INTERNATIONAL STANDARD

**ISO 8537**

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

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



Reference number
ISO 8537:2007(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.

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 8537 was prepared by Technical Committee ISO/TC 84, *Devices for administration of medicinal products and intravascular catheters*.

This second edition cancels and replaces the first edition (ISO 8537:1991) and its Amendment 1 (ISO 8537:1991/Amd.1:2000), which have been technically revised.

# Introduction

This International Standard deals with products primarily intended for use with humans and provides performance requirements, but permits some variations of design and of the methods of packaging and sterilization by individual manufacturers.

Materials to be used for the construction and lubrication of sterile syringes and needles for single use are not specified as their selection will depend to some extent upon the design, process of manufacture and sterilization method employed by individual manufacturers.

Syringes and needles should be manufactured and sterilized in accordance with recognized national or international codes of good manufacturing practice for medical devices, and should be free from defects affecting appearance, safety and serviceability for their intended use.

Certain grades of polypropylene, polystyrene and styrene/acrylonitrile copolymer have been extensively used for the barrels of sterile syringes for single use. A high quality natural rubber composition is frequently used for the piston, although other materials such as silicone rubber are also used, the surface of the piston being lubricated with polydimethylsiloxane. For 2 ml syringes, high density polyethylene is frequently used for the seal of the two-component design of syringe in combination with a polypropylene barrel containing a fatty acid amide slip additive.



When selecting materials, make the following considerations:



— Clarity of barrel: Materials used in the construction of the wall of the syringe barrel should be of sufficient clarity to enable dosages to be read without difficulty and for air bubbles to be seen.

— Compatibility with insulin preparations: The materials of syringes and needles (including lubricant) and packaging should not, in their final form after sterilization and under conditions of normal use, detrimentally affect the efficacy, safety and acceptability of insulin preparations: neither should the construction materials themselves be affected physically or chemically by insulin preparations.

— Biocompatibility: The materials should not cause the syringes and needles to yield, under conditions of normal use, significant amounts of toxic substances and should permit them to satisfy the appropriate national requirements or regulations for freedom from pyrogenic materials and abnormal toxicity. For testing these properties, an extract as specified in Annex H may be used.

It is strongly recommended that regulatory authorities, pharmacopoeia and relevant trade associations should recognize the need for further testing, especially for incompatibility between the insulins and syringes when they are in contact for prolonged periods.

In some countries national regulations are legally binding and the requirements may take precedence over this International Standard.

This International Standard describes syringes with or without needles for use with 40 units of insulin/ml (U-40) and 100 units of insulin/ml (U-100). It is recommended that syringes graduated for only one strength of insulin be used in each country to avoid accidents. For those countries using more than one strength of insulin, the importance of having individual syringes appropriately graduated for only one strength of insulin as specified in this International Standard is emphasized. Serious problems may result if a syringe is used with a strength of insulin for which it is not designed. If the syringe is used for mixing different types of insulin, it is strongly recommended that the procedure is performed in the same order each time.

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

## 1 Scope

This International Standard specifies requirements and test methods for sterile syringes, with or without needles, solely for the injection of insulin. The syringes are single-use only, primarily for use in humans. It covers syringes for use with 40 units of insulin/ml (U-40) and 100 units of insulin/ml (U-100).

Sterile syringes specified in this International Standard are intended for use soon after filling as they are not suitable for containing insulin over extended periods of time.

## 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 594-1:1986, *Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 1: General requirements*

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



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

## 3 Terms and definitions

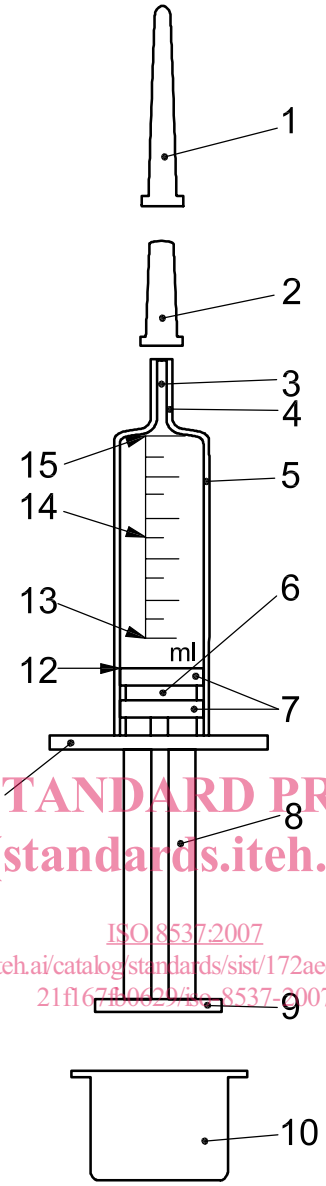
For the purposes of this document the following terms and definitions apply. The nomenclature of some components of syringes for single use is given in Figure 1.

