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Packaging — Tamper verification features for medicinal product packaging

Emballage — Témoins d'effraction pour emballages de médicaments

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

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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 122, *Packaging.*

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

Requirements for tamper verification features on medicinal product packaging are emerging and expanding globally to reduce risk and improve patient safety.

This document is to support the harmonization and implementation of tamper verification features to the packaging of medicinal products worldwide.

The knowledge and experience gained in EN 16679:2014 has been used for developing this document. The background for the creation of a European Standard for tamper verification features for medicinal product packaging (EN 16679) was the European Directive 2001/83/EC[6], as amended by Directive 2011/62/EU[7], the latter commonly referred to as the "Falsified Medicines Directive" (FMD).

The packaging of medicinal products placed on the market and incorporating tamper verification features in accordance with this document meets, as an example but not limited to, the requirements of Directive 2001/83/EC[6] as amended by Directive 2011/62/EU[7]. Article 54(o) of the Directive stipulates, that on the outer packaging of certain medicinal products or, where there is no outer packaging, on the immediate packaging must appear, among others, "a device allowing verification of whether the outer packaging has been tampered with".

Packaging — Tamper verification features for medicinal product packaging

1 Scope

This document specifies requirements and provides guidance for the application, use and check of tamper verification features to the packaging of medicinal products.

The principles in this document can be applied in other sectors, as appropriate.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

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

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

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

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

3.1
falsified medicinal product
medicinal products (3.6) that deliberately/fraudulently misrepresent their identity, composition or source

[SOURCE: WHO, Definitions of Substandard and Falsified (SF) Medical Products, 2017[17]]

3.2
finished product
authorized *medicinal product* (3.6) which has undergone all stages of production including packaging in its final container as it is dispensed, sold or otherwise supplied

3.3
immediate packaging
primary packaging
container or other form of packaging directly in contact with the *medicinal product* (3.6)

3.4
manufacturing authorization holder
natural or legal person or entity that is authorized for total or partial manufacture

Note 1 to entry: This includes replacement of safety and *tamper verification features* (3.9) (in accordance with Directive 2001/83/EC[6], Article 47a(1)(b) as amended by Directive 2011/62/EU[7]).

3.5
marketing authorization holder
natural or legal person or entity responsible for placing the *medicinal product* (3.6) on the market

3.6
medicinal product
substance or combination of substances that may be administered to human beings (or animals) for treating or preventing disease, with the aim/purpose to making a medical diagnosis or to restore, correct or modify physiological functions

[SOURCE: ISO 11615:2017, 3.1.50, modified — "Pharmaceutical product" has been replaced by "substance" in the definition. The Notes to entry have been deleted.]

3.7
outer packaging
secondary packaging
packaging designed to contain one or more primary packagings together with any protective materials where required

[SOURCE: ISO 21067-1:2016, 2.2.4, modified — "Outer packaging" has been added as an admitted term.]

3.8
tampering
unauthorized attempt to open, manipulate or re-use the packaging or elements of it

3.9
tamper verification feature
characteristic(s) allowing *verification* (3.10) of whether the *outer packaging* (3.7) of *medicinal products* (3.6) or, where there is no outer packaging, the immediate packaging has been opened or tampered with

Note 1 to entry: Tamper verification features may be referred to as "anti-tampering devices".

3.10
verification
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

[SOURCE: ISO 9000:2015, 3.8.12, modified — The Notes to entry have been deleted.]

4 General requirements

4.1 Tamper verification features

Tamper verification features shall be applied to packaging of medicinal products as required, or may be applied for other situations.

4.2 Purpose of tamper verification features

Tamper verification features should provide an indication that the packaging of a finished product has been opened or tampered with, i.e. indicating a possible adulteration or unauthorized attempt to open the packaging or entry of falsified medicinal products into the legitimate supply chain. Tamper verification features limit the ability to replace the contents of genuine packs.

Tamper verification features are only one element of possible safety features against falsification and do not, by themselves, prevent falsification of medicinal products.

4.3 Application and use of tamper verification features

The application of tamper verification features shall not compromise the readability of statutory information which can include tactile markings. The statutory text on the packaging should remain readable after opening the pack.

Applying tamper verification features can increase the physical strength needed to open the packaging.

The immediate packaging of medicinal products may also provide tamper verification. However, this alone does not necessarily meet the tamper verification requirements in certain jurisdictions.

4.4 Check of tamper verification features

The tamper verification feature shall enable a visual check for its presence and any evidence of tampering (see 5.2 to 5.11 for details).

5 Categories of tamper verification features

5.1 General

Tamper verification technologies applied on the packaging are constantly evolving. Ten broad categories of tamper verification features are described in this document (see 5.2 to 5.11). Other tamper verification features can exist or be developed and they shall meet the requirements of this document as appropriate (see 5.12). The features illustrated in Clause 5 are non-exhaustive.

Annex A provides additional information on tamper verification features as listed in 5.2 to 5.11.

If there is no outer packaging, the immediate packaging (e.g. bottles and tubes) shall be equipped with a tamper verification feature.

