INTERNATIONAL STANDARD

ISO 7886-1

First edition
1993-10-01

Sterile hypodermic syringes for single use —

Part 1:
Syringes for manual use

Seringues hypodermiques stériles, non réutilisables —
Partie 1: Seringues pour utilisation manuelle

Reference number
ISO 7886-1:1993(E)

Contents

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

Annexes

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 7886-1 was prepared by Technical Committee ISO/TC 84, *Medical devices for injections*, Sub-Committee SC 1, *Syringes, needles and intravascular catheters for single use*.

This first edition of ISO 7886-1 cancels and replaces ISO 7886:1984. It was decided to divide the Standard into two parts, ISO 7886-1 retaining essentially the scope of ISO 7886:1984, and ISO 7886-2 (in course of preparation) being applicable to sterile, single-use syringes for use with power-driven syringe pumps. The major differences between this part of ISO 7886 and ISO 7886:1984 are as follows.

a) In order to reflect the demand for syringes of sizes other than those listed in ISO 7886:1984, this part of ISO 7886 does not specify a range of syringe sizes and allows the syringes to be marked with graduations at greater than the nominal capacity.

b) An informative annex on forces required to operate the syringe plunger has been introduced.

c) The tests for toxicity given in ISO 7886:1984 have been replaced by an informative cross-reference to ISO 10993-1.

d) The informative annex on test methods for compatibility between syringes and injection fluids has been revised.

e) This part of ISO 7886 permits the use on package labelling of the ISO symbol for "do not re-use", but continues to require the written word. Manufacturers are encouraged to use the symbol so as to increase familiarity with it among purchasers and users.

ISO 7886 consists of the following parts, under the general title *Sterile hypodermic syringes for single use*:

— *Part 1: Syringes for manual use*

— *Part 2: Syringes for use with syringe pumps*

Annexes A, B, C and D form an integral part of this part of ISO 7886. Annexes E, F, G, H and J are for information only.

Introduction

This part of ISO 7886 does not give requirements or test methods for freedom from biological hazard. Guidance on biological tests relevant to hypodermic syringes is given in ISO 10993-1, and it is suggested that manufacturers take this guidance into account when evaluating products. Such an evaluation should include the effects of the process whereby the syringes are sterilized. However, national regulations may exist in some countries, and these will override the guidance in ISO 10993-1.

Materials to be used for the construction of syringes are not specified as their selection will depend to some extent upon the design, process of manufacture and method of sterilization employed by individual manufacturers. Guidance on some aspects of the selection of materials is given in annex E.

The materials of the syringe should be compatible with injection fluids. If this is not the case, the attention of the user should be drawn to the exception by labelling the primary container. It is not practicable to specify a universally acceptable test method for incompatibility. However, recommended methods are given in annex F. These test methods can be regarded only as a means of indicating compatibility. The only conclusive test is that of an individual injection fluid with a specific syringe.

Manufacturers of pharmaceuticals use solvents in injectable preparations. Such solvents should be tested by the manufacturer of the injectable preparation for any possible incompatibility with the materials frequently used in syringe construction. The types of material that have received wide acceptance are included in annex E. If an incompatibility exists, the injection should be suitably labelled. The impossibility of testing any one injection fluid with all available syringes is recognized and it is strongly recommended that regulatory authorities and relevant trade associations should recognize the problem and take appropriate measures to assist manufacturers.

Hypodermic syringes specified in this part of ISO 7886 are intended for use with hypodermic needles specified in ISO 7864.

This part of ISO 7886 does not cover syringes for the injection of insulin (see ISO 8537).

In some countries, national pharmacopoeia or government regulations are legally binding and their requirements may take precedence over this part of ISO 7886.

Sterile hypodermic syringes for single use —

Part 1:
Syringes for manual use

1 Scope

This part of ISO 7886 specifies requirements for sterile single-use hypodermic syringes made of plastics materials and intended for the aspiration of fluids or for the injection of fluids immediately after filling.

It excludes syringes for use with insulin (see ISO 8537), single-use syringes made of glass, syringes with needles permanently attached, syringes for use with power-driven syringe pumps, syringes pre-filled with the injection by the manufacturer and syringes supplied with the injection as a kit for filling by a pharmacist.

NOTE 1 A second part of ISO 7886 is being prepared to cover syringes for use with power-driven syringe pumps.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this part of ISO 7886. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this part of ISO 7886 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 594-2:1991, *Conical fittings with a 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 2: Lock fittings.*

ISO 3696:1987, *Water for analytical laboratory use — Specification and test methods.*

ISO 8601:1988, *Data elements and interchange formats — Information interchange — Representation of dates and times.*

3 Definitions

For the purposes of this part of ISO 7886, the following definitions apply.

3.1 nominal capacity: Capacity of the syringe as designated by the manufacturer.

NOTE 2 Examples are 1 ml, 5 ml, 50 ml.

3.2 graduated capacity: Volume of water at (20 ± 5) °C [or, for tropical countries (27 ± 5) °C] expelled from the syringe when the fiducial line on the piston traverses a given scale interval or intervals.

