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Infusion equipment for medical use —

Part 2:
Closures for infusion bottles

Matériel de perfusion à usage médical —

Partie 2: Bouchons pour flacons de perfusion

[Revision of second edition (ISO 8536-2:2001)]

ICS 11.040.20

ISO/CEN PARALLEL PROCESSING

This 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.

This draft is hereby submitted to the ISO member bodies and to the CEN member bodies for a parallel five-month enquiry.

Should this draft be accepted, a final draft, established on the basis of comments received, will be submitted to a parallel two-month approval vote in ISO and formal vote in CEN.

To expedite distribution, this document is circulated as received from the committee secretariat. ISO Central Secretariat work of editing and text composition will be undertaken at publication stage.

Pour accélérer la distribution, le présent document est distribué tel qu'il est parvenu du secrétariat du comité. Le travail de rédaction et de composition de texte sera effectué au Secrétariat central de l'ISO au stade de publication.

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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.

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 8536-2 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

This third edition cancels and replaces the second edition (ISO 8536-2:2001), which has been technically revised in order to align this Standard with ISO 8871-1, ISO 8871-4 and ISO 8871-5.

ISO 8536 consists of the following parts, under the general title *Infusion equipment for medical use*:

— *Part 1: Infusion glass bottles*

— *Part 2: Closures for infusion bottles*

— *Part 3 Aluminium caps for infusion bottles*

— *Part 4: Infusion sets for single use, gravity feed*

— *Part 5: Burette infusion sets for single use, gravity feed*

— *Part 6: Freeze drying closures for infusion bottles*

— *Part 7: Caps made of aluminium-plastics combinations for infusion bottles*

— *Part 8: Infusion equipment for use with pressure infusion apparatus*

— *Part 9: Fluid lines for use with pressure infusion equipment*

— *Part 10: Accessories for fluid lines for use with pressure infusion equipment*

— *Part 11: Infusion filters for use with pressure infusion equipment*

Introduction

The purpose of this part of ISO 8536 is to specify the shape and dimensions of and the requirements for elastomeric closures intended for infusion bottles. In order to provide seal integrity of the container closure systems the dimensions of the elastomeric closures have to be compatible with the dimensions of the infusion bottles and the caps as specified in corresponding parts of ISO 8536.

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 in e. g. ISO 15378 or GMP Guidelines as published by the European Community and the United States of America.

Infusion equipment for medical use —

Part 2:
Closures for infusion bottles

1 Scope

This part of ISO 8536 specifies the shape, dimensions, material, performance requirements and labelling of closures for infusion bottles as specified in ISO 8536-1.

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

Closures specified in this part of ISO 8536 are intended for single use only.

NOTE The potency, purity, stability and safety of a medicinal product during its manufacture and storage can strongly be 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 (all parts), *Rubber — Tolerances for products*

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

ISO 8536-1, *Infusion equipment for medical use — Part 1: Infusion glass bottles*

ISO 8536-3, *Infusion equipment for medical use — Part 3: Aluminium caps for infusion bottles*

ISO 8871-1, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 1: Extractables in aqueous autoclavates*

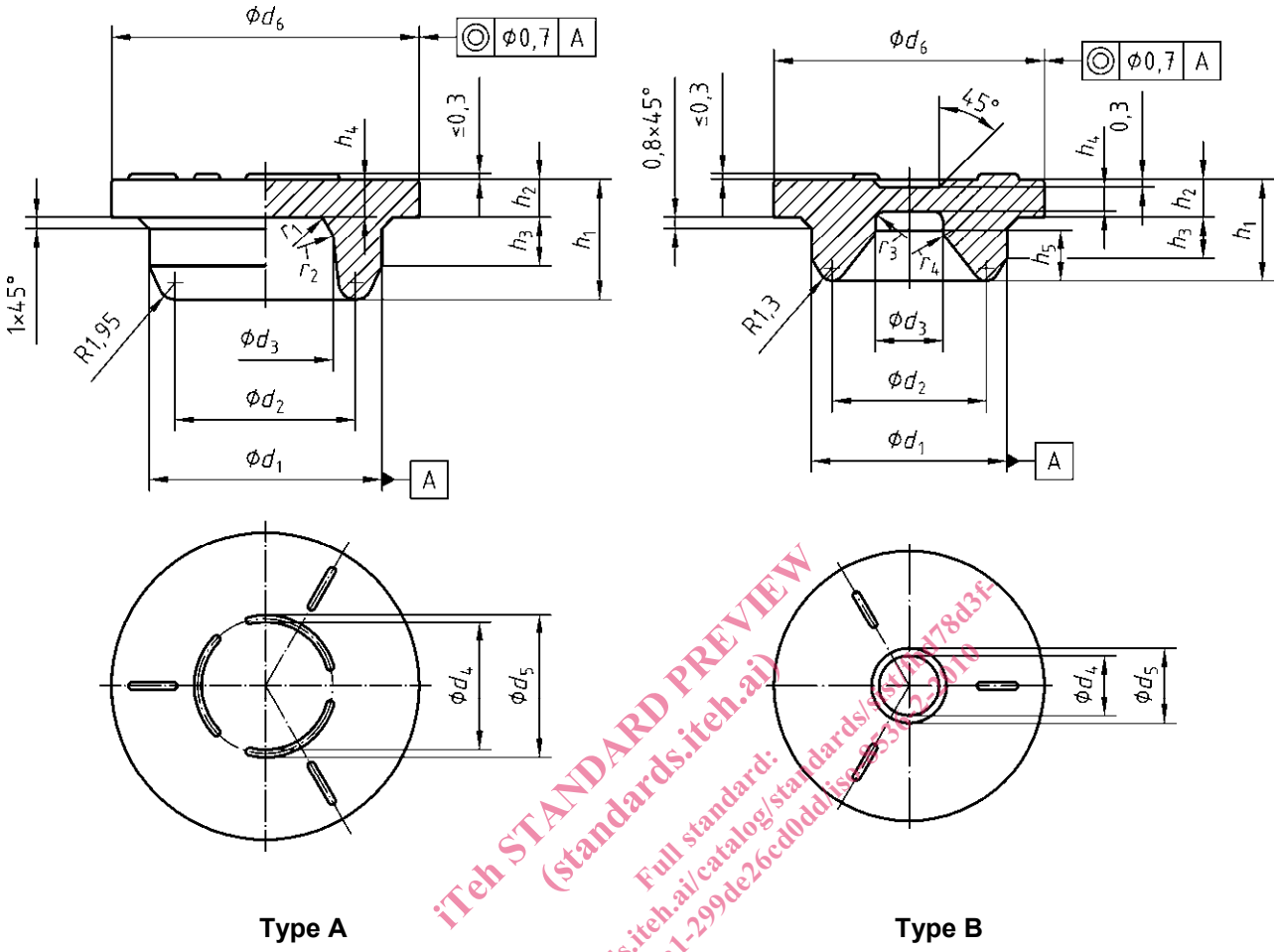
ISO 8871-4, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 4: Biological requirements and test methods*