Tamper verification features shall meet the requirements of Clause 4.

The marketing authorization holder or the manufacturing authorization holder, as appropriate, shall decide on appropriate tamper verification feature(s).

This choice should be based on an assessment that takes into account a number of factors including technical feasibility, appropriateness, effectiveness, other safety features used on the product, and overall cost.

5.2 Folding boxes closed with glue

5.2.1 Description

A glue (e.g. hot melt, polyurethane, dispersion or other glues, or a combination of glues) is applied to close the folding box. These boxes may incorporate perforations to facilitate the opening of the pack.

5.2.2 Criteria of tamper verification

Folding boxes closed with glue shall be cut or torn to gain access to the product. The box cannot be opened without visible signs of tear-off/ripping-off of the carton board surface and/or other parts of the folding box.

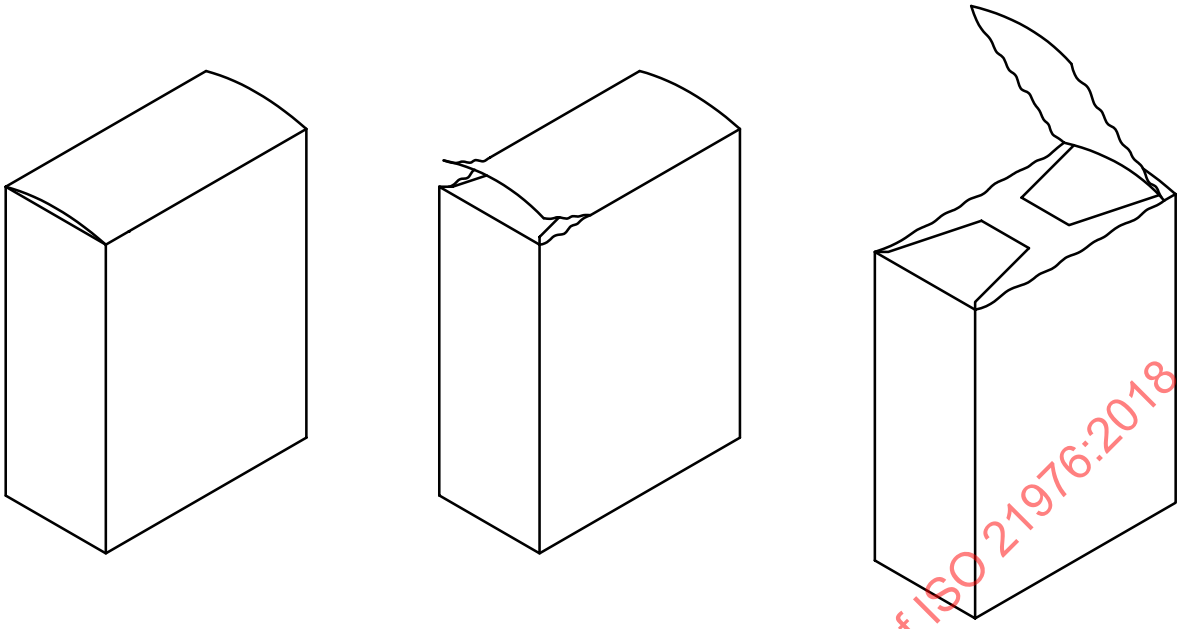
5.2.3 Verification

First time opening of the folding box leads to visible, irreversible damage of the folding box integrity, for example (see Figure 1 and Figure 2):

— damage of one or more of the flaps, see Figure 1 b) and Figure 1 c);

— damage of perforations, see Figure 2 b) and Figure 2 c);

— damage of other parts of the folding box.