3.3 total graduated capacity: Capacity of the syringe at the graduation line furthest from the zero graduation line.

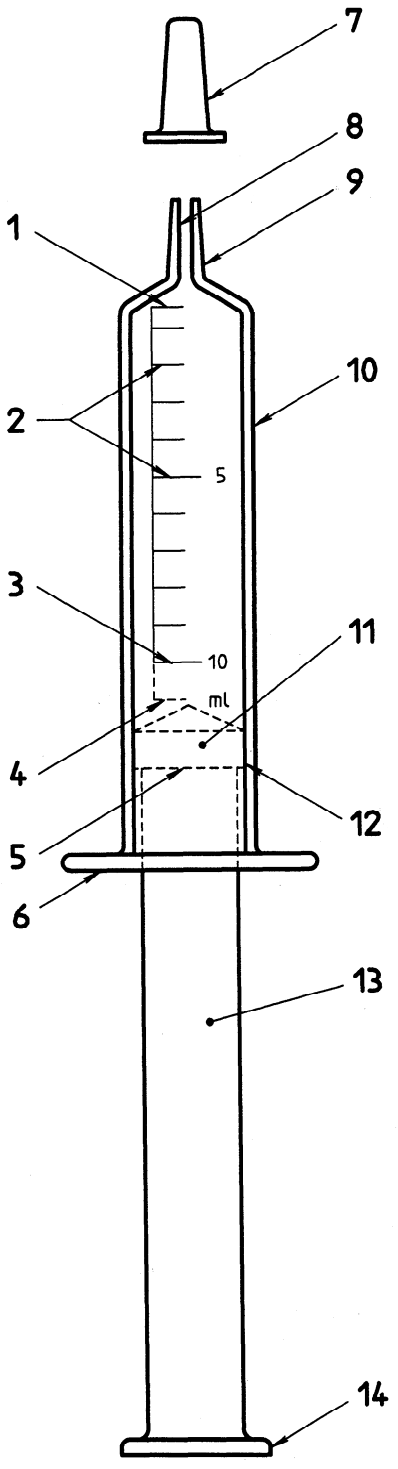
NOTE 3 The total graduated capacity may be equal to, or greater than, the nominal capacity.

3.4 maximum usable capacity: Capacity of the syringe when the piston is drawn back to its furthest functional position.

3.5 fiducial line: Line circumscribing the end of the piston for determining the capacity corresponding to any scale reading of the syringe.

4 Nomenclature

The nomenclature for components of hypodermic syringes for single use is shown in figure 1.



1. Zero graduation line
2. Graduation lines
3. Nominal capacity graduation line
4. Total graduated capacity line
5. Fiducial line
6. Finger grips
7. Nozzle cap
8. Nozzle lumen
9. Nozzle
10. Barrel
11. Piston
12. Seal
13. Plunger
14. Push-button

NOTE — The drawing is intended to be illustrative of components of a syringe. The piston/plunger assembly may or may not be of integral construction and may or may not incorporate more than one seal.

Figure 1 — Schematic representation of hypodermic syringe for single use

5 Cleanliness

When inspected by normal or corrected-to-normal vision without magnification under an illuminance of 300 lx to 700 lx, the surface of the hypodermic syringe which comes in contact with injection fluids during normal use shall be free from particles and extraneous matter.

6 Limits for acidity or alkalinity

When determined with a laboratory pH meter and using a general purpose electrode, the pH value of an extract prepared in accordance with annex A shall be within one unit of pH of that of the control fluid.

7 Limits for extractable metals

When tested by a recognized microanalytical method, for example by an atomic absorption method, an extract prepared in accordance with annex A shall, when corrected for the metals content of the control fluid, contain not greater than a combined total of 5 mg/l of lead, tin, zinc and iron. The cadmium content of the extract shall, when corrected for the cadmium content of the control fluid, be lower than 0,1 mg/l.

8 Lubricant

If the interior surfaces of the syringe, including the piston, are lubricated, the lubricant shall not be visible, under normal or corrected-to-normal vision, as droplets or particles.

An acceptable lubricant, applied undiluted, for three-piece syringes is polydimethylsiloxane complying with a national or the European pharmacopoeia. The quantity of lubricant used should not exceed 0,25 mg per square centimetre of the internal surface area of the syringe barrel.

An acceptable lubricant for two-piece syringes is fatty acid amides of erucic and/or oleic acids. The quantity of lubricant should not exceed 0,6 % (*m/m*) of the mass of the barrel, but attention is drawn to the fact that some national regulations may specify a lower maximum concentration.

9 Tolerance on graduated capacity

The tolerances on the graduated capacity shall be as given in table 1.

