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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

Reference number
ISO 11607-2:2006(E)

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. 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 document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 11607-2 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

ISO 11607-1 and ISO 11607-2 cancel and replace ISO 11607:2003, which has been technically revised.

ISO 11607 consists of the following parts, under the general title *Packaging for terminally sterilized medical devices*:

— *Part 1: Requirements for materials, sterile barrier systems and packaging systems*

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

Introduction

Medical devices delivered in a sterile state should be designed, manufactured and packed to ensure that they are sterile when placed on the market and remain sterile, under documented storage and transport conditions, until the sterile barrier system is damaged or opened. Additionally, medical devices delivered in a sterile state should have been manufactured and sterilized by an appropriate, validated method.

One of the most critical characteristics of a sterile barrier system and packaging system for sterile medical devices is the assurance of sterility maintenance. 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 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 sterile barrier system integrity are forming, sealing, capping or other closure systems, cutting and process handling. This part of ISO 11607 provides the framework of activities and requirements to develop and validate the process used to make and assemble the packaging system. ISO 11607-1 and ISO 11607-2 are designed to meet the Essential Requirements of the European Medical Device Directives.

One significant barrier to harmonization was terminology. The terms “package”, “final package”, “final pack”, “primary pack”, and “primary package” all have different connotations around the globe and choosing one of these terms to be the harmonized basis for this part of ISO 11607 was considered a barrier to successful completion of this document. As a result, the term “sterile barrier system” was introduced 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 healthcare facilities for use in internal sterilization are considered as 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 part of ISO 11607 specifies the requirements for 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.

This part of ISO 11607 is applicable to industry, to health care facilities, and wherever medical devices are packaged and sterilized.

This part of ISO 11607 does not cover all requirements for packaging medical devices that are manufactured aseptically. Additional requirements may also be necessary for drug/device combinations.

2 Normative references

The following referenced documents are indispensable for the application 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, *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.

3.1
expiry date
indication of the date, by which the product should be used, expressed at least as the year and month

3.2
installation qualification
IQ
process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification

[ISO/TS 11139:2006]

3.3
labelling
written, printed, electronic or graphic matter affixed to a medical device or its packaging system; or accompanying a medical device

NOTE Labelling is related to identification, technical description and use of the medical device but excludes shipping documents.

3.4
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[ISO/TS 11139:2006]

3.5
packaging system
combination of the sterile barrier system and protective packaging

[ISO/TS 11139:2006]

3.6
performance qualification
PQ
process of obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields product meeting its specification

[ISO/TS 11139:2006]

3.7
preformed sterile barrier system
sterile barrier system that is supplied partially assembled for filling and final closure or sealing

EXAMPLE Pouches, bags and open reusable containers

[ISO/TS 11139:2006]

3.8
process development
establishing the nominal values and limit(s) for critical process parameters

3.9
product
result of a process

[ISO 9000:2000]

NOTE For the purpose of sterilization standards, product is tangible and can be raw material(s), intermediate(s), sub-assembly(ies) and health care product(s).

[ISO/TS 11139:2006]

3.10
protective packaging
configuration of materials designed to prevent damage to the sterile barrier system and its contents until the point of use

[ISO/TS 11139:2006]

3.11
repeatability
closeness of the agreement between the results of successive measurements of the same particular quantity subject to measurement (measurand) carried out under the same conditions of measurement

NOTE 1 These conditions are called repeatability conditions.

NOTE 2 Repeatability conditions can include the following:

— the same measurement procedure;

— the same observer;

— the same measuring instrument, used under the same conditions;

— the same location; and

— repetition over a short period of time.

NOTE 3 Repeatability may be expressed quantitatively in terms of the dispersion characteristics of the results.

NOTE 4 Adapted from *International Vocabulary of Basic and General Terms in Metrology*,1993, definition 3.6.

3.12
reproducibility
closeness of the agreement between the results of measurements of the same particular quantity subject to measurement (measurand) carried out under changed conditions of measurement

NOTE 1 A valid statement of reproducibility requires specification of the conditions changed.

NOTE 2 The changed conditions may include:

— principle of measurement;

— method of measurement;

— observer;

— measuring instrument;

— reference standard;

— location;

— conditions of use; and

— time.

NOTE 3 Reproducibility may be expressed quantitatively in terms of the dispersion characteristics of the results.

NOTE 4 Adapted from *International Vocabulary of Basic and General Terms in Metrology*,1993, definition 3.7.

