INTERNATIONAL STANDARD

ISO 8537

Third edition
2016-03-15

Sterile single-use syringes, with or without needle, for insulin

Seringues à insuline, stériles, non réutilisables, avec ou sans aiguille

Reference number
ISO 8537:2016(E)

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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 84, *Devices for administration of medicinal products and catheters*.

This third edition cancels and replaces the second edition (ISO 8537:2007), which has been technically revised to include the following changes:

a) revised the introduction;

b) revised the scope to include various concentrations of insulin, specified plastic materials and excluded, e.g. single-use syringes made of glass;

c) added some normative references;

d) added new definitions;

e) added new colour codes for higher concentration of insulin;

f) clarified the drawing to illustrate the component of the syringe;

g) included general requirements;

h) revised test methods for syringes;

i) revised the labelling requirement;

j) moved the syringe sizes and graduated scales in Annex H;

k) deleted Annex I.

Introduction

This International Standard covers insulin syringes primarily intended for human use and provides performance and testing requirements. It permits broader variation in design so as to not limit innovation in technology or methods of packaging. Its appearance and layout are consistent with other TC 84 International Standards, which are designed to be more performance-based than design-prescriptive.

Manufacturers are expected to follow a risk-based approach and employ usability engineering during the design, development and manufacture of insulin syringes.

This edition introduces general requirements as design guidelines for manufacturers. This edition retains a number of limits on requirements, which were originally based on consensus opinion but subsequently have been confirmed in practice.

This International Standard does not specify materials to be used for the construction and lubrication of sterile insulin syringes and needles for single use because their selection will depend, to some extent, upon the manufacturer's specific syringe design, process of manufacture, and sterilization method.

Insulin syringes and needles are to be manufactured and sterilized in accordance with recognized national or international codes of good manufacturing practice for medical devices.

This International Standard emphasizes the importance of having individual syringes that are appropriately graduated and labelled for only one concentration of insulin. Serious problems can result if a syringe is used with a concentration of insulin that is different from the one for which it was designed. Hazards associated with dosing errors with highly concentrated insulin (U300 and U500) are considered higher than the experience with U40 and U100.

It is preferred that when more than one insulin concentration is in a market, the new concentration be provided in a dedicated delivery system that make miss-dosing less likely.

In acknowledgement that insulin in higher concentrations in vials are available in some markets, new formulations are under development and dedicated delivery systems other than syringes are not always appropriate for all markets, this International Standard introduces new colour codes to differentiate syringes for the new higher concentrations of insulin.

The sampling plans for inspection selected for this International Standard are intended to verify the design at a high confidence level. The sampling plans for inspection do not replace the more general manufacturing quality systems that appear in standards on quality systems, for example, the ISO 9000 series and ISO 13485.

Guidance on transition periods for implementing the requirements of this International Standard is given in ISO/TR 19244, developed by ISO/TC 84.

Sterile single-use syringes, with or without needle, for insulin

1 Scope

This International Standard specifies requirements and test methods for empty, sterile, single-use syringes, with or without needles, made of plastic materials and intended solely for the injection of insulin, with which the syringes are filled by the end user. This International Standard covers syringes intended for single-use only in humans and with insulins of various concentrations.

The insulin syringes specified in this International Standard are intended for use (i.e. insulin injection) immediately after filling and are not intended to contain insulin for extended periods of time.

This International Standard excludes single-use syringes made of glass, syringes for use with power-driven syringe pumps, syringes that are pre-filled by the manufacturer, and syringes intended to be stored after filling (e.g. in a kit intended for filling by a pharmacist).

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 594-1[1)], *Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 1: General requirements*

ISO 3696, *Water for analytical laboratory use — Specification and test methods*

ISO 7864, *Sterile hypodermic needles for single use*

ISO 9626, *Stainless steel needle tubing for the manufacture of medical devices*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 11608–1, *Needle-based injection systems for medical use — Requirements and test methods — Part 1: Needle-based injection systems*

ISO 11608–5, *Needle-based injection systems for medical use — Requirements and test methods — Part 5: Automated functions*

ISO 14971, *Medical devices — Application of risk management to medical devices*

ISO 15223-1:2012, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*

ISO 23908, *Sharps injury protection — Requirements and test methods — Sharps protection features for single-use hypodermic needles, introducers for catheter and needles used for blood sampling*

ISO/IEC 80369-7, *Small bore connectors for liquids and gases in healthcare applications — Part 7: Connectors with 6 % (Luer) taper for intravascular or hypodermic applications (under development)*

IEC 62366-1, *Medical devices — Part 1: Application of usability engineering to medical devices*

1) To be replaced by ISO 80369–7.

3 Terms and definitions

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

NOTE The nomenclature used for some components of syringes intended for single use is shown in Figure 2.

