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Snap-on bottles for metering pumps —

Part 2: Moulded glass

Flacons encliquetables pour pompes doseuses —

Partie 2: Verre moulé

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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 of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

A list of all parts in the ISO 24166 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

This document is part of a series of International Standards for containers made from different materials used in combination with metering pumps for medicinal applications.

Glass containers are mainly used for that purpose. Plastic containers can be used as an alternative.

This document can be used for the development of standardized filling and assembling equipment.

Based on the dimensions of the containers, appropriate components, such as metering pumps and other closure systems can also be standardized. As such this document provides important inputs for developing entire packaging systems for medicinal applications.

Primary packaging materials are an integral part of medicinal products. Thus, depending on the jurisdiction, the principles of the current Good Manufacturing Practices (cGMP) can apply to the manufacturing of these components (e.g. ISO 15378).

Snap-on bottles for metering pumps —

Part 2:
Moulded glass

1 Scope

This document specifies the shape, dimensions, fill capacities and performance requirements of moulded glass bottles for metering pumps. It also specifies the material for the manufacturing of such containers as well as the secondary packaging.

This document also provides requirements for packaging of the moulded glass bottles and addresses nonsterile, ready to sterilize or sterile as three possible options.

This document is applicable to colourless or amber glass containers moulded from borosilicate or soda-lime-silica glass and intended to be used in the packaging, storage or transportation of products intended for medicinal use.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 719, *Glass — Hydrolytic resistance of glass grains at 98 °C — Method of test and classification*

ISO 720, *Glass — Hydrolytic resistance of glass grains at 121 °C — Method of test and classification*

ISO 4802-1, *Glassware — Hydrolytic resistance of the interior surfaces of glass containers — Part 1: Determination by titration method and classification*

ISO 4802-2, *Glassware — Hydrolytic resistance of the interior surfaces of glass containers — Part 2: Determination by flame spectrometry and classification*

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 11607-2, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
base foil
packaging component for protection of the pallet load from contamination

3.2
bottle
vial
container made of a suitable material, which is intended for packaging, storage and application of liquid medicinal products

EXAMPLE Tubular glass, moulded glass or plastic.

3.3
brimful capacity
volume of water required to fill a container, placed on a flat, horizontal surface

[SOURCE: ISO 4802-1:2016, 3.3]

3.4
chemical indicator
test system that reveals change in one or more pre-defined process variables based on a chemical change resulting from exposure to a process

[SOURCE: ISO 11139: 2018, 3.43, modified — "pre-specified" was replaced with "pre-defined", "or physical" was deleted.]

3.5
customer
business entity that purchases bottles for metering pumps and conducts further processing or filling as appropriate

[SOURCE: ISO 21882:2019, 3.1 modified — “sterilized ready for filling vials” was replaced with “bottles for metering pumps”.]

3.6
dip-tube
conduit, part of the metering pump, which delivers the product from the bottle to the metering mechanism

3.7
foil bag
gas permeable or non-permeable bag

Note 1 to entry: Foil bags can be used as *sterile barrier system* (3.16) or as *protective packaging* (3.13), depending on final usage.

3.8
label
written, printed or graphic information appearing on the item itself, on the packaging of each item or on the packaging of multiple items

[SOURCE: IMDRF/GRRP WG/N52:2019, 3.17, modified – replaced "unit" and "devices" with "item".]

3.9
manufacturer
business entity that manufactures or is otherwise responsible for the manufacturing of the bottles ready to be filled by the *customer* (3.5)

[SOURCE: ISO 21882:2019, 3.4. modified — “performs” was replaced with “manufactures”, “vials” was replaced with “bottles”.]

