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Packaging for terminally sterilized medical devices —

Part 2: Validation requirements for forming, sealing and assembly processes

Emballages des dispositifs médicaux stérilisés au stade terminal —

Partie 2: Exigences de validation pour les procédés de formage, scellage et assemblage

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

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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 the following URL: www.iso.org/iso/foreword.html.

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

This second edition cancels and replaces the first edition (ISO 11607-2:2006), which has been technically revised. It also incorporates the amendment ISO 11607-2:2006/Amd.1:2014.

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

— terms and definitions for “process variable”, “process parameter” and “monitoring of processes” have been added;

— various definitions have been aligned with the latest version of ISO 11139;

— the terminology of “critical” process parameters has been discontinued and the concept of a process specification has been introduced to include all elements required to manufacture a product that consistently meets specifications.

A list of all parts in the ISO 11607 series can be found on the ISO website.

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

Packaging for terminally sterilized medical devices should be designed and manufactured to ensure that the medical device can be sterilized and remain sterile under documented storage and transport conditions until the sterile barrier system is damaged or opened.

One of the most critical characteristics of a sterile barrier system and packaging system for sterile medical devices is the assurance of sterility maintenance. Medical devices delivered in a sterile state should have been manufactured, packed and sterilized by appropriate, validated methods. The development and validation of packaging processes are crucial to ensure that sterile barrier system integrity is attained and will remain so until opened by the users of sterile medical devices.

There should be a documented process validation programme demonstrating the efficacy and reproducibility of all packaging and sterilization processes. Along with the sterilization process, some of the packaging operations that can affect sterile barrier system integrity are sealing, capping or other closure systems, cutting, form/fill/seal, assembly processes and subsequent handling. This document provides the framework of activities and requirements to develop and validate the process used to make and assemble the packaging system. Guidance for ISO 11607 series can be found in ISO/TS 16775.

The term “sterile barrier system” was introduced in 2006 to describe the minimum packaging required to perform the unique functions required of medical packaging: to allow sterilization, to provide an acceptable microbial barrier, and to allow for aseptic presentation. “Protective packaging” protects the sterile barrier system, and together they form the packaging system. “Preformed sterile barrier systems” would include any partially assembled sterile barrier systems such as pouches, header bags or hospital packaging reels.

The sterile barrier system is essential to ensure the safety of terminally sterilized medical devices. Regulatory authorities recognize the critical nature of sterile barrier systems by considering them as an accessory or a component of a medical device. Preformed sterile barrier systems sold to health care facilities for use in internal sterilization are considered medical devices in many parts of the world.

Packaging for terminally sterilized medical devices —

Part 2: Validation requirements for forming, sealing and assembly processes

1 Scope

This document specifies requirements for the development and validation of processes for packaging medical devices that are terminally sterilized. These processes include forming, sealing and assembly of preformed sterile barrier systems, sterile barrier systems and packaging systems.

It is applicable to industry, to health care facilities, and to wherever medical devices are packaged and sterilized.

It does not cover all requirements for packaging medical devices that are manufactured aseptically. Additional requirements can be necessary for drug/device combinations.

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 11607-1:2018, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

3 Terms and definitions

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

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

— ISO Online browsing platform: available at http://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
aseptic presentation
transfer of sterile contents from its sterile barrier system using conditions and procedures that minimize the risk of microbial contamination

[SOURCE: ISO 11139:2018, 3.13]

3.2
closure
<packaging> means used to complete a sterile barrier system where no seal is formed

EXAMPLE By a reusable container gasket or sequential folding to construct a tortuous path.

[SOURCE: ISO 11139:2018, 3.51, modified — The example has been added.]

3.3
control
regulation of variables within specified limits

[SOURCE: ISO 11139:2018, 3.63]

3.4
expiry date
date by which product should be used

Note 1 to entry: For the purpose of this document and ISO 11607-1, expiry date refers to the medical device in a sterile barrier system. The term "use by date" is used to describe the shelf life of packaging materials and *preformed sterile barrier systems* (3.13) prior to assembly into a *sterile barrier system* (3.25).

[SOURCE: ISO 11139:2018, 3.110, modified — The Note 1 to entry has been added.]

3.5
installation qualification
IQ
process of establishing by objective evidence that all key aspects of the process equipment and ancillary system installation comply with the approved specification

[SOURCE: ISO 11139:2018, 3.220.2]

3.6
labelling
label, instructions for use and any other information that is related to identification, technical description, intended purpose and proper use of the health care product but excluding shipping documents

[SOURCE: ISO 13485:2016, 3.8, modified — The term "medical device" has been replaced by "health care product".]

