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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—

Foreword	ix
Introduction	xi
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	7
5.1.3 Dimensions for staked needle (SN) syringes	10
5.1.4 Front end design for staked needle syringe	11
5.2 Functional testing of Luer connection	12
5.3 Material	12
5.4 Performance requirements	13
5.4.1 Hydrolytic resistance glass barrel	13
5.4.2 Annealing quality	13
5.4.3 Lubrication of the inner surface	13
5.4.4 Flange breakage resistance	13
5.4.5 Front end breakage resistance	13
6 Sterilized subassembled syringes ready for filling	13
6.1 General	13
6.1.1 Design	13
6.1.2 Raw materials properties	13
6.1.3 Documentation	14
6.2 Sterility	14
6.3 Pyrogenicity/endotoxins	14
6.4 Particulate matter	14
6.5 Additional requirements to specific components of sterilized subassembled syringes ready for filling	15
6.5.1 Syringe barrel	15
6.5.2 Needle	16
6.5.3 Syringe closure system	17

6.6	Syringe closure system tightness	18
7	Packaging.....	18
8	Labelling.....	18
Annex A (informative)	Examples of types of sterilized subassembled syringes ready for filling	19
Annex B (informative)	Additional components for a subassembled syringe ready for filling	22
Annex C (normative)	Test methods for syringe barrels	24
Annex D (informative)	Sample preparation for endotoxin and particulate determination.....	32
Annex E (informative)	Glide force test method.....	35
Annex F (informative)	Needle penetration test	38
Annex G (normative)	Test methods for front end components	43
Annex H (informative)	Tightness test.....	63
Bibliography	65

Foreword — vii

Introduction — ix

1 — Scope — 1

2 — Normative references — 1

3 — Terms and definitions — 2

4 — General requirements — 3

4.1 — Quality systems — 3

4.2 — Testing — 3

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 — 8

5.1.4 — Specific Dimension for front end design of staked needle — 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	13
6.5.1	Syringe barrel	13
6.5.2	Needle	13
6.5.3	Closure system	14
6.6	Closure system tightness	15
7	Packaging	15
8	Labelling	15
Annex A (informative)	Examples of types of sterilized subassembled syringes ready for filling	17
A.1	Components	17
A.2	Description of front end closure systems	17
A.2.1	General	18
A.2.2	Closures for syringes with 6 % Luer slip	18
A.2.3	Closures for syringes with 6 % Luer slip for Luer connectors	18
A.2.4	Closures for syringes with staked needle	18
Annex B (informative)	Example of additional components needed for testing	19
Annex C (normative)	Test methods for syringe barrels	20
C.1	Flange breakage resistance	20
C.1.1	Principle	20
C.1.2	Materials	20
C.1.3	Apparatus	20
C.1.4	Preparation and preservation of test samples	21
C.1.5	Procedure	21
C.1.6	Expression of results	23
C.1.7	Test report or documentation	23
C.2	Front end breakage resistance	23
C.2.1	Principle	23
C.2.2	Materials	23
C.2.3	Apparatus	23
C.2.4	Procedure	24

C.2.5	Expression of results	25
C.2.6	Test report or documentation	25
Annex D (informative) Sample preparation for endotoxin and particulate determination		26
D.1	Endotoxins	26
D.1.1	General	26
D.1.2	Materials and equipment	26
D.1.3	Procedure	26
D.2	Particulates	27
D.2.1	General	27
D.2.2	Materials and equipment	27
D.2.3	Procedure	27
Annex E (informative) Glide force test method		29
E.1	Purpose	29
E.2	Materials	29
E.3	Apparatus	29
E.4	Procedure	30
E.5	Test report or documentation	31
Annex F (informative) Needle penetration test		32
F.1	Principle	32
F.2	Apparatus	32
F.3	Materials	32
F.4	Procedure	32
F.5	Test report or documentation	34
Annex G (normative) Test methods for closure systems		36
G.1	Needle pull-out force	36
G.1.1	Principle	36
G.1.2	Materials	36
G.1.3	Apparatus	36
G.1.4	Preparation and preservation of test samples	36
G.1.5	Procedure	36
G.1.6	Expression of results	37
G.1.7	Test report/documentation	37
G.2	Closure system liquid leakage test	38
G.2.1	Principle	38
G.2.2	Reagents and materials	38
G.2.3	Apparatus	38
G.2.4	Preparation and preservation of test samples	38
G.2.5	Procedure	38
G.2.6	Expression of results	39

G.2.7	Test report or documentation	39
G.3	Luer lock adaptor collar pull-off force	40
G.3.1	Principle	40
G.3.2	Materials	40
G.3.3	Apparatus	41
G.3.4	Preparation and preservation of test samples	41
G.3.5	Procedure	41
G.3.6	Expression of results	42
G.3.7	Test report or documentation	42
G.4	Luer lock adaptor collar torque resistance	42
G.4.1	Principle	42
G.4.2	Materials	42
G.4.3	Apparatus	42
G.4.4	Preparation and preservation of test samples and test pieces	43
G.4.5	Procedure	43
G.4.6	Expression of results	44
G.4.7	Test report or documentation	44
G.5	Luer lock rigid tip cap unscrewing torque	44
G.5.1	Principle	44
G.5.2	Materials	44
G.5.3	Apparatus	44
G.5.4	Preparation and preservation of test samples and test pieces	45
G.5.5	Procedure	45
G.5.6	Expression of results	45
G.5.7	Test report/documentation	45
G.6	Pull-off force of the tip cap or the needle shield	46
G.6.1	Method 1	46
G.6.1.1	Principle	46
G.6.1.2	Materials	46
G.6.1.3	Apparatus	47
G.6.1.4	Procedure	47
G.6.1.5	Expression of results	47
G.6.1.6	Test report or documentation	47
G.6.2	Method 2	48
G.6.2.1	Principle	48
G.6.2.2	Materials	48
G.6.2.3	Apparatus	48
G.6.2.4	Procedure	49
G.6.2.5	Expression of results	49

G.6.2.6 Test report or documentation	49
Annex H (informative) Dye solution tightness test	51
H.1 General	51
H.2 Principle	51
H.3 Apparatus, equipment, and reagents	51
H.4 Preparation and preservation of test samples and test pieces	52
H.5 Procedure	52
H.6 Test report/documentation	52
Bibliography	54

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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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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 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:~~

~~The main changes are as follows:~~ — **update of Clause 3;**

— **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.

~~— update of Figures in Annex A;~~

~~— figures in Annex A have been updated;~~

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

— ~~—~~ general update of ~~Annexes~~ annexes.

A list of all parts in the ISO11040 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.htm~~ www.iso.org/members.html.

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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.

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*

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.

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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