
Prefilled syringes —

Part 5:

Plunger stoppers for injectables

Seringues préremplies —

Partie 5: Bouchons-pistons pour produits injectables

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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web 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.

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 11040-5 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

This third edition cancels and replaces the second edition (ISO 11040-5:2001), which has been technically revised by:

- adjusting the title of this part of ISO 11040;
- aligning this International Standard with the ISO 8871 series;
- revising the requirements on the height of the spacers and requirements on material and hardness;
- adding requirements on resistance to ageing.

ISO 11040 consists of the following parts, under the general title *Prefilled syringes*:

- *Part 1: Glass cylinders for dental local anaesthetic cartridges*
- *Part 2: Plunger stoppers for dental local anaesthetic cartridges*
- *Part 3: Seals for dental local anaesthetic cartridges*
- *Part 4: Glass barrels for injectables and ready-to-use prefillable syringes*
- *Part 5: Plunger stoppers for injectables*
- *Part 6: Plastics barrels for injectables*

The following parts are under preparation:

- *Part 7: Packaging systems for prefillable ready-to-use syringes*

Introduction

Primary packaging components made of elastomeric materials are an integral part of medicinal products. Therefore, the principles of current good manufacturing practices (cGMP) apply to the manufacturing of these components.

Principles of cGMP are described in e.g. ISO 15378 or in the GMP Guidelines published by the European Community and the United States of America.

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Prefilled syringes —

Part 5: Plunger stoppers for injectables

1 Scope

This part of ISO 11040 specifies the shape, dimensions, material, performance requirements and labelling of plunger stoppers for glass barrels (single-chamber design) for injection preparations in accordance with ISO 11040-4.

Plunger stoppers specified in this part of ISO 11040 are intended for single use only.

This part of ISO 11040 is not applicable to barrier-coated plunger stoppers.

NOTE The potency, purity, stability and safety of a medicinal product during its manufacture and storage can be significantly affected by the nature and performance of the primary packaging.

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 3302-1, *Rubber — Tolerances for products — Part 1: Dimensional tolerances*

ISO 7619-1, *Rubber, vulcanized or thermoplastic — Determination of indentation hardness — Part 1: Durometer method (Shore hardness)*

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

ISO 8871-4, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 4: Biological requirements and test methods*

ISO 11040-4, *Prefilled syringes — Part 4: Glass barrels for injectables*

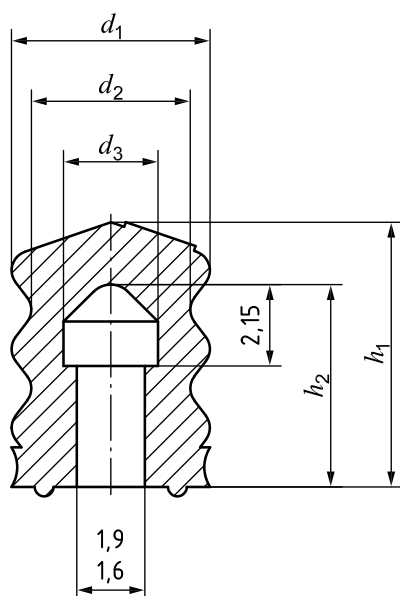
3 Classification

Plunger stoppers shall be classified as follows:

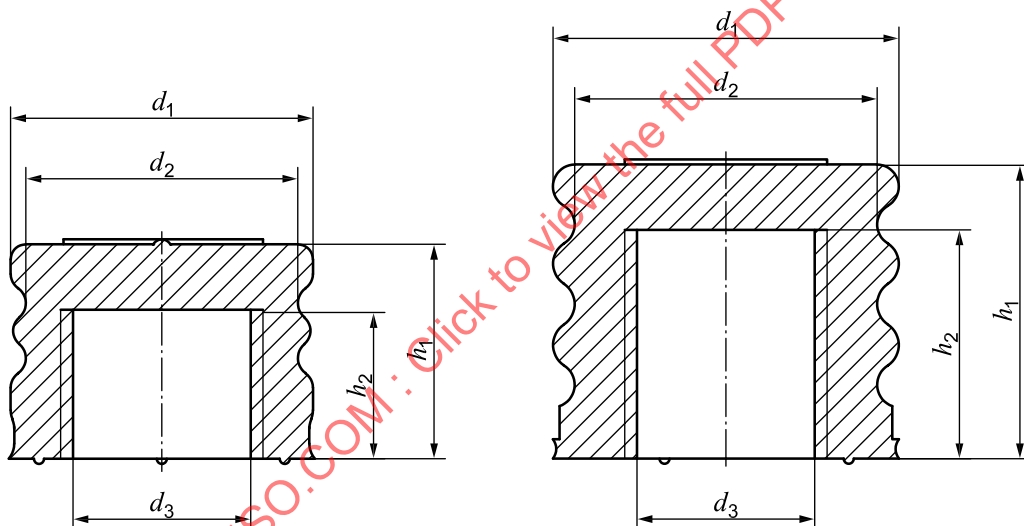
- type PSL: plunger stoppers with snap lid;
- type PST: plunger stoppers with thread.