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

3 Shape and dimensions

3.1 The shape and dimensions of closures shall be as shown in Figure 1 and as given in Table 1. Figure 1 illustrates two typical designs of closures, types A and B.

Dimensions in millimetres



Type A Type B

Figure 1 — Dimensions and configuration of type A and type B closures

Table 1 — Dimensions of infusion closures

Dimensions in millimetres

Type	Nominal size	d_1 ± 0,2	d_2 max.	d_3 min.	d_4 min.	d_5 max.	d_6 ± 0,3	h_1 ± 0,4	h_2 ± 0,3	h_3	h_4[a] ± 0,3	h_5
A	32	23,6	18,2	13	13	14	30,8	12,2	4	5,1	4	-
B	28	19,6	15,5	6,9	6,1	7,1	27,1	10,2	3,4	4,2	2,5	5,1

[a] Indentations may reduce the piercing thickness.

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

3.3 In order to facilitate the production process, the flange of the closure may have a slightly conical shape (max. 0,8 mm related to the diameter). The trimming edge of the flange shall comply with the tolerances specified for the diameter of the flange.

3.4 The diameter d_4 which defines the piercing area shall not exceed d_3. Marks and indentations may be placed in the piercing area. The height of the marks shall not exceed 0,3 mm.

NOTE The spacers in Figure 1 for type A and type B closures are shown for illustrative purposes only and do not form part of the requirements of this part of ISO 8536.

3.5 All edges of the closure may be rounded.

4 Designation

Closures can be designated according to their type, see Figure 1. The designation is expressed as the number of this part of ISO 8536 followed by the nominal size of the infusion bottle followed by the type letter.

EXAMPLE A type A closure for infusion bottles of nominal size 32 mm complying with the requirements laid down in this part of ISO 8536 is designated as follows:

Infusion closure ISO 8536-2 - 32 - A

5 Material

The elastomeric material used shall meet the requirements specified in Clause 6.

The elastomeric material shall withstand two sterilization cycles when autoclaving in saturated steam at (121 ± 2) °C for 30 min without exceeding the specified limits and without the impairment of its performance characteristics under the conditions of normal use. In case of other sterilization methods, e. g. irradiation, the suitability of the material has to be evaluated.

NOTE For use with infusion solutions, resistance to two steam sterilization cycles may not be needed because only terminal sterilization is applied.

Closures shall be made of elastomeric formulation originally tested and approved by the end-user. The closure manufacturer shall ensure the conformance of each delivery with the type sample and the compliance with previously agreed functional parameters and compendium requirements.

6 Performance

6.1 General

The requirements specified in 6.2 to 6.4 represent minimum requirements which refer to the condition of the elastomeric closures on receipt by the user.

6.2 Physical requirements

6.2.1 Hardness

The hardness agreed between manufacturer and user shall not differ from the nominal value by more than ± 5 Shore A when tested in accordance with ISO 7619-1 on special test specimen. Alternatively, the hardness can be tested on the closures according to ISO 48. If tested according to ISO 48, the microhardness shall not differ by more than ± 5 IRHD from the type sample.

6.2.2 Fragmentation

When tested for fragmentation in accordance with Annex A, not more than 20 fragments of diameter equal to or greater than 50 µm per 10 piercings shall be observed.