

BS ISO 13926-3:2012



BSI Standards Publication

Pen systems

Part 3: Seals for pen-injectors
for medical use

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National foreword

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The UK participation in its preparation was entrusted to Technical Committee CH/212, IVDs.

A list of organizations represented on this committee can be obtained on request to its secretary.

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Pen systems —

Part 3:

Seals for pen-injectors for medical use

Systèmes de stylos-injecteurs —

Partie 3: Joints pour stylos-injecteurs à usage médical



Reference number
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Foreword

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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 13926-3 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

ISO 13926 consists of the following parts, under the general title *Pen systems*:

- *Part 1: Glass cylinders for pen-injectors for medical use*
- *Part 2: Plunger stoppers for pen-injectors for medical use*
- *Part 3: Seals for pen-injectors for medical use*

Introduction

Primary packaging components made of elastomeric materials are an integral part of medicinal products. As such, the principles of current Good Manufacturing Practices (cGMP) are applicable to the manufacturing of these components.

Principles of cGMP are described in, for example, ISO 15378 and GMP Guidelines published by the European Community and the United States of America.

Pen systems —

Part 3: Seals for pen-injectors for medical use

1 Scope

This part of ISO 13926 specifies the shape, dimensions, material, performance requirements and labelling of seals for pen-injectors for medical use.

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 (all parts), *Rubber — Tolerances for products*

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

ISO 7885:2010, *Dentistry — Sterile injection needles for single use*

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 8871-5:2005, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 5: Functional requirements and testing*

ISO 8872, *Aluminium caps for transfusion, infusion and injection bottles — General requirements and test methods*

ISO 11608-3, *Needle-based injection systems for medical use — Requirements and test methods — Part 3: Finished containers¹⁾*

ISO 13926-1, *Pen systems — Part 1: Glass cylinders for pen-injectors for medical use*

ISO 13926-2, *Pen systems — Part 2: Plunger stoppers for pen-injectors for medical use*

3 Classification

Seals shall be classified as follows:

- type A: seals with a mono-layer disc;
- type B: seals with a double-layer disc.

1) To be published.

4 Shape and dimensions

4.1 The shapes and dimensions of seals shall be as shown in Figure 1 and as given in Table 1.

Dimensions in millimetres

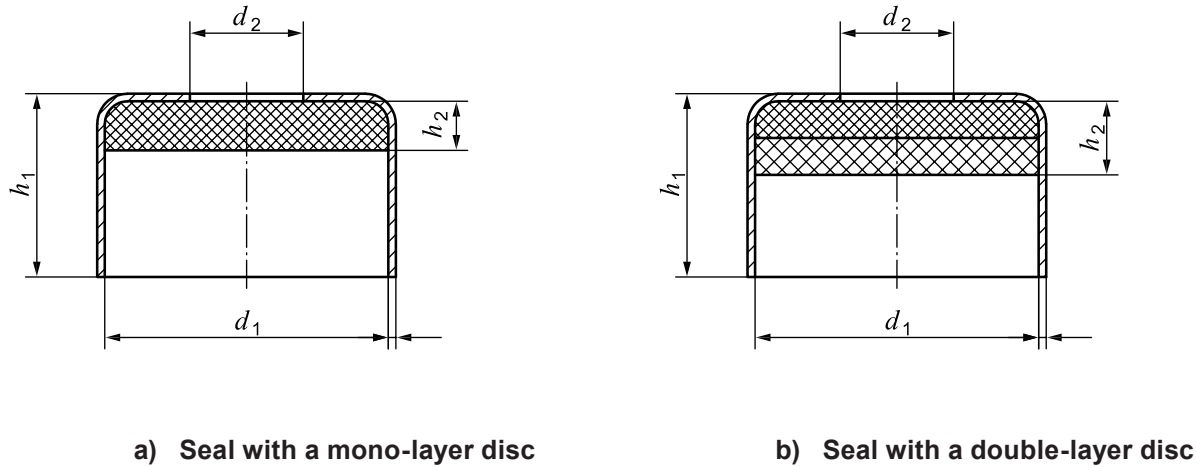


Figure 1 — Shape and dimensions of seals for pen-injectors for medical use

Table 1 — Dimensions of seals

Dimensions in millimetres

Nominal size	Type	Total cap height ^a	Thickness of disc	Inner cap diameter	Bore diameter
		h_1 $\pm 0,15$	h_2 $\pm 0,15$	d_1 $\pm 0,05$	d_2 $\pm 0,2$
7,5	A	4,85 to 4,9	1,3 to 1,5	7,5	3,0
7,5	B	4,85 to 5,3	1,45 to 1,95	7,5	3,0
10,0	A	4,85 to 4,9	1,3 to 1,5	9,85	4,0
10,0	B	4,85 to 5,3	1,45 to 1,95	9,85	4,0

^a The height of the seal depends on the thickness and hardness of the disc.

4.2 For type B seals, both single layers shall be continuous. The ratio of thickness of the single layers shall be agreed upon between the supplier and the user.