3.7
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

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

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

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

— supporting or sustaining life;

— control of conception;

— disinfection of medical devices;

— providing information by means of *in vitro* examination of specimens derived from the human body;

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

Note 1 to entry: Products which may be considered to be medical devices in some jurisdictions but not in others include:

— items specifically intended for cleaning or sterilization of medical devices;

— pouches, reel goods, sterilization wrap and reusable containers for packaging of medical devices for sterilization;

— disinfection substances;

— aids for persons with disabilities;

— devices incorporating animal and/or human tissues;

— devices for *in vitro* fertilization or assisted reproduction technologies.

[SOURCE: ISO 13485:2016, 3.11, modified — The first two list items in Note 1 to entry have been added.]

3.8
microbial barrier
property of a sterile barrier system to minimize the risk of ingress of microorganisms

[SOURCE: ISO 11139:2018, 3.169]

3.9
monitoring
continual checking, supervising, critically observing or determining the status in order to identify change from the performance level required or expected

[SOURCE: ISO Guide 73:2009, 3.8.2.1, modified — The note has been deleted.]

3.10
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[SOURCE: ISO 11139:2018, 3.220.3]

3.11
packaging system
combination of a *sterile barrier system* (3.25) and *protective packaging* (3.18)

[SOURCE: ISO 11139:2018, 3.192]

3.12
performance qualification
PQ
process of establishing by objective evidence that the process, under anticipated conditions, consistently produces a *product* (3.17) which meets all predetermined requirements

[SOURCE: ISO 11139:2018, 3.220.4]

3.13
preformed sterile barrier system
sterile barrier system (3.25) that is supplied partially assembled for filling and final closure or sealing

EXAMPLE Pouches, bags and open *reusable containers* (3.21).

[SOURCE: ISO 11139:2018, 3.201, modified — The example has been added.]

3.14
process parameter
specified value for a *process variable* (3.16)

Note 1 to entry: The specification for a process includes the process parameters and their tolerances.

[SOURCE: ISO 11139:2018, 3.211]

3.15
process specification
documented procedure that includes all equipment, process parameters, monitors and materials required to manufacture a product that consistently meets requirements

3.16
process variable
chemical or physical attribute within a cleaning, disinfection, packaging or sterilization process, changes in which can alter its effectiveness

EXAMPLE Time, temperature, pressure, concentration, humidity, wavelength.

[SOURCE: ISO 11139:2018, 3.213]

3.17
product
tangible result of a process

EXAMPLE Raw material(s), intermediate(s), sub-assembly(ies), healthcare product(s).

Note 1 to entry: For the purposes of this document and ISO 11607-1, products include *preformed sterile barrier systems* (3.13), *sterile barrier systems* (3.25) and contents within them.

[SOURCE: ISO 11139:2018, 3.217, modified — Note 1 to entry has been added.]

3.18
protective packaging
configuration of materials designed to prevent damage to the *sterile barrier system* (3.25) and its contents from the time of their assembly until the point of use

[SOURCE: ISO 11139:2018, 3.219]

3.19
repeatability
condition of measurement, out of a set of conditions that includes the same measurement procedure, same operators, same measuring system, same operating conditions and same location, and replicate measurements on the same or similar objects over a short period of time

[SOURCE: ISO/IEC Guide 99:2007, 2.20, modified — The term name has been simplified and the notes omitted.]

3.20
reproducibility
condition of measurement, out of a set of conditions that includes different locations, processors, measuring systems, and replicate measurements on the same or similar objects

Note 1 to entry: The different measuring systems may use different measurement procedures.

Note 2 to entry: A specification should give the conditions changed and unchanged to the extent practical.

[SOURCE: ISO/IEC Guide 99:2007, 2.24, modified — The term has been simplified.]

3.21
reusable container
rigid *sterile barrier system* (3.25) designed to be used repeatedly

[SOURCE: ISO 11139:2018, 3.235]

3.22
seal
<packaging> result of joining surfaces together by fusion to form a microbial barrier

Note 1 to entry: Surfaces can be joined together by, for example, adhesives or thermal fusion.

[SOURCE: ISO 11139:2018, 3.244 modified — The Note 1 to entry has been added.]

3.23
seal strength
mechanical capacity of the seal to withstand force

[SOURCE: ISO 11139:2018, 3.246]

3.24
sterile
free from viable microorganisms

[SOURCE: ISO 11139:2018, 3.271]

3.25
sterile barrier system
SBS
minimum package that minimizes the risk of ingress of microorganisms and allows aseptic presentation of the sterile contents at the point of use

[SOURCE: ISO 11139:2018, 3.272]

3.26
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

EXAMPLE The interior of the tubing for administration of an intravenous fluid.