3.10
metering pump
device actuated by the user to deliver a specific dose of liquid

3.11
packaging system
combination of a sterile barrier system and protective packaging

[SOURCE: ISO 11139:2018, 3.192]

3.12
pallet
construction for transportation and storage of goods

3.13
protective packaging
configuration of materials designed to prevent damage to the sterile barrier system and its contents from the time of their assembly until the point of use

[SOURCE: ISO 11139:2018, 3.219]

3.14
sealing ring
bottle feature on top of the flange to support tightness

3.15
snap-on bottle
container with press-fit for metering pumps

3.16
sterile barrier system
SBS
minimum package that minimizes the risk of ingress of microorganisms and allows aseptic presentation of the sterile contents at the point of use

[SOURCE: ISO 11139:2018, 3.272]

3.17
transport cover
outside packaging layer protecting against environmental hazards and keeping the package units in place

4 Symbols

t bottom concavity

d_1 outer diameter body

h_1 total length

h_2 length cylindrical part of the body

h_3 inner depth

r_1 shoulder radius

r_2 bottom radius

M moulded

5 Dimensions

5.1 General

The dimensions including tolerances are a function of manufacturing processes and materials.

To achieve the specified dimensions and tolerances, it is recommended that the offset of the mould halve and insert for forming the neck finish are horizontally max. 0,1 mm.

The dimensions and tolerances are established to achieve a neck that allows a snap-on functionality with the metering pump. This functionality can be challenged by a tightness test. An example of a snap-on process including positioning of the dip-tube as well as a typical tightness test is given in Annex A and Annex B.

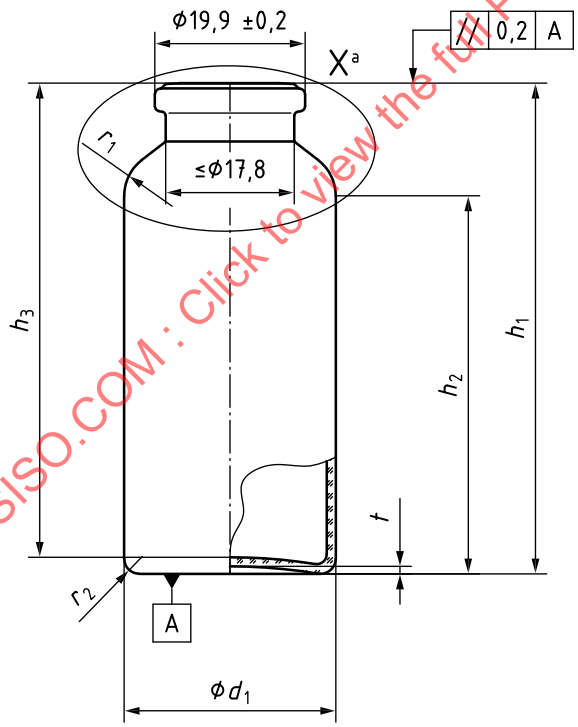
A test method for the inner depth as shown in Table 1 and Table 2 is described in Annex C.

The bottles can be manufactured with or without a sealing ring.

5.2 Bottles without sealing ring

The dimensions of snap-on bottles made of moulded glass shall meet the requirements of Figure 1 and Figure 2, as appropriate, and Table 1. The brimful capacity shall be as shown in Table 1.

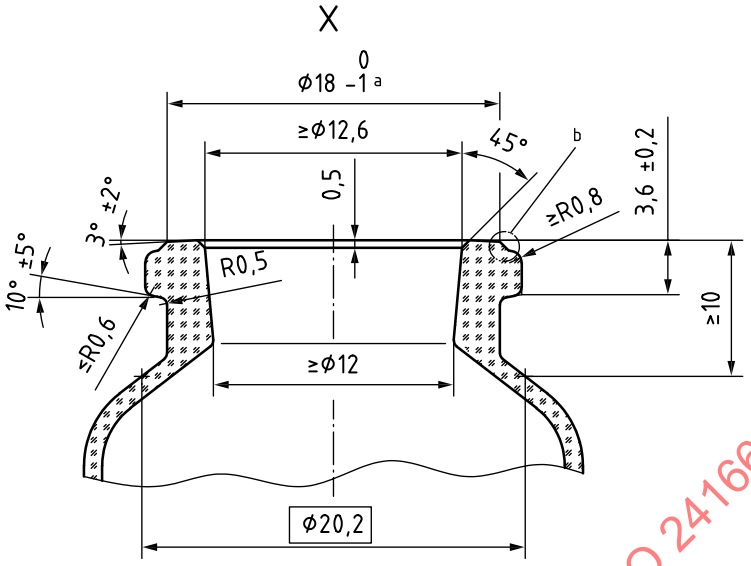
Dimensions in millimetres



a See Figure 2.

