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Second edition
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Prefilled syringes —

Part 7: Packaging systems for sterilized subassembled syringes ready for filling

Seringues préremplies —

Partie 7: Systèmes d'emballage pour les seringues pré-assemblées stérilisées préremplissables

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Contents

Page

Foreword

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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 document 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).

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This document was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

This second edition cancels and replaces the first edition (ISO 11040-7:2015), which has been technically revised.

The main changes are as follows:

— Clause 3 was updated;

— former Annex B was removed because this specific method for determination of nest deflection was not commonly adopted by the industry;

— former Annex F was removed because the specific measurement method of determining the distance between the edge of the protective bag to rear end of the tub is not commonly adopted by the industry;

— a new Annex E was added to support automated processing;

— in Annex A, Annex B, the existing market ranges and tolerances have been revised and updated because fully automated and/or high-speed processes require smaller variations of certain tolerances;

— Table D.1 for bag sizes was revised. Bags and header bags are combined, and two main groups of bag sizes have been defined based on market experience and future expectations. They were entered into Table D.1 as column “recommended dimensions for 3” and 4” tub and “recommended dimensions for 4” tub”.

A list of all parts in the ISO 11040 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

At the start of prefilled syringe processing by the pharmaceutical industry, syringes made of tubing glass were delivered to the pharmaceutical companies in the form of a so called non-sterile “bulkware” only. The process steps such as washing, drying, inner lubrication, sealing the syringe with a closure system, sterilization, as well as filling, and closing were then performed by the pharmaceutical companies. Since their introduction to the market and with the emergence of specialized process equipment, sterilized subassembled syringes have more and more replaced the non-sterile “bulkware” to become the preferred approach for pre-filled syringe filling operations.

In the case of sterilized subassembled syringes ready for filling, responsibility for the aforementioned process steps relevant to the injectable product lies within the manufacturer of the subassembled syringes. Following the assembly of the needle shield on syringes with a staked needle or tip caps for the Luer cone version, the subassembled syringes are placed into so called nests. The nests, in turn, are placed into a plastic tub. The syringes in the nest are protected by means of an insert liner and the tub itself is sealed by a sealing lid (which is currently, and so far, primarily achieved using a porous material). Thus, the tub properly sealed with the sealing lid represents the “sterile barrier system”. The sealed tub is then wrapped into a sealable bag and, thus, ready for sterilization, which is currently, and so far, primarily performed using ethylene oxide.

In this form, the sterilized subassembled syringes ready for filling are delivered to the pharmaceutical companies in a sterile condition where they are processed on suitable machines.

The packaging design and material maintain sterility and should be compatible with the process of the customer. The packaging characteristics, material, thickness, shape, and resistance to deformations among others are such that they maintain, up to the point of use, the integrity of the product and a validated barrier against particulate and bacterial contamination.

The objective is to support the development of standardized equipment with automatic debagging process steps for aseptic processing.

Prefilled syringes —

Part 7: Packaging systems for sterilized subassembled syringes ready for filling

1 Scope

This document specifies a packaging system that is used to deliver sterilized subassembled syringes ready for filling in tubs and nests.

Downstream processes (processes after filling such as in house/outside transport, reprocessing) can result in specific requirements on the packaging system used to deliver sterilized subassembled syringes ready for filling. However, these requirements are not within the scope of this document.

NOTE 1 Glass barrels and sterilized subassembled syringes ready for filling, plunger stoppers, and plastic barrels for injectables are specified in ISO 11040-4, ISO 11040-5 and ISO 11040-6.

NOTE 2 ISO 11607-2 addresses validation requirements of sealing and packaging processes for medical devices.