[SOURCE: ISO 11139:2018, 3.273]

3.27
terminally sterilized
condition of a product that has been exposed to a sterilization process in its sterile barrier system

[SOURCE: ISO 11139:2018, 3.296]

3.28
validation
confirmation process, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled

Note 1 to entry: The objective evidence needed for a validation is the result of a test or other form of determination such as performing alternative calculations or reviewing documents.

Note 2 to entry: The word "validated" is used to designate the corresponding status.

Note 3 to entry: The use conditions for validation can be real or simulated.

[SOURCE: ISO 9000:2015, 3.8.13, modified — "process" has been added to the definition.]

4 General requirements

4.1 Quality systems

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

NOTE ISO 9001, ISO 13485, and ANSI/AAMI ST90 contain requirements for suitable quality systems. Additional requirements can be specified by a country or region.

4.2 Risk management

The activities described within this document shall consider risk management to medical devices.

NOTE ISO 14971 contains requirements for risk management to medical devices. Additional requirements can be specified by a country or region.

4.3 Sampling

The sampling plans used for testing of materials, sterile barrier systems or packaging systems shall be applicable to materials, sterile barrier systems or packaging systems being evaluated. Sampling plans shall be based upon statistically valid rationale.

NOTE Common statistically based sampling plans as given, for example, in ISO 2859-1 or ISO 186 (with appropriate modifications if necessary) can be applied to materials, sterile barrier systems or packaging systems. Additional sampling plans can be specified by countries or regions. For further guidance, see ISO/TS 16775.

4.4 Test methods

4.4.1 A rationale for the selection of appropriate tests for the packaging system shall be established and recorded.

4.4.2 A rationale for acceptance criteria shall be established and recorded.

NOTE Pass/fail is a type of acceptance criterion.

4.4.3 All test methods used to show conformity to this document shall be validated and documented by the laboratory performing the test.

NOTE Annex B of ISO 11607-1 contains a list of test methods. Publication of a method by a standards body does not make it validated in any laboratory.

4.4.4 The test method validation shall demonstrate the suitability of the method as used. The following elements shall be included:

— determination of test method repeatability;

— determination of test method reproducibility;

— establishment of test method sensitivity for integrity tests.

4.5 Documentation

4.5.1 Demonstration of conformity with the requirements of this document shall be recorded.

4.5.2 All records shall be retained for a specified period of time. The retention period shall consider factors such as applicable requirements, expiry date and traceability of the medical device or sterile barrier system.

4.5.3 Records of conformity with the requirements shall include, but is not limited to, performance data, specifications and test results from validated test methods as well as validation protocols, conclusions and any necessary actions.

4.5.4 Electronic records, electronic signatures and handwritten signatures executed to electronic records that contribute to validation, process control or other quality decision-making processes shall remain legible, readily identifiable and retrievable.

5 Validation of packaging processes

5.1 General

5.1.1 Preformed sterile barrier systems and sterile barrier system manufacturing processes shall be validated.

NOTE Examples of these processes include, but are not limited to, the following:

— pouch, reel, or bag forming and sealing;

— form/fill/seal automated processes;

— kit assembly and wrapping, including application of tape;

— assembly of sterile fluid-path products;

— tray/lid sealing;

— filling and closing of reusable containers;

— sterilization sheets folding and wrapping, including application of tape.

5.1.2 Process validation shall include, at a minimum, an installation qualification (IQ), an operational qualification (OQ), and a performance qualification (PQ), in this order.

5.1.3 A process specification shall be established for forming, assembly and sealing processes, including, but not limited to, the following elements:

— the required process output;

— the process variables and process (and/or product) attributes to be monitored in order to maintain the process in a state of control and capability;

— the process parameters for control to produce the specified process output.

NOTE 1 Process development, while not formally part of process validation, is considered an integral part of forming and sealing (see Annex A).

NOTE 2 Validation of existing products can rely on data from previous validations of existing products. That data can be used for determining the tolerances for process parameters.

5.1.4 When similar preformed sterile barrier systems and sterile barrier system manufacturing processes are validated, a rationale for establishing similarities and identifying the worst case configuration shall be documented. As a minimum, the worst case configuration shall be validated to determine conformity with this document.

NOTE For example, similarity can be established by different sizes of preformed sterile barrier systems made of the same or comparable raw materials.

5.2 Installation qualification

5.2.1 The IQ shall be performed including, as minimum, all elements to be listed in the process specification.

The following shall be considered:

— equipment design features;

— installation conditions, such as wiring, utilities, functionality, etc.;

— safety features;

— equipment operating within the stated design parameters;

— supplier documentation, prints, drawings and manuals;

— spare-parts lists;

— software and/or firmware validation;

— environmental conditions such as cleanliness, temperature, humidity, lighting;

— documented operator training;

— operating manual or procedure.

5.2.2 Tests shall be performed to confirm that process variables can be controlled as specified.

NOTE For further guidance, see Annex A.