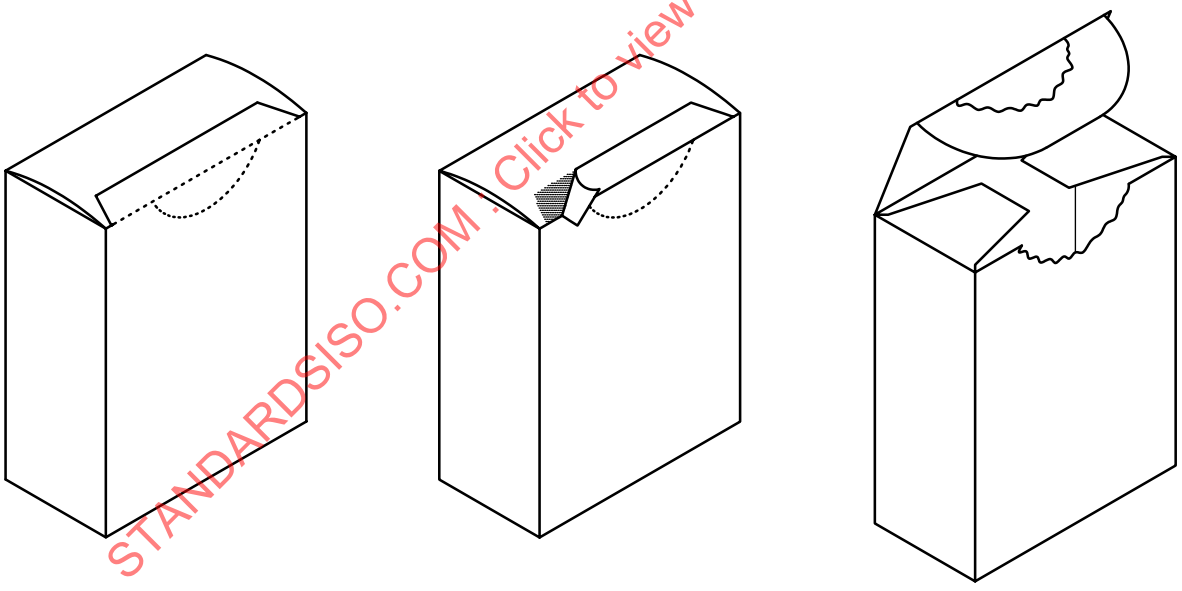


a) Original condition

b) Where the opening of the box has been tried

c) Opened

Figure 1 — Example of a folding box closed with glue



a) Original condition

b) Where the opening of the box has been tried

c) Opened

Figure 2 — Example of a folding box with perforations closed with glue

5.3 Specially constructed folding boxes

5.3.1 Description

The flaps and the body of the folding box are constructed in such a way that the feature is activated/enabled by inserting the flaps by the manufacturer to close the folding box. First time opening leads to

a visible, irreversible change of the folding box appearance in such way that parts of the flaps or of the folding box are damaged.

5.3.2 Criteria of tamper verification

The closure is set up in such a way that, the first time the box is opened, parts of the flaps or of the folding box are ripped off and/or torn.

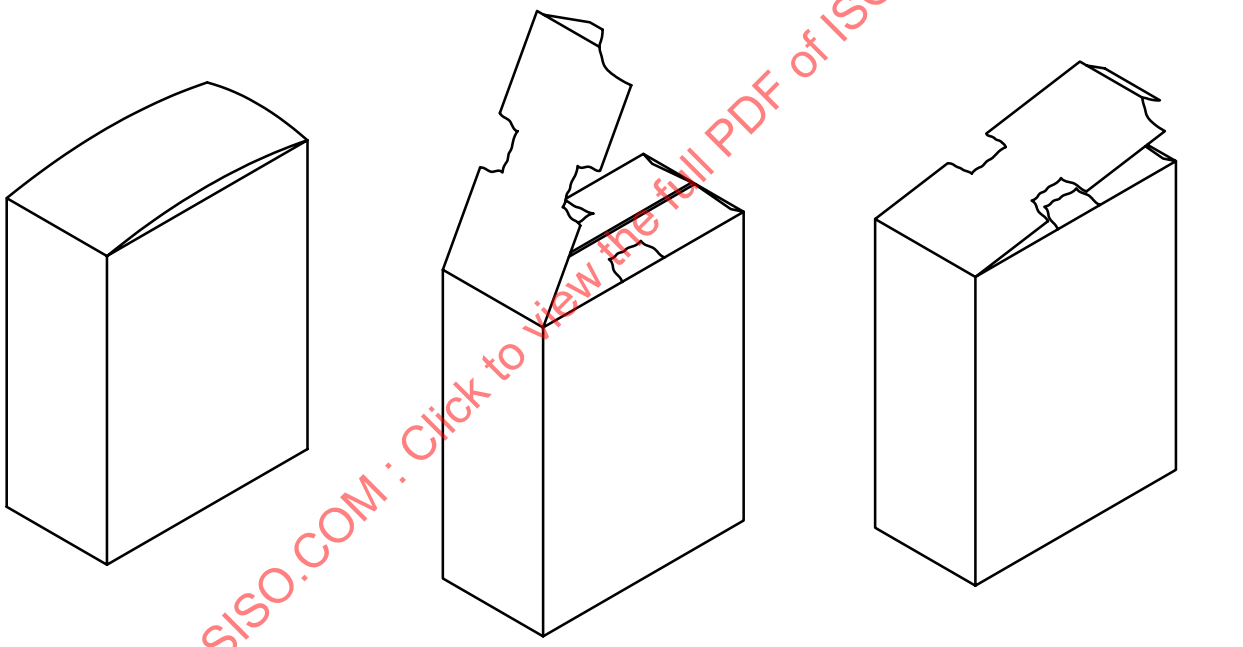
5.3.3 Verification

First time opening leads to visible, irreversible damage of the folding box integrity, for example (see Figure 3):

— damage of one or more of the flaps, see Figure 3 b) and Figure 3 c);

— damage of perforations and/or scores/half cuts, if applicable;

— damage of other parts of the folding box.



a) Original condition **b) Opened** **c) Condition in which the re-closing of the opened condition shows the first time opening**

Figure 3 — Example of a specially constructed folding box

5.4 Sealing labels and tapes

5.4.1 Description

A label or tape (e.g. from paper, film or laminate) is applied in order to seal the packaging of medicinal products. The packaging to be sealed may incorporate perforations to facilitate the opening of the pack. The sealing label or tape shall provide the integrity of the sealed packaging.