**3.1**
**graduated capacity**
volume of water at 20 °C ± 3 °C or 27 °C ± 3 °C expelled from the syringe when the fiducial line on the piston traverses a given scale interval or intervals

**3.2**
**needle cap**
protective end cap intended to maintain the sterility of the needle tube and to protect physically the needle tube and needle hub, if present

**3.3**
**needle sheath**
cover intended to provide physical protection to the needle tube

**3.4**
**protective end caps**
covers intended to enclose the projecting portion of the plunger and push-button at one end and the nozzle and/or the needle at the other end






**Key**

| | | | |
|---|---|---|---|
| 1 | needle cap | 9 | push-button |
| 2 | protective end cap | 10 | protective end cap |
| 3 | nozzle lumen | 11 | finger grips |
| 4 | nozzle | 12 | fiducial line |
| 5 | barrel | 13 | nominal capacity |
| 6 | piston | 14 | graduation lines |
| 7 | seals | 15 | zero line |
| 8 | plunger | | |

NOTE This figure is intended to be illustrative of components of a syringe only. It does not show a detachable needle or a permanently attached needle tube, and does not form part of the specification. The piston/plunger assembly might or might not be of integral construction and might incorporate more than one seal.

**Figure 1 — Schematic representation of insulin syringe for single use**

## 4 Types of syringe

The types of syringe shall be designated as follows in relation to their packaging and combinations with needles:

**Type 1:** Syringe having a 6 % (Luer) male conical fitting, supplied without a needle and packaged in a unit container.

**Type 2:** Syringe having a 6 % (Luer) male conical fitting, and supplied without a needle and fitted with protective end caps.

**Type 3:** Syringe having a 6 % (Luer) male conical fitting, and supplied with a detached or detachable needle and packaged in a unit container.

**Type 4:** Syringe having a 6 % (Luer) male conical fitting, and supplied with a detachable needle and fitted with protective end caps.

**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 container.

**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.

**Type 7:** Syringe with fixed needle tube and packaged in a unit container.

**Type 8:** Syringe with fixed needle tube and fitted with protective end caps.



NOTE 1 Eight types are designated to encompass different presentations, but it is likely that the number of types in use in a particular country will be less than eight.



NOTE 2 In addition safety syringes with insulin graduation are available in most markets. At time of publication, a general standard relating to medical sharps prevention features is in development.

## 5 Freedom from extraneous matter

The surfaces of the syringe and needle, which come in contact with insulin, shall be clean and free from extraneous matter when viewed by normal or corrected vision without magnification.

## 6 Limits for extraneous matter

### 6.1 Limits for acidity or alkalinity

The pH value of the extract prepared as described in Annex A shall be determined with a laboratory potentiometric pH meter using a general purpose electrode, and shall be within one pH unit of that of the control fluid.

### 6.2 Limits for extractable metals

An extract prepared as described in Annex A shall contain not more than a combined total of 5 mg/kg of lead, tin, zinc and iron when tested by a recognized micro-analytical method, for example by an atomic absorption method. The cadmium content of the extract shall be less than 0,1 mg/kg.

## 7 Lubrication of syringes and needles

If the interior surface of the syringe, including the piston, and the exterior surface of the needle tube are lubricated, the lubricant shall not form pools of fluid on the interior surface of the syringe nor drops on the exterior surface of the needle tube or in the bore.

## 8 Range of sizes

The range of sizes of syringes and graduations shall be as given in Table 1.

**Table 1 — Insulin syringes, range of sizes, graduated scale and tolerance on graduated capacity**

| Unit scale | Nominal capacity<br>ml | Minimum length of scale<br>mm | Scale interval<br>units | Tolerance on graduated capacity | |
|---|---|---|---|---|---|
| | | | | Volumes less than half the nominal capacity | Volumes equal to or greater than half the nominal capacity |
| | 0,3 | 41 | 0,5 | | |
| U-100 | 0,3 | 41 | 1 | ± 1 ½ % of the nominal capacity + 2 % of the expelled volume | ± 5 % of the expelled volume |
| | 0,5 | 43 | 1 | | |
| | 1,0 | 57 | 1 | | |
| | 1,0 | 57 | 2 | | |
| U-40 | 0,5 | 43 | 0,5 | | |
| | 0,5 | 43 | 1 | | |
| | 1,0 | 50 | 1 | | |
| | 2,0 | 60 | 1 | | |
| | 2,0 | 60 | 2 | | |



NOTE Syringes having different nominal capacities and scale intervals are designated to encompass different presentations, but the number of types in use in a particular country can be fewer than those given in Table 1.