4.3 The diameter of the rubber discs shall be such that a sufficient press-fit in the aluminium cap is achieved and that the discs cannot fall out.

4.4 If not otherwise specified, general dimensional tolerances shall be in accordance with ISO 3302.

4.5 The surface of the discs can be structured in order to avoid sticking.

5 Designation

Seals can be designated according to their type (see Clause 3 and Figure 1). The designation shall be expressed as the word “Seal”, followed by a reference to this part of ISO 13926, followed by the nominal size, followed by the type letter.

EXAMPLE Designation of a seal type A (mono-layer disc) for a nominal head size of the cartridge of 7,5 mm complying with the requirements in this part of ISO 13926:

Seal ISO 13926-3 – 7,5 – A

6 Material

6.1 Cap

General requirements for aluminium caps shall be in accordance with ISO 8872.

In addition, the cap shall be anodized or suitably lacquered.

6.2 Disc

Discs shall be made from the elastomeric formulation originally tested and approved by the end user. The manufacturer of the discs shall ensure 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 ± 2) °C for 30 min without impairment of its function under the conditions of normal use. In case of other sterilization methods, 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 represent minimum requirements which refer to the condition of the seals on receipt by the user.

7.2 Physical requirements

7.2.1 Hardness of the disc

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 discs according to ISO 48. If tested according to ISO 48, the micro-hardness shall not differ by more than ± 5 IRHD from the type sample.

The manufacturer should provide suitable test specimens upon requests.

7.2.2 Fragmentation

The requirements and test method specified in ISO 8871-5:2005, 4.2, shall apply, using a needle with an outer diameter of 0,4 mm, conforming to ISO 7885:2010, 5.3 (butt end).

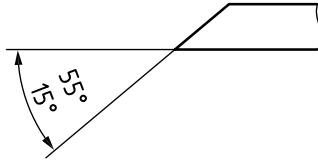


Figure 2 — Schematic representation of butt-end angle

7.2.3 Freedom from leakage

The cartridge shall be free from leakage at the seal when tested in accordance with Annex A.

7.2.4 Resealability

ISO 11608-3 applies.

7.2.5 Resistance to ageing

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

The seals 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 the storage and handling conditions. A guide to storing vulcanized rubber is given in ISO 2230.

7.3 Chemical requirements

The requirements in ISO 8871-1 shall apply for the disc.

7.4 Biological requirements

The requirements in ISO 8871-4 shall apply.

Toxicity tests apply to the disc only.

8 Labelling

Packed seals which meet the requirements of this part of ISO 13926 can be labelled with the designation given in Clause 5.

Annex A (normative)

Leakage test

A.1 Principle

Water-filled cartridges are prepared, using the seals to be tested. By means of a suitable device, a force is applied to the seal during a defined time interval. Any observed leakage is recorded.

The leakage test of the seals and the plunger stoppers (see ISO 13926-2) can be combined.

A.2 Apparatus

A.2.1 Cartridge cylinders with a silicone-treated inner surface in accordance with ISO 13926-1.

A.2.2 Seals to be tested.

A.2.3 Plunger stoppers in accordance with ISO 13926-2.

A.2.4 Suitable equipment to prepare water-filled cartridges.

A.2.5 Cartridge holder, for example, as described in ISO 11608-3.

A.2.6 Device, capable of applying a force as calculated in accordance with A.3.2.

A.3 Procedure

A.3.1 Take 10 cartridges and fill them, using the seals to be tested, with water that is as air-free as possible.

NOTE The water can be replaced by a coloured solution in order to improve the visibility of the leakage.

A.3.2 Place the first cartridge, mounted in the cartridge holder (A.2.5), into the pressurizing device (A.2.6), and apply a force, F , as calculated in accordance with Formula (A.1) for 1 min.

$$F = 0,64 \text{ N/mm}^2 \times d^2 \quad (\text{A.1})$$

where

F is the force to be applied, in newtons;

d is the inner diameter of the glass cylinder, in millimetres, in accordance with ISO 13926-1 (in ISO 13926-1, the inner diameter of the glass cylinder is designated d_2)

Check for leakage at the seal.

SAFETY PRECAUTIONS — Adequate safety measures should be in place to protect the operator.

A.3.3 Repeat the operation described in A.3.2 on the remaining cartridges.

A.4 Expression of results

Report the number of leakages observed at the seal.

Report whether the testing of the seals and the plunger stoppers (see ISO 13926-2) has been combined.

Bibliography

- [1] ISO 48, *Rubber, vulcanized or thermoplastic — Determination of hardness (hardness between 10 IRHD and 100 IRHD)*
- [2] ISO 2230, *Rubber products — Guidelines for storage*
- [3] ISO 15378, *Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2008, with reference to Good Manufacturing Practice (GMP)*
- [4] EC Guide to Good Manufacturing Practice for Medicinal Products, III/2244/87, Rev. 3 – January 1998, as amended
- [5] US/FDA Code of Federal Regulations

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