INTERNATIONAL STANDARD

ISO 15759

First edition
2002-04-01

Medical infusion equipment — Plastics caps with inserted elastomeric liner for containers manufactured by the Blow-Fill-Seal (BFS) process

Matériel de perfusion à usage médical — Capsules plastiques avec un joint à base d'élastomère pour récipients (flacons plastiques) produits par le procédé simultané d'extrusion/soufflage/remplissage (ESR)

Reference number
ISO 15759:2002(E)

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Printed in Switzerland

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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 3.

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 International Standard may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 15759 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

Annexes A, B, C, D, E, F, G, H and I form a normative part of this International Standard.

Introduction

The materials used to manufacture Blow-Fill-Seal containers are primary packaging materials suitable for storing infusion solutions until they are administered. This International Standard deals with plastic caps with inserted elastomeric liners for use with Blow-Fill-Seal containers and describes their dimensional and functional requirements. This International Standard takes into account that the cap is not a primary packaging component.

Medical infusion equipment — Plastics caps with inserted elastomeric liner for containers manufactured by the Blow-Fill-Seal (BFS) process

1 Scope

This International Standard specifies the dimensional and functional requirements for plastics caps with inserted elastomeric liners, attached to the infusion container (BFS container) by welding or by collar technique. These caps are intended for use in the packaging and handling of liquid drugs for parenteral delivery.

2 Normative references

The following normative documents contain provisions which, through reference in this text, constitute provisions of this International Standard. For dated references, subsequent amendments to, or revisions of, any of these publications do not apply. However, parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the normative documents indicated below. For undated references, the latest edition of the normative document referred to applies. Members of ISO and IEC maintain registers of currently valid International Standards.

ISO 48:1994, *Rubber, vulcanized or thermoplastic — Determination of hardness (hardness between 10 IRHD and 100 IRHD)*

ISO 2768-1:1989, *General tolerances — Part 1: Tolerances for linear and angular dimensions without individual tolerance indications*

ISO 3302-1:1996, *Rubber — Tolerances for products — Part 1: Dimensional tolerances*

ISO 7500-1:1999, *Metallic materials — Verification of static uniaxial testing machines — Part 1: Tension/compression testing machines — Verification and calibration of the force-measuring system*

ISO 7864:1993, *Sterile hypodermic needles for single use*

ISO 8536-4:1998, *Infusion equipment for medical use — Part 4: Infusion sets for single use, gravity feed*

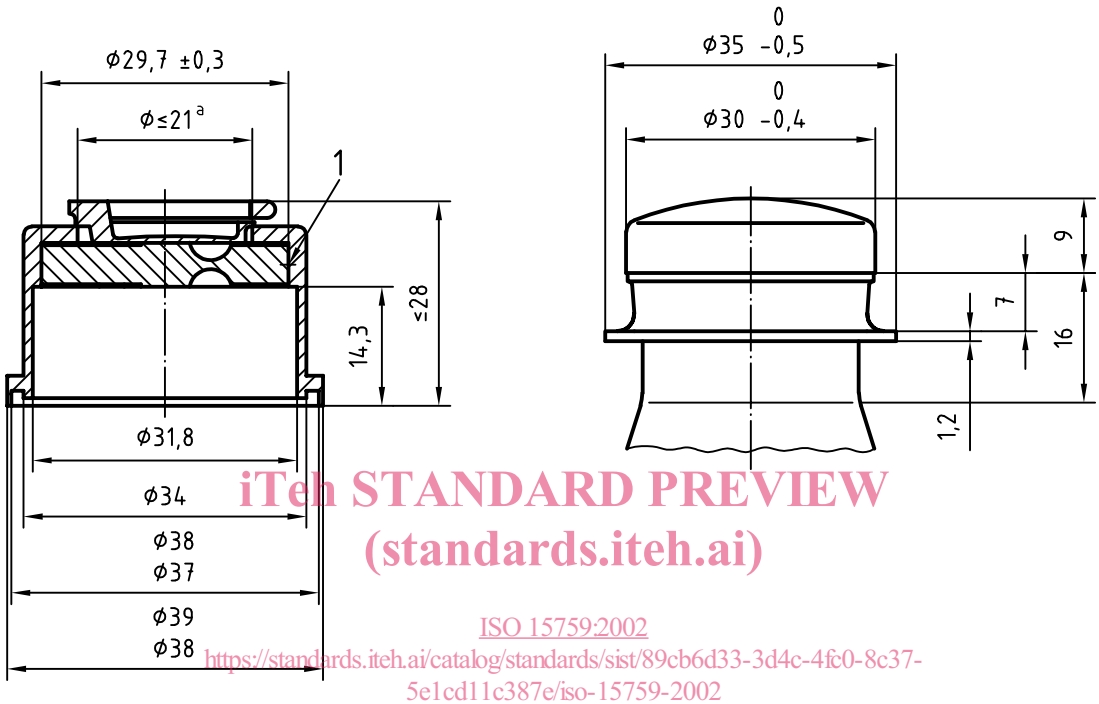
ISO 8871:1990, *Elastomeric parts for aqueous parenteral preparations*

