INTERNATIONAL STANDARD

ISO 8537

First edition
1991-05-01

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

Seringues à insuline stériles non réutilisables avec ou sans aiguille

Reference number
ISO 8537:1991(E)

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International Organization for Standardization
Case Postale 56 • CH-1211 Genève 20 • Switzerland
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.

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.

International Standard ISO 8537 was prepared by Technical Committee ISO/TC 84, *Syringes for medical use and needles for injections*.

Annexes A, B, C, D, E, F and G form an integral part of this International Standard. Annexes H and J are for information only.

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 the following should be considered:

— **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 be themselves 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, pharmacopoeiae 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 their 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 intended for single use solely for the injection of insulin and primarily 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 standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

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

ISO 7864:1988, *Sterile hypodermic needles for single use.*

3 Definitions and nomenclature

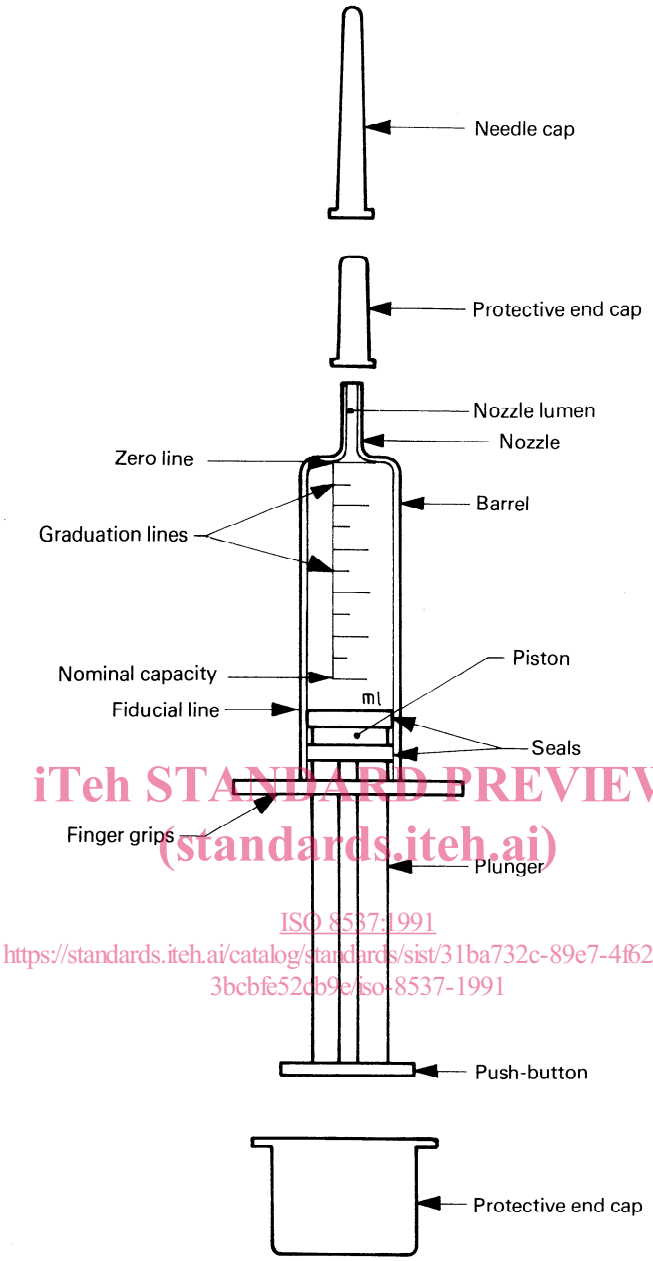
For the purposes of this International Standard, the following definitions apply. The nomenclature of some components of syringes for single use is given in figure 1.

3.1 gratuated 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.



NOTE — The drawing 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 may or may not be of integral construction and may 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 end 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.

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 extractable 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.

NOTE 2 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 could be less than those given in table 1.

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

Unit scale	Nominal capacity	Minimum length of scale	Scale interval	Tolerance on graduated capacity	
				Volumes less than half the nominal capacity	Volumes equal to or greater than half the nominal capacity
	ml	mm	units		
U-100	0,3	41	1	± (1 1/2 % 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		

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 3 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.

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.

9.3 Overall length of scale

The overall length of the scale shall be in accordance with table 1.

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 Fiducial line

There shall be a visible and defined edge serving as the fiducial line at the end of the piston for determining the graduated capacity corresponding to any syringe scale reading. The fiducial line shall be in contact with the inner surface of the barrel.

For three-part syringes it is recommended that material of a dark colour be used for that part of the piston which forms the fiducial line.

11.3 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 Needles

Needles of syringes of types 3, 4, 5, 6, 7 and 8 shall be of length not less than 12 mm and of external diameter not greater than 0,45 mm. Needles of external diameter 0,45 mm shall be in accordance with ISO 7864. Needles of external diameter less than 0,45 mm shall have the properties given in annex D, as determined by the methods given in 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 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.

14.3 Liquid and air leakage past piston

When tested as described in annex F, there shall be no leakage of water past the piston seal.