Figure 1 — Snap–on bottle without sealing ring

Dimensions in millimetres



a The mould split should be in between a diameter of 17 mm and 18 mm.

b The geometry in this area of the bottle neck finish can be designed as an offset or as a chamfer (free design).

Figure 2 — Neck finish without sealing ring

Table 1 — Brimful capacity and dimensions of snap-on bottles made of moulded glass without sealing ring

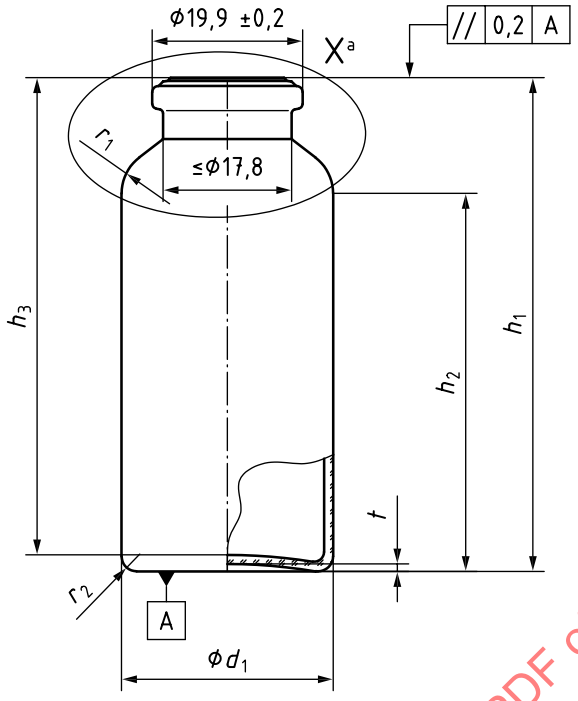
Dimensions in millimetres

Size of the bottle	Brimful capacity	d_1		h_1		h_2	h_3		r_1	r_2	t
	ml		Tol.		Tol.	min.		Tol.			
10M	15,0	25,4	±0,4	53,3	±0,6	35,3	49,0	±1,5	10,0	2,0	1,0
20M	23,5	28,0	±0,6	64,7	±0,5	50,0	58,9		3,8	2,0	2,0
30M	35,0	31,8		75,2	±0,8	57,0	69,4		7,8	2,5	1,5
50M	60,0	39,0	±0,5	82,9	±0,8	59,0	78,6	±2,0	14,0	2,0	2,0
100M	106,0	45,5	±0,8	102,9		76,5	97,2		14,0	3,0	2,0

5.3 Bottles with sealing ring

The dimensions of snap-on bottles made of moulded glass shall meet the requirements of Figure 3 and Figure 4, as appropriate, and Table 2. The brimful capacity shall be as shown in Table 2.