3.1
needle cap
cover intended to protect physically the needle tube prior to use and, for syringes with a fixed needle tube (type 8), to maintain the sterility of the needle

3.2
plunger stopper
component connected to the leading end of the plunger and seals the open end of the syringe barrel

3.3
plunger cap
cover intended to maintain the sterility of the syringe and to enclose the projecting portion of the plunger and push button, if present

3.4
fiducial line
leading edge of the *plunger stopper* (3.2), which is in contact with and perpendicular to the syringe barrel and aligns with the zero marking on the syringe barrel when the piston is fully inserted

3.5
graduated capacity

volume of water, at a temperature of 18 °C to 28 °C, expelled from the syringe when the *fiducial line* (3.4) on the piston traverses a given scale interval or intervals

3.6

total graduated capacity
capacity of the syringe at the graduation line farthest from the zero graduation line

Note 1 to entry: The total graduated capacity may be equal to, or greater than, the nominal capacity.

3.7
piston
assembled component of plunger and *plunger stopper* (3.2)

3.8
unit packaging
packaging of an individual device, intended to maintain its sterility

3.9
self-contained syringe
syringe with protective end caps intended to maintain the sterility of the interior of the syringe

Note 1 to entry: Protective end caps may be *plunger cap* (3.3), nozzle cap or *needle cap* (3.1).

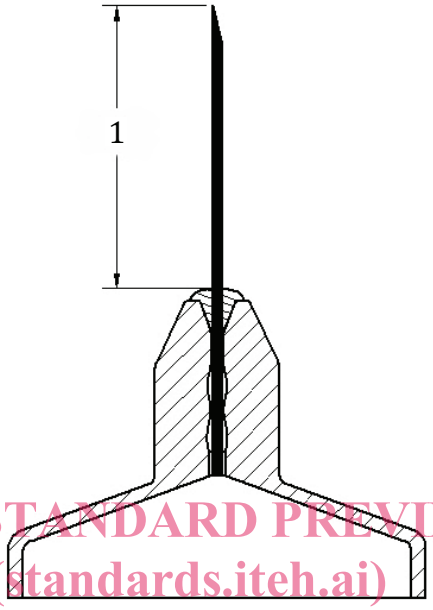
3.10
user packaging
packaging, which contains one or more items of unit packaging, designed to provide labelling information to the user

3.11
needle length
usable length of needle

Note 1 to entry: Needle length is shown in Figure 1.

3.12
nozzle cap
sheath intended to protect physically the needle hub prior to use

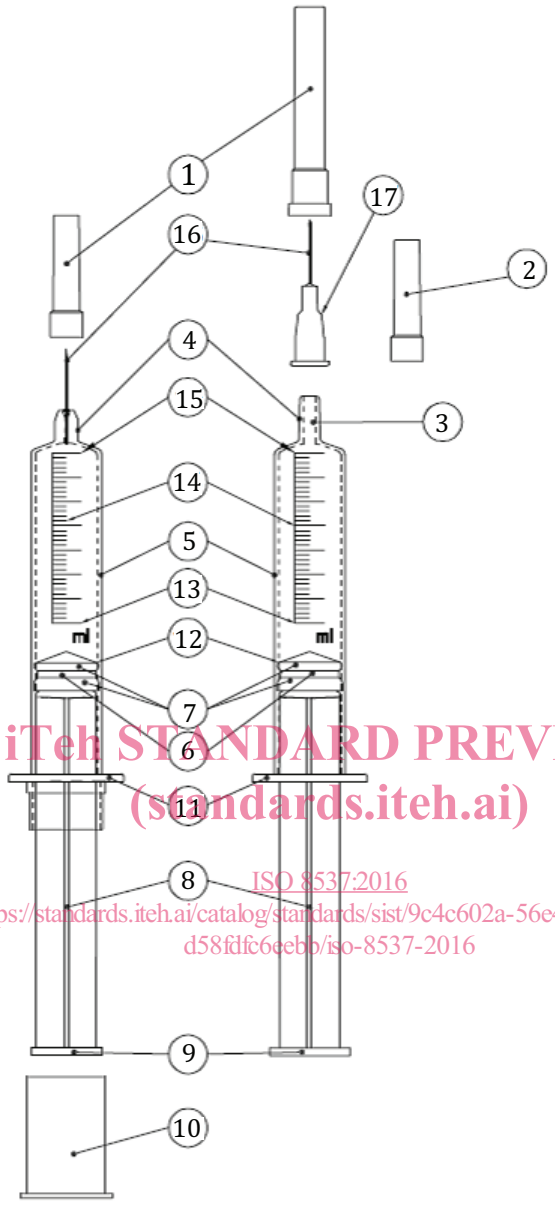
3.13
plunger delivery
device mechanism which advances the *plunger stopper* (3.2) to deliver the medicinal product



Key

1 needle length

Figure 1 — Needle length



Key

1	needle cap	10	plunger cap
2	nozzle cap	11	finger grips
3	nozzle lumen	12	fiducial line
4	nozzle	13	nominal capacity
5	barrel	14	graduation lines
6	plunger stopper	15	zero line
7	seals	16	needle tube
8	plunger	17	hub
9	push-button		

Note This figure is only intended to be illustrative of the components of a syringe. The piston might or might not be of integral construction and might incorporate more than one seal.