Table 1 — Capacity tolerance, dead space, scale dimensions and test forces

Nominal capacity of syringe, V	Tolerance on any graduated capacity		Maximum dead space	Minimum overall length of scale to nominal capacity mark	Scale interval	Increment between graduation lines to be numbered	Forces for leakage testing (see annex D)	
	Less than half nominal capacity	Equal to or greater than half nominal capacity					Side force (± 5 %)	Axial pressure (gauge) (± 5 %)
ml			ml	mm	ml	ml	N	kPa
$V < 2$	± (1,5 % of V + 2 % of expelled volume)	± 5 % of expelled volume	0,07	57	0,05	0,1	0,25	300
$2 \leqslant V < 5$	± (1,5 % of V + 2 % of expelled volume)	± 5 % of expelled volume	0,07	27	0,2	0,5 or 1	1,0	300
$5 \leqslant V < 10$	± (1,5 % of V + 1 % of expelled volume)	± 4 % of expelled volume	0,075	36	0,5	1	2,0	300
$10 \leqslant V < 20$	± (1,5 % of V + 1 % of expelled volume)	± 4 % of expelled volume	0,10	44	1,0	5	3,0	300
$20 \leqslant V < 30$	± (1,5 % of V + 1 % of expelled volume)	± 4 % of expelled volume	0,15	52	2,0	10	3,0	200
$30 \leqslant V < 50$	± (1,5 % of V + 1 % of expelled volume)	± 4 % of expelled volume	0,17	67	2,0	10	3,0	200
$50 \leqslant V$	± (1,5 % of V + 1 % of expelled volume)	± 4 % of expelled volume	0,20	75	5,0	10	3,0	200

10 Graduated scale

10.1 Scale

10.1.1 The syringe shall have either only one scale or more than one identical scales, which shall be graduated at least at the intervals given in table 1. The unit of volume shall be marked on the barrel.

NOTE 4 This requirement does not preclude the provision of additional graduation marks within the scale or as extensions to the scale.

10.1.2 If the scale is extended beyond the nominal capacity, the extended portion shall be differentiated from the rest of the scale.

Examples of means of differentiation are

a) encircling the scale number of the nominal capacity line;

b) the use of smaller scale numbers for the extra graduation lines;

c) the use of shorter graduation lines for the extra graduation lines;

d) the use of a broken line for the optional vertical line of the extra scale length.

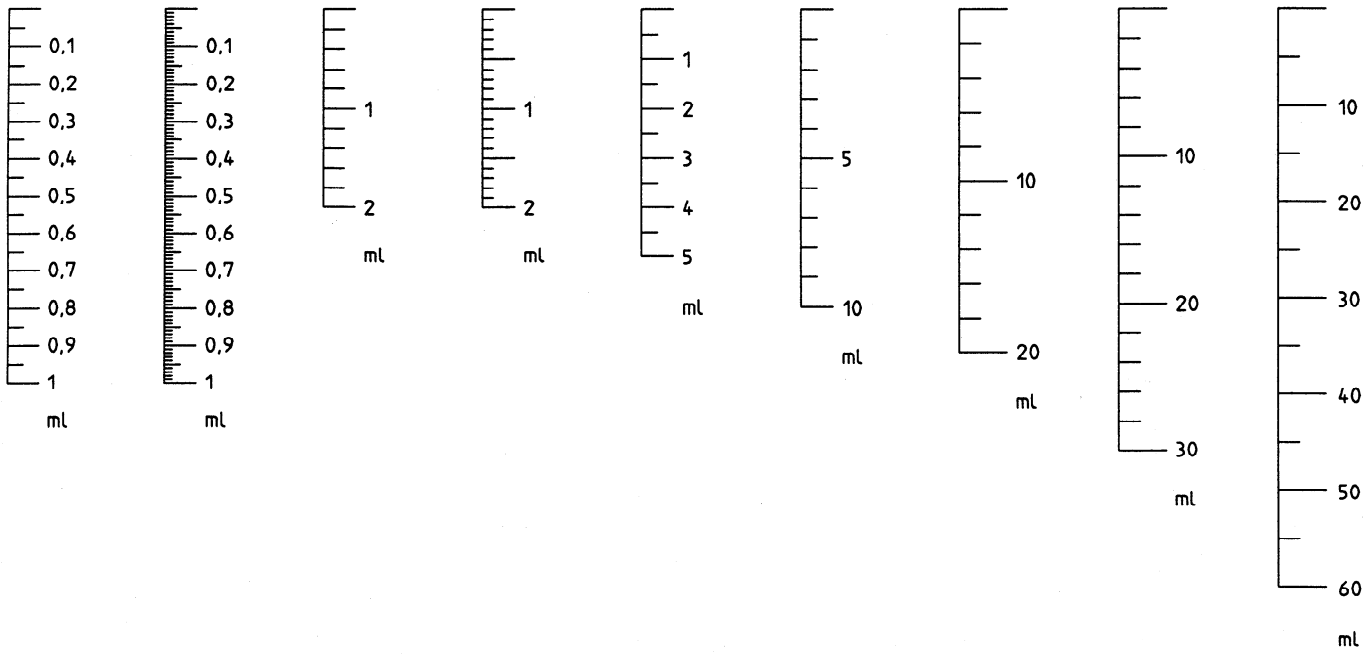
10.1.3 The graduation lines shall be of uniform thickness. They shall lie in planes at right angles to the axis of the barrel.