3.13
reusable container
rigid sterile barrier system designed to be repeatedly used

3.14
sterile barrier system
minimum package that prevents ingress of microorganisms and allows aseptic presentation of product at the point of use

[ISO/TS 11139:2006]

3.15
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

NOTE An example of sterile fluid-path packaging would be the interior of the tubing for administration of an intravenous fluid.

3.16
validation
〈process〉 documented procedure for obtaining, recording and interpreting the results required to establish that a process will consistently yield product complying with predetermined specifications

NOTE Adapted from ISO/TS 11139:2006.

4 General requirements

4.1 Quality systems

4.1.1 The activities described within this part of ISO 11607 shall be carried out within a formal quality system.

NOTE ISO 9001 and ISO 13485 contain requirements for suitable quality systems. Additional requirements may be specified by countries or regions.

4.1.2 It is not necessary to obtain third-party certification of the quality system to fulfil the requirements of this part of ISO 11607.

4.1.3 Health care facilities may use the quality system required by their country or region.

4.2 Sampling

The sampling plans used for selection and testing of packaging systems shall be applicable to the process being evaluated. Sampling plans shall be based upon a statistically valid rationale.

NOTE Examples of suitable sampling plans are specified in ISO 2859-1 or ISO 186. Additional sampling plans may be specified by countries or regions.

4.3 Test methods

4.3.1 All test methods used to show compliance with this part of ISO 11607 shall be validated and documented.

NOTE Annex B in ISO 11607-1:2006 contains a list of suitable test methods.

4.3.2 Test method validation shall demonstrate the suitability of the method used. The following elements shall be included:

— establishment of a rationale for the selection of the appropriate tests for the packaging system;

— establishment of acceptance criterion;

NOTE Pass/fail is a type of acceptance criterion.

— determination of test method repeatability;

— determination of test method reproducibility;

— determination of test method sensitivity for integrity tests.

4.3.3 Unless otherwise specified in the test methods, test samples shall be conditioned at (23 ± 1) °C and (50 ± 2) % relative humidity for a minimum of 24 h.

4.4 Documentation

4.4.1 Demonstration of compliance with the requirements of this part of ISO 11607 shall be documented.

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

4.4.3 Documentation of compliance with the requirements may include, but is not limited to, performance data, specifications, test results from validated test methods, and protocols and results from IQ, OQ, PQ.

4.4.4 Electronic records, electronic signatures, and handwritten signatures executed to electronic records that contribute to validation, process control or other quality decision-making processes shall be reliable.

5 Validation of packaging processes

5.1 General

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

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

— rigid and flexible blister forming;

— pouch, reel, or bag forming and sealing;

— form/fill/seal automated processes;

— kit assembly and wrapping;

— assembly of sterile fluid-path products ;

— tray/lid sealing;

— filling and closing of reusable containers;

— sterilization sheets folding and wrapping

5.1.2 Process validation shall include, at a minimum, an installation qualification, an operational qualification, and a performance qualification in this order.

5.1.3 Process development, while not formally part of process validation, should be considered as an integral part of forming and sealing (see Annex A).

5.1.4 Validation of existing products may rely on data from previous installation and operation qualification. That data can be used for determination of the tolerances for critical parameters.

5.1.5 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 compliance with this part of ISO 11607.

NOTE For example, similarity could be established by different sizes of preformed sterile barrier systems.

5.2 Installation qualification (IQ)

5.2.1 Installation qualification shall be performed.

Some installation qualification considerations are:

— 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 validation;

— environmental conditions such as cleanliness, temperature, humidity;

— documented operator training;

— operating manual or procedure.

5.2.2 Critical process parameters shall be defined.

5.2.3 Critical process parameters shall be controlled and monitored.

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

5.2.5 Critical process instruments, sensors, displays, controllers, etc. shall be certified as calibrated and have written calibration schedules. Calibration should be performed before and after performance qualification.

5.2.6 There shall be written preventive maintenance and cleaning schedules.

5.2.7 The application of software systems, such as programmable logic controller, data collection, and inspection systems, shall be validated to ensure that they function as intended. Functional tests shall be performed to verify the correct functioning of the software and hardware, and especially the interfaces. The system shall be checked (e.g. by entering correct and incorrect data, by simulating a loss of electrical power) to detect the availability, reliability, identity, accuracy and traceability of data or records.

5.3 Operational qualification (OQ)

5.3.1 Process parameters shall be challenged to assure that they will produce preformed sterile barrier systems, and sterile barrier systems, that meet all defined requirements under all anticipated conditions of manufacturing.