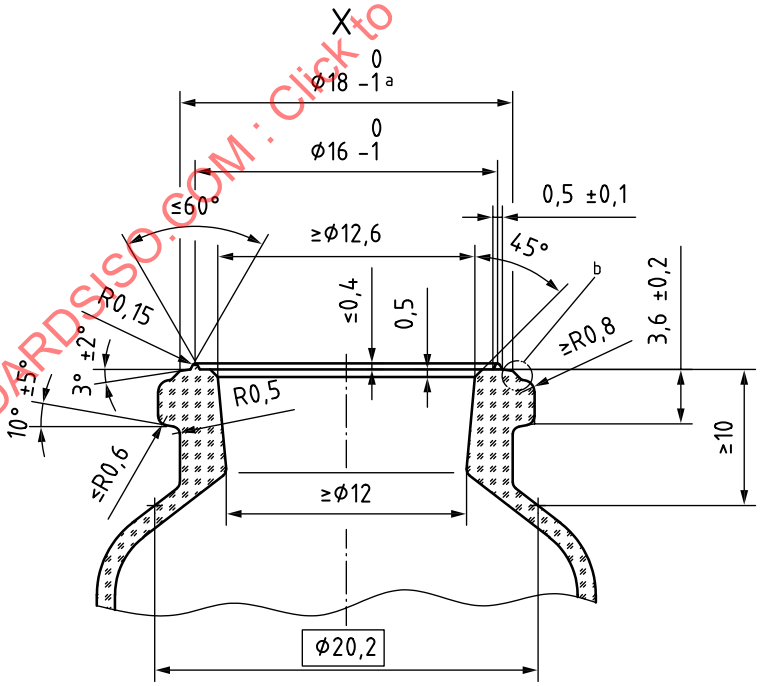
Dimensions in millimetres



a See Figure 4.

Figure 3 — Snap-on bottle with sealing ring

Dimensions in millimetres



a The mould split should be in between a diameter of 17 mm and 18 mm.

b The geometry in this area of the bottle neck finish can be designed as an offset or as a chamfer (free design).

Figure 4 — Neck with sealing ring

Table 2 — Brimful capacity and dimensions of snap-on bottles made of moulded glass with sealing ring

Dimensions in millimetres

Size of the bottle	Brimful capacity	d_1		h_1		h_2	h_3		r_1	r_2	t
	ml		Tol.		Tol.	min.		Tol.			
10M	15,0	25,4	±0,4	53,7	±0,6	35,3	49,4	±1,5	10,0	2,0	1,0
20M	23,5	28,0	±0,6	65,1	±0,5	50,0	59,3		3,8	2,0	2,0
30M	35,0	31,8		75,6	±0,8	57,0	69,8		7,8	2,5	1,5
50M	60,0	39,0	±0,5	83,3	±0,8	59,0	79,0	±2,0	14,0	2,0	2,0
100M	106,0	45,5	±0,8	103,3		76,5	97,2		14,0	3,0	2,0

6 Material

Materials for glass bottles for use with metering pumps shall be suitable for the manufacturing process, the sterilization method, storage, and fill-finish process with assembly of metering pumps.

Colourless (cl) or amber (br) borosilicate glass or soda-lime glass of one of the following hydrolytic resistance grain classes shall be used:

— ISO 720 – HGA 1;

— ISO 719 – HGB 3 or ISO 720 – HGA 2.

The following should be considered depending on the application and the intended use, as specified by the customer:

— conformity to applicable pharmacopoeia monographs;

— material composition requirements to meet specific drug/container interactions;

— shelf-life limitation requirements.

7 Requirements

7.1 General requirements

The following requirements shall be met to enable the functionality between the bottle and the metering pump:

— snap-on bottle sealing surfaces shall be free from grooves, ripples and undulations sufficient to affect the sealing performance when combined with the metering pump;

— the bottom shall have a shape and an inner surface that allows the dip-tube of the metering pump moving into a position of the bottle to minimize the residual volume;

— the supplier and the customer shall agree on the specifications for such sealing and bottom surfaces.

7.2 Physical requirements

7.2.1 Vertical Force

The bottles shall resist a vertical force of min. 900 N. The supplier and the customer shall agree on an Acceptable Quality Limit (AQL) for this limit value.

The test method is given in Annex D.

7.2.2 Particulate contaminations

Glass bottles for snap-on metering pumps shall be manufactured by processes that minimize the risk of particulate contamination.

The manufacturer and the customer should agree upon the size and number of visible particles and the test method.

NOTE 1 Currently no particle specifications are assigned for sub-visible particles regarding devices for non-parenteral products.

NOTE 2 Current pharmacopoeias identify visible particulates as undesirable but do not define the size or put a limit on the allowable number for non-parenteral products.

7.3 Chemical requirements

Glass bottles shall have hydrolytic resistance requirements as described in ISO 4802-1 and/or ISO 4802-2.

