



**International
Standard**

ISO 8871-5

**Elastomeric parts for parenterals and
for devices for pharmaceutical use —**

**Part 5:
Functional requirements and testing**

*Éléments en élastomère pour administration parentérale et
dispositifs à usage pharmaceutique —*

Partie 5: Exigences fonctionnelles et essais

**Third edition
2025-03**

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Contents

	Page
Foreword	iv
Introduction	vi
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 Requirements	2
4.1 Penetrability.....	2
4.2 Fragmentation.....	2
4.3 Self-sealing.....	2
4.4 Dye solution tightness.....	2
5 Preparation of closures for testing	2
5.1 Sampling.....	2
5.2 Cleaning.....	3
5.3 Sterilization.....	3
Annex A (normative) Test for penetrability	4
Annex B (normative) Test for fragmentation	5
Annex C (normative) Test for self-sealing	7
Annex D (normative) Test for dye solution tightness	9
Bibliography	11

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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*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 205, *Non-active medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This third edition cancels and replaces the second edition (ISO 8871-5:2016), which has been technically revised.

The main changes are as follows:

- "aqueous solution tightness" has been replaced with "dye solution tightness";
- definition for fragmentation has been clarified;
- definitions for "filling volume" and "nominal volume" have been added;
- information on the fragmentation test and new information on the fragment size have been added;
- "pore size of 0,5 µm" has been replaced with "pore size of maximum 5,0 µm" to be aligned with ISO 11608-3;
- clarification on the fragments counting measurements has been added;
- "dye solution tightness" from the self-sealing test has been removed;
- "solution of methylene blue" has been replaced by "appropriate dye solution" and new information on the dye solution;
- "methylene blue" has been replaced by "dye solution";
- references to USP <788> and USP <1207> have been added.

A list of all parts in the ISO 8871 series can be found on the ISO website.

ISO 8871-5:2025(en)

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.

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Introduction

The elastomeric parts specified in the ISO 8871 series are produced from rubber and thermoplastic elastomers (TPE). These pharmaceutical use closures are used in combination with vials and many times in conjunction with piercing devices. There are three functional parameters which are important to the piercing process. These are penetrability, fragmentation and self-sealing. The three functional tests described in this document can be used as a reference method for testing closures that are pierced using injection needles made from metal. In addition, the dye solution tightness test can be used to verify the effectiveness of the sealing of a specific closure/vial combination.

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Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 5: Functional requirements and testing

1 Scope

This document specifies requirements and test methods for functional parameters of closures used in combination with vials and when pierced by an injection needle.

NOTE Functional testing with spikes is specified in ISO 8536-2, ISO 8536-6, ISO 8362-1 and ISO 8362-4.

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 7864, *Sterile hypodermic needles for single use — Requirements and test methods*

ISO 8362-1, *Injection containers and accessories — Part 1: Injection vials made of glass tubing*

ISO 8362-3, *Injection containers and accessories — Part 3: Aluminium caps for injection vials*

ISO 8362-4, *Injection containers and accessories — Part 4: Injection vials made of moulded glass*

ISO 8362-6, *Injection containers and accessories — Part 6: Caps made of aluminium-plastics combinations for injection vials*

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

penetrability

force required for piercing a closure

3.2

fragmentation

formation of elastomeric particles that are generated when the component that forms part of the primary container closure is pierced by a needle, spike or other access device for filling or delivery

Note 1 to entry: Coring is one mechanism to generate fragments.

[SOURCE: ISO 11608-3:2022, 3.4, modified — change "disc coring" to "coring", "disc or other elastomeric" deleted.]

3.3

self-sealing

measure of the resealing efficiency of closures following penetration and withdrawal of a needle

3.4

dye solution tightness

measure for the effective sealing of a specific closure/vial combination

3.5

filling volume

90 % of the brimful capacity

[SOURCE: United States Pharmacopoeia Convention, USP <660>]

3.6

nominal volume

volume indicated by marking on the device or its packaging

[SOURCE: ISO 28620:2020, 3.10]

4 Requirements

4.1 Penetrability

Penetrability shall be tested in accordance with [Annex A](#). The force required for piercing shall not be greater than 10 N for each closure.

4.2 Fragmentation

Fragmentation shall be tested in accordance with [Annex B](#). The number of elastomeric fragments generated by the total of 48 piercings (i.e. 4 piercings/12 closures) shall not be greater than 5. The test conditions and acceptance criteria (limits for minimum fragment size and allowable number of fragments) shall be adapted in certain circumstances and can be agreed between the supplier and the customer. For example, use of spike/needle with different characteristics or use of closed-system transfer devices.

