American National Standard

ANSI/AAMI/ISO 11607:2000

Packaging for terminally sterilized medical devices

AAMI Association for the Advancement of Medical Instrumentation

The Objectives and Uses of AAMI Standards and Recommended Practices

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

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

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

Although a device standard is primarily directed to the manufacturer, it may also be of value to the potential purchaser or user of the device as a fume of reference for device evaluation. Similarly, even though a recommended practice is usually oriented towards health care professionals, it may be useful to the manufacturer in better understanding the environment in which a medical device will be used. Also, some recommended practices, while not addressing device performance criteria, provide guidelines to industrial personnel on such subjects as sterilization processing, methods of collecting data to establish safety and efficacy, human engineering, and other processing or evaluation techniques; such guidelines may be useful to health care professionals in understanding industrial practices.

In determining whether an AAMI standard or recommended practice is relevant to the specific needs of a potential user of the document, several important concepts must be recognized:

All AAMI standards and recommended practices are *voluntary* (unless, of course, they are adopted by government regulatory or procurement authorities). The application of a standard or recommended practice is solely within the discretion and professional judgment of the user of the document.

Each AAMI standard or recommended practice reflects the collective expertise of a committee of health care professionals and industrial representatives, whose work has been reviewed nationally (and sometimes internationally). As such, the consensus recommendations embodied in a standard or recommended practice are intended to respond to clinical needs and, ultimately, to help ensure patient safety. A standard or recommended practice is limited, however, in the sense that it responds generally to perceived risks and conditions that may not always be relevant to specific situations. A standard or recommended practice is an important *reference* in responsible decision-making, but it should never *replace* responsible decisionmaking.

Despite periodic review and revision (at least once every five years), a standard or recommended practice is necessarily a static document applied to a dynamic technology. Therefore, a standards user must carefully review the reasons why the document was initially developed and the specific rationale for each of its provisions. This review will reveal whether the document remains relevant to the specific needs of the user.

Particular care should be taken in applying a product standard to existing devices and equipment, and in applying a recommended practice to current procedures and practices. While observed or potential risks with existing equipment typically form the basis for the safety and performance criteria defined in a standard, professional judgment must be used in applying these criteria to existing equipment. No single source of information will serve to identify a particular product as "unsafe". A voluntary standard can be used as one resource, but the ultimate decision as to product safety and efficacy must take into account the specifics of its utilization and, of course, cost-benefit considerations. Similarly, a recommended practice should be analyzed in the context of the specific needs and resources of the individual institution or firm. Again, the rationale accompanying each AAMI standard and recommended practice is an excellent guide to the reasoning and data underlying its provision.

In summary, a standard or recommended practice is truly useful only when it is used in conjunction with other sources of information and policy guidance and in the context of professional experience and judgment.

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Requests for interpretations of AAMI standards and recommended practices must be made in writing, to the Manager for Technical Development. An official interpretation must be approved by letter ballot of the originating committee and subsequently reviewed and approved by the AAMI Standards Board. The interpretation will become official and representation of the Association only upon exhaustion of any appeals and upon publication of notice of interpretation in the "Standards Monitor" section of the *AAMI News.* The Association for the Advancement of Medical Instrumentation disclaims responsibility for any characterization or explanation of a standard or recommended practice which has not been developed and communicated in accordance with this procedure and which is not published, by appropriate notice, as an *official interpretation* in the *AAMI News.*

American National Standard

ANSI/AAMI/ISO 11607:2000
(Revision of ANSI/AAMI/ISO 11607:1997)

Packaging for terminally sterilized medical devices

Approved 16 October 2000 by
Association for the Advancement of Medical Instrumentation

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American National Standards Institute, Inc.

Abstract: This standard specifies the requirements for single-use materials and reusable containers used for packaging of terminally sterilized medical devices, whether produced industrially or in health care facilities.

Keywords: packaging, terminally sterilized, medical device, seal

AAMI Standard

This Association for the Advancement of Medical Instrumentation (AAMI) standard implies a consensus of those substantially concerned with its scope and provisions. The existence of an AAMI standard does not in any respect preclude anyone, whether they have approved the standard or not, from manufacturing, marketing, purchasing, or using products, processes, or procedures not conforming to the standard. AAMI standards are subject to periodic review, and users are cautioned to obtain the latest editions.

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Glossary of equivalent standards

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

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

International designation	U.S. designation	Equivalency
IEC 60601-1-2:2001	ANSI/AAMI/IEC 60601-1-2:2001	Identical
IEC 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 & Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:1998	Major technical variations
ISO 5840:1996	ANSI/AAMI/ISO 5840:1996	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996	Identical
ISO 10993-1:1997	ANSI/AAMI/ISO 10993-1:1997	Identical
ISO 10993-2:1992	ANSI/AAMI/ISO 10993-2:1993/(R)2001	Identical
ISO 10993-3:1992	ANSI/AAMI/ISO 10993-3:1993	Identical
ISO 10993-4:1992	ANSI/AAMI/ISO 10993-4:1993	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:1994	ANSI/AAMI/ISO 10993-6:1995/(R)2001	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995/(R)2001	Identical
ISO 10993-8:2000	ANSI/AAMI/ISO 10993-8:2000	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999	Identical
ISO 10993-10:2001	ANSI/AAMI/ISO 10993-10:2001	Identical
ISO 10993-11:1993	ANSI/AAMI 10993-11:1993	Minor technical variations
ISO 10993-12:1996	ANSI/AAMI/ISO/CEN 10993-12:1996	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999	Identical
ISO 10993-14:2001	ANSI/AAMI/ISO 10993-14:2001	Identical
ISO 10993-15:2000	ANSI/AAMI/ISO 10993-15:2000	Identical
ISO 10993-16:1997	ANSI/AAMI/ISO 10993-16:1997	Identical
ISO 10993-17:2001	ANSI/AAMI/ISO 10993-17:2001	Identical
ISO 11134:1994	ANSI/AAMI/ISO 11134:1993	Identical
ISO 11135:1994	ANSI/AAMI/ISO 11135:1994	Identical
ISO 11137:1995	ANSI/AAMI/ISO 11137:1994	Identical
ISO 11138-1:1994	ANSI/AAMI ST59:1999	Major technical variations