5.4.2 Criteria of tamper verification

Tampering of the sealing label or tape or opening of the packaging shall lead to visible, irreversible damage or change of the packaging and/or of the label or tape.

5.4.3 Verification

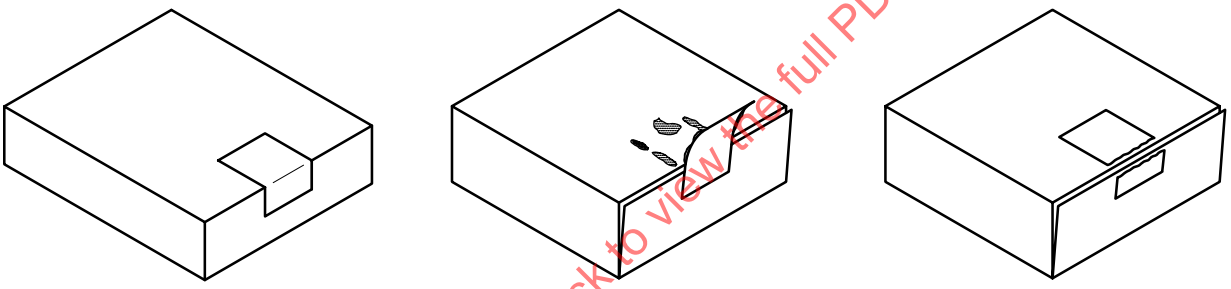
Verification of typical categories of sealing labels or tapes (see Figure 4 and Figure 5) are:

a) **Fibre-tear seal**: By tampering/tearing off the sealing label or tape, the fibre or the surface of the packaging is torn or ripped off and, thus, clearly indicates a visible, irreversible damage or change of the packaging.

b) **Void seal**: By tampering/tearing off the sealing label or tape, a hidden pattern or text of the sealing label or tape becomes irreversibly visible on the sealing label or tape and/or on the packaging.

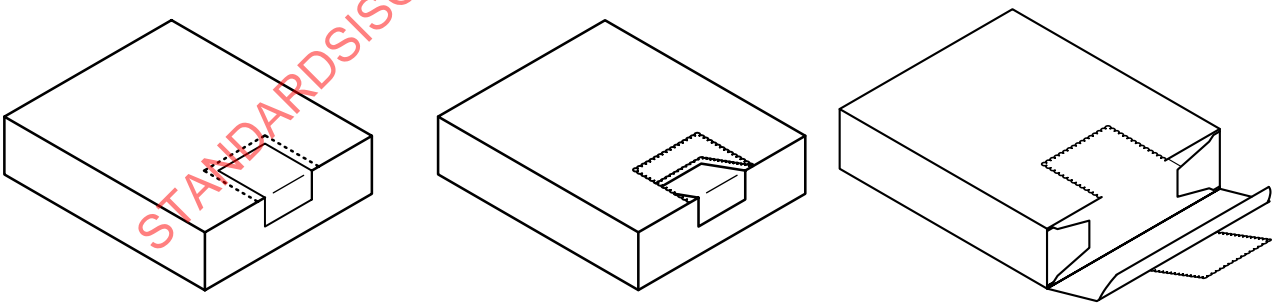
c) **Seal made with opening strips or perforations**: By tampering or opening or tearing off the sealing label or tape, the sealing label or tape becomes irreversibly torn, broken or peeled off and indicates that the individual product container has previously been sealed.

d) **Seal made of fragile material**: By tampering or opening or tearing off the sealing label or tape, the sealing label or tape becomes irreversibly torn or broken.



a) Original condition **b) Opened = torn-off** **c) Opened = cut**

Figure 4 — Example of a sealing label or tape



a) Original condition **b) Where the opening of the flap has been tried** **c) Opened**

Figure 5 — Example of a folding box with perforations closed with a label or tape

NOTE Further examples for sealing labels or tapes are bespoke tamper-evident void seals and seals with opening strip.

5.5 Film wrappers

5.5.1 Description

The product container or part of it is wrapped in film ensuring the product is appropriately sealed. The film shall be torn to gain access to the product.

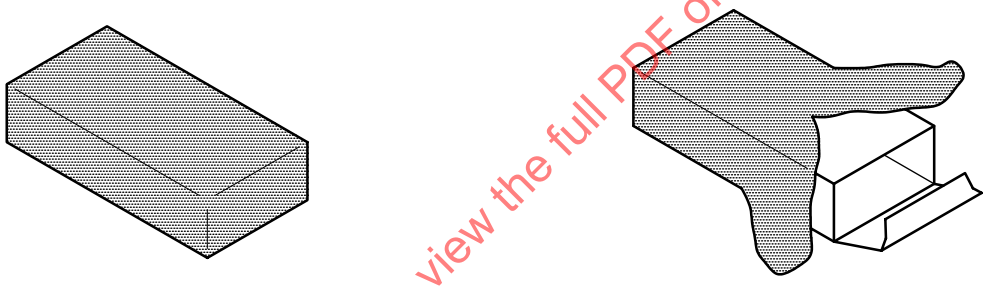
5.5.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible damage or change of the film wrapper and show visible evidence of tampering.