4.3 Self-sealing

Self-sealing characteristic shall be tested in accordance with [Annex C](#). None of the vials shall contain any trace of dye coloured solution when observed with the naked eye. This requirement applies to multi-dose containers only, i.e. containers which utilize closures that are pierced multiple times.

Materials that meet the requirements are not required to undergo further testing in accordance with [4.4](#).

4.4 Dye solution tightness

Dye solution tightness shall be tested in accordance with [Annex D](#). None of the vials shall contain any trace of dye coloured solution when observed with the naked eye.

5 Preparation of closures for testing

5.1 Sampling

The number of closures required for each test is as follows:

— Penetrability:	10
— Fragmentation:	12
— Self-sealing:	10
— Dye solution tightness:	10

In practice, it is recommended that more than the minimum required number of closures be prepared for testing.

5.2 Cleaning

Closures shall be sterilized in the as-delivered condition. If samples from regular production cleaning processes are not available, the stoppers shall be cleaned in accordance with the following procedure.

Introduce an appropriate number of closures in a suitable glass container, cover with particle-free water, boil for 5 min, then rinse five times with cold particle-free water.

5.3 Sterilization

The closures shall be tested after having been subjected to the sterilization method actually used.

NOTE For already sterilized samples, there is no need to sterilize again.

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Annex A (normative)

Test for penetrability

A.1 General

Many closures for pharmaceutical use are used in conjunction with injection needles. The force necessary to penetrate or pierce a closure is an important parameter in evaluating the suitability of the closure for its intended use.

A.2 Principle

The force necessary to completely pierce a closure is measured using a suitable apparatus.

A.3 Apparatus, equipment and reagents

A.3.1 10 closures, prepared in accordance with [Clause 5](#).

A.3.2 10 clean vials, in accordance with ISO 8362-1 or ISO 8362-4, neck finish size to match the size of closures ([A.3.1](#)) (e.g. 13 mm, 20 mm).

A.3.3 10 aluminium or plastic/aluminium crimp seals, in accordance with ISO 8362-3 or ISO 8362-6, sized to match the size of closures ([A.3.1](#)) (e.g. 13 mm, 20 mm), and crimping apparatus.

A.3.4 10 lubricated long-bevel [bevel angle $(11 \pm 2)^\circ$] **metal hypodermic needles**, external diameter of 0,8 mm in accordance with ISO 7864.

A.3.5 Apparatus, capable of measuring a force of 10 N with an accuracy of $\pm 0,25$ N.

A.4 Procedure

A.4.1 Close the vials ([A.3.2](#)) with the closures ([A.3.1](#)) to be tested and secure with a crimp seal ([A.3.3](#)).

A.4.2 Fit the force-measuring apparatus ([A.3.5](#)) with a hypodermic needle ([A.3.4](#)) and pierce a closure perpendicular to the surface. Record the maximum force. Use a new needle for each of the 9 remaining closures and repeat the procedure.

A.5 Expression of results

Record the force required for piercing each closure and compare the test results with the requirement in [4.1](#).

Annex B (normative)

Test for fragmentation

B.1 General

Many closures for pharmaceutical use are used in conjunction with injection needles. Elastomeric fragments can be released upon penetration with these injection needles. The number and size of these fragments can affect the quality of drug products with which the closures are used.

B.2 Principle

Closures for injection vials are pierced with an injection needle. Elastomeric fragments which have been caused by piercing are collected on a filter and counted.

B.3 Apparatus, equipment and reagents

B.3.1 12 closures, prepared in accordance with [Clause 5](#).

B.3.2 12 clean vials, in accordance with ISO 8362-1 or ISO 8362-4, neck finish size to match the size of closures ([B.3.1](#)) (e.g. 13 mm, 20 mm).

B.3.3 12 aluminium or plastic/aluminium crimp seals, in accordance with ISO 8362-3 or ISO 8362-6, size to match the size of closures ([B.3.1](#)) (e.g. 13 mm, 20 mm), and crimping apparatus.

B.3.4 Particle-free water, to fit the filling volumes of the vials ([B.3.2](#)) and syringe ([B.3.6](#)).

B.3.5 12 lubricated long-bevel [bevel angle $(11 \pm 2)^\circ$] **metal hypodermic needles**, external diameter of 0,8 mm in accordance with ISO 7864.

B.3.6 Syringe, capable of being fitted with the needles in [B.3.5](#).

B.3.7 Filter, with a pore size of maximum 5,0 μm .

B.3.8 Filtering apparatus, capable of holding a filter ([B.3.7](#)) with a pore size of maximum 5,0 μm .

B.3.9 Laboratory microscope or a magnification glass.