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

10.1.5 When the syringe is held vertically, the ends of all graduation lines of similar length shall be vertically beneath each other.

10.1.6 The lengths of the short graduation lines on each scale shall be approximately half the length of the long lines.

Examples of scales and the numbering of graduation lines are shown in figure 2.



NOTE — The vertical line of the scale may be omitted.

Not to scale.

Figure 2 — Examples of scale graduations

10.2 Numbering of scale

10.2.1 The graduation lines shall be numbered at the volume increments given in table 1. In addition, the line denoting the nominal capacity or the lines denoting the nominal capacity and the total graduated capacity, if these differ, shall be numbered.

Examples of scale numbering are shown in figure 2.

10.2.2 When the syringe is held vertically with the conical tip uppermost and with the scale to the front, the numbers shall appear vertical 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.

10.3 Overall length of scale to nominal capacity line

The overall length of the scale shall be as given in table 1.

10.4 Position of scale

When the plunger is fully inserted, that is as near to the nozzle end of the barrel as it will go, the zero graduation line of the scale shall coincide with the fiducial line on the piston to within a quarter of the smallest scale interval.

11 Barrel

11.1 Dimensions

The length of the barrel shall be such that the syringe has a maximum usable capacity of at least 10 % more than the nominal capacity.

11.2 Finger grips

The open end of the barrel shall be provided with finger grips that shall ensure that the syringe will not roll more than 180° when it is placed on a flat surface 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.

12 Piston/plunger assembly

12.1 Design

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. When tested in accordance with annex B , the piston shall not become detached from the plunger.

The plunger should be of a length adequate to allow the piston to traverse the full length of the barrel, but it should not be possible easily to withdraw the plunger completely from the barrel.

The projection of the plunger and the configuration of the push-button should be such as to allow the plunger to be operated without difficulty. When the fiducial line of the piston coincides with the zero graduation line, the preferred minimum length of the plunger from the surface of the finger grips nearer to the push-button should be:

a) 8 mm for syringes of nominal capacity up to but excluding 2 ml;

b) 9 mm for syringes of nominal capacity of 2 ml up to but excluding 5 ml;

c) 12,5 mm for syringes of nominal capacity of 5 ml and greater.

12.2 Fit of piston in barrel

When the syringe is filled with water and held vertically with first one end and then the other end uppermost, the plunger shall not move by reason of its own mass.

NOTE 5 A suggested test method and performance criteria for the forces required to move the plunger are given in annex G. It is recommended that this test be used to generate data on which to decide whether to make this test mandatory in a future revision of this part of ISO 7886.

12.3 Fiducial line

There shall be a visible and defined edge serving as the fiducial line at the end of the piston. The fiducial line shall be in contact with the inner surface of the barrel.

13 Nozzle

13.1 Conical fitting

The male conical fitting of the syringe nozzle shall be in accordance with ISO 594-1.

If the syringe has a locking fitting, it shall be in accordance with ISO 594-2.

13.2 Position of nozzle on end of barrel

13.2.1 On syringes of nominal capacity up to but not including 5 ml, the syringe nozzle shall be situated centrally, i.e. it shall be coaxial with the barrel.

13.2.2 On syringes of nominal capacity 5 ml and greater, the syringe nozzle shall be situated either centrally or eccentrically.

13.2.3 If the syringe nozzle is eccentric, its axis shall be vertically below the axis of the barrel when the syringe is lying on a flat surface with the scale uppermost. The distance between the axis of the nozzle and the nearest point on the internal surface of the bore of the barrel shall be not greater than 4,5 mm.

13.3 Nozzle lumen

The nozzle lumen shall have a diameter of not less than 1,2 mm.

14 Performance

14.1 Dead space

When tested in accordance with annex C, the volume of liquid contained in the barrel and the nozzle when the piston is fully inserted shall be as given in table 1.

14.2 Freedom from air and liquid leakage past piston

When tested in accordance with annex D, there shall be no leakage of water past the piston or seal(s).

When tested in accordance with annex B, there shall be no leakage of air past the piston or seal(s), and there shall be no fall in the manometer reading.

15 Packaging

15.1 Primary container

Each hypodermic syringe shall be sealed in a primary container.

The materials of the container should not have detrimental effects on the contents. The material and design of the container should be such as to ensure:

a) the maintenance of sterility of the contents under dry, clean and adequately ventilated storage conditions;

b) the minimum risk of contamination of the contents during opening of the container and removal of the contents;

c) adequate protection of the contents during normal handling, transit and storage;

d) that once opened, the container cannot be easily resealed, and it should be obvious that the container has been opened.

15.2 Secondary container

One or more primary containers shall be packaged in a secondary container.

The secondary container should be sufficiently robust to protect the contents during handling, transit and storage.

One or more secondary containers may be packaged in a storage and/or transit container.