5.2.3 Functions that allow process variable monitoring shall be checked or certified in place.

5.2.4 Alarms, warning systems or machine stops shall be challenged in the event that process variables exceed predetermined limits.

5.2.5 Specified instruments, sensors, displays, controllers, etc., shall be calibrated and have written calibration schedules.

5.2.6 There shall be written preventive maintenance and cleaning schedules.

5.2.7 The application of software systems shall be validated.

NOTE For software validation, see also ISO 13485:2016, 7.5.6 and Reference [14].

5.3 Operational qualification

5.3.1 Process variables shall be challenged to determine the upper and lower parameter limits that produce preformed sterile barrier systems and/or sterile barrier systems that meet all predetermined specifications.

NOTE See Annex A.

5.3.2 As a minimum, preformed sterile barrier systems and sterile barrier systems shall be produced at both the upper and lower process limits (see 5.3.1) and exhibit the properties that meet predefined specifications.

The following quality properties shall be considered.

a) For forming/assembly:

— sterile barrier system completely formed/assembled;

— product fits into the sterile barrier system;

— essential dimensions are met.

b) For sealing:

— seal strength;

— intact seal for a specified seal width;

— absence of channels or open seals;

— absence of punctures or tears;

— absence of material delamination for seals designed to be opened.

c) For other closure systems:

— continuous closure;

— absence of punctures or tears;

— absence of material delamination or separation.

5.4 Performance qualification

5.4.1 The PQ shall demonstrate that the process will consistently produce preformed sterile barrier systems and sterile barrier systems that meet predetermined requirements under anticipated operating conditions.

5.4.2 The PQ shall include the following:

— the actual or simulated contents, unless a rationale can be established that the contents are not required for process validation activities;

— nominal process parameters established in the OQ;

— verification of product/package requirements;

— assurance of process control and capability;

— process repeatability and reproducibility.

5.4.3 Challenges to the process shall include conditions anticipated to be encountered during manufacture.

NOTE These challenges can include, but are not limited to, machine set-up and change-over procedures; process start-up and restart procedures; power failure and variations; and multiple shifts, if applicable.

5.4.4 The PQ of the process shall include at least three production runs to assess variability within a run and reproducibility between different runs.

NOTE These process variations include, but are not limited to, machine warm up until equilibrium is reached, breaks and shift changes, normal starts and stops, and material lot-to-lot differences.

5.4.5 Documented procedures and/or process specifications for the forming, assembly, sealing or closing operations shall be established and incorporated into the PQ.

5.4.6 Specified process variables shall be monitored and recorded.

5.4.7 The process shall be under control and capable of consistently producing products according to predetermined requirements.

5.5 Formal approval of the process validation

5.5.1 Review and formal approval of the process validation shall be carried out and documented as a final step in the validation program.

5.5.2 The documentation shall summarize and reference all protocols and results, and state conclusions regarding the validation status of the process.

5.6 Process control and monitoring

5.6.1 Procedures shall be established, implemented and maintained to ensure that the packaging process is under control and within the established parameters during routine operation and consistently producing the specified process output.

5.6.2 Specified process variables shall be routinely monitored and records shall be maintained.

5.7 Process changes and revalidation

5.7.1 Processes concerning forming, assembly, sealing or closing shall be covered by a change-control procedure for documenting, verifying and authorizing change.

NOTE The change control procedure can include a check for the need to revalidate.

5.7.2 Processes shall be revalidated if changes are made to the equipment, contents, packaging materials or packaging process that compromise the original validation.

NOTE 1 The following list gives examples of changes that usually affect the status of a validated process:

— raw material changes that can impact the process variables;

— changes or exchanges to a main part of the equipment which can affect one or more of the established parameters;

— modification or refurbishment of equipment;

— transfer of processes and/or equipment from one facility or location to another, or relocation within the same facility;

— negative trends in quality or process control indicators.

NOTE 2 Installation of a new piece of equipment is not included in changes requiring revalidation but rather new process validation.

5.7.3 The need for revalidation shall be evaluated and documented. If the situation does not require that all aspects of the original validation be repeated, this revalidation does not have to be as extensive as the initial validation.

NOTE It is acceptable practice to keep design validation separate from process validation to allow for targeted root cause analysis in case of issues and to limit the effort of revalidation to only those aspects that are really affected.

5.7.4 Minor process changes shall be documented and can require review of the validation status.

NOTE Multiple minor changes are considered to be able to cumulatively affect the validation status of the packaging system.

6 Assembly

6.1 The sterile barrier system shall be assembled under appropriate environmental conditions to minimize the risk posed by contaminants to the medical device.

6.2 The packaging system assembly process shall follow controlled labelling and processing procedures to prevent mislabelling.

