INTERNATIONAL STANDARD

ISO 8362-5

Second edition
2008-10-15

Injection containers and accessories —

Part 5: Freeze drying closures for injection vials

Récipients et accessoires pour produits injectables —

Partie 5: Bouchons à lyophilisation pour flacons d'injection

Reference number
ISO 8362-5:2008(E)

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

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 8362-5 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

This second edition cancels and replaces the first edition (ISO 8362-5:1995) which has been technically revised in order to align this International Standard with ISO 8871-2, ISO 8871-4 and ISO 8871-5.

ISO 8362 consists of the following parts, under the general title *Injection containers and accessories*:

— *Part 1: Injection vials made of glass tubing*

— *Part 2: Closures for injection vials*

— *Part 3: Aluminium caps for injection vials*

— *Part 4: Injection vials made of moulded glass*

— *Part 5: Freeze drying closures for injection vials*

— *Part 6: Caps made of aluminium-plastics combinations for injection vials*

— *Part 7: Injection caps made of aluminium-plastics combinations without overlapping plastics part*

Introduction

Freeze drying closures are put on the top of a glass container after filling, leaving sufficient openings for the sublimation process and vacuum. At the end of the drying process, they are fully inserted into the glass container by hydraulic or mechanical means in the vacuum chamber.

Freeze drying closures can pick up water during shipping, storage, washing and steam sterilization cycles, which is difficult to remove in a subsequent drying cycle. As a consequence, the freeze drying closures are usually loaded with residual moisture. Depending upon the mass of the freeze dried product and the degree of its sensitivity to water, the residual moisture in the rubber material can spoil the freeze dried preparation during storage.

These specific process requirements have been addressed in this part of ISO 8362 by specifying relevant requirements for freeze drying closures, including a test method for determining residual moisture.

Primary packaging components made of elastomeric materials are an integral part of medicinal products and thus the principles of current Good Manufacturing Practices (cGMP) apply to the manufacturing of these components.

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

Injection containers and accessories —

Part 5:
Freeze drying closures for injection vials

1 Scope

This part of ISO 8362 specifies the shape, dimensions, material, performance requirements and labelling for the type of closure for injection vials, as described in ISO 8362-1 and ISO 8362-4, which is used in connection with the freeze drying (or lyophilization) of drugs and biological materials.

The dimensional requirements are not applicable to barrier-coated closures.

Closures specified in this part of ISO 8362 are intended for single use only.

NOTE The potency, purity, stability and safety of a medicinal product during its manufacture and storage can be strongly 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 48, *Rubber, vulcanized or thermoplastic — Determination of hardness (hardness between 10 IRHD and 100 IRHD)*

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

ISO 3302-2, *Rubber — Tolerances for products — Part 2: Geometrical 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 8871-5:2005, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 5: Functional requirements and testing*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
freeze drying
lyophilization
drying process designed to remove solvents from both aqueous and non-aqueous systems by sublimation and desorption

3.2
freeze drying closure
closure that enables the drying of a frozen pharmaceutical preparation in a vacuum chamber

4 Shape and dimensions

4.1 The dimensions of freeze drying closures shall be as given in Table 1. Figure 1 illustrates the general design of a freeze drying closure.

Table 1 — Dimensions of freeze drying closures

Dimensions in millimetres

Nominal size	d_1 ± 0,2	d_2[a] min.	h_2 ± 0,25	h_3 min.	h_4 min.
13	12,5	7,5	2,0	2,0	1,8
20	18,8	13,0	3,3	2,0	2,0

[a] The value of d_2 is applied in that area which is defined by h_3.

4.2 If not otherwise specified, general dimensional tolerances shall be in accordance with ISO 3302-1 and ISO 3302-2.

4.3 If spacers are located on the top of the flange, they shall not interfere with the marks for the piercing area (see Figure 1). The height of the spacers shall not exceed 0,3 mm.

NOTE The spacers in Figure 1 are shown for illustrative purposes only and do not form part of the requirements of this part of ISO 8362.

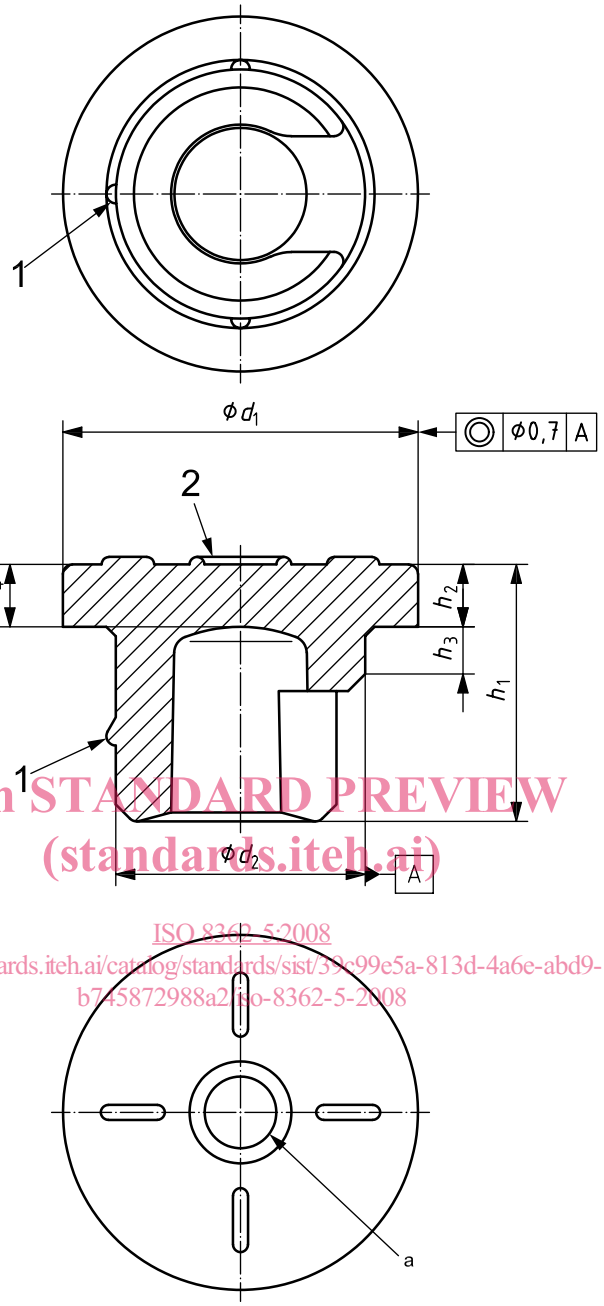
On the top surface there may be marks or indentations.

4.4 If the flange of the closure has a slightly conical shape, it shall be 0,3 mm maximum in relation to the diameter in order to facilitate production. The tolerances of the trimming edge of the flange shall comply with the tolerances specified in Table 1 for diameter d_1.

4.5 The plug part shall provide slits, channels or other appropriate means, in conjunction with protruding or positioning elements at the outer diameter, which enable insertion on a drying (halfway) position during the sublimation process.

4.6 The design of the positioning element to hold the freeze drying closure firmly in the sublimation position should not compromise the full insertion of the closure into the neck of the vial.

4.7 The design of the flange part in conjunction with the plug design shall permit both the reconstitution of the freeze dried product with the appropriate solvent and the removal of the dissolved product by means of a piercing device.



NOTE The total height of the freeze drying closure, h_1, can vary and is subject to mutual agreement between manufacturer and user.

Key

1 positioning element
2 spacer

[a] The inner diameter shall not be wider than the inner lumen.

Figure 1 — Example of a freeze drying closure design