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Prefilled syringes —

Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling

Seringues préremplies —

Partie 4: Cylindres en verre pour produits injectables et seringues pré-assemblées stérilisées préremplissables

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Contents

Page

Foreword ..... **v**
Introduction ..... **vii**
1 Scope **1**
2 Normative references **1**
3 Terms and definitions **2**
4 General requirements **4**
4.1 Quality systems 4
4.2 Testing 4
4.3 Documentation 4
5 Syringe barrel **4**
5.1 Design including dimensions 4
5.1.1 Dimensions for 6 % Luer slip and 6 % Luer slip for Luer lock adapter front end syringes 4
5.1.2 Specific dimensions for front end design for 6 % Luer slip and 6 % Luer slip for Luer lock adapter 6
5.1.3 Dimensions for staked needle (SN) syringes 7
5.1.4 Front end design for staked needle syringe 9
5.2 Functional testing of Luer connection 10
5.3 Material 10
5.4 Performance requirements 10
5.4.1 Hydrolytic resistance glass barrel 10
5.4.2 Annealing quality 10
5.4.3 Lubrication of the inner surface 10
5.4.4 Flange breakage resistance 10
5.4.5 Front end breakage resistance 11
6 Sterilized subassembled syringes ready for filling **11**
6.1 General 11
6.1.1 Design 11
6.1.2 Raw materials properties 11
6.1.3 Documentation 11
6.2 Sterility 11
6.3 Pyrogenicity/endotoxins 12
6.4 Particulate matter 12
6.5 Additional requirements to specific components of sterilized subassembled syringes ready for filling 12
6.5.1 Syringe barrel 12
6.5.2 Needle 13
6.5.3 Syringe closure system 14
6.6 Syringe closure system tightness 15
7 Packaging **15**
8 Labelling **16**
Annex A (informative) **Examples of types of sterilized subassembled syringes ready for filling** **17**
Annex B (informative) **Additional components for a subassembled syringe ready for filling** **19**
Annex C (normative) **Test methods for syringe barrels** **20**
Annex D (informative) **Sample preparation for endotoxin and particulate determination** **26**
Annex E (informative) **Glide force test method** **29**
Annex F (informative) **Needle penetration test** **32**
Annex G (normative) **Test methods for front end components** **35**

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Annex H (informative) **Tightness test** **50**
Bibliography **52**

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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 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 fourth edition cancels and replaces the third edition (ISO 11040-4:2015), which has been technically revised.

The main changes are as follows:

— Clause 3 has been updated;

— update on general requirements have been added on quality systems, testing and documentation;

— additional requirements to specific components of sterilized subassembled syringes ready for filling have been revised;

— requirements on syringes barrels have been revised by:

  — addition of specification for finger flange breakage resistance,

  — addition of specification for cone breakage resistance,

  — addition of requirements specifically for staked needle syringes,

  — addition of performance requirements for non-lubricated syringes.

— figures in Annex A have been updated;

— information of former Annex B has been implemented in 5.1; new Annex B shows information of typical components of a finished prefilled syringe;

— general update of annexes.

A list of all parts in the ISO 11040 series can be found on the ISO website.

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Introduction

In the past, ampoules and injection vials were mainly used for (parenteral) injectable products. However, for the injection of the products contained in those ampoules and vials, a hypodermic syringe combined with the appropriate injection needle is also needed. This means the injectable product must be transferred by the user into the hypodermic syringe before its final use. This procedure is not only time-consuming, but also presents a great number of possibilities for contamination.

To ensure safe use of an injectable product, prefilled syringes for single use are on the market for many years. Without a doubt, such prefilled syringes permit immediate injection of the product contained after relatively simple handling. These syringes can also be used in injectors with automated functions where further and particular requirements apply.

Based on the diameter of the prefilled syringes, appropriate components, such as plunger stoppers, tip caps, needle shields, and other syringe closure systems can also be standardized. In conjunction with the right sealing components, they offer a system for (parenteral) injectable use. The producers of filling machines can use this document to standardize the equipment of the machines.

In the beginning of prefilled syringe processing by the pharmaceutical industry, syringes made of tubing glass were delivered to the pharmaceutical companies in the form of so called non-sterile “bulkware” only. The process steps washing, drying, inner surface lubrication, sealing the syringe with a syringe closure system, sterilization, as well as filling and closing, were then performed in the pharmaceutical companies. Processing of “bulkware” is still performed this way. Sterilized subassembled syringes have partially replaced non-sterile “bulkware”.

In the case of sterilized subassembled syringes ready for filling, responsibility for the aforementioned process steps relevant to the injectable product lies with the manufacturer of the primary packaging material. Following the assembly of the needle shield on syringes with a staked needle or tip caps for the Luer slip 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 against contamination 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 gas permeable 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.

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Prefilled syringes —

Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling

1 Scope

This document specifies materials, dimensions, quality, and performance requirements, as well as relevant test methods.

This document also specifies components that are part of the sterilized subassembled syringe ready for filling.

This document is applicable to

— tubing-glass barrels (single-chamber design) for injection preparations, and

— sterilized subassembled syringes ready for filling.

Glass barrels and sterilized subassembled syringes ready for filling in accordance with this document are intended for single use only.

Components to complete the subassembled syringe, such as plunger stopper and plunger rod, are outside the scope of this document.

NOTE National or regional regulations such as Ph.Eur., USP, or JP can 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 720, *Glass — Hydrolytic resistance of glass grains at 121 °C — Method of test and classification*

ISO 4802-1, *Glassware — Hydrolytic resistance of the interior surfaces of glass containers — Part 1: Determination by titration method and classification*

ISO 4802-2, *Glassware — Hydrolytic resistance of the interior surfaces of glass containers — Part 2: Determination by flame spectrometry and classification*

ISO 7864:2016, *Sterile hypodermic needles for single use*

ISO 8871-1, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 1: Extractables in aqueous autoclavates*

ISO 9626, *Stainless steel needle tubing for the manufacture of medical*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

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

ISO 80369-1, *Small-bore connectors for liquids and gases in healthcare applications — Part 1: General requirements*

ISO 80369-7, *Small-bore connectors for liquids and gases in healthcare applications — Part 7: Connectors for intravascular or hypodermic applications*

ISO 80369-20, *Small-bore connectors for liquids and gases in healthcare applications — Part 20: Common test methods*

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
business entity which purchases syringe barrels or sterilized subassembled syringes ready for filling and conducts further processing or filling as appropriate

3.2
Luer connector
small-bore connector that contains a conical mating surface with a 6 % (Luer) taper intended for use in intravascular or hypodermic applications of medical devices and related accessories

Note 1 to entry: A Luer connector can be either a Luer slip connector or a Luer lock connector.

Note 2 to entry: Male Luer connectors are referenced as cone and female Luer connectors are referenced as socket to align as recommended in ISO 80369-7.

EXAMPLE Hypodermic needle systems (ISO 7864).

[SOURCE: ISO 80369-7:2021, 3.2, modified — Note 2 to entry was deleted, a new Note 2 to entry and an example were added]

3.3
Luer lock adapter
Luer connector that contains a locking mechanism which is connected to a 6 % Luer slip

Note 1 to entry: See Figure 2.

3.4
manufacturer
business entity which performs or is otherwise responsible for the manufacturing of the syringe barrels (bulkware) or for the sterilized subassembled syringes ready for filling by the customer

3.5
needle shield
elastomeric syringe closure system, which seals the front end of staked needle syringe, designed to protect the needle tip/bevel from damage and allows sterilization of the syringe

3.5.1
rigid needle shield
needle shield (3.5) covered by a rigid housing

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