5.5.3 Verification

First time opening leads to visible, irreversible damage of the film wrapper and provides the indication that the packaging has been tampered with. The film wrapper cannot be removed and resealed without showing visible evidence of tampering (see Figure 6).

It can be appropriate to indicate that a film wrapper should be present.



a) Original condition **b) Opened**

Figure 6 — Example of a film wrapper

5.6 Sleeves

5.6.1 Description

A film is shrunk around the immediate packaging or at least around its closure, where the film adapts to the outer shape. The sleeve shall be ripped or broken to gain access to the product.

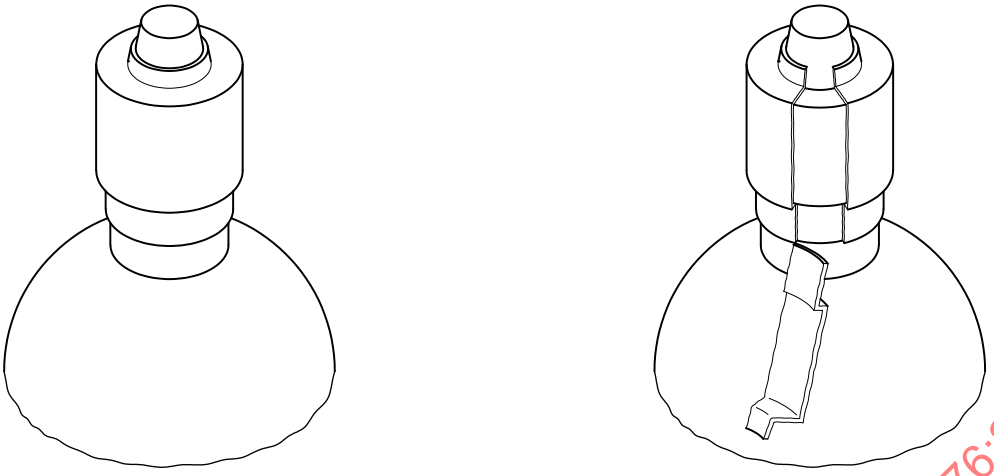
5.6.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible damage or change of the sleeve and show visible evidence of tampering.

5.6.3 Verification

First time opening leads to visible, irreversible damage of the sleeve and provides the indication that the immediate packaging or its closure has been tampered with. The sleeve cannot be removed and resealed without showing visible evidence of tampering (see Figure 7).

It can be appropriate to indicate that a sleeve should be present.



a) Original condition b) Opened

Figure 7 — Example of a sleeve shrunk around a closure of a bottle

5.7 Breakable or tear-away closure

5.7.1 Description

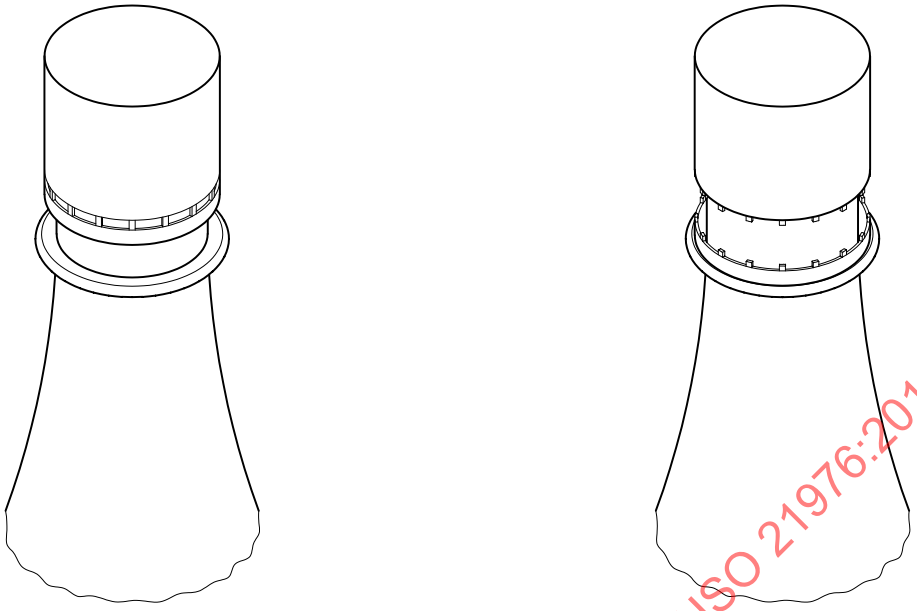
The product container is closed with a breakable or tear-away closure (e.g. metal, plastic) that has a portion that breaks on opening.

5.7.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible change in the closure and show visible evidence of tampering.