International designation	U.S. designation	Equivalency
ISO 11138-2:1994	ANSI/AAMI ST21:1999	Major technical variations
ISO 11138-3:1995	ANSI/AAMI ST19:1999	Major technical variations
ISO TS 11139:2001	ANSI/AAMI/ISO 11139:2002	Identical
ISO 11140-1:1995 and Technical Corrigendum 1:1998	ANSI/AAMI ST60:1996	Major technical variations
ISO 11607:2003	ANSI/AAMI/ISO 11607:2000	Identical
ISO 11737-1:1995	ANSI/AAMI/ISO 11737-1:1995	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO TR 13409:1996	AAMI/ISO TIR 13409:1996	Identical
ISO 13485:1996	ANSI/AAMI/ISO 13485:1996	Identical
ISO 13488:1996	ANSI/AAMI/ISO 13488:1996	Identical
ISO 14155:1996	ANSI/AAMI/ISO 14155:1996	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998	Identical
ISO 14161: 2000	ANSI/AAMI/ISO 14161:2000	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO 14969:1999	ANSI/AAMI/ISO 14969:1999	Identical
ISO 14971:2000	ANSI/AAMI/ISO 14971:2000	Identical
ISO 15223:2000	ANSI/AAMI/ISO 15223:2000	Identical
ISO 15223/A1:2002	ANSI/AAMI/ISO 15223:2000/A1:2001	Identical
ISO 15225:2000	ANSI/AAMI/ISO 15225:2000	Identical
ISO 15674:2001	ANSI/AAMI/ISO 15674:2001	Identical
ISO 15675:2001	ANSI/AAMI/ISO 15675:2001	Identical
ISO TS 15843:2000	ANSI/AAMI/ISO TIR15843:2000	Identical
ISO TR 15844:1998	AAMI/ISO TIR15844:1998	Identical
ISO TR 16142:1999	ANSI/AAMI/ISO TIR16142:2000	Identical

Committee representation

Association for the Advancement of Medical Instrumentation
Sterilization Standards Committee

The adoption of ISO 11607:2000 as an American National Standard was initiated by the AAMI Packaging Working Group, which also functions as the U.S. Technical Advisory Group to the relevant work in the International Organization for Standardization (ISO). The AAMI Packaging Working Group functions under the auspices of the AAMI Sterilization Standards Committee. U.S. representatives from the AAMI Packaging Working Group (U.S. Sub-TAG for ISO/TC 198/WG 7, *Packaging*) played an active role in developing the International Standard.

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

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

Background of ANSI/AAMI adoption of ISO 11607:2000

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.

ISO 11607 was developed by ISO Technical Committee 198, *Sterilization of health care products,* to fill a need for an international standard for packaging for terminally sterilized medical devices. U.S. participation in ISO/TC 198 is organized through the U.S. Technical Advisory Group (TAG) for ISO/TC 198, administered by the Association for the Advancement of Medical Instrumentation on behalf of the American National Standards Institute (ANSI). The United States made a considerable contribution to this standard.

AAMI encourages its committees to harmonize their work with international standards as much as possible. Upon review of the Final Draft International Standard (FDIS) of ISO 11607:2003, the AAMI Sterilization Standards Committee and the AAMI Packaging Working Group (WG) decided to adopt ISO 11607 verbatim as a revision of the ANSI/AAMI standard. Owing to delays by ISO in issuing the final text, the year of the AAMI adoption precedes the year of ISO publication. In spite of this, ANSI/AAMI/ISO 11607:2000 is identical to ISO 11607:2003. The WG also amended its technical information report, TIR22, which provides additional guidance for those parties wishing to implement the requirements of ANSI/AAMI/ISO 11607, to correspond to ANSI/AAMI/ISO 11607:2000 (second edition).

As noted, this is the second edition of ANSI/AAMI/ISO 11607. The goal of the second edition was to harmonize the materials sections of ISO 11607 and EN 868-1, *Packaging materials and systems for medical devices which are to be sterilized—Part 1: General requirements and method*, as much as practicable. These changes were primarily organizational and editorial in nature. Consequently, there are many new notes in the second edition that outline the requirements that would have to be met if compliance with EN 868-1 is desired. While it was the committee's desire that these notes be self explanatory, additional information can be obtained by referring to EN 868-1. General requirements (quality systems, sampling, test methods, responsibilities, and documentation) that were dispersed throughout the first edition of the standard have been compiled and now constitute section 4 in the second edition.

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 comes to light.

Suggestions for improving this standard are invited. Comments and suggested revisions should be sent to: Standards Department, AAMI, 1110 N. Glebe Rd., Suite 200, Arlington, VA 22201-4795.

NOTE—Beginning with the ISO foreword on page ix, this American National Standard is identical to ISO 11607:2000.

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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 3.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this International Standard may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 11607 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This second edition cancels and replaces the first edition (ISO 11607:1997), which has been extensively revised.

Annex A forms a normative part of this International Standard. Annexes B and C are for information only.

Introduction

Many global medical device manufacturers and sterile packaging producers seek the ability to comply with both ISO 11607 and EN 868-1, *Packaging materials and systems for medical devices which are to be sterilized—Part 1: General requirements and test method*. However, differences remain where unharmonized ISO and EN standards exist and are referenced in one of the documents.

The goal of this revision is to enable the user to identify the differences that exist between ISO 11607 and EN 868-1. The specific differences are indicated in notes which describe the differences in general terms and provide a reference to specific clauses of EN 868-1:1997. It is necessary that those wishing to demonstrate compliance with EN 868-1 obtain a copy of that standard and not depend on the information on EN 868-1 contained in this International Standard.

The process of designing and developing a package for a terminally sterilized medical device is a complicated and critical endeavor. The device components and the package system should combine to create a total product that performs efficiently, safely, and effectively in the hands of the user.

The specific nature of the medical device; the intended sterilization method(s); and the intended use, shelf life, transport, and storage all influence the package design and choice of packaging materials.

Clause 5 of this International Standard specifies the basic attributes required of materials intended for use in packaging for terminally sterilized medical devices while considering the wide range of potential materials, medical devices, packaging designs, and sterilization methods that are available.

Based upon the complexities outlined above, determination that a material is appropriate for packaging of terminally sterilized medical devices should not be made without reference to this International Standard. European standards providing specifications for particular materials are published as the EN 868 series (see Bibliography).

The basic requirements described in this International Standard allow either the producer or the manufacturer to conduct a formal qualification to determine if a potential packaging material meets the performance requirements. Once it has been determined that a material adequately meets the performance requirements, product specifications may be established by the producer, manufacturer, or a regulatory body. From that point in time, compliance qualification of the material can be conducted to demonstrate that the material meets these stated specifications.

The development and validation of packaging operations are crucial to ensure package integrity to the users of sterile medical devices. There should be a documented process validation program demonstrating the efficacy and reproducibility of all sterilization and packaging processes. Along with the sterilization process, some of the packaging operations that can affect package integrity are forming, sealing, capping, or other closure systems, cutting, and process handling. Clause 6 provides manufacturers with a framework of activities to validate the process used to make and assemble the package.