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 11040-1, *Prefilled syringes — Part 1: Glass cylinders for dental local anaesthetic cartridges*

ISO 11040-2, *Prefilled syringes — Part 2: Plunger stoppers for dental local anaesthetic cartridges*

ISO 11040-3, *Prefilled syringes — Part 3: Seals for dental local anaesthetic cartridges*

ISO 11040-4, *Prefilled syringes — Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling*

ISO 11040-5, *Prefilled syringes — Part 5: Plunger stoppers for injectables*

ISO 11040-6, *Prefilled syringes — Part 6: Plastic barrels for injectables and sterilized subassembled syringes ready for filling*

ISO 11040-8, *Prefilled syringes — Part 8: Requirements and test methods for finished prefilled syringes*

ISO 11138-1, *Sterilization of health care products — Biological indicators — Part 1: General requirements*

ISO 11138-2, *Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes*

ISO 11138-3, *Sterilization of health care products — Biological indicators — Part 3: Biological indicators for moist heat sterilization processes*

ISO 11138-4, *Sterilization of health care products — Biological indicators — Part 4: Biological indicators for dry heat sterilization processes*

ISO 11138-5, *Sterilization of health care products — Biological indicators — Part 5: Biological indicators for low-temperature steam and formaldehyde sterilization processes*

ISO 11138-7, *Sterilization of health care products — Biological indicators — Part 7: Guidance for the selection, use and interpretation of results*

ISO 11138-8, *Sterilization of health care products — Biological indicators — Part 8: Method for validation of a reduced incubation time for a biological indicator*

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.

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

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

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

3.1
customer
person or organization that could or does receive a product or a service that is intended for or required by this person or organization

[SOURCE: ISO 9000:2015, 3.2.4, modified — Deletion of EXAMPLE and Note 1 to entry.]

3.2
insert liner
sheet to cover the filled nest

3.3
manufacturer
organization or person that manufactures a product

3.4
nest
plastic plate with a defined hole pattern for the suspension of the syringe bodies

3.5
protective bag
plastic bag or sealing around the tub

Note 1 to entry: There can be more than one protective bags around the tub.

3.6
sealing lid
microbial barrier material for sealing the tub

3.7
packaging system
combination of the sterile barrier system and protective packaging

[SOURCE: ISO 11139:2018, 3.192]

3.8
protective packaging
configuration of materials designed to prevent damage to the sterile barrier system and its contents from the time of their assembly until the point of use

[SOURCE: ISO 11139:2018, 3.219]

3.9
sterile barrier system
minimum package that minimizes the risk of ingress of microorganisms and allows aseptic presentation of the sterile contents at the point of use

Note 1 to entry: For packaging systems for sterilized subassembled syringes ready for filling, the sterile barrier system is formed by the assembled tub and sealing lid.

[SOURCE: ISO 11139:2018, 3.272, modified — Adding Note 1 to entry.]

3.10
tub
plastic container to accommodate the filled nest

4 Requirements for the packaging system

4.1 General

4.1.1 The packaging system intended to contain the ready for filling subassembled syringes shall protect the subassembled syringes and their sterile barrier system during handling, distribution and storage, to maintain the sterility as well as the functional and cosmetic characteristics over the claimed shelf-life.

4.1.2 The materials, the sterile barrier system, and the packaging system that enable sterilization, protect the product and maintain sterility until the point of aseptic filling, shall be in accordance with the requirements of ISO 11607-1.

4.1.3 The packaging system shall have acceptable microbiological and particulate levels to support the introduction of the sterilized syringes into an aseptic filling environment and related designated cleanrooms. Requirements should be agreed upon by the manufacturer and the customer.

NOTE The introduction of sterilized packaged syringes into an aseptic filling environment poses a risk of microbiological and/or particulate contamination of the drug product.

4.1.4 Tubs, nests, lids, inserts and protective bags shall allow the necessary process steps of the sterilized subassembled syringes over their shelf-life. The process steps to be considered include, but are not limited to, the following:

a) for tubs including sealing lid and insert liner:

— lid sealing and lid opening;

— conveying;

— nest insertion and extraction;

— stacking and destacking;

— sterilization and decontamination.

b) for nests:

— subassembled syringe insertion (nesting) and removal (denesting);

— filling;

— plunger stopper insertion;

— stacking and destacking;

— sterilization and decontamination.

c) for protective bag:

— sealing;

— folding;

— sterilization and decontamination;

— cutting and opening.

