TECHNICAL SPECIFICATION

ISO/TS 16775

Second edition

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

Emballages des dispositifs médicaux stérilisés au stade terminal — Lignes directrices relatives à l'application de l'ISO 11607-1 et l'ISO 11607-2

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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*.

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 current editions of ISO 11607-1 and ISO 11607-2;

— 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 to 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, 1 and ISO 11607-2:2019, 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 an SBS, 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 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 which case the rationale for these similarities should be documented. Risk management plans and related documentation for packaging systems can be combined with the 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.

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.

This initial estimation can be used for sample size calculations.

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, the rationale for the selection of an appropriate test shall 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