitive to moisture, the packaging can provide a barrier or resistance to moisture ingress.
- c) Light: Determine if there are any limitations on the exposure of the medical device to ultraviolet (UV) or visible light.
- d) Oxygen: Determine whether the medical device is sensitive to oxygen.
- e) Shock forces: Determining the amount of shock the medical device can handle in the absence of packaging will help determine the amount of shock protection required from the packaging system (e. g. force resulting from drop/impact). It is also important to understand if the medical device is more susceptible to shock forces in a particular orientation. Healthcare users should refer to instructions for use for more information on this topic.
- f) Vibration: Determine if the medical device is sensitive to vibration. It is often helpful in the design of a packaging system to know the resonant frequency of the medical device; this will help determine the amount of protection required.
- g) Duration: the amount of time the medical device needs to be protected by the SBS and/or packaging system.

See Annex C of this document for the use of FMEA (Failure Mode and Effect Analysis) or risk management techniques to address risk of the product and/or packaging system.

Healthcare users should refer to the handling, distribution and storage checklist in Annex H of this document.

5.21 Sterile fluid path (ISO 11607-1:2019, 6.2.4, 6.2.5)

5.21.1 Intent

When sterile fluid path assemblies are considered an SBS, they are to be identified as such and follow key requirements.

5.21.2 Guidance

Sterile fluid path packaging is defined as the system of protective port covers and/or packaging designed to maintain sterility of the portion of the medical device intended for contact with fluids.

NOTE For example, the interior of the tubing for administration of an intravenous fluid needs to be sterile while the sterility of the outer surfaces could not be required.

Sterile fluid path packaging is typically closed with tortuous path closures. Examples of closures are luer caps, spike caps, drip chamber caps, etc.

A sterile fluid path is a special case when it comes to an SBS, which is why there is a specific definition in ISO 11607-1. In a sterile fluid path system, fluids flow through a lumen. The critical characteristic is that the inside of the tube is sterile. This contrasts with a typical medical device, where it is critical that the outside of the instrument is sterile. The sterility of the sterile fluid path system is maintained by the closure system of the fluid path, and it should be demonstrated that the closure system maintains sterility until point of use. Sterility validation is usually conducted by exposure to an aerosol of spores followed by sterility testing of the lumen.

Simulated distribution (e. g. shock and vibration) should be done to assure that the integrity of the sterile fluid path remains intact, i.e. closures do not fall off or become loose. Acceptance criteria for the integrity of the sterile fluid path closures should be developed.

As many sterile fluid path systems are packaged in pouches, a common SBS, it is important to determine in each case what (e. g. the pouch or the closures such as luer cap, spike caps, etc.) is providing the sterile barrier and to make sure that the package is labelled accordingly. Without such labelling an end user could assume the pouch is providing the sterile barrier. If the sterile fluid pathway is labelled as such, then the pouch enclosing can be considered protective packaging and validated as part of the packaging system.



Figure 1 — Sterile fluid path symbol — ISO 7000-3084

The symbol in Figure 1, when placed on the medical device packaging, indicates the presence of a sterile fluid path within the medical device in cases when other parts of the medical device, including the exterior, might not be supplied sterile.

To make sure the end users understand the function of a pouch containing the sterile fluid path, it is recommended to use the symbols referred to under 5.17 of this document.

NOTE ISO 15223-1^[58] includes symbols for SBSs (see also 5.17.2 of this document).

Some examples of sterile fluid path products include:

- Collection devices: drainage bags, vials, syringes.
- Administration devices: feeding bags, syringes.

5.22 Usability evaluation for aseptic presentation (ISO 11607-1:2019, 7.1, 7.2 and 7.3)

5.22.1 Intent

The intent of these subclauses is to describe specific requirements for a usability evaluation to demonstrate that an SBS allows for aseptic presentation.

5.22.2 Guidance

The SBS should facilitate an adequate opening performance in order to allow for the medical device to be dispensed aseptically to reduce the risk of microbial contamination of the contents. Usability evaluation is intended to address these risks and demonstrate effective risk control. This is fundamental for sterile medical device packaging. If the SBS is difficult to open, the likelihood of contamination can increase. When a sterile medical device is contaminated, it should not be used. Seal fiber tear is an example of an opening defect that could be considered a source of contamination by a healthcare user.

The usability evaluation may be conducted in real or simulated environments. ISO 11607-1:2019 requires that the study give consideration of the different end users, for example:

- Healthcare environment: trained personnel for opening SBS, trained in sterile field, experienced, accustomed to several different SBS forms. The study can consider a healthcare user with minimal training and/or experience.
- Home environment: lay person, no training, potentially no experience opening these sorts of packages. Patients could have limited strength and dexterity limiting their ability to easily open an SBS.