The microbial barrier properties of packaging materials, together with suitable forming and sealing, are critical for ensuring package integrity and product safety. If no validated final package challenge method is available or applicable, the barrier properties of materials should be evaluated separately from the effectiveness of forming and sealing.

Clause 7 is intended to assist in the selection of tests and to provide criteria that can be used to evaluate the performance of packages for terminally sterilized medical devices.

It is intended that historical data and supporting rationale are acceptable for use in the verification of requirements of this International Standard.

NOTE—EN 868-1 was developed as a means to show compliance with relevant European Directives. If European health care facilities, e.g., hospitals, do not place medical devices on the market, they are not covered by the European Directives. Nevertheless, such health care facilities can fulfill the same requirements as manufacturers but can use alternative means to demonstrate conformity to EN 868-1.

Packaging for terminally sterilized medical devices

1 Scope

1.1 This International Standard specifies the requirements for single-use materials and reusable containers used for packaging of terminally sterilized medical devices, whether produced industrially or in health care facilities (see clause 6).

1.2 This International Standard outlines principal requirements for packaging process development and validation for the manufacturer of terminally sterilized medical devices (see clause 7). Forming and sealing are considered to be the most critical processes. Other process operations that can affect the final package are addressed also. Guidelines are provided for the most common practices and techniques.

1.3 This International Standard specifies requirements for essential criteria used to evaluate the performance of packages for sterile medical devices (see clause 7). The intent is to provide designers and manufacturers of medical devices with a framework of laboratory tests and evaluations that can be used to qualify the overall performance of the package used to protect device components during handling, distribution, and storage.

1.4 This International Standard does not cover all requirements for packaging for products manufactured aseptically; in such cases, additional requirements are necessary to ensure that the packaging and packaging process do not present a source of contamination of the product.

1.5 This International Standard is not applicable to protocols for sampling plans or the number and duration of replicate runs.

NOTE—For the purposes of this International Standard, hospitals or other organizations that package medical devices are considered to be manufacturers.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 5636-5:1986, *Paper and board—Determination of air permeance (medium range)—Part 5: Gurley method*

ISO 11140-1:1995, *Sterilization of health care products—Chemical indicators—Part 1: General requirements*

3 Terms and definitions

For the purposes of this International Standard, the following terms and definitions apply.

3.1 bioburden: Population of viable microorganisms on an item.

3.2 closure: Means used to close a package where no seal is formed.

EXAMPLE—Repeated folding to construct a tortuous path.

3.3 closure integrity: Condition of the closure that ensures that the closure presents a microbial barrier to at least the same extent as the rest of the packaging.

NOTE—In EN 868-1 the definition of this term differs slightly.

3.4 compliance qualification: Documented evidence that packaging meets the requirements for packaging for terminally sterilized medical devices based on testing for conformity to an agreed material specification.

3.5 development: Process of refining a prototype design or process to meet established product criteria.

3.6 failure: Event in which a component of the package does not perform one or more of its required functions within the specified limits under specified conditions.

3.7 failure analysis: Logical, systematic examination of an item to identify and analyze the probability, causes, and consequences of potential and real failures.

3.8 final package: Primary containment system in which the product is sterilized (excluding shelf cartons and shipping containers) that protects contents to the intended level over a specific period of time (c.f. **primary package** 3.18).

NOTE 1—The intended level may be e.g., a barrier to physical, microbial, or chemical challenges.

NOTE 2—In EN 868-1 the term “primary pack” is synonymous with the above definition. In EN 868-1 the term “pack” is synonymous with the term “package” used in this International Standard.

3.9 labeling system: Assembly of the package label and any supplied information on usage that is included within or in contact with the final package.

3.10 manufacturer: Natural or legal person, individual, or organization with the responsibility for packaging and/or sterilizing the medical device.

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

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

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

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

— control of conception;

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological, or metabolic means, but which may be assisted in its function by such means.

3.12 microbial barrier: Attribute of the packaging system that prevents the ingress of microorganisms under specified conditions.

NOTE—In EN 868-1 the definition of this term differs slightly.

3.13 package integrity: Unimpaired physical condition of a final package.

3.14 packaging compatibility: Attribute of the packaging material and/or system to allow it to achieve the required performance without detrimental effect on the medical device during transport, storage, or use.

3.15 packaging material: Any material used in the fabrication or sealing of a packaging system or primary package.

3.16 packaging system: One or more packaging materials assembled into a single unit intended as part or all of a primary package.

3.17 performance qualification: Documented evidence that packaging meets the appropriate requirements for sterile packaging based on testing of the particular packaging material for compliance with the applicable requirements of this International Standard.

3.18 primary package: Sealed or closed packaging system that forms a microbial barrier, enclosing a medical device.

3.19 producer: Natural or legal person, individual, or organization with the responsibility for manufacturing the packaging material and/or system.

3.20 product: Combination of both the medical device and/or additional components with the final package.

3.21 qualification: Documented evidence that all specified design and performance requirements are met.

3.22 revalidation: Documented procedure to reconfirm an established validation.

3.23 seal: Result of joining of packaging layers.

NOTE—A seal may be created, e.g., by use of adhesives or thermal fusion.

3.24 seal integrity: Condition of the seal that ensures that it presents a microbial barrier to at least the same extent as the rest of the packaging.

NOTE—In EN 868-1 the definition of this term differs slightly.

3.25 seal strength: Mechanical strength of the seal.

3.26 sterile: Free from viable microorganisms.

NOTE—For the purposes of EN 868-1, the term "sterile" is defined in EN 556.

3.27 sterile fluid-path packaging: System of protective port covers and/or packaging designed to ensure sterility of the portion of the medical device intended for contact with fluids.

3.28 sterilization compatibility: Attributes of the packaging material and/or system that allow it to both withstand the sterilization process and attain the required conditions for sterilization within the final package.

3.29 terminally sterilized: Term for medical devices that are sterilized after being completely sealed or enclosed in at least the primary package.

3.30 user: Natural or legal person, individual, or organization having the responsibility for making use of the product.

3.31 validation: Documented procedure for obtaining, recording, and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications.

NOTE—Validation is considered to be a total process that includes written protocol, evidence that the equipment as installed meets design criteria and specifications (equipment qualification), use of calibrated instruments to collect data, and evidence that the equipment can deliver the process within specified tolerances under established operating conditions and is reproducible as demonstrated by replicate runs and process challenges (process performance qualification).

4 General requirements

4.1 Quality systems

The activities described within this International Standard shall be carried out within a formal quality system.