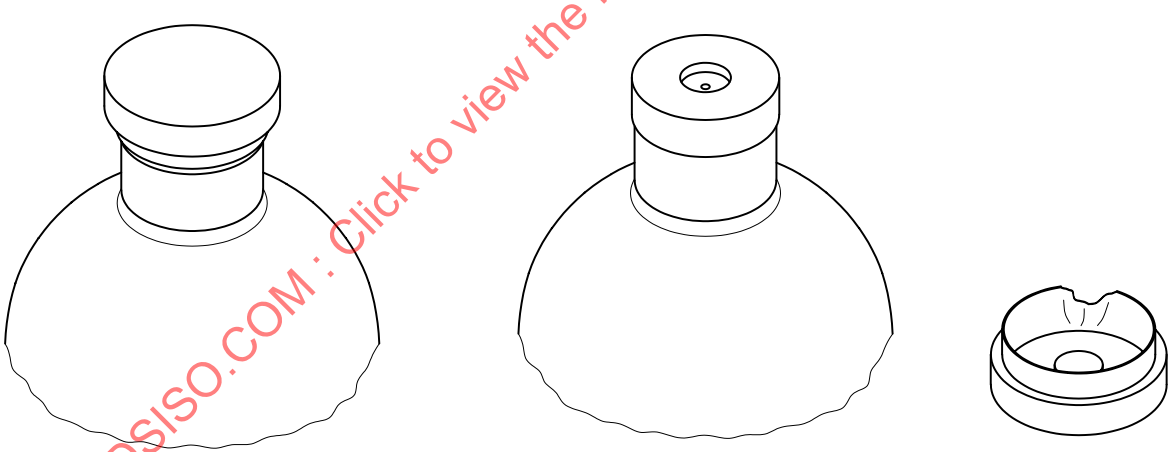
5.7.3 Verification

First time opening leads to visible, irreversible change in the closure. The closure cannot be removed and reapplied in its original state without showing visible evidence of tampering (see Figure 8 and Figure 9).



a) Original condition b) Opened

Figure 8 — Example of a breakable closure



a) Original condition b) Opened

Figure 9 — Example of a tear-away closure

5.8 Container inner seal or membrane

5.8.1 Description

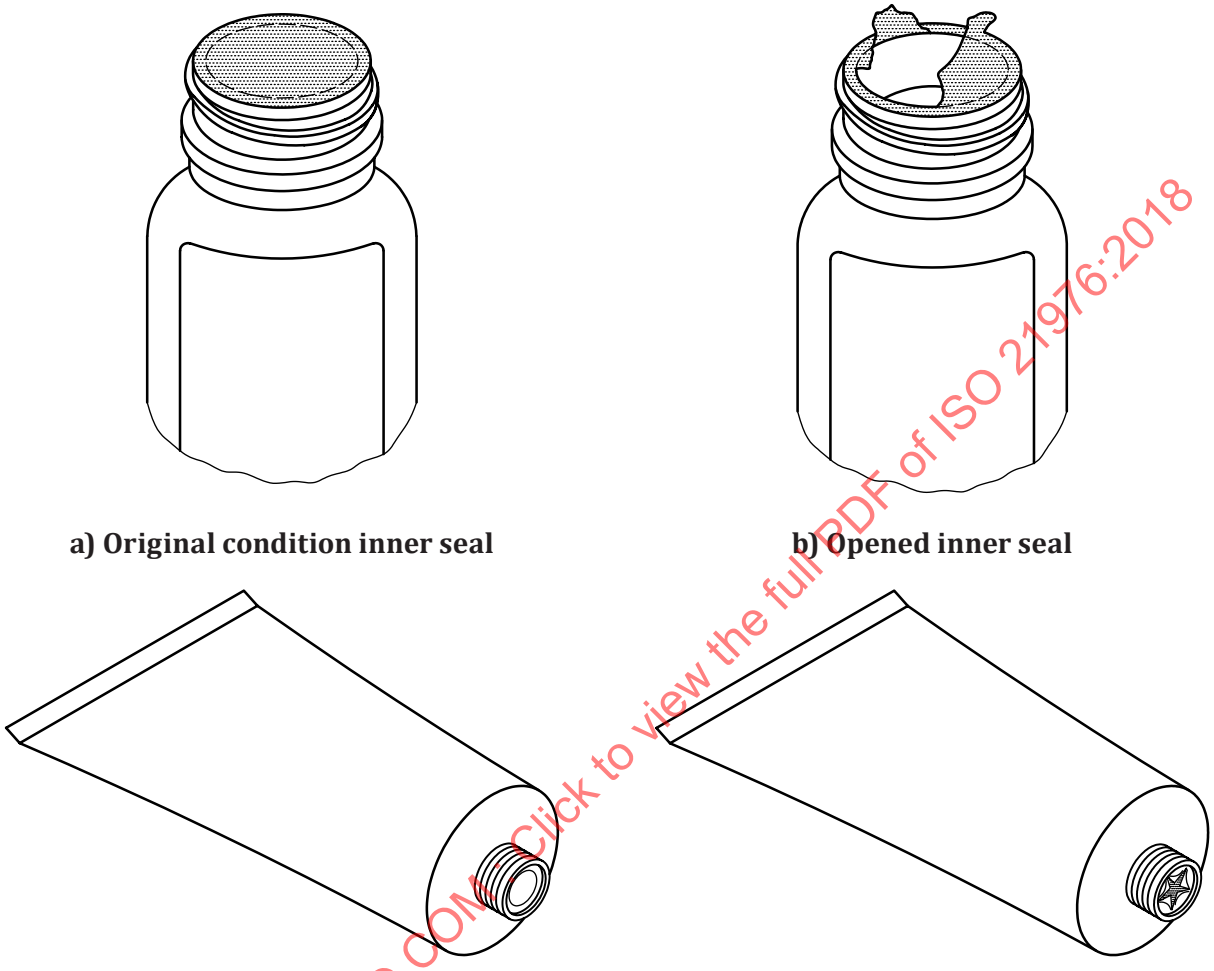
The product is sealed to the opening/mouth of a container under the cap with e.g. a paper, thermal plastic, polystyrene foam, plastic film, foil, or combinations thereof. It shall be removed, punctured or broken to gain access to the product.The inner seal or membrane shall be intact and sealed all the way around.