Figure 2 — Schematic representation of insulin syringe for single use

4 Types of syringes

The type of syringe shall be designated as follows.

— **Type 1**; syringe having a 6 % (Luer) male conical fitting, supplied with no needle and packaged in unit packaging.

— **Type 2**; syringe having a 6 % (Luer) male conical fitting, supplied with no needle and fitted with protective end caps and packaged.

— **Type 3**; syringe having a 6 % (Luer) male conical fitting, and supplied with a detached or detachable needle and packaged in a unit packaging.

— **Type 4**; syringe having a 6 % (Luer) male conical fitting and supplied with a detachable needle and fitted with protective end caps and packaged.

— **Type 5**; syringe having a fitting other than a 6 % (Luer) taper, supplied with a needle not intended to be detached and packaged in a unit packaging.

— **Type 6**; syringe having a fitting other than a 6 % (Luer) taper, supplied with a needle not intended to be detached and fitted with protective caps and packaged.

— **Type 7**; syringe with fixed needle tube and packaged in a unit packaging.

— **Type 8**; syringe with fixed needle tube and fitted with protective end caps and packaged.

NOTE This International Standard provides designations for eight types of syringes to encompass different product configurations, but the number of types in use in a particular country is likely to be fewer than eight.

5 Requirements

5.1 General requirements

The general requirements listed below are considered to be design guidelines for manufacturers.

a) Given the likelihood that multiple insulin concentrations and concentration-specific syringes will exist in a particular country or locality, the manufacturer shall develop risk mitigation strategies to minimize the occurrence of “wrong dose” medication errors.

b) The syringe shall indicate, through visual means, the insulin concentration it is intended to contain.

The insulin syringes should also indicate, through non-visual means (e.g. tactile), the insulin concentration it is intended to contain.

c) Syringes designed to contain a specific concentration of insulin (e.g. U-100) shall be adequately differentiated visually from other dedicated syringes. This differentiation shall be determined based on a risk assessment and confirmed through usability validation testing.

d) The syringe and needle should be free from defects affecting safety, serviceability for their intended use, and appearance.

e) The syringe scale shall be graduated in increments corresponding to units of only one concentration of insulin. The syringe scale graduation and numbering increments shall be determined through risk analysis and confirmed through usability validation testing.

NOTE 1 Annex H offers guidance from prior versions of ISO 8537 for graduation and numbering increments on U-40 and U-100 syringes.

f) The nominal capacity of the syringe shall be designated in millilitres (ml).

g) The tolerances on the graduated capacity shall be in accordance with Table H.1.

h) Syringes indicated for use with devices or accessories that provide automated functions (e.g. needle insertion and retraction) shall comply with applicable requirements of ISO 11608-1 and ISO 11608-5.

i) Syringes with integrated or add-on sharps protection shall comply with ISO 23908.

j) Syringes with Luer attachment features shall comply with ISO 80369-7.

k) The length of the barrel shall be sufficient to allow the expulsion of any air bubbles without affecting the syringe's nominal capacity.

NOTE 2 Compliance with this requirement may be demonstrated, for example, by meeting the requirements in 5.6.1.

l) The syringe's finger grips shall be of adequate size, shape and strength for the intended purpose. The design specifications for the finger grips shall be determined through risk analysis and confirmed through usability validation testing.

m) The materials used in the syringe shall be tested and qualified according to ISO 10993-1.

n) The self-contained syringes with sterile interiors and syringes provided in its unit packaging shall have been subjected to a validated sterilization process.

NOTE 3 For testing these properties, the manufacturer may use an extract, as specified in Annex G.

5.2 Material selection

With regard to material selection,

— materials used for fabrication of the syringe barrel shall be of sufficient clarity to enable dosages to be read and for air bubbles to be seen without difficulty, and

— materials used for fabrication of syringes and needles (including lubricant) and packaging shall not, in their final form after sterilization and under conditions of intended use, adversely affect the efficacy, safety and acceptability of insulin preparations. The fabrication materials shall also not be affected, either physically or chemically, by insulin preparations.

5.3 Colour coding

Colour coding of syringes intended for dedicated use with specific insulin concentrations is as follows.

— The barrel of the insulin syringe shall be clear, with graduation markings of a colour that contrasts clearly with the syringe.

— The colour used to indicate the insulin concentration shall appear on at least one component of the syringe (e.g. needle cap, plunger cap, plunger, a portion of the barrel that does not interfere with visibility of the graduation lines).

— For insulin syringes with fixed needles, the colour of the needle cap shall be the colour designated for the insulin concentration.

— The colour coding used on the syringes shall be repeated and explained on the user packaging and, if applicable, on the unit packaging.

NOTE 1 The presence of colour coding on a syringe or package does not absolve the user of the responsibility to check the marked insulin concentration of the syringe.

— No additional colours, other than black and white, shall be used on the syringe barrel.

NOTE 2 In acknowledgement that established syringes on the market use red to indicate the U40 insulin strength on the barrel, these syringes are exempted.