NOTE 1—ISO 9001 gives requirements for suitable quality systems. It is not necessary to obtain third party certification of the quality system to fulfill the requirements of this International Standard.

NOTE 2—Health care facilities may use the quality system appropriate for their country or region.

4.2 Sampling

The sampling plans used for selection and testing of packaging materials and/or system shall be chosen by agreement between the producer and manufacturer, e.g. acceptable quality limit (AQL) in accordance with ISO 2859-1 or ISO 186:2002, or statistical process control (SPC). For each plan chosen, a rationale shall be documented.

4.3 Test methods

4.3.1 All test methods used to show compliance with this International Standard shall be validated. The selection of test methods, the variables to be determined, and the acceptance criteria shall be documented.

4.3.2 For some of the requirements, internationally accepted standardized test methods may be available. The use of these test methods is recommended, but these methods, as well as any other applied methods, shall be validated and documented.

Unless otherwise specified in the test methods for materials, test samples should be conditioned in accordance with ISO 187 at (23 $\pm$ 1) °C and (50 $\pm$ 2) % relative humidity.

NOTE 1—For compliance with EN 868-1, the above becomes a requirement (EN 868-1:1997, 5.2).

NOTE 2—The test methods listed in annexes B and C of this International Standard do not eliminate the need for validation nor do they exclude other validated test methods.

4.4 Responsibilities for package validation and for compliance and performance qualification

4.4.1 It shall be the responsibility of the manufacturer to ensure that the final package is validated in accordance with this International Standard.

4.4.2 The responsibility for conducting compliance qualification tests on materials shall rest with the producer.

NOTE—This does not preclude voluntary assumption of this responsibility by the manufacturer.

4.4.3 The responsibility for conducting performance qualification tests shall rest with the manufacturer.

4.5 Documentation

All procedures, and the results obtained used to demonstrate compliance with the requirements of this International Standard, shall be fully documented and retained securely in accordance with a formal quality system or for a specified period of time, considering factors such as expiry date of the packaging material and/or system, and traceability.

NOTE—When compliance with EN 868-1 also is desired, additional documentation is required (EN 868-1:1997, clause 6).

5 Packaging materials

5.1 General requirements

The intention of packaging for terminally sterilized medical devices is to maintain the sterility of the product with respect to its intended use, shelf life, transport, and storage conditions. The conditions under which the packaging material and/or system is produced, stored, transported, and handled shall be established, controlled, and documented, if applicable, in order to ensure that

— the conditions are compatible with the use for which the packaging material and/or system is designed,

— the performance characteristics of the packaging material and/or system is maintained.

As a minimum, the following shall be considered for all packaging materials and/or systems:

— temperature range;

— pressure range;

— humidity range;

— maximum rate of change of the above, where necessary;

— exposure to sunlight or UV light;

— cleanliness; and

— bioburden.

NOTE—The bioburden of the packaging material and/or system should be considered when determining the sterilization process parameters.

5.1.2 Raw materials used for the manufacture of packaging materials may be virgin or reclaimed materials, provided that the source, history, and traceability of all raw materials, especially recycled materials, is known and controlled to ensure that the finished product will consistently meet the requirements of this International Standard.

NOTE—With current commercial technologies, it is unlikely that reclaimed material other than manufacturing waste will be sufficiently controlled to allow its safe use for medical device packaging.

5.1.3 The packaging design and processing requirements shall be reviewed and applied against the material chosen. This should include effects of the sterilization process. Clauses 6 and 7 provide relevant performance criteria.

5.1.4 The following material properties shall be evaluated with appropriate test methods agreed upon by the producer and manufacturer:

a) microbial barrier;

b) toxicological attributes;

c) physical and chemical properties;

d) compatibility with respect to sterilization processes with which the material is intended to be used;

e) compatibility with respect to forming and sealing processes (see clause 6); and

f) any shelf-life limitations for pre-sterilization and post-sterilization storage of the packaging material.

5.1.5 Listed in 5.1.6 through 5.1.9 are some essential performance requirements that shall be considered for packaging for terminally sterilized medical devices. This list is not intended to be all-inclusive. The manufacturer shall decide the material characteristics that are necessary for each particular application. Materials which have characteristics not listed in clause 5 can be evaluated using the performance criteria given in clauses 6 and 7.

5.1.6 General packaging materials, e.g. wrapping materials, paper, plastic film, or nonwoven high density polyethylene (HDPE), shall meet the following general performance requirements.

a) Materials shall be non-leaching and odorless to such an extent that neither performance nor safety is impaired and the medical devices with which they are in contact are not adversely affected.

b) Materials shall be free of holes, cracks, tears, creases, or localized thickening and/or thinning sufficient to impair functioning.

c) Basis weight shall be consistent with the producer's stated value.

d) Materials shall exhibit an acceptable level of cleanliness.

e) Specific or minimum physical properties, such as tensile strength, thickness variation, tear resistance, air permeance, and burst strength, shall be established to meet the requirements of the medical device, packaging or sterilization process, or final package.

f) Specific chemical properties, such as pH value and chloride and sulfate contents, shall be established to meet the requirements of the medical device or packaging or sterilization process.

g) Packaging materials and/or systems shall not release material known to be toxic in sufficient quantity to cause a health hazard either before, during, or after sterilization under the conditions of use.

   NOTE—Evidence that the packaging material and/or systems does not contain material known to be toxic in sufficient quantity to cause a health hazard should be sufficient to meet this requirement.

h) If necessary, the biocompatibility of the packaging materials and/or systems shall be assessed with regard to the intended use of the medical device.

   NOTE—For selection of test methods for biocompatibility, see ISO 10993-1 for guidance.

5.1.7 In addition to the requirements given in 5.1.6, adhesive-coated materials shall meet the requirements listed below.

a) Coating patterns shall be continuous without skips or breaks in the pattern sufficient to cause a discontinuity in the seal.

b) Coating mass shall be consistent with the producer's stated value.

c) Materials shall demonstrate a minimum specified seal strength.

5.1.8 Formed packages shall meet the additional requirements listed below.

a) Components, e.g., materials, adhesive coating, ink, or chemical indicators, shall not react with, contaminate, transfer to, or adversely affect the product before, during, or after sterilization.

b) In addition to meeting the materials requirements given in 5.1.6 and, if appropriate, 5.1.7, formed packaging (e.g. paper bags, heat-sealable pouches and reels) shall comply with the requirements listed below.

   1) Packages shall meet producer's and manufacturer's specifications for seal width, burst, and/or seal strength.

   2) Process indicators printed on packages shall comply with ISO 11140-1.