16 Labelling

16.1 Primary container

The primary container shall be marked with at least the following information:

a) a description of the contents, including the nominal capacity and the type of nozzle;

b) the word "STERILE";

c) the words "FOR SINGLE USE" or equivalent (excepting the term "disposable"); the symbol given in annex H may also be given;

d) a warning of solvent incompatibility if necessary, for example "Not to be used with paraldehyde" (see remarks on compatibility given in the Introduction);

e) the lot number, prefixed by the word "LOT";

f) the name, trademark, trade name or logo of the manufacturer or supplier.

16.2 Secondary container

The secondary container shall be marked with at least the following information:

a) a description of the contents, including the nominal capacity, the type of nozzle and the number;

b) the word "STERILE";

c) the words "FOR SINGLE USE" or equivalent (excepting the term "disposable"); the symbol given in annex H may also be given;

d) a warning to check the integrity of each primary container before use;

e) the lot number, prefixed by the word "LOT";

f) the date (year and month expressed as specified in subclause 5.2.1.1 of ISO 8601:1988) of sterilization (the date of sterilization may be incor-

porated in the first several digits of the lot number);

g) the name and address of the manufacturer or supplier;

h) information for handling, storage and transportation.

16.3 Storage container

If secondary containers are packaged in a storage container, the storage container shall be marked with at least the following information:

a) a description of the contents as specified in 16.2 a);

b) the lot number, prefixed by the word "LOT";

c) the word "STERILE";

d) the date of sterilization as specified in 16.2 f);

e) the name and address of the manufacturer or supplier;

f) information for handling, storage and transportation of the contents.

16.4 Transport wrapping

If a storage container is not used but the secondary containers are wrapped for transportation, the information required by 16.3 shall either be marked on the wrapping or shall be visible through the wrapping.

Annex A
(normative)

Method for preparation of extracts

A.1 Principle

The syringe is filled with water in order to extract soluble components.

A.2 Apparatus and reagents

A.2.1 Freshly distilled or deionized water, of grade 3 in accordance with ISO 3696.

A.2.2 Selection of laboratory borosilicate glassware.

A.3 Procedure

A.3.1 Fill at least three syringes to the nominal capacity graduation line with water (A.2.1), expel air bubbles and maintain the syringes at a temperature of $(37\ ^{+3}_{0})$ °C for 8 h $^{+15}_{0}$ min.

Eject the contents and combine them in a vessel made of borosilicate glass (A.2.2).

A.3.2 Prepare the control fluid by reserving a portion of the unused water (A.2.1).

Annex B
(normative)

Test method for air leakage past syringe piston during aspiration, and for separation of piston and plunger

B.1 Principle

The syringe nozzle is connected to a reference female conical hub and the syringe partially filled with water. A negative pressure is applied through the nozzle, and the syringe inspected for leakage past the piston and seal(s) and to determine if the piston becomes detached from the plunger.

B.2 Apparatus and reagents

B.2.1 Reference steel female conical fitting, in accordance with ISO 594-1.

B.2.2 Support and device that clamps the syringe plunger, in a fixed position.

B.2.3 Equipment for producing, controlling and measuring vacuum, as shown in figure B.1, comprising a vacuum pump with air bleed control, a manometer and a vacuum-tight valve.

B.2.4 Freshly boiled water, cooled to a temperature of (20 ± 5) °C.

B.3 Procedure

B.3.1 Draw into the syringe a volume of water (B.2.4) of not less than 25 % of the nominal capacity.

B.3.2 With the nozzle uppermost, withdraw the plunger axially until the fiducial line is at the nominal capacity graduation line and clamp (B.2.2) the plunger in this position as shown in figure B.1.

B.3.3 Connect the syringe nozzle to the reference steel female conical fitting (B.2.1).

B.3.4 Arrange the test equipment (B.2.3) as shown in figure B.1. Switch on the vacuum pump with the air bleed control open.

B.3.5 Adjust the bleed control so that a gradual reduction in pressure is obtained and a manometer reading of 88 kPa[1)] below ambient atmospheric pressure is reached.

B.3.6 Examine the syringe for leakage of air past the piston or seal(s).

B.3.7 Isolate the syringe and manometer assembly by means of the vacuum-tight valve.

B.3.8 Observe the manometer reading for (60 $^{+5}_{0}$) s and record any fall in the reading.

B.3.9 Examine the syringe to determine if the piston has become detached from the plunger.