7.4 Sterilization

If the glass bottles are provided sterile, the sterilization method shall be validated in accordance with a suitable sterilization International Standard (e.g. ISO 11135, ISO 17665-1, ISO 11137-1 or ISO 14937).

NOTE Gamma Irradiation is typically not used for clear glass as it causes a yellow discoloration.

8 Marking of the bottle

The specification of the marking applied to the bottle, e.g. cavity number, is subject to agreement between customer and the manufacturer.

9 Packaging options

9.1 General packaging requirements

In general, there are three different conditions of packaging for the bottles due to the requirements of the customer. The product can be provided nonsterile, ready to sterilize or sterile.

The packaging shall protect the product from alteration, contamination or damage when exposed to expected conditions and hazards during processing, storage, handling and distribution.

All packaging configurations shall include the following parts (from outside to inside):

— pallet;

— label;

— transport cover;

— foil bags.

A base foil can be added as optional component to protect the pallet load from particles, dust, environmental hazards, etc. that could be necessary for certain types of pallets. An example is given in Annex E.

9.2 Packaging for nonsterile glass bottles

This packaging configuration is not designed for sterilization of the bottles. In addition to the packaging components specified in 9.1, the glass bottles shall be packaged in double foil bags with a closure or seal that prevents contamination of the content.

9.3 Ready to sterilize or sterile glass bottles

The packaging shall be designed and validated as a packaging system with protective packaging and sterile barrier system(s) in accordance with the requirements of ISO 11607-1 and ISO 11607-2 and compatible with the selected sterilization process. In addition to the packaging components specified in 9.1, the following requirements apply:

— the bottles shall be sealed in minimum 2 layers of foil bags. As a minimum, the last inner layer foil bag shall be designed and validated as a SBS. Further foil bags can be validated as a SBS depending on the requirement of the customer.

— the packaging shall be provided with an appropriate chemical indicator that indicates that the product has been exposed to the specified sterilization process.

Annex A
(informative)

Snap-on considerations

The following considerations are important for an efficient and safe snap-on process:

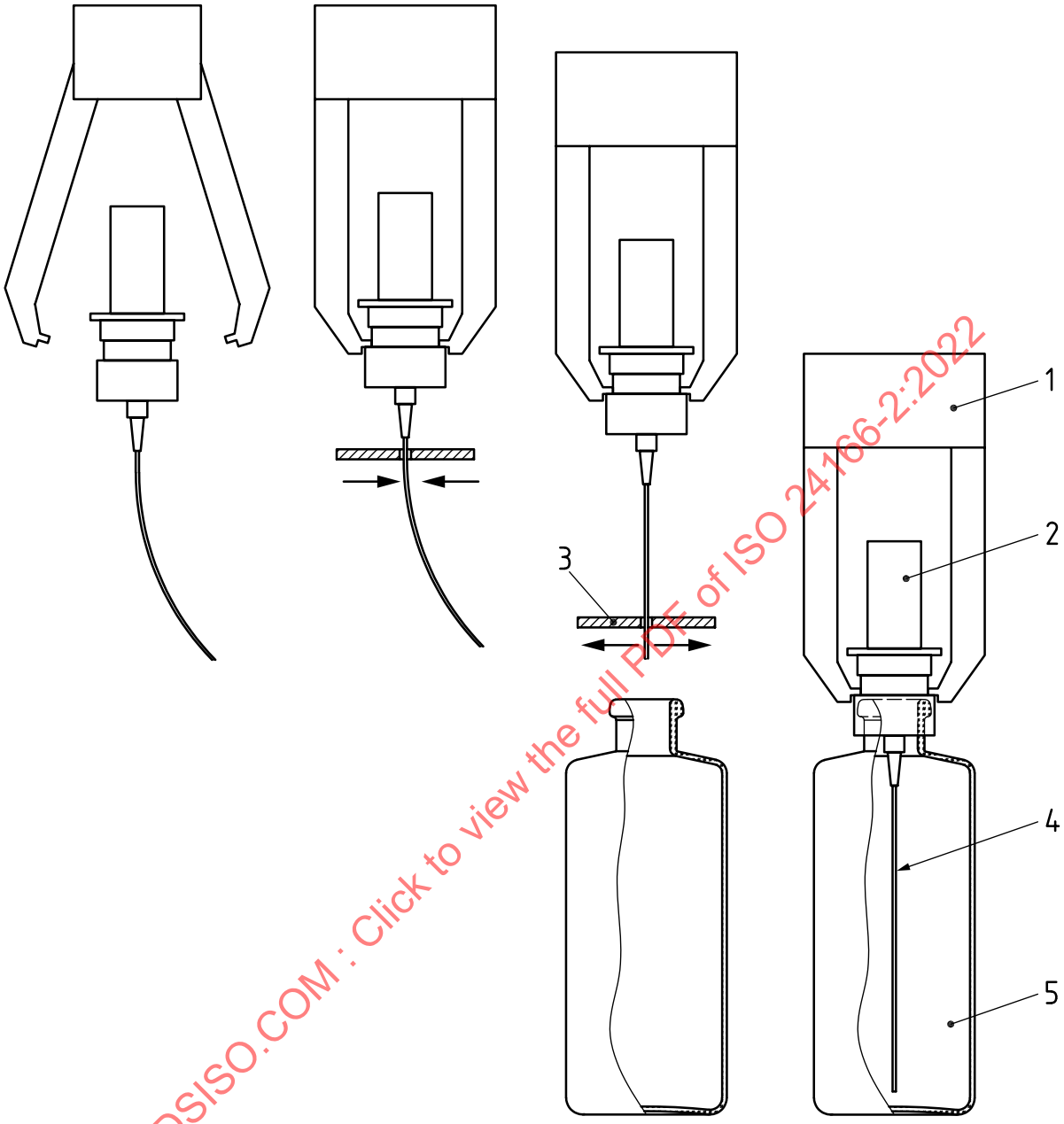
— the neck finish dimensions (see Clause 5);