   3) Packages that have peel-open characteristics shall have a peel that is continuous and homogeneous without delamination or tearing of the material that can affect aseptic presentation.

NOTE—Paper bags and heat-sealable pouches and reels have construction and package design requirements as well as performance requirements.

5.1.9 In addition to the general materials requirements given in 5.1.6 and, if appropriate, 5.1.7, reusable containers shall meet the requirements given below.

a) Each container shall be fitted with a tamper-evident system to provide a clear indication when the closure integrity has been compromised.

b) The sterilant port shall provide a barrier to microorganisms during removal from the sterilizer, transport, and storage (see 5.1.4).

c) Gaskets/seals shall provide a barrier to microorganisms as specified in 5.2.4.

d) The container shall be constructed to facilitate visual inspection of all essential parts. The producer shall specify the acceptance criteria to be used on visual inspection prior to each reuse.

e) The producer shall specify the service, cleaning procedures, and the manner of inspection, maintenance, and replacement of components.

5.2 Validation requirements

5.2.1 Packaging materials and systems shall meet the following requirements for sterilization process compatibility.

5.2.1.1 Means shall be provided to ensure that all packaging used in routine production is within the limits determined to be suitable for the sterilization process.

5.2.1.2 In specific cases where multiple sterilization cycles are required, the performance of the packaging materials shall be evaluated to ensure that the material performance remains within specified limits. This shall be the responsibility of the manufacturer.

5.2.1.3 Determination of suitability for the intended purpose shall include consideration of material variations that will occur during normal routine supply.

Where the product is enclosed by multiple wrappings, different limits on material properties may be set for inner and outer layers of packaging.

Determination of suitability may be carried out concurrently with validation of the sterilization process(es) to be used.

Testing of materials should assess the effect that the random variation of essential attributes can have on the performance of the material (e.g., thickness and/or pore size of porous materials).

5.2.1.4 Regarding the sterilization process specified, it shall be demonstrated and documented that the packaging material and/or system is suitable for use in the sterilization process for which it is intended by the producer of the packaging material and/or system (e.g., for ethylene oxide sterilization, this would include permeability to ethylene oxide gas, water vapor, and air). This shall include a demonstration that packaging materials and/or systems have, when necessary, sufficient permeance to air and the sterilant in order to permit the attainment of the required conditions for sterilization and to permit removal of sterilant after sterilization when assembled into a specified form for loading into the sterilizer. In addition, the physical properties of the material shall not be adversely affected over time by the sterilization process.

NOTE—If compliance with EN 868-1 is desired, sterilization compatibility should be determined using a sterilizer designed, constructed, and operated in accordance with the requirements of the relevant European Standard (EN 285, EN 550, EN 552, EN 554, EN 1422). Efforts are under way to harmonize these European Standards with International Standards.

5.2.1.5 When a sterilization process is not specified or when the packaging material and/or system is not specified as intended for the sterilization process to be used, the suitability of the packaging material and/or system for the sterilization process shall be established. This shall be done by validation of the final package in the sterilization process.

5.2.2 The following requirements shall be met regarding compatibility with the product to be packaged.

a) The suitability of the packaging material and/or system for use with the particular medical device shall be determined by the manufacturer. This shall include limiting values for physical characteristics of both the medical device as well as the stresses that will be imposed during sterilization and subsequent transport and storage.

b) Factors to be considered shall include:

   1) the mass and configuration of the medical device to be packed;

   2) the presence of sharp edges or protrusions;

   3) the need for physical and other protection; and

   4) the sensitivity of the medical device to particular risks, e. g., radiation, moisture, mechanical shock, static discharge.

NOTE—Documented historical evidence can be used for packaging materials and/or systems that have previously been used satisfactorily.

c) The manufacturer shall be responsible for ensuring that the packaging materials in combination with the specified sterilization and packaging processes do not adversely affect the safety and efficacy of the medical device.

d) The suitability of the packaging for use in protecting the particular medical device shall be determined by the manufacturer.

5.2.3 The following requirements shall be met regarding compatibility with the labeling system.

The labeling system shall:

a) not adversely affect the compatibility of the packaging material and/or system with the sterilization process to be used;

b) not be rendered illegible by the sterilization process to be used; and

c) not be printed or written in ink of a type which may be transferred to the medical device nor react with the packaging material and/or system to impair the utility of the packaging material and/or system nor change color to an extent which renders the label illegible.

For labels fixed to the surface of the packaging material and/or system, the attachment system shall withstand exposure to the sterilization process and the manufacturer's defined storage and transport conditions.

NOTE—Labels can take a number of forms, including labeling printed or written directly on the packaging material and/or system, or labels consisting of another layer of material attached to the surface of the packaging material and/or system by adhesion, fusion, or other means.

5.2.4 The following requirements shall be met regarding microbial barrier properties.

The microbial barrier properties of packaging materials are critical for ensuring package integrity and product safety. The methods used for evaluation of the microbial barrier properties are divided into two categories: those that are appropriate for impermeable materials and methods appropriate for porous materials.

a) The impermeability of a material shall be determined in accordance with annex A. Demonstrating that the material is impermeable shall satisfy the microbial barrier requirement.

b) The following requirements shall be met regarding porous materials.

   1) Porous materials shall provide an adequate microbial barrier to microorganisms in order to provide sterile package integrity and product safety.

   NOTE—There is no universally applicable method of demonstrating microbial barrier properties. Evaluation of the microbial barrier properties of porous materials is typically conducted by challenging samples with an aerosol of bacterial spores or particulates under a set of test conditions which specify the flowrate through the material, microbial challenge to the sample, and duration of the test. The microbial barrier properties of the material under these specified test conditions are determined by comparing the extent of bacterial or particulate penetration through the material with the original challenge. These methods provide a relative ranking of materials and do not predict performance under conditions other than the specified test conditions.

2) The producer of the material shall determine if the microbial barrier properties are adequate for the intended use as sterile packaging.

3) The manufacturer shall determine if the microbial barrier properties of a given material meet the criteria required for a specific package design.

c) The following requirements shall be met regarding microbial barrier test methods.

The microbial challenge method used to determine the microbial barrier properties shall first be validated by establishing a protocol, demonstrating acceptable repeatability of the method, and demonstrating the ability to differentiate among packaging materials, examples of which are described in national Pharmacopoeias and national standards.

NOTE 1—Test methods for determining the microbial barrier properties are available and in the course of preparation, but none has been accepted as a standardized international procedure at the time of publication of this International Standard.

NOTE 2—If a validated physical test method is found to correlate with a validated microbiological challenge method, the data from the physical test method are considered acceptable for determining the microbial barrier properties.