B.4 Test report

The test report shall contain at least the following information:

a) the identity and nominal capacity of the syringe;

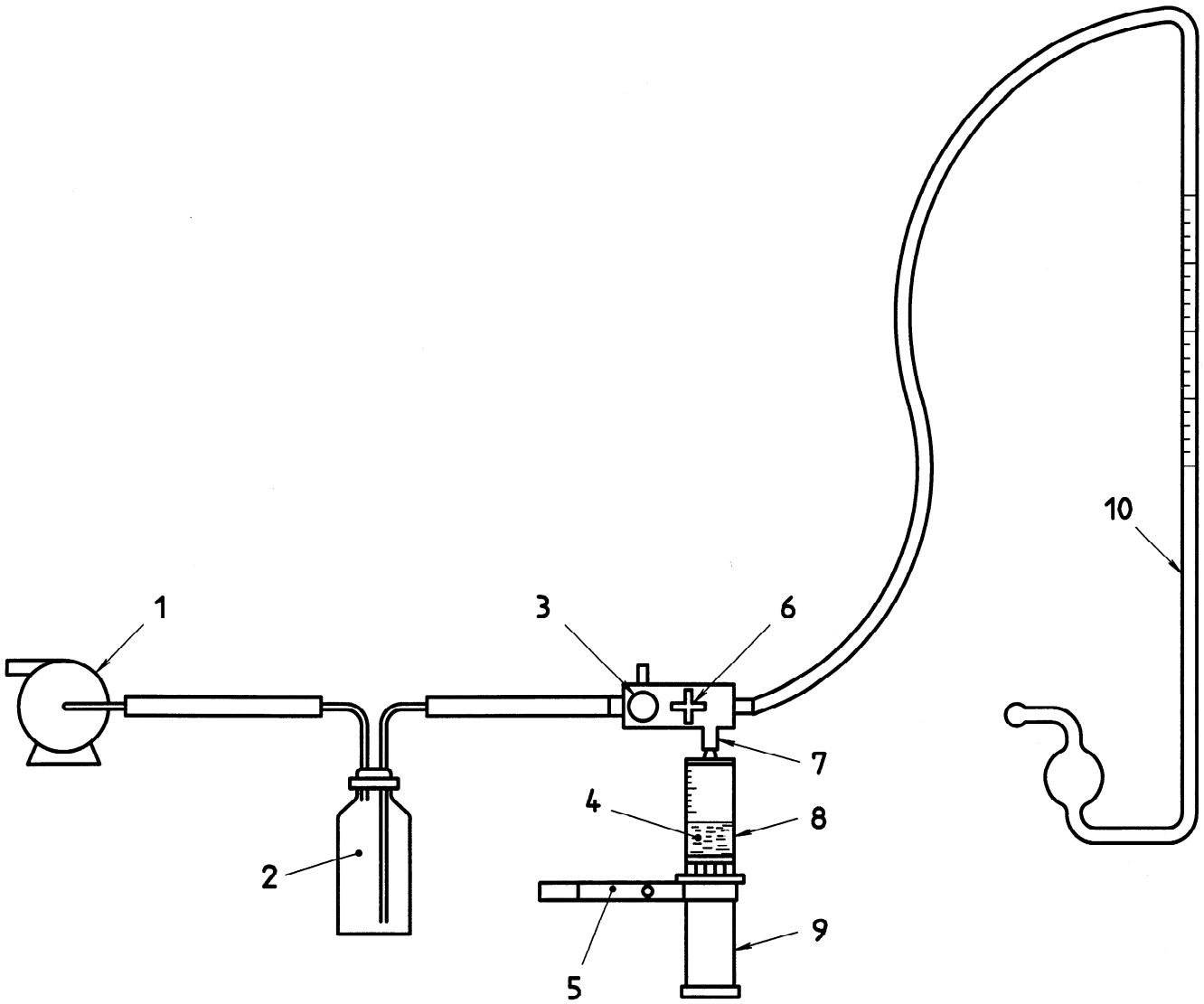
b) whether leakage past the piston or seal(s) was observed;

c) the fall, if any, in the manometer reading;

d) whether the piston became detached from the plunger;

e) the date of testing.

1) 1 kPa = 7,5 mmHg



1. Vacuum pump
2. Bottle trap
3. Fine bleed control
4. Nominal capacity graduation line
5. Clamp
6. Vacuum-tight valve
7. Female conical fitting complying with ISO 594-1
8. Water to not less than 25% of nominal capacity
9. Syringe
10. Manometer

Figure B.1 — Apparatus for aspiration test

Annex C
(normative)

Method for determination of dead space

C.1 Principle

The syringe is weighed dry and after having been filled with, and emptied of, water. The dead space is inferred from the mass of the residual water.

C.2 Apparatus and reagents

C.2.1 Balance, capable of determining a difference in mass of 0,2 g or less to an accuracy of 7 mg.

C.2.2 Distilled or deionized water, of grade 3 in accordance with ISO 3696.

C.3 Procedure

C.3.1 Weigh (C.2.1) the empty syringe.

C.3.2 Fill the syringe to the nominal capacity graduation line with water (C.2.2), taking care to expel all air bubbles and to ensure that the level of the meniscus of the water coincides with the end of the nozzle lumen.

C.3.3 Expel the water by fully depressing the plunger, and wipe dry the outer surfaces of the syringe.

C.3.4 Reweigh the syringe.

C.4 Calculation of results

Determine the mass, in grams, of water remaining in the syringe by subtracting the mass of the empty syringe from the mass of the syringe after expulsion of the water. Record this value as the dead space in millilitres, taking the density of water as 1 000 kg/m^3.