— the material of the bottle;

— the correct positioning of metering pump, dip-tube and bottle;

— the way how the force is applied to achieve the snap on.

Figure A.1 shows an example of a snap-on process using a mechanical gripper system and a dip-tube stripper prism that maintains the dip-tube in a middle position. In this example, the force is transferred over the metering pump snap body, and not over the nasal adapter, to ensure that the resulting pressure is distributed evenly over the entire closure sealing rim.



Key

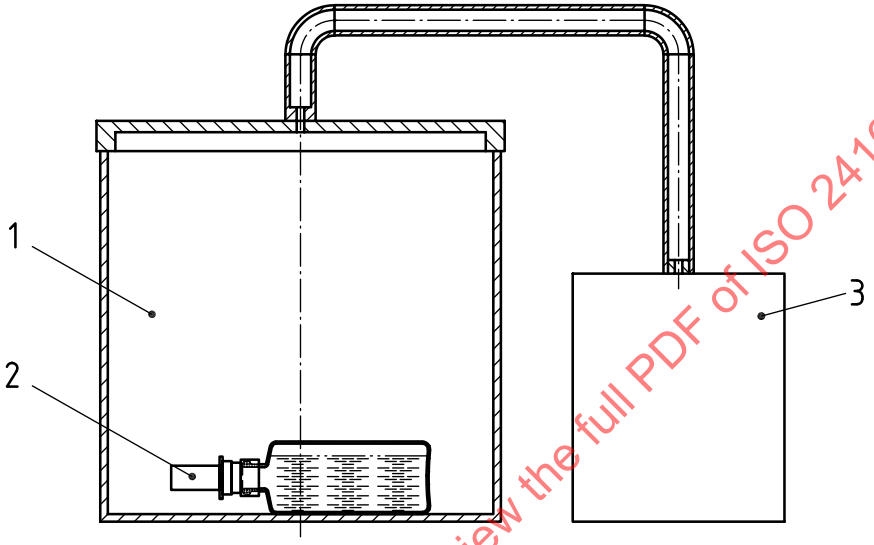
1 mechanical gripper system
2 metering pump
3 dip-tube stripper prism
4 dip-tube
5 bottle

Figure A.1 — Snap-on process

Annex B
(informative)

Tightness test

This annex proposes a test method suitable for verifying the integrity of the entire system. An example of a test equipment is shown in Figure B.1.