NOTE 3—As validated microbial challenge methods for materials and final packages (e.g., reusable containers) become available, they will be considered for inclusion in future editions of this International Standard.

NOTE 4—There are differences in the approach taken by ISO 11607 and EN 868-1 regarding microbial barrier testing. See EN 868-1:1997, 4.6.

5.3 Storage and Transport

5.3.1 The packaging material and/or system shall be wrapped to provide the protection necessary to maintain the performance characteristics of the packaging material and/or system during storage and transport under the specified conditions, if applicable.

5.3.2 As packaging materials can deteriorate during storage, the manufacturer shall ensure that the performance characteristics of the packaging material remain within specified limits (see 5.1 and 5.2) by either:

a) demonstrating retention of these characteristics under the manufacturer's defined storage conditions, or

b) ensuring that storage conditions remain within specified limits. These limits and conditions shall be determined by the producer.

5.4 Design Considerations

5.4.1 The packaging material and/or system shall be designed to minimize the safety hazard to user or patient under the intended specified use.

5.4.2 Once the appropriate packaging materials have been selected, the design of the final package shall include consideration of at least the following:

a) the compatibility of the packaging material and/or system with the medical device (i.e., that the packaging has no adverse effect on the medical device and vice-versa [see 5.2.2]);

b) the compatibility of the packaging material and/or system with the sterilization process (see 5.2.1);

c) the compatibility of the packaging material and/or system with the labeling system (see 5.2.3.);

d) the physical, chemical, and microbial protection provided by the packaging material and/or system; and

e) the compatibility of the packaging material and/or system with the user’s requirements at the point of use, e.g., aseptic opening.

NOTE—The requirements for the evaluation of the performance of the package design are included in clause 7.

6 Package forming and sealing

6.1 Equipment qualification

Before starting final process development, it shall be demonstrated that the process equipment and ancillary systems are capable of consistently operating within established design and operating limits and tolerances, including the following:

a) the ability to monitor key parameters;

b) written calibration specifications and schedules with certified calibration of all relevant instruments, sensors, displays, controllers, etc.;

c) documented inspection of forming/sealing or other closure systems, fixtures (tooling);

d) written preventive maintenance schedules and cleaning procedures;

e) software validation, if applicable; and

f) documented operator training.

6.2 Process development

6.2.1 The manufacturer shall conduct a process assessment to establish appropriate and necessary upper and lower processing limits. The assumption is made that materials have been selected in accordance with the requirements of clause 5 and the package design qualified in accordance with clause 7 to include compatibility with the intended sterilization process.

6.2.2 The following material compatibility requirements apply.

a) It is the responsibility of the manufacturer to ensure that all incoming packaging materials for forming and sealing meet predetermined requirements or specifications, including those of clause 5, and to select producers who have been assessed for their capability to produce materials which consistently meet design requirements.

b) Lot-to-lot variations will still exist in received lots of accepted materials that can influence the quality of the package produced. These variations shall be considered by the manufacturer during process development.

6.2.3 The following process design requirements apply.

a) The material characteristics shall be evaluated to determine those which have an effect on the final package.

b) Essential processing parameters shall be evaluated. These may include, but are not limited to:

   1) temperature;

   2) pressure/vacuum, including rate of change;

   3) dwell time (line speed);

   4) energy levels/frequency (radio frequency/ultrasonic); and

   5) torque limits for lid/cap closure systems.

c) The selected essential parameters shall produce a process that is capable of yielding final packages that meet predetermined design specifications.

It is recommended that a package failure analysis be conducted to establish process conditions that result in unacceptable packages. This analysis ensures that the upper and lower process limits are sufficiently removed from marginal and failure conditions.

6.2.4 The following process verification requirements apply.

a) Process verification shall be performed to challenge the process limits.

b) Packages shall be produced at both the upper and lower parameter limits and shall exhibit the properties that the manufacturer has defined for the final package (see clause 7). The following quality properties shall be considered

   1) For forming/assembling:

      — package completely formed/assembled;

      — product fits appropriately into package; and

      — essential dimensions met.

2) For sealing:

— total continuous seal width;

— punctures or tears;

— material delamination or separation; and

— channels or open seals.

3) For other closure systems:

— continuous closure;

— punctures or tears; and

— material delamination or separation.

c) Physical package performance testing (see 7.5) shall be performed with packages made at the upper and lower process limits or those made at worst-case conditions.

6.3 Process performance qualification

6.3.1 The process performance qualification shall include multiple production runs at specified operating conditions and shall demonstrate the effectiveness and reproducibility of the process.

NOTE—The results of the process development provide the supporting documentation for the process performance qualification.

6.3.2 Documented procedures and specifications for process control elements of packaging operations shall be established and incorporated into the process performance qualification. For machine systems these shall include

a) machine set-up procedures;

b) sealing and forming process parameters such as temperature, pressure, torque, and dwell time, including setting and tolerances;

c) valid test methods for package quality attributes such as seal width, continuity, and integrity; and

d) process start-up procedures.

6.3.3 Documented protocols shall specify an adequate number of test samples and replicate process runs to demonstrate reproducibility and variability within and between different runs. Essential process variables shall be monitored and recorded.

6.4 Process control

6.4.1 Either during or after the process validation, the manufacturer shall establish procedures to ensure that the packaging process will be under control during routine operation.

6.4.2 The manufacturer shall demonstrate adequate methods of process control and documentation.

6.4.3 Packaging and sealing process documents, including selection of packaging materials, shall be covered by a procedure for documenting, verifying, and authorizing change.

6.5 Process certification and revalidation

6.5.1 Process certification is a documented review and approval process carried out as a final step in the validation program. Supporting documentation shall be available in a technical summary. It may include:

a) a summary of the development and/or qualification work that has been done;

b) quantitative, qualitative, and/or statistically significant results;

c) references to the location of background technical data; and/or

d) discussion of major problems and corrective action taken to solve them.

6.5.2 Processes shall be revalidated if changes are made to the equipment, product, packaging materials, or packaging process which compromise the original validation and affect the sterility, safety, or efficacy of sterile medical devices.

7 Final (product) package

7.1 Test selection and sampling

7.1.1 The sampling plans used for selecting the test units shall be chosen by the medical device manufacturer based upon that manufacturer's requirements (e.g., AQL, SPC). For each method chosen, a rationale shall be documented.

7.1.2 Each test selection cannot be considered as a stand-alone procedure for final package acceptance. The tests shall be considered in their entirety to ensure a validated package system.

NOTE—Additional tests may be required for specific medical devices (e.g. antistatic properties for electronic components).