The following practices can be employed to create a robust usability evaluation:

- a) The evaluation should address the hazardous situations that have been identified in the design process for aseptic presentation following the requirements under 5.13 c) of this document.
- b) Evaluation participants should represent end users, and should wear appropriate surgical/clinical attire, as applicable.
- c) Attributes of the use environment should be represented in the evaluation.
- d) Observe and document participant behaviour to assess participants' adherence to the instructions and to identify errors/problems.
- e) Afterwards, ask the participants about difficulties, problems or hesitations, and for feedback regarding unclear instructions (wording/symbols/graphics) in case instructions for use are being used. Validate significant changes to the instructions.
- f) It is recommended to include potential use scenarios not aligned with the intended use by the designer/manufacture (intentional or unintentional misuse of the SBS, abnormal use as defined in IEC 62366-1^[60]). This could also be a regulatory requirement in some jurisdictions.

Usability evaluations for aseptic presentation can be done together with usability evaluations for the devices, and sample sizes can be aligned.

NOTE Reference IEC 62366-1^[60] for further guidance.

5.23 Leveraging usability evaluations (ISO 11607-1:2019, 7.4)

5.23.1 Intent

It can be an efficient and cost-effective way to evaluate the usability of SBS families by using the worst-case configuration to evaluate the design.

5.23.2 Guidance

It is common for both manufacturers and healthcare facilities to utilize similar SBS configurations for families of products that are similar. In these situations, organizations can embark on an efficient approach by grouping SBSs that can be considered equivalent based on a number of factors. Such factors could include:

- a) multiple sizes of preformed SBSs that are common to industry (e.g. chevron opening, corner-peel, etc.);
- b) multiple sizes of rigid SBS (tray/lid) in which the means of opening and dispensing of the contents present an equivalent risk of contamination (e.g. same clearance for a gloved hand to pick contents).

For legacy SBSs that have been in the market, historical data can be leveraged to document the evaluation of the usability for aseptic presentation.

Manufacturers should review the impact on aseptic presentation in case of design changes to the device. Post market surveillance can be a data source for understanding the usability of the marketed SBS. Historical data can often be leveraged when adopting a new but similar product into an established/validated SBS. Leveraging historical data is applicable to both healthcare facilities and medical device manufacturers.

5.24 Usability evaluation failures (ISO 11607-1:2019, 7.5)

5.24.1 Intent

When the steps for the usability evaluation are conducted and the requirement is not met, additional information can be provided to the end user or the SBS could be redesigned to achieve the objective. If a redesign is made or additional information is provided, ISO 11607-1:2019 requires that a subsequent usability evaluation is conducted.

5.24.2 Guidance

In the event, that the usability evaluation fails to demonstrate the steps outlined in ISO 11607-1:2019, 7.2, risk management is deployed to resolve this issue as described below.

If the steps outlined in ISO 11607-1:2019, 7.2 are not initially met:

- a) Investigate:
 - Document the failure(s) and determine any primary and contributing root causes. It is very important to understand if the cause of a failure can be attributed to the design of the SBS or to the end user's comprehension of how to use the SBS.
- b) Correct:
 - Based on the results of the investigation and the documented root cause, perform corrective actions.
 - If the root cause was the design of the SBS, a design change or redesign should be performed.
 - If the root cause was end user comprehension, additional information can be provided to the end user to aid the usability of the SBS.
- c) Re-evaluate usability:
 - If the SBS design is changed based on the results of a usability evaluation, ISO 11607-1:2019, 7.2 requires that the redesigned SBS demonstrate that the steps can be met. If the design change addresses only one design feature, then the subsequent usability evaluation can focus on usability of that specific feature.
 - If additional information is to be provided to the end user, ISO 11607-1:2019, 7.2 requires that the usability evaluation include an assessment of the ability for an end user to follow that information and subsequently perform the steps successfully.

5.24.3 Guidance on formative and summative studies

Usability testing is a methodology for assessing whether a design is meeting its intended use (or ease of use) when an end user is interacting with the design. This methodology can be approached by formative studies gaining insights of end user's acceptance of the design, which can then be demonstrated with a summative study confirming design acceptance by end users.

5.24.3.1 Formative studies

The following questions can be useful in a formative study for usability:

- a) Initial evaluation of the design usability. A formative study can indicate how intuitive a design is for the end user to interpret how to use the SBS. The formative study is an optional study; one can proceed directly to a summative study.

- Is labelling sufficient?
- Is opening location understood?
- Is the opening technique and dispensing method understood?

NOTE Usability evaluation can also be an opportunity to verify if disposal is understood, if applicable and required by regional regulations.

- b) Outcome of the formative study can be a refinement in the design or labelling, or it can confirm readiness for a summative evaluation.

5.24.3.2 Summative studies

- a) Final confirmation of the usability requirement.
- b) The outcome of the summative study is the demonstration that an end user can aseptically open and dispense the contents of the SBS by meeting the steps in ISO 11607-1:2019, 7.2.