4 Shape and dimensions

4.1 The shape and dimensions of plunger stoppers shall be as shown in Figure 1 and given in Table 1.



a) Plunger stopper with snap lid (PSL)



NOTE Thread: 16 pitch on 25,4 mm; for 1 ml (long), 17 pitch on 25,4 mm.

b) Plunger stopper with thread (PST)

Shape and dimensions of plunger stoppers for a prefilled syringe

Dimensions of plunger stoppers

Dimensions in millimetres

Nominal inner diameter d_2^b	Nominal volume ml	Type	d_1^a		d_2^a		d_3^a		h_1^a		h_2^a	
			nom.	tol.	nom.	tol.	nom.	tol.	nom.	tol.	nom.	tol.
4,65 ± 0,1	0,5	PSL	5,2 to 5,3		4,1 to 4,2		2,5	±0,2	6,85 to 7,0		5,3	±0,35
6,35 ± 0,1	1 (long)	PST	6,8 to 7		5,9 to 6		2,6		7,65 to 7,85		4,5	
8,65 ± 0,2	1 to 3		9,05 to 9,25		7,6 to 8		4,7		7,7 to 7,85		4	
11,85 ± 0,2	5		12,5 to 12,7	10,5 to 11,15	5,2 to 5,6	8,5	6,0					
14,25 ± 0,2	10		15 to 15,3	13,5 to 13,75	7,4 to 7,6	8,5 to 10	6 to 6,2					
19,05 ± 0,2	20		19,9 to 20,1	±0,15	18,4 to 18,6	±0,15	10,7	13,45 to 13,50	7	±0,3		

^a The nominal diameter shall be agreed upon between the manufacturer and the user within the given range.

^b In accordance with ISO 11040-4.

4.2 If not otherwise specified, general dimensional tolerances shall be Class M3 in accordance with ISO 3302-1.

4.3 In order to prevent the plunger stoppers from adhering to each other, there shall be spacers. The height of the spacers shall not exceed 0,3 mm.

The shape of the spacers should be agreed upon between the manufacturer and the cartridge assembler.

4.4 Sprues, if present on the surface of the plunger stopper, shall not protrude beyond the surface of the plunger stopper.

4.5 The performance and dimensions of the plunger stopper thread shall be compatible with the plunger rod. The plunger stopper shall not detach itself from the rod under normal use, e.g. aspiration.

5 Designation

Plunger stoppers are designated according to their type. The designation shall comprise, in the following order, the descriptor "Plunger", a reference to this part of ISO 11040, the type of plunger [snap lip (PSL) or threaded (PST)], the volume of the barrel for which the plunger stopper is intended, and the letters "lg" if it is the long version.

EXAMPLE 1 Designation of a plunger stopper with snap lip for a glass barrel of 0,5 ml nominal volume, complying with the requirements in this part of ISO 11040:

Plunger ISO 11040-5 - PSL - 0,5

EXAMPLE 2 Designation of a threaded plunger stopper for a glass barrel of 1 ml nominal volume, long version, complying with the requirements in this part of ISO 11040:

Plunger ISO 11040-5 - PST - 1 - lg

6 Material

The elastomeric material used shall meet the requirements specified in Clause 7.

Plunger stoppers shall be made from the elastomeric formulation originally tested and approved by the end user. The manufacturer of the plunger stopper shall ensure the conformance of each delivery with the type sample and compliance with previously agreed functional and compendial requirements.

The elastomeric material shall withstand two sterilization cycles when autoclaving in saturated steam at $(121 \pm 2) ^\circ\text{C}$ for 30 min without impairment of its function under conditions of normal use. If other sterilization methods are used, e.g. irradiation, the suitability of the material shall be evaluated.

7 Requirements

7.1 General

The requirements specified in 7.2 to 7.4 constitute minimum requirements concerning the condition of the elastomeric plunger stopper on receipt by the user.

7.2 Physical requirements

7.2.1 Hardness

The hardness agreed between the manufacturer and the user shall not differ from the nominal value by more than ± 5 Shore A when tested in accordance with ISO 7619-1 on a special test specimen. Alternatively, the hardness can be tested on the plunger stoppers in accordance with ISO 48. If tested according to ISO 48, the microhardness shall not differ by more than ± 5 IRHD from the type sample.

The manufacturer should provide suitable test specimens upon request.

7.2.2 Resistance to ageing

The maximum time between the date of manufacture of the plunger stoppers and their pharmaceutical use should be agreed upon between the manufacturer and the user.

The plunger stoppers shall maintain their performance characteristics throughout the entire shelf-life of the medicinal product, which is tested as part of the stability test by the user.

NOTE Ageing depends on storage and handling conditions. A guide to storage of vulcanized rubber is given in ISO 2230.

7.3 Chemical requirements

The aqueous extractables of the plunger stopper material shall not exceed the limits specified for elastomeric parts defined in ISO 8871-1.

7.4 Biological requirements

The requirements in ISO 8871-4 shall apply.

8 Labelling

Packed plunger stoppers that meet the requirements of this part of ISO 11040 can be labelled with the designation given in Clause 5.