4.1.5 The packaging configuration including the arrangement of the product shall be agreed with the customer to allow for adequate processing.

NOTE The process steps described include those at the premises of the manufacturer and of the customer.

4.2 Nest and tub configuration

4.2.1 Ready for filling subassembled syringes shall be packaged in a plastic nest, which is placed within a plastic tub.

4.2.2 The nest shall maintain distance between the subassembled syringes to protect against breakage during transportation. Depending on a particular subassembled syringe's dimensions, nests can contain different numbers and sizes of cavities.

4.2.3 The subassembled syringes shall be covered with a protective insert liner and the tub shall be sealed with a sealing lid. Once sealed, the tub and lid assembly shall serve as a sterile barrier system to maintain sterility of the contents following sterilization of the packaging system.

4.3 Nest

4.3.1 This subclause covers nests used for sterilized subassembled syringes ready for filling. Nested formats can also be used for plunger stoppers/pistons.

4.3.2 For the nest, the following information shall be provided:

— external dimensions;

— deflection;

— cavities for the syringes;

— centering/lifting features (i.e. openings, columns);

— defined free space where the lifting tool can engage.

4.3.3 The customer and manufacturer shall agree upon the dimensions and tolerances of the finished product as delivered.

NOTE See Annex A.

4.3.4 The design of the nest shall facilitate the insertion and removal of the sterilized subassembled syringes ready for filling [e.g. Luer lock adapter (LLA)-syringes] by adding bevels or other means.

NOTE For information on the design, see Annex A.

4.3.5 The maximum acceptable nest deflection shall be agreed upon by the manufacturer and customer.

4.4 Tub

4.4.1 External dimensions including reinforcements/beads and radii, for tubs, information on dimensions including tolerances shall be shared with the customers based on the customer and manufacturer agreement.

4.4.2 The tub shall allow the sealing of the lid.

4.4.3 If sterilization indicators are applied to the tubs, they shall conform with ISO 11138-1, ISO 11138-2, ISO 11138-3, ISO 11138-4, ISO 11138-5, ISO 11138-7 and ISO 11138-8, ISO 11040-1, ISO 11040-2, ISO 11040-3, ISO 11040-4, ISO 11040-5, ISO 11040-6 and ISO 11040-8, as applicable. The customer and manufacturer shall agree upon the dimensions and tolerances of the finished product as delivered.

NOTE See Annex B.

4.5 Insert liner

4.5.1 The syringes shall be covered by an insert liner as a protection from particles generated during opening. The insert liner shall be, where appropriate, permeable for the sterilization agent (e.g. made of nonwoven material of polyolefin).

4.5.2 The insert liner can consist of several layers in order to ensure sufficient shielding of the glass against electron beam irradiation during the decontamination process. To enable proper removal, the layers should be connected with each other (e.g. by means of sealing points).

4.5.3 Corners may be rounded or chamfered. The shape and dimensions of the insert liner shall match with the protection demands.

4.6 Sealing lid

4.6.1 The sealing lid (e.g. made from nonwoven polyolefin material) shall be sealable to the tub and completely peelable from the tub while minimizing the risk of releasing particles. The seal properties (e.g. seal strength, seal width) and integrity shall be tested in accordance with a validated test method. For examples of test methods, see ISO 11607-1.

4.6.2 The sealing lid should be designed and positioned to ensure sealing lid overhang beyond the edge of the sealing to support peeling without delamination or tearing.

4.6.3 The sealing lid shall be, where appropriate, permeable for the sterilization agent.

4.6.4 The materials and seals shall be compatible with the decontamination processes, as applicable (e.g. electron beam and vaporized hydrogen peroxide), prior to transfer of the packaging into the aseptic filling area.

4.7 Protective bag

4.7.1 The protective bag shall be permanently sealed and shall enable the selected sterilization method. Testing of the seal properties (e.g. seal strength, seal width and integrity) shall be performed in accordance with a validated test method (for examples of test methods, see ISO 11607-1). As a minimum, the protective