Key

1 desiccator
2 test device filled with liquid, e.g. methylene blue solution
3 vacuum pump

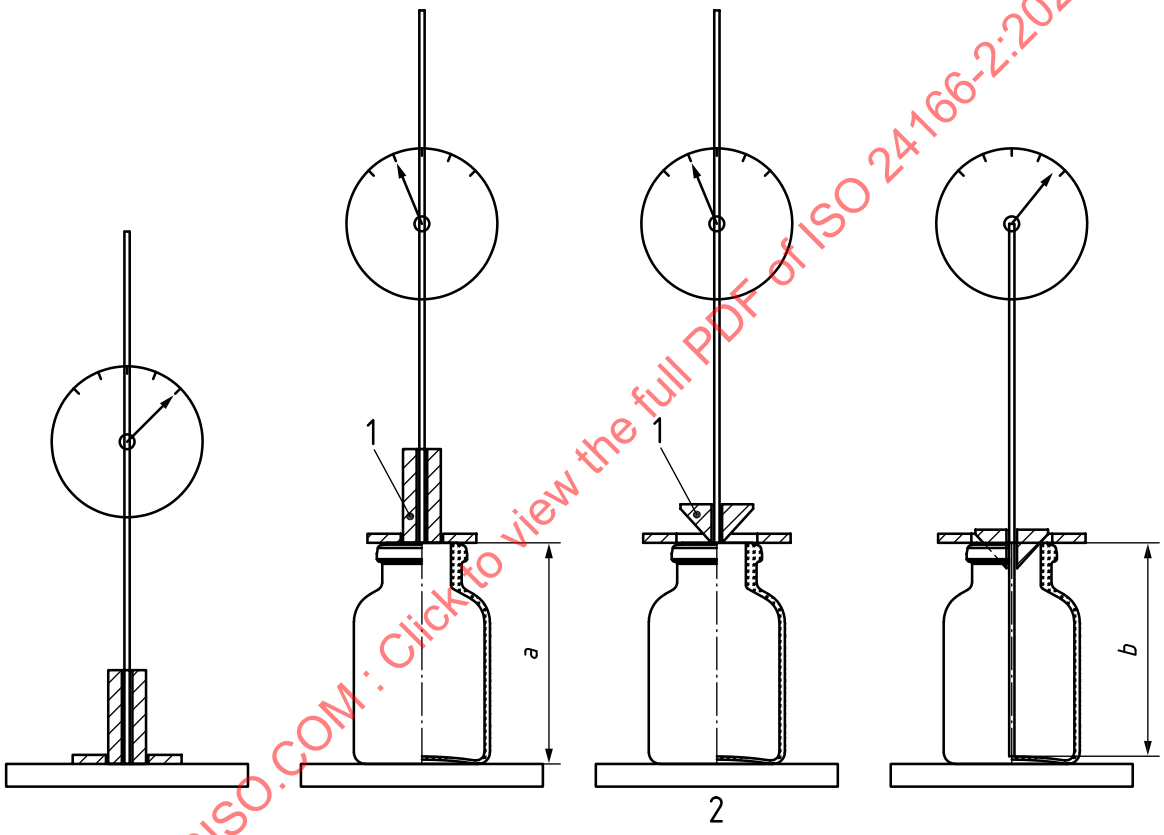
Figure B.1 — Schematic test description

The filled device is placed for 10 min in a desiccator at 500 hPa absolute pressure. After the storage time the system is checked if any liquid leaked from the container. If yes, the test failed.

Annex C
(informative)

Inner depth measuring

Place the bottle on a flat, horizontal surface. The inner depth of the bottle results from the approached highest point at the neck finish area and the centre of the bottom of the bottle. An example of a measuring device is shown in Figure C.1.



Key

1 centring
2 90° rotated view
a bottle height
b inner depth

Figure C.1 — Bottle inner depth measurement