3 Dimensions and designation

3.1 Plastics cap for attachment by welding technique (Form A)

General tolerances for Form A plastics caps shall be in accordance with ISO 2768-1; dimensions shall be in accordance with Figure 1. Elastomeric liners for such caps shall be in accordance with ISO 3302-1.

Dimensions in millimetres



Key

1 Measuring point at the centre

[a] Diameter of score line.

Figure 1

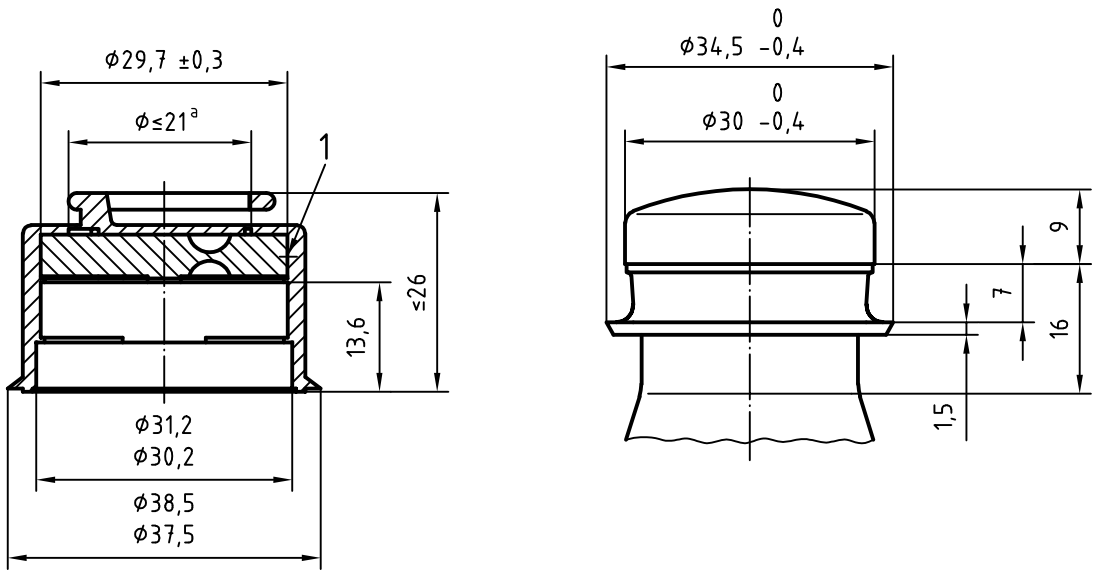
Plastics cap(s) of Form A in accordance with this International Standard shall be designated as follows:

Cap ISO 15759-BFS-A

3.2 Plastics cap for attachment by collar technique (Form B)

Dimensions for Form B plastics caps shall be in accordance with Figure 2.

Dimensions in millimetres



Key

1 Measuring point at the centre

[a] Diameter of score line.

Figure 2

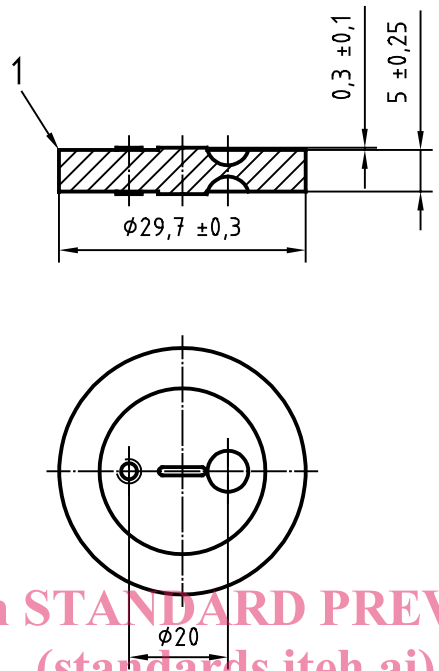
Plastics cap(s) of Form B in accordance with this International Standard shall be designated as follows:

Cap ISO 15759-BFS-B

3.3 Elastomeric liner

Dimensions for elastomeric liners for plastics caps of Form A or Form B shall be in accordance with Figure 3.