C.5 Test report

The test report shall contain at least the following information:

a) the identity and nominal capacity of the syringe;

b) the dead space, expressed in millilitres;

c) the date of testing.

Annex D
(normative)

Test method for liquid leakage at syringe piston under compression

D.1 Principle

The syringe is filled with water, the syringe nozzle sealed, the plunger arranged in the most disadvantageous orientation in relation to the barrel and a force applied in an attempt to induce leakage past the piston and seal(s).

D.2 Apparatus and reagents

D.2.1 Device for sealing or occluding the syringe nozzle.

NOTE 6 This may comprise the reference steel female conical fitting in accordance with ISO 594-1, suitably sealed or occluded.

D.2.2 Device for applying a sideways force to the syringe plunger, in the range 0,25 N to 3 N.

D.2.3 Device for applying an axial force to the barrel and/or plunger, to generate pressures of 200 kPa and 300 kPa.

D.2.4 Water.

D.3 Procedure

D.3.1 Draw into the syringe a volume of water (D.2.4) exceeding the nominal capacity of the syringe.

D.3.2 Expel air and adjust the volume of water in the syringe to the nominal capacity.

D.3.3 Seal (D.2.1) the syringe nozzle.

D.3.4 Apply a sideways force (D.2.2) to the push-button at right angles to the plunger to swing the plunger radially about the piston seal(s) with a force as given in table 1.

Orientate the plunger to permit the maximum deflection from the axial position.

D.3.5 Apply an axial force (D.2.3) to the syringe so that the pressure given in table 1 is generated by the relative action of the piston and barrel. Maintain the pressure for $(30\ ^{+5}_{0})$ s.

D.3.6 Examine the syringe for leakage of water past the piston seal(s).

D.4 Test report

The test report shall contain at least the following information:

a) the identity and nominal capacity of the syringe;

b) whether leakage past the piston or seal(s) was observed;

c) the date of testing.

Annex E
(informative)

Guidance on materials

Materials used in the construction of syringes should be suitable for the process to be used for their sterilization. Attention is drawn to the work in progress in ISO/TC 198 on the sterilization of medical devices.

Materials used in the construction of syringes should not cause them to be detrimentally affected, physically or chemically, by the normal use of injectable preparations.

Certain grades of polypropylene, polystyrene and styrene/acrylonitrile copolymer have been extensively used for the barrels of sterile syringes for hypodermic use. A high-quality natural or synthetic rubber composition is frequently used for the piston, the surface of the piston being lubricated with polydimethylsiloxane. High-density polyethylene is used for the seal of the two-component design in combination with a polypropylene barrel containing an amide slip additive.

Materials used in the construction of the wall of the syringe barrel should have sufficient clarity to enable dosages to be read without difficulty.

Annex F
(informative)

Examples of test methods for incompatibility between syringes and injection fluids

F.1 General

F.1.1 This annex contains a selection of test methods that are recommended for the investigation of the compatibility of syringes with injection fluids. These tests are not yet fully developed and the details of apparatus and methodology have not been finalized; neither have compliance criteria been finalized. This annex should therefore be viewed as being of a provisional nature. Nonetheless, manufacturers are encouraged to perform these tests with a view both to validating the methodology and to producing data that can be used to develop pass/fail criteria. Note that these tests are intended to provide a general assessment, and that the only conclusive test is that of particular injectable preparation with a particular type and brand of syringe.

F.1.2 Three types of tests are given, namely;

— visual/organoleptic (odour) evaluation;

— chemical/physical analysis of syringe extracts (reducing substances, absorption spectra, resistivity);

— evaluation of ease of plunger movement.

F.2 Matrix of tests

A matrix showing which tests are to be performed with each test fluid is shown in table F.1

Table F.1 — Matrix of compatibility tests

Test	Test fluid			
	A (water)	**B** (aqueous ethyl alcohol)	**C** (aqueous benzyl alcohol)	**D** (aqueous potassium chloride)
Visual (clarity, colour, presence of particles) (F.6.1)	X	X		
Organoleptic (odour) (F.6.2)	X	X		
Reducing substances (F.6.3)	X			
UV light absorbtion spectrum (F.6.4)	X	X		
Visual light absorbtion spectrum (F.6.4)	X	X		
Resistivity (F.6.5)				X
Ease of plunger movement (F.6.6)	X		X	
X = tests to be performed				

F.3 Test fluids

F.3.1 Test fluid A, comprising purified water.

F.3.2 Test fluid B, comprising a solution of ethyl alcohol (analytical grade reagent) in purified water, $c(C_2H_5OH) = 10,85$ mol/l.

F.3.3 Test fluid C, comprising a solution of benzyl alcohol (analytical grade reagent) in purified water, $c(C_6H_5CH_2OH) = 0,28$ mol/l.

F.3.4 Test fluid D, comprising purified water, the resistivity of which has been adjusted to a known value in the range 350 000 Ω·cm to 450 000 Ω·cm by the addition of potassium chloride.