B.4 Procedure

B.4.1 Place in each of the 12 clean vials ([B.3.2](#)) a volume of particle-free water ([B.3.4](#)) equivalent to the nominal volume minus 4 ml (e.g. place 21 ml in a 25 ml vial). Close the vials with the closures ([B.3.1](#)) to be tested and secure with a crimp seal ([B.3.3](#)).

B.4.2 Pierce each closure using a hypodermic needle ([B.3.5](#)) fitted to a clean syringe ([B.3.6](#)) filled with particle-free water ([B.3.4](#)), and inject into the vial 1 ml of water and remove 1 ml of air. Carry out this

ISO 8871-5:2025(en)

operation four times for each closure, piercing each time at a different site. Use a new needle for each closure and check that the needle is not blunted during the test.

B.4.3 Pass the liquid from each of the 12 vials through a filter ([B.3.7](#)) having a pore size of maximum 5,0 µm and count the presence of visible particulates in the sample.

It is assumed that visibility of particles starts in the size range of 100 µm to 150 µm. The counting of the fragments can be confirmed by measurements made with a microscope having a stage micrometre in order to determine size and nature ([B.3.9](#)). Additional information on the microscope particle count test method and settings is given in Reference [[3](#)].

B.5 Expression of results

Record the total number of fragments and compare to the limit given in [4.2](#).

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Annex C (normative)

Test for self-sealing

C.1 General

Closures for pharmaceutical use are commonly used in conjunction with vials. The closure ensures an appropriate seal with the vial. Poor closure/vial seal integrity and/or poor self-sealing can affect the sterility of the vial contents, product volume and concentration of doses.

Many closures for pharmaceutical use are used in conjunction with injection needles. For multiple-dose containers, the closures may be pierced many times over the course of delivering all the doses. Self-sealing or reseal of the incision made by the needle is important to the container integrity. For additional information on container closure integrity testing methods, see Reference [4].

C.2 Principle

Closures for injection vials are pierced several times with an injection needle and examined for leakage forced by a pressure differential across the closure.

C.3 Apparatus, equipment and reagents

C.3.1 10 closures, prepared in accordance with [Clause 5](#).

C.3.2 10 clean vials, in accordance with ISO 8362-1 or ISO 8362-4, neck finish size to match the size of closures ([C.3.1](#)) (e.g. 13 mm, 20 mm).

C.3.3 10 aluminium or plastic/aluminium crimp seals, in accordance with ISO 8362-3 or ISO 8362-6, size to match the size of closures ([C.3.1](#)) (e.g. 13 mm, 20 mm), and crimping apparatus.

C.3.4 Particle-free water, to fit the filling volumes of the vials ([C.3.2](#)).

C.3.5 Appropriate dye solution, including a colorant and possibly a surfactant.

NOTE Suitable dyes are methylene blue, rhodamine B, and fluorescein. A possible surfactant is Tween 80.¹⁾

The dye solution should be filtered through a filter (pore size <1 µm) and stored in a clean, particulate-free container until use.

C.3.6 10 lubricated long-bevel [bevel angle (11 ± 2)°] **metal hypodermic needles**, external diameter of 0,8 mm in accordance with ISO 7864.

C.3.7 Vacuum chamber, capable of maintaining a pressure (27 kPa below atmospheric pressure) for 10 min.

1) Tween 80 is an example of a suitable product available commercially. This information is given for the convenience of users of this document and does not constitute an endorsement by ISO of these products.

C.4 Procedure

C.4.1 Place in each of the 10 clean vials ([C.3.2](#)) a volume of particle-free water ([C.3.4](#)) equivalent to the nominal volume (e.g. place 25 ml in a 25 ml vial). Close the vials with the closures ([C.3.1](#)) to be tested and secure with a crimp seal ([C.3.3](#)).

C.4.2 Using a new hypodermic needle ([C.3.6](#)) for each closure, pierce each closure 10 times, piercing each time at a different site within the target area. Immerse the vials upright in a container holding the dye coloured solution ([C.3.5](#)). Ensure that the vials are completely immersed in the solution. Place the container of vials in a vacuum chamber ([C.3.7](#)) and reduce the pressure by 27 kPa. Hold the vacuum for 10 min, then restore to atmospheric pressure. Allow the vials to remain immersed in the dye coloured solution for an additional 30 min, then remove them from the chamber. Rinse the outside of the vials with water. Inspect the vial contents visually for any traces of the dye coloured solution.

NOTE For further information, see Reference [\[4\]](#).

C.5 Expression of results

Report if the vials contain any trace of dye coloured solution and compare to the requirements in [4.3](#).

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