7.1.3 When test packages are not assembled on validated manufacturing lines, the packages shall be built using systems and processes that simulate anticipated manufacturing conditions as closely as possible.

7.2 Visual testing for sterile package integrity

7.2.1 General requirements for visual evaluation of package integrity

7.2.1.1 Any visual evaluation shall be performed by an inspector with normal visual acuity (corrected if necessary) under specified conditions of distance, illumination, illumination source, time, and magnification (if required).

7.2.1.2 All assessed defects shall be assigned categories that define actions to be taken by the manufacturer in the event that such defects are detected during normal production runs.

7.2.2 Inspection method

7.2.2.1 The external surface of the final package shall be inspected for defects such as

a) irregularities in or on the sterile barrier materials, such as tears, cracks, holes, or fractures;

b) presence of foreign material;

c) dimensional accuracy;

d) seal integrity (open or incomplete seals); and/or

e) presence of humidity, moisture, or staining.

7.2.2.2 Opened package samples shall be inspected for defects such as

a) foreign material, particularly on the device components;

b) any irregularities on the inside surfaces of the sterile barrier material, including tears, cracks, holes, and fractures;

c) seal attributes (irregular, non-homogeneous, or non-continuous seals); and/or

d) the presence of unacceptable humidity, moisture, or staining.

7.3 Seal/closure evaluation

7.3.1 The properties of the closure or seal of the package sample shall be evaluated in accordance with 7.3.2 to 7.3.5.

7.3.2 Regarding seal integrity, it shall be sufficient to demonstrate that the seal is impermeable and continuous by using physical tests. This, together with microbial barrier property testing of materials (5.1.4), establishes sterile package integrity.

7.3.3 The following requirements regarding seal strength apply.

7.3.3.1 The seal strength shall be determined at the upper and lower limits of defined critical sealing process variables and shall be demonstrated to be suitable for the intended purpose.

NOTE—When evaluating whether the package sealing process is under control, it is helpful to look for variations in seal strength values.

7.3.3.2 In determining the required limits for the seal strength, consideration shall be given to the strength of the material and whether or not the seal is intended to be peeled apart during aseptic removal of the product.

Various methods can be used to determine seal strength, e.g., tensile strength testing and burst/creep pressure testing. Examples of such methods include the following.

a) Tensile seal strength test (ASTM F-88, ASTM D-903 or equivalent)

   This test method measures the strength of the package seal by tensile testing a portion of that seal. It does not measure seam continuity or any other seal properties beyond the force required to tear (peel) apart the seal between two materials.

b) Burst/creep pressure test (ASTM F-1140 or equivalent)

   A final package pressure test used to evaluate overall minimum seal strength of the package by pressurizing the entire package to a point of failure (burst) or to a known critical value for a period of time (creep).

NOTE—There is no general correlation between tensile strength and burst/creep testing. They are separate tests and the results obtained have entirely different implications regarding package/seal strength.

7.3.4 The following requirements regarding closure integrity apply.

7.3.4.1 If a package is not closed by sealing (such as, but not limited to, sterilization wraps, packaging for sterile fluid-path products, and reusable containers), the closure system shall be demonstrated to provide acceptable microbial barrier properties.

7.3.4.2 For any performance requirement for the closure given in this International Standard, it shall be sufficient for the user to demonstrate that the closure is formed in strict accordance with the manufacturer's operating instructions.

7.3.5 The following requirements regarding peelable seals apply.

The seal shall be demonstrated to be uniform and, upon peeling, it shall be demonstrated that fiber shedding, and splitting or tearing of the package material are within limits specified by the manufacturer to ensure that the utility of the medical device is not impaired.

7.4 Physical testing for sterile package integrity

7.4.1 The following package integrity testing requirements apply.

The manufacturer shall demonstrate the integrity of the sterile package by testing the package. This can be accomplished by physical tests.

NOTE—When evaluating package integrity, it is assumed that the package design has met the requirements of 7.5, which documents the package's ability to protect the contents from damage and maintain sterile package integrity.

7.4.1.2 Specific methods and test values shall be determined by the manufacturer to take into consideration the specific package materials, design, and medical device.

7.4.1.3 Each test method shall have rationale statements, detailed test plans, step-by-step procedures, and good data collection.

Some examples of such physical test methods are described below.

a) Internal pressure test: Increase the internal pressure of the sterile package while it is submerged in water and note any escaping air bubbles.

b) Dye penetration test: Fill the package with a liquid containing a penetrating dye and observe any paths in the seal area or holes in the packaging material.

c) Gas sensing test: Pressurize the sterile package with a traceable gas and use appropriate gas sensors or other measuring equipment to detect holes in the materials or open paths in the seals.

d) Vacuum leak test: Immerse sealed packages in a test solution and apply vacuum. When the vacuum is released, the difference in pressure will force the test solution through any openings in the package.

7.4.2 The following sterilization compatibility testing requirements apply.

7.4.2.1 Final packages shall be tested for compatibility with the sterilization process. This should include both demonstration of attainment of sterilizing conditions within the package and the integrity and performance of the package after the sterilization process.

7.4.2.2 In instances where more than one sterilization run is allowed due to, for example, out-of-specification runs and/or correction of packaging defects, the manufacturer shall ensure that the final package remains suitable for use.

NOTE—Reprocessed packages may require further validation of residual sterilant levels. Reprocessed packages may also require enhanced levels of inspection for any detrimental effect of the medical device or sterilization process on the package, seal, or closure.

7.4.3 The following procedures for maintenance of package integrity requirements apply.

7.4.3.1 The ability of the final package to maintain its integrity over time can be evaluated using the same functional tests that are used to test the packaging material's microbial barrier properties (5.1.4), seal/closure integrity (7.3.2 and 7.3.4), and whole-package integrity (7.4.1).

NOTE—The loss of final-package integrity is usually regarded as event-related rather than time-related.

7.4.3.2 The manufacturer shall demonstrate that, under the rigors of distribution, storage, handling, and aging, the integrity of the final package is maintained at least for the claimed shelf life of the medical device under storage conditions specified by the manufacturer, as long as the package is undamaged or unopened.

7.4.3.3 Microbial barrier properties of the package shall be evaluated after exposure to the environmental stresses expected for a finished package.

This shall include demonstration of attainment of sterilizing conditions within the package and the integrity of the package after the sterilization process.

The environmental stresses should include consideration of forming the package, sterilization, handling, and storage.

NOTE—Whole-package microbial barrier testing is often impracticable. Equivalent evidence may be obtained by a combination of data from testing component materials, seals, etc., of the package.

7.4.3.4 For medical devices with a defined shelf life, the manufacturer shall have documented evidence that the performance of the packaging is not adversely affected by storage under specified conditions for a period not less than the shelf life of the medical device.

