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8362-5**

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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

Please see the administrative notes on page iii

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ISO/CEN PARALLEL PROCESSING

This final draft has been developed within the International Organization for Standardization (ISO), and processed under the **ISO-lead** mode of collaboration as defined in the Vienna Agreement. The final draft was established on the basis of comments received during a parallel enquiry on the draft.

This final draft is hereby submitted to the ISO member bodies and to the CEN member bodies for a parallel two-month approval vote in ISO and formal vote in CEN.

Positive votes shall not be accompanied by comments.

Negative votes shall be accompanied by the relevant technical reasons.

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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 documents 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).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information.

The committee responsible for this document is 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 8362-5:2008), which has been technically revised to include a new 7.5.

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 documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. 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
lyophilizaion
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 given in Table 1 while 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.

There may be marks or indentations on the top surface.

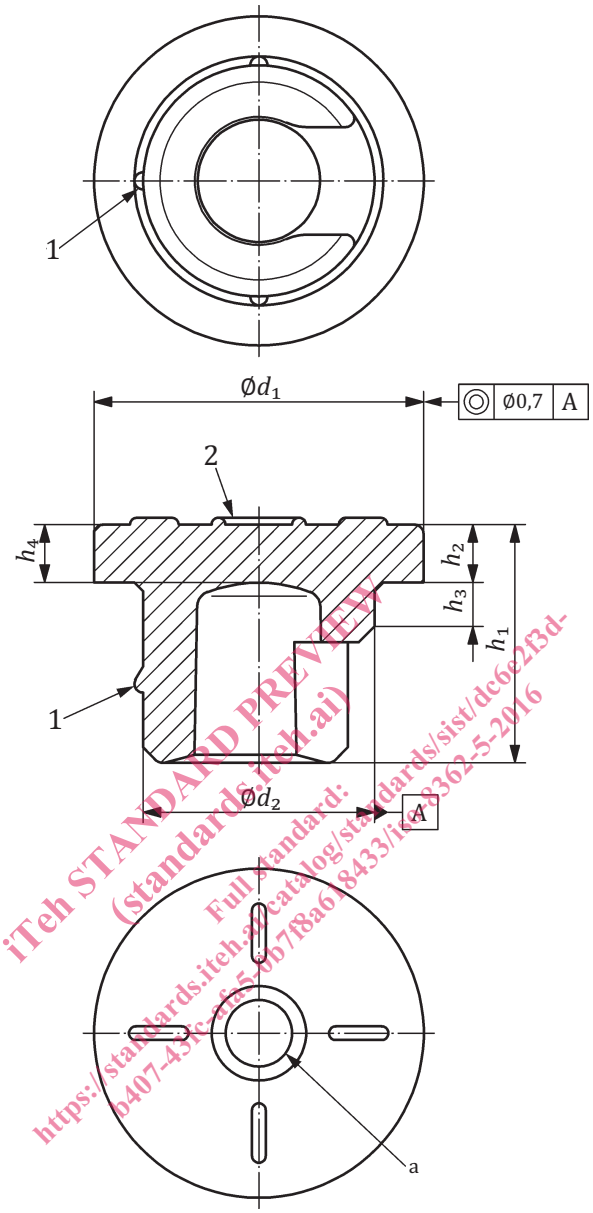
4.4 If the flange of the closure has a slightly conical shape, it shall be 0,3 mm maximum in relation to the diameter in order to facilitate production. The tolerances of the trimming edge of the flange shall comply with the tolerances specified in Table 1 for diameter d_1.

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.

Dimensions in millimetres



Key

1 positioning element

2 spacer

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

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

Figure 1 — Example of a freeze drying closure design

4.8 The freeze drying closure shall be designed and manufactured in such a way that the removal of the reconstituted product with a hypodermic needle can be visually controlled in order to minimize the amount of residual product.