5.8.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible damage or change of the inner seal or membrane and show visible evidence of tampering.

5.8.3 Verification

First time opening of the inner seal or membrane leads to visible, irreversible damage. The inner seal or membrane cannot be opened and reapplied in its original state without showing visible evidence of tampering (see Figure 10).



a) Original condition inner seal

b) Opened inner seal

c) Original condition membrane

d) Opened membrane

Figure 10 — Two examples of a container inner seal or membrane

5.9 Display blister pack

5.9.1 Description

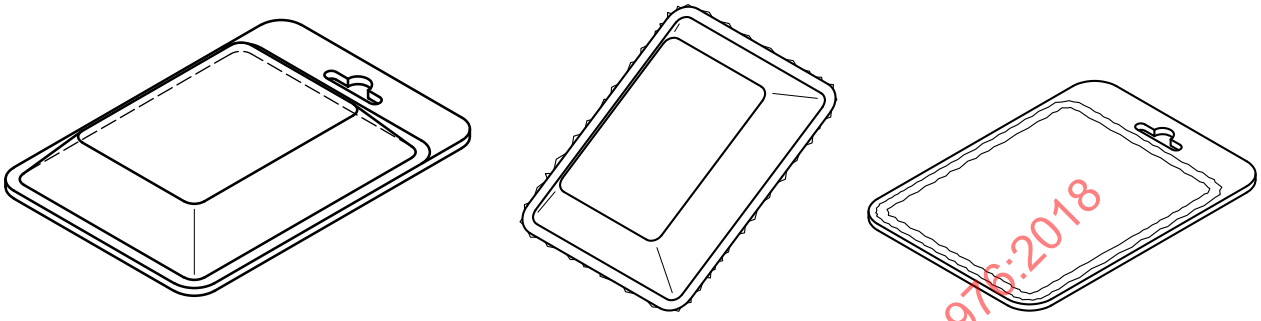
The product is sealed into a display blister pack which shall be cut or broken to gain access to the product. The display blister pack shall be intact and sealed all the way around.

5.9.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible damage or change of the display blister pack and show visible evidence of tampering.

5.9.3 Verification

First time opening leads to visible, irreversible damage of the display blister pack and/or its sealing. The display blister pack cannot be opened and reclosed without showing visible evidence of tampering (see Figure 11).



a) Original condition **b) Opened**

Figure 11 — Example of a display blister pack

5.10 Flexible packaging

5.10.1 Description

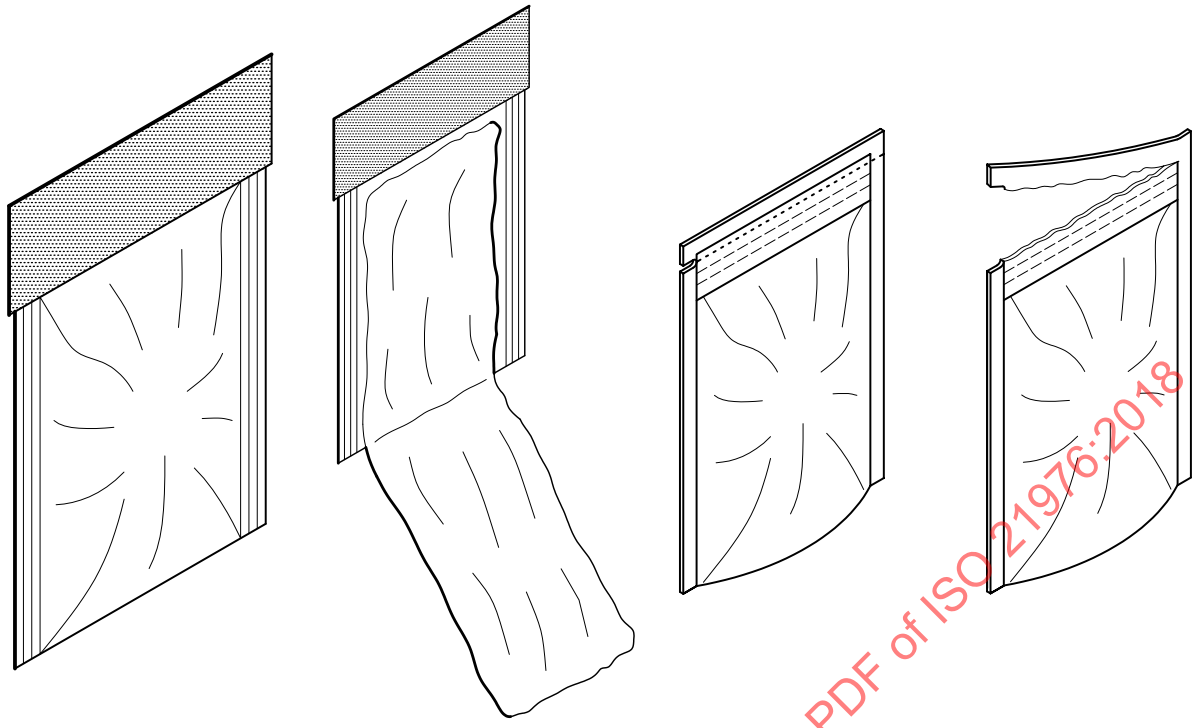
The medicinal product is sealed into a film or foil or combination thereof (e.g. pouches, sachets). The packaging shall be cut or torn to gain access to the product.