This shall be demonstrated by real-time aging tests. Accelerated aging tests may be undertaken in addition to real time aging tests by storage under conditions of increased severity. If accelerated aging tests are performed, a documented rationale for the accelerated aging conditions and test duration chosen shall be established. Accelerated aging may be regarded as sufficient evidence for claimed shelf life on the introduction of new products. This does not preclude the requirement to perform real-time aging tests.

These aging tests may be carried out on final packages, with or without including the medical device; it should be noted that the presence of a medical device could stress the package and cause changes in performance.

7.4.3.5 It shall be demonstrated that all the material properties given in 5.1 remain within the validated limits of the performance specification after exposure to the sterilization process and during storage under the manufacturer's specified conditions after sterilization.

7.4.3.6 The storage conditions before or after the materials are formed into packages can affect the nature and rate of deterioration. The storage and distribution conditions for the sterilized product in its packaging shall be defined by the manufacturer.

The following conditions shall be considered for all packaging:

a) temperature range;

b) pressure range;

c) humidity range;

d) where applicable, the maximum rate of change of the conditions a), b), and c); and

e) exposure to light.

NOTE 1—The flowrate of air through a permeable-barrier packaging material is influenced by the porosity of the material, the rate of temperature and pressure changes, the ratio of porous surface area to package volume, and package flexibility. The filtration efficiency of a material can be markedly affected by air flowrate.

NOTE 2—The storage conditions defined for the product by the manufacturer of the medical device could require tighter limits than are necessary for the packaging alone.

7.5 Physical testing of package performance

7.5.1 The performance of the package in providing adequate protection to the medical device through the handling, distribution, and storage systems shall be evaluated.

7.5.2 The packaging system shall ensure retention of the product in the correct orientation for aseptic removal.

7.5.3 The manufacturer shall define the limiting conditions for handling, distribution, and storage.

7.5.4 The manufacturer shall select test methods that are appropriate to determine whether the performance of the packaging is adversely affected by the distribution, storage, and handling system.

NOTE—For examples of tests that could be used to evaluate package performance in the handling, storage, and distribution systems, see annex B.

7.6 Documentation of testing

7.6.1 Before any performance testing is started, a test protocol shall be documented. This test protocol shall include

a) the design configuration to be qualified;

b) the tests to be performed;

c) the test sequence; and

d) product information such as mass, fragility levels, transport methods that will be used, and definitions of the product unit of sale configuration(s) to be qualified (e.g., one sterile barrier package, multipack container, pallet load).

7.6.2 This protocol shall also include pass/fail criteria for each attribute evaluated.

The test protocol should also include anticipated storage conditions and information regarding manufacturing systems and methods.

Annex A
(normative)

Test method for resistance of impermeable materials to the passage of air

A.1 Impermeable packaging materials shall be tested for air permeance in accordance with ISO 5636-5.

Test criterion: After not less than 1 h there shall be no visible movement of the cylinder, within the tolerance of ± 1 mm.

A.2 Other test methods may be used for routine monitoring and production testing. Those methods shall be validated against the reference test method for the material used. Examples of such methods are the method for dye penetration as described in annex C and the Schopper method for determination of air permeance, in accordance with ISO 5636-2.

NOTE—Conversion factors for different types of apparatus used in various methods for determination of air permeance are given in ISO 5636-1.

Annex B
(informative)

Evaluating package performance in distribution, storage, and handling systems

B.1 Evaluating package performance in the distribution system

Several methodologies are used to evaluate the performance of package design in the distribution environment. These protocols are used most often because they allow the engineer flexibility in developing a final test regime that matches the distribution environment of the manufacturer. They include:

a) ASTM D-4169, for shipping containers and systems;

b) ISTA Procedures 1 and 1A**,** for packaged products destined for shipment within the continent of origin;

c) ISTA Procedures 2 and 2A, for packaged products destined for export shipment outside the continent of origin.

B.2 Evaluating package performance in the storage system

The following method can aid in developing specific test protocols:

ASTM D-4332, *Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing*.

Other methods are being researched and documented, and may be considered in evaluating the performance of the package in the storage system.

B.3 Evaluating package performance in the handling system

B.3.1 The methodology for fabricating packages should be documented, and defined critical processing and handling steps should be evaluated for any effects detrimental to the finished end product. These steps would include:

a) cleaning;

b) forming/sealing/closure operations;

c) sterilization/subsequent processing; and

d) material handling and storage of incomplete package assemblies.

B.3.2 There are no documented test methodologies that detail these specific conditions. It is the responsibility of the manufacturer to develop specific conditions around this processing system. It is important to understand the interaction between all the manufacturing systems involved, to duplicate those systems with typical production-built quantities, equipment, tooling, and procedures, and to evaluate the packages for the effects of those systems.

Annex C
(informative)

Dye penetration test

C.1 Apparatus and reagents

The following equipment is necessary to perform the dye penetration test:

C.1.1 Weighted sponge, made from a block of cellulose sponge of nominal dimensions 100 mm × 75 mm × 82 mm bonded with a waterproof adhesive to a steel plate 110 mm × 75 mm such that the total mass is (800 ± 50) g.

C.1.2 Shallow tray, not less than 15 mm deep and of minimum dimensions 130 mm × 95 mm.

C.1.3 Absorption paper, white, medium, or medium/fast absorption filter, or chromatography paper.

C.1.4 Flat glass surface.

C.1.5 Dye solution, 1 g amaranth red per 100 mL aqueous solution containing 0.005 % cetrimide (a mixture of dodecyl-, tetradecyl-, and hexadecyltrimethylammonium bromide) as a wetting agent.

C.2 Sampling

Take five conditioned test specimens each with dimensions of not less than 250 mm x 105 mm. Identify the surface that will be on the inside of the final pack.

C.3 Test procedure

Place a piece of absorption paper (C.1.3) of size similar to the test specimen on the flat glass surface (C.1.4), and place the inside surface of the test specimen in contact with the absorption paper.

Pour the dye (C.1.5) into the shallow tray (C.1.2) and stand the sponge (C.1.1) in the tray for 1 min. Remove the sponge, draining surplus liquid off the edge of the tray.

Place the sponge on the test specimen, ensuring that the edge of the sponge is not within 15 mm of the edge of the test specimen, and allow to stand for 2 min.

Remove the sponge and test specimen, and examine the absorption paper for staining due to penetration of the dye through the test specimen. Repeat the procedure for the remaining test specimens.

C.4 Test report

Identify the origins of the test specimens.

Report the number of specimens for which staining of the absorption paper occurs.

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