NOTE The IEC 62366-1^[60] standard and US FDA guidance “Applying Human Factors and Usability Engineering to Medical Devices^[61]” contain significantly more detail on performing usability evaluations and can be a valuable resource when evaluating the usability of an SBS.

5.25 Packaging system performance and stability (ISO 11607-1:2019, 8.1)

5.25.1 Intent

The intent of ISO 11607-1:2019, 8.1 is to set performance and stability testing requirements to the final design, and to describe the purpose and importance of integrity testing and also the difference between performance and stability testing as outlined in ISO 11607-1:2019, 8.2 and 8.3.

5.25.2 Guidance

5.25.2.1 Significance of integrity testing

After sterility is achieved in a validated sterilization process, the most important acceptance criterion of the packaging system design is retaining/maintaining this sterility. This can be confirmed by testing the integrity of the SBS. Testing for sterility is often considered a less effective method for several reasons:

- risk of false negatives and false positives;
- impossibility of demonstrating the presence of one viable microorganism in one million sterilized products by testing (need to test minimum 1 million negatives);
- sterility result is only the status at a single point in time and depends on several aspects, e.g. if exposure to dry conditions or high temperature was conducted just before testing for sterility, then SBSs could be broken but sterile contents could likely pass sterility testing as typical bacteria would likely not survive the exposures.

Thus, SBS integrity becomes an essential element for a medical device that is supplied in the sterile state. The SBS integrity provides confidence that the medical device remains in a sterile condition to the point of use and facilitates the aseptic delivery of that medical device. ISO 11607-1:2019 regards the loss of sterility as event related rather than time related. Such events occur during the handling, distribution and storage of medical device products and are usually catastrophic in nature, i.e. occurs in conjunction with a physical breach of the SBS. Exposures to excessive and frequent temperature and pressure variations during storage and transport or wetting of SBSs are also considered as events.

Test methods associated with package integrity can be used to discover possible physical breaches in the SBS, which jeopardize the microbial barrier.

5.25.2.2 Before testing

SBSs submitted for the packaging system design validation should be manufactured under standard operating procedures. Packaging systems need to be sterilized using a validated sterilization process. The sterilization challenge should be elevated by considering worst-case, multiple sterilization cycles and/or sterilizer process tolerances, as applicable. If a manufacturer decides to validate multiple sterilizations to be able to resterilize a load, then this needs to be applied to the packaging system as well. The packaging systems for performance testing should contain the actual medical device or a surrogate of the medical device (which is suitable in terms of mass and surface geometry), appropriate labelling, and IFUs expected to be included in the final market packaging system.

If sufficient stability or performance data of similar SBS design exists, it should not be necessary to redo testing unless it is evident that the contents inside the system could pose a risk to the SBS or materials. An example could be a new size of a plastic syringe in the same sterile pouch used for other sizes. The effects of physical interaction by a heavier syringe would be shown in performance testing and not in stability studies.

5.25.2.3 Separation of performance and stability testing

ISO 11607-1:2019 is clear regarding the separation of SBS stability testing from packaging system performance testing and regards them as separate entities. The standard does not preclude the user from combining these tests but doing so imposes unrealistic stresses on the test samples which can result in failures not experienced during normal storage and distribution. There are several reasons why stability testing and packaging system performance testing should not be combined.

- Combining both stability and design performance tests could expose the packaging systems to excessive conditions and stresses not seen in normal distribution environments. For example, accelerated aging quite often exposes SBS samples to continuously elevated temperatures (e.g. 55 °C) for extended periods of time (several months). Protective packaging can be significantly weakened to an extent that could cause failures during performance testing.
- If a failure occurs during performance testing of aged packaging systems or SBS, it is difficult if not impossible to determine the root cause. Was it a failure due to aging (time) or was it a package design performance issue (event)?

Users should also refer to Annex I of this document for guidance on failure investigations.

5.25.2.4 Different methods for integrity testing

SBS integrity can be measured in different ways. Annex B of ISO 11607-1:2019 lists several applicable tests for sterile barrier integrity, including:

- Visual inspection: Channel defects in SBS seals can be detected with good probability by applying ASTM F1886/F1886M^[62]. Despite certain material limitations, for example pinholes and minute tears, it is a valuable method for monitoring of seal integrity. Other tools that have also been useful include polarized light and black light. These are generally not employed as the sole methods by which SBSs are evaluated during initial SBS and/or packaging system, but frequently serve as an in-process check during regular SBS and/or packaging system production.
- Dye penetration: ASTM F1929^[63] involves the wicking of a dye solution through a seal channel defect with porous materials and ASTM F3039^[64] involves the wicking of a dye solution through a material defect or a seal channel defect on nonporous materials. This is a common test for seal validation if seal quality has not yet been correlated with visual inspection. Dye tests can be affected by the materials used, and operator training and experience. Depending on the nature of the materials and particularly if they are porous, it is essential to perform the dye test following the recommendations of ASTM F1929^[63] in terms of timing to avoid the dye from wicking into the