5.10.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible damage or change of the flexible packaging and show visible evidence of tampering.

5.10.3 Verification

First time opening leads to visible, irreversible damage of the flexible packaging and/or its sealing. The flexible packaging cannot be opened and reclosed without showing visible evidence of tampering (see Figure 12).



a) Original condition b) Opened c) Original condition d) Opened

Figure 12 — Two examples of a flexible packaging

5.11 Blow-fill-and-seal-container (BFS)

5.11.1 Description

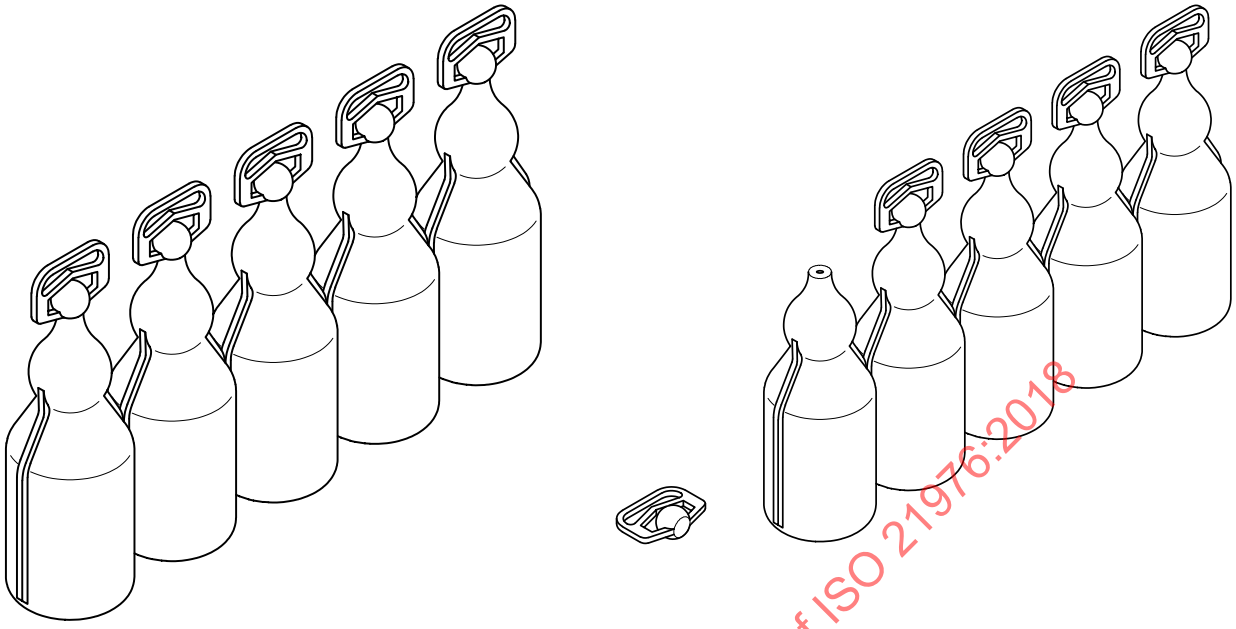
The BFS container is made from plastic material and is formed, filled and sealed in a continuous process. The BFS container shall be penetrated or the integrated closure shall be broken to gain access to the product.

5.11.2 Criteria of tamper verification

Tampering or opening shall lead to visible, irreversible damage or change of the BFS container and show visible evidence of tampering.

5.11.3 Verification

First time opening leads to visible, irreversible damage of the BFS container. The BFS container cannot be opened and reclosed without showing visible evidence of tampering (see Figure 13). Squeezing may be recommended in order to check that the BFS container does not leak.



a) Original condition **b) Opened**

Figure 13 — Example of a blow-fill-and-seal-container

5.12 New and emerging technologies

Other tamper verification features may be developed and shall meet the requirements of this document as appropriate.