Dimensions in millimetres



Key

1 Trimming edge max. ∅ 30,2

Figure 3

Elastomeric liners in accordance with this International Standard shall be designated as follows:

Elastomeric liner ISO 15759

Figure 3 illustrates a typical liner design. Other liner designs are permitted.

4 Materials for cap and liner

4.1 Materials shall be in accordance with the requirements in clauses 6, 7, 8 and 9. The choice of plastic and elastomeric materials shall be subject to agreement between manufacturer and customer.

4.2 Resistance to ageing depends largely on presterilization techniques, storage and handling conditions. The period during which cap and liner shall comply with the requirements of this International Standard is subject to agreement between manufacturer and customer.

4.3 The shelf life of the liner while in contact with the drug is determined by compatibility tests to be carried out by the user.

4.4 ISO 2230 describes storage guidelines for vulcanized elastomeric parts.

5 Plastics cap — Physical requirements and testing

5.1 Leaktightness

When testing the leaktightness of the covered piercing area in accordance with annex H, no leakage shall be observed.

5.2 Opening force

When testing the opening force needed to expose the piercing area in accordance with annex I, the required force shall not exceed 80 N, and shall not tear the cap outside the piercing area.

6 Liner — Physical requirements and testing

6.1 General requirements

6.1.1 Injection gates and sprues are not allowed in the sealing area, i.e. between cap and liner.

6.1.2 Marks, indentations and spacers are allowed. The height of spacers shall not exceed 0,3 mm.

6.2 Hardness

Hardness requirements shall be agreed between manufacturer and customer. The hardness shall not differ from the nominal value by more than ± 5 IRHD when tested in accordance with ISO 48.

6.3 Fragmentation (coring)

When testing for fragmentation in accordance with annex A, no more than two fragments of diameter equal to or greater than 50 μm shall be observed per 10 piercings.

6.4 Penetration force

When testing for penetration in accordance with annex B, the force required to penetrate the liner shall not exceed 80 N. The average value shall not exceed 75 N.

6.5 Dynamic spike-retention capability

When tested in accordance with annex C, the measured retention force shall not fall below 20 N.

6.6 Static spike-retention capability

When tested in accordance with annex D, no leakage shall be observed between the spike and liner during a period of 4 h.

6.7 Resealability

When piercing the liner with a hypodermic needle in accordance with annex E, the requirements concerning resealability shall be fulfilled, and no air shall escape.

7 Plastics cap — Chemical requirements and testing

The plastics material used to manufacture the cap shall be physiologically harmless.

8 Liner — Chemical requirements and testing

The characteristics of the liner material shall not exceed the limits specified in Table 1, when tested in accordance with ISO 8871.

Table 1 — Chemical limits for elastomeric liner

Characteristics	Limits	Test method as described in ISO 8871:1990
Reducing matter (oxidizables)	$\leqslant$ 7,0 ml $c(KMnO_4) = 2$ mmol/l per 20 ml	Annex C
Heavy metals (calculated as Pb^{2+})	$\leqslant$ 10 µg Pb^{+2}/10 ml	Annex D
Ammonium (calculated as NH_4^+)	$\leqslant$ 20 µg NH_4^+/10 ml	Annex E
Acidity/alkalinity	$\leqslant$ 1,0 ml $c(HCl)$ or $c(NaOH) = 5$ mmol/l per 20 ml	Annex G
Residue on evaporation (total solids)	$\leqslant$ 4 mg/100 ml	Annex H
Volatile sulfides (at pH $\approx$ 2)	Coloration of lead acetate paper $\leqslant$ 50 µg Ma_2S/20 cm^2 of closure	Annex J
Zinc (calculated as Zn^{2+})	$Zn^{2+} \leqslant$ 50 µg/10 ml	Annex K
Conductivity	$\leqslant$ 40 µS/cm	Annex L
Turbidity	Not exceeding the opalescence of suspension No. 3	Annex M

9 Biological requirements for plastics cap and liner

Biological requirements are not part of this International Standard; however, since biological tests are required by most of the national Pharmacopoeia or other health authority regulations, they are mandatory for manufacturers and users in countries where such regulations exist. Where none exists, reference should be made to biological tests, e.g. as described in the United States Pharmacopeia or other pharmacopoeia.

10 Packaging

The packaging shall protect the plastics caps and liners during transportation and storage in such a way that their function is not impaired and they remain clean.

11 Storage

Prior to end use, the plastics caps and liners shall be stored between 0 °C and 40 °C and shall not be exposed to UV radiation. Under these conditions, they shall comply with the requirements of this International Standard throughout a storage period of six years.

12 Marking

The packaging of plastics caps and liners which comply with the requirements of this International Standard shall be marked as specified in clause 3, e.g.

Cap ISO 15759-BFS-B