5.3.2 Preformed sterile barrier systems, and sterile barrier systems, shall be produced at both the upper and lower parameter limits, and shall exhibit the properties that meet predefined requirements. 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:

— intact seal for a specified seal width;

— channels or open seals;

— punctures or tears;

— material delamination or separation.

NOTE See EN 868-5:1999, 4.3.2 for an example of a seal width specification.

c) For other closure systems:

— continuous closure;

— punctures or tears;

— material delamination or separation.

5.4 Performance qualification (PQ)

5.4.1 The performance qualification shall demonstrate that the process will consistently produce acceptable preformed sterile barrier systems, and sterile barrier systems, under specified operating conditions.

5.4.2 Performance qualification shall include:

— the actual or simulated product;

— process parameters established in the operational qualification;

— 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 expected 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 Challenges to the process shall include at least three production runs with adequate sampling to demonstrate variability within a run and reproducibility between different runs. The duration of a production run should account for process variables.

NOTE These variables include, but are not limited to, machine equilibrium, breaks and shift changes, normal starts and stops, and material lot-to-lot differences.

5.4.5 Documented procedures and specifications for the forming, sealing and assembly operations shall be established and incorporated into the performance qualification.

5.4.6 Essential process variables shall be monitored and recorded.

5.4.7 The process shall be under control and capable of consistently producing product 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 to ensure that the packaging process is under control and within the established parameters during routine operation.

5.6.2 Critical process parameters shall be routinely monitored and documented.

5.7 Process changes and revalidation

5.7.1 Documents concerning packaging and sealing process shall be covered by a change-control procedure for documenting, verifying and authorizing change.

5.7.2 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.

NOTE The following is a list of changes which could affect the status of a validated process:

— raw material changes that would impact the process parameters;

— a new piece of equipment is installed;

— transfer of processes and/or equipment from one facility or location to another;

— sterilization-process changes;

— negative trends in quality or process control indicators.

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.

5.7.4 Periodic revalidation or reviews should be considered since multiple minor changes could cumulatively affect the validation status of the process.

6 Packaging system 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 package system assembly process shall follow controlled labelling and processing procedures to prevent mislabelling.

NOTE Additional guidance can be found in DIN 58953-7 and DIN 58953-8.

6.3 Package systems shall be assembled and filled according to the instructions based on a validated process that assures sterilization in a defined sterilization process. These instructions should include configuration of contents and organizing inserts, total weight, inner wrapping, and absorbent materials.

7 Use of reusable sterile barrier systems

In addition to the requirements listed in Clause 6, instructions and restrictions for use as specified in 5.1.10 and 5.1.11 of ISO 11607-1:2006 shall be followed (e.g. assembly, disassembly, maintenance, repair, storage).

NOTE For additional guidance on reusable containers, see EN 868-8, DIN 58953-9, and AAMI/ANSI ST33. For additional guidance on reusable fabrics, see EN 13795-1 and ANSI/AAMI ST65.

8 Sterile fluid-path packaging

8.1 Assembly of sterile fluid-path components and closures shall meet the requirements of Clauses 5 and 6.

8.2 Medical devices labelled “sterile fluid path” shall maintain sterility of the fluid path by the construction of the device in combination with its closures.

NOTE 1 The requirements for microbial barrier properties and sterile barrier system integrity are provided in ISO 11607-1. The requirements apply to the device itself.

NOTE 2 For the purpose of interpreting the requirements of this part of ISO 11607, the device and its closures constitute the sterile barrier system.

Annex A
(informative)

Process development

Process development, while not a formal part of process validation, should be considered as an integral part of forming and sealing. Process development or process design requires an assessment to identify and evaluate critical parameters, along with their operating ranges, settings and tolerances.

A process assessment is conducted to establish appropriate and necessary upper and lower processing limits, as well as the expected normal operating conditions. These process limits should be sufficiently removed from failure or marginal conditions. One technique could be the creation of seal-strength curves with accompanying visual examples of seal results that could aid in the selection of an optimal process window.

Potential failure modes and action levels having the greatest impact on the process should be identified and addressed (failure mode and effects analysis, cause and effect analysis).

Statistically valid techniques, such as screening experiments and statistically designed experiments to optimize the process, should be used.

Essential processing parameters that are evaluated may include, but are not limited to:

— temperature;

— pressure/vacuum, including rate of change;

— dwell time (line speed);

— energy levels/frequency (radio frequency/ultrasonic);

— torque limits for lid/cap closure systems.

The selected essential parameters will be selected such that they will produce a process that is in control, and capable of yielding sterile barrier systems and packaging systems that meet predetermined design specifications.

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