
**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

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005



PDF disclaimer

This PDF file may contain embedded typefaces. In accordance with Adobe's licensing policy, this file may be printed or viewed but shall not be edited unless the typefaces which are embedded are licensed to and installed on the computer performing the editing. In downloading this file, parties accept therein the responsibility of not infringing Adobe's licensing policy. The ISO Central Secretariat accepts no liability in this area.

Adobe is a trademark of Adobe Systems Incorporated.

Details of the software products used to create this PDF file can be found in the General Info relative to the file; the PDF-creation parameters were optimized for printing. Every care has been taken to ensure that the file is suitable for use by ISO member bodies. In the unlikely event that a problem relating to it is found, please inform the Central Secretariat at the address given below.

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005

© ISO 2005

All rights reserved. Unless otherwise specified, no part of this publication may be reproduced or utilized in any form or by any means, electronic or mechanical, including photocopying and microfilm, without permission in writing from either ISO at the address below or ISO's member body in the country of the requester.

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

Published in Switzerland

Contents

Page

Foreword	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 Requirements	2
5 Preparation of elastomeric closures for testing	2
Annex A (normative) Test for penetrability	4
Annex B (normative) Test for fragmentation	5
Annex C (normative) Test for self-sealing and container closure seal integrity test	7
Annex D (normative) Test for container closure seal integrity	9
Bibliography	10

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005

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 8871-5 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

This first edition of ISO 8871-5, together with ISO 8871-1, ISO 8871-2, ISO 8871-3 and ISO 8871-4, cancels and replaces ISO 8871:1990 and its Amendment 1:1995, which have been technically revised.

ISO 8871 consists of the following parts, under the general title *Elastomeric parts for parenterals and for devices for pharmaceutical use*:

- *Part 1: Extractables in aqueous autoclavates*
- *Part 2: Identification and characterization*
- *Part 3: Determination of released particle count*
- *Part 4: Biological requirements and test methods*
- *Part 5: Functional requirements and testing*

Introduction

Elastomeric or rubber closures for pharmaceutical use 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 part of ISO 8871 can be used as a reference method for testing elastomeric closures that are pierced using injection needles made from metal. In addition, the container/closure seal integrity test can be used to verify the effectiveness of the sealing of a specific closure/vial combination.

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005

Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 5: Functional requirements and testing

1 Scope

This part of ISO 8871 specifies requirements and test methods for functional parameters of elastomeric closures used in combination with vials and when pierced by an injection needle.

NOTE Functional testing with spikes is specified in ISO 8536-2 and in ISO 8536-6.

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 7864, *Sterile hypodermic needles for single use*

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 for injectables 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.

3.1

penetrability

force required for piercing an elastomeric closure

3.2

fragmentation

measure of the number of elastomeric particles which are generated by the piercing process

3.3

self-sealing

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

3.4

container closure seal integrity

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

4 Requirements

4.1 Penetrability

When tested in accordance with Annex A, the force required for piercing shall not be greater than 10 N for each closure.

4.2 Fragmentation

When tested in accordance with Annex B, the number of elastomeric fragments per 48 piercings visible with the naked eye shall not be greater than 5.

4.3 Self-sealing and container closure seal integrity

When tested in accordance with Annex C, none of the vials shall contain any trace of coloured solution when observed with the naked eye. This requirement applies to multidose containers only, i.e. containers which utilize elastomeric 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 Container closure seal integrity

When tested in accordance with Annex D, none of the vials shall contain any trace of coloured solution when observed with the naked eye.

5 Preparation of elastomeric closures for testing

5.1 Sampling

The number of closures required for each test is:

— penetrability	10
— fragmentation	12
— self-sealing and container closure seal integrity	10
— container closure seal integrity	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 rubber 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

Place the pretreated closures in a wide-necked flask and add enough of particle-free water to cover the closures. Cover the mouth of the flask with an inverted borosilicate-glass beaker or similar type closure. Heat in an autoclave so that a temperature of $(121 \pm 2) ^\circ\text{C}$ is reached within 20 min to 30 min and maintain at this temperature for 30 min. At the end of the autoclave cycle, remove the flask from the autoclave. Decant the water and allow the closures to dry.

Other sterilization methods, e.g. gamma sterilization or ethylene oxide sterilization, can have an influence on the functional properties. Their impact on the functional properties should therefore be evaluated accordingly.

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005

Annex A (normative)

Test for penetrability

A.1 General

Many elastomeric or elastomeric closures for pharmaceutical use are used in conjunction with injection needles. The force necessary to penetrate or pierce a rubber 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 an elastomeric 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, finish sized to match the size of closures (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 (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 with the closures to be tested and secure with a crimp seal.

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 requirements in 4.1.

Annex B (normative)

Test for fragmentation

B.1 General

Many elastomerics or elastomeric closures for pharmaceutical use are used in conjunction with injection needles. Elastomeric fragments may 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 elastomeric closures are used.

B.2 Principle

Elastomeric 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, finish size to match the size of closures (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 (e.g. 13 mm, 20 mm), and crimping apparatus.

B.3.4 Particle-free water, to fit the fill volumes of the vials and syringe.

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 One filter, with a pore size of 0,5 μm .

B.3.8 Filtering apparatus, capable of holding a filter with a pore size of 0,5 μm .

B.3.9 Laboratory microscope or a **magnification glass**, with a minimum magnification of 6 \times .

B.4 Procedure

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

B.4.2 Pierce each closure using a hypodermic needle (B.3.5) fitted to a clean syringe filled with particle-free water, and inject into the vial 1 ml of water and remove 1 ml of air. Carry out this 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 having a pore size of 0,5 µm and count the number of particles visible with the naked eye. The count is based on the assumption that fragments with a diameter equal to or greater than 50 µm are visible with the naked eye. In cases of doubt or dispute, count the rubber fragments with a microscope or magnifying glass to verify their size and nature.

B.5 Expression of results

Record the total number of fragments and compare to the limit in 4.2.

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005

Annex C (normative)

Test for self-sealing and container closure seal integrity test

C.1 General

Many elastomeric or elastomeric 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. Poor self-sealing can affect the sterility, volume and concentration of doses.

Elastomeric 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 can affect sterility of the vial contents.

C.2 Principle

Elastomeric 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, finish size to match the size of closures (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 (e.g. 13 mm, 20 mm), and crimping apparatus.

C.3.4 Particle-free water, to fit the fill volumes of the vials.

C.3.5 Solution of methylene blue, 1 g/l.

C.3.6 10 lubricated long-bevel [bevel angle $(11 \pm 2)^\circ$] **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.

C.4 Procedure

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

C.4.2 Using a new hypodermic needle 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 solution of methylene blue. Ensure that the vials are completely immersed in the solution. Place the container of vials in a vacuum chamber 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 methylene blue 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 blue-coloured solution of methylene blue.

C.5 Expression of results

Report if the vials contain any trace of coloured solution and compare to the requirements in 4.3.

STANDARDSISO.COM : Click to view the full PDF of ISO 8871-5:2005