## 9 Graduated scale

### 9.1 Scale

The scale shall be graduated in units of insulin and shall refer to one strength of insulin only. The nominal capacity shall be designated in millilitres (ml).

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

NOTE The graduated capacity can be conveniently determined by weighing the expelled fluid. See 3.1.

The graduation lines shall be of a uniform thickness between 0,2 mm and 0,4 mm. They shall lie in planes at right angles to the axis of the barrel.

The graduation lines shall be evenly spaced along the longitudinal axis between the zero line and the line for the total graduated capacity.

When the syringe is held vertically, the ends of all graduation lines of similar length shall be vertically beneath each other with a tolerance of ± 0,5 mm.

The length of the short graduation lines shall be approximately half the length of the long lines.

The scale and scale numbers should be legible and of a colour that contrasts clearly with the syringe.

### 9.2 Numbering of scale

The graduation lines shall be numbered at every five units for the 0,3 ml and 0,5 ml syringes and at every 10 units for the 1,0 ml and 2,0 ml syringes.

The minimum height of the figures should be at least 3 mm.

When the syringe is held vertically with the zero line uppermost and with the scale to the front, the numbers shall appear upright on the scale and in a position such that they would be bisected by a prolongation of the graduation lines to which they relate. The numbers shall be close to, but shall not touch, the ends of the graduation lines to which they relate.

## 10 Barrel

### 10.1 Dimensions

The barrel length shall be such that the syringe has a usable capacity of at least 10 % more than the nominal capacity or 5 mm of plunger travel beyond the scale marking, whichever is less.

### 10.2 Finger grips



The open end of the barrel shall be provided with finger grips which shall ensure that the syringe will not roll when it is placed with the scale uppermost on a flat surface inclined at an angle of 10° to the horizontal.



The finger grips shall be free from flash and sharp edges.

Finger grips should be of adequate size, shape and strength for the intended purpose and should enable the syringe to be held securely during use.

## 11 Piston/plunger assembly

### 11.1 General

The design of the plunger and push-button of the syringe shall be such that when the barrel is held in one hand the plunger can be depressed by the thumb of that hand. The piston shall not become detached from the plunger during the test described in Annex B.

The projection of the plunger and the configuration of the push-button should be such as to enable the plunger, when in the fully inserted position, to be grasped and drawn back without difficulty.

### 11.2 Fit of piston in barrel

When the syringe is filled with water and held vertically with first one and then the other end uppermost, the plunger shall not move by reason of its own mass and the mass of the water contained. When a needle is secured to the syringe in accordance with the instructions of the manufacturer, the force required to initiate movement of the plunger to expel water from the syringe shall not exceed 15 N when measured in accordance with Annex C.

The fit of the piston in the barrel should be such that the piston slides smoothly throughout the graduated length of the barrel.

## 12 Nozzle

### 12.1 Conical fitting

The male conical fitting of the syringe nozzle on syringe types 1, 2, 3 and 4 shall comply with the requirements of ISO 594-1.

### 12.2 Position of nozzle on end of barrel

The syringe nozzle shall be situated centrally, i.e. shall be co-axial with the barrel.

## 13 Needle tubing and needles

### 13.1 Needles for syringes of types 3 and 4

Needles for syringes of types 3 and 4 shall be in accordance with ISO 7864, except for the dimensions and test parameters which shall be in accordance with Annex D of this International Standard.

### 13.2 Needle tubing for syringes of types 5, 6 ,7 and 8

Needle tubing for syringes of types 5, 6, 7 and 8 shall be in accordance with ISO 9626, except for the dimensions and test parameters which shall be in accordance with Annex D of this International Standard. The needle point shall be in accordance with ISO 7864.



## 14 Performance of assembled syringe



### 14.1 Dead space

When tested in accordance with Annex E, the dead space shall not exceed the limits given in Table 2.

**Table 2 — Maximum dead space**

| Type of syringe | Maximum dead space<br>ml |
|---|---|
| 1 and 2 | 0,07 |
| 3 and 4 | 0,10 |
| 5 and 6 | 0,02 |
| 7 and 8 | 0,01 |

### 14.2 Freedom from leakage at needle

When tested as described in Annex F, there shall be no leakage of water sufficient to form a falling drop within 30 s from the unions listed in F.2.9.

When tested as described in Annex G, there shall be no continued formation of air bubbles from the unions listed in G.2.6.