F.4 Apparatus and reagents

F.4.1 Apparatus for volumetric titration, of class B accuracy as specified in ISO 384.

F.4.2 Spectrophotometer and silica cells.

F.4.3 Resistivity meter, having platinum electrodes operating on alternating current so as to avoid polarization effects on the electrodes.

F.4.4 Apparatus to depress syringe plunger, with known, adjustable force.

F.4.5 Stop-watch.

F.4.6 Selection of laboratory borosilicate glassware.

F.4.7 Sulfuric acid, solution in purified water, $c(H_2SO4) = 1$ mol/l.

F.4.8 Potassium permanganate, solution in purified water, $c(KMnO_4) = 0,002$ mol/l.

F.4.9 Sodium thiosulfate, solution in purified water, $c(Na_2S_2O_3) = 0,01$ mol/l.

F.4.10 Starch indicator solution.

F.4.11 Membrane filter, of pore size not less than 5 µm and not more than 25 µm, and filter holder.

F.4.12 Balance, capable of weighing from 1 g to 160 g, with an accuracy of 0,1 mg.

F.4.13 Water bath.

F.4.14 Potassium iodide, solid.

F.4.15 Apparatus for clamping syringe.

NOTE 7 All reagents are analytical reagent grade.

F.5 Procedure for preparation of extracts

F.5.1 Fill the requisite number of sterile syringes to the nominal capacity with the selected test fluid. Divide the filled syringes into four equal groups and maintain the syringes and contents under the following conditions:

— Group 1: (20 ± 1) °C for (60 ± 3) min

— Group 2: (20 ± 1) °C for (24 ± 1) h

— Group 3: (37 ± 1) °C for (60 ± 3) min

— Group 4: (37 ± 1) °C for (24 ± 1) h

F.5.2 Eject the contents of each group of syringes into a borosilicate glass vessel. Seal the vessel and store at room temperature until required for testing. Do not allow more than 1 h to elapse before testing.

F.6 Test procedures

NOTE 8 Unless otherwise specified, all procedures are to be carried out at (20 ± 5) °C.

F.6.1 Visual examination

F.6.1.1 Procedure

F.6.1.1.1 Filter the requisite quantity of test fluid A (F.3.1) through a membrane filter (F.4.11) and bring the filtrate to a temperature of (37 ± 2) °C.

F.6.1.1.2 Draw into the syringe a volume of filtered test fluid equal to half the nominal capacity and then draw air into the syringe until the fiducial line on the piston is at the nominal capacity graduation line on the scale.

F.6.1.1.3 Shake the syringe vigorously by hand for (30 ± 2) s. Expel the contents into a borosilicate glass vessel (F.4.6), and examine the fluid under normal or corrected-to-normal vision for the presence of coloration, turbidity and particles. Record the observations.

F.6.1.1.4 Repeat F.6.1.1.2 and F.6.1.1.3.

F.6.1.1.5 Repeat F.6.1.1.1 to F.6.1.1.3 using test fluid B (F.3.2).

F.6.1.2 Proposed compliance criterion

The proposed criterion is that no turbidity, coloration or particles shall be visible in the fluids expelled from the syringe.

F.6.2 Organoleptic (odour) examination

F.6.2.1 Procedure

Proceed as described in F.6.1.1. Compare the odour of the syringe contents (see F.6.1.1.3 and F.6.1.1.5) with that of test fluids A and B and record the observations.

F.6.2.2 Proposed compliance criterion

The proposed criterion is that no difference shall be perceived between the odour of the fluid expelled from the syringe and that of the corresponding test fluid.

F.6.3 Reducing substances

F.6.3.1 Procedure

F.6.3.1.1 Prepare extracts of groups of syringes using test fluid A (F.3.1), as described in F.5.

F.6.3.1.2 Add to a titration flask, by means of the titration apparatus (F.4.1), 20 ml of extract, 2 ml of sulfuric acid (F.4.7) and 20 ml of potassium permanganate solution (F.4.8). Bring the mixture to boiling point (F.4.13) and maintain at this temperature for (180 ± 2) s. Cool the mixture quickly to room temperature.

F.6.3.1.3 Add 1 g of potassium iodide crystals (F.4.14) and 0,25 ml starch indicator solution (F.4.10). Titrate with sodium thiosulfate solution (F.4.9) and record the volume of sodium thiosulfate solution added.

F.6.3.1.4 Repeat F.6.3.1.2 and F.6.3.1.3 using test fluid A in place of the syringe extract. Calculate and report the difference in titres between the test fluid and the syringe extract.

F.6.3.2 Proposed compliance criterion

The proposed criterion is that the difference in titre shall not exceed 0,5 ml between any of the four different extraction conditions.

F.6.4 Spectrophotometry

F.6.4.1 Procedure

F.6.4.1.1 Prepare extracts of groups of syringes using test fluid A (F.3.1) and test fluid B (F.3.2), as described in F.5.

F.6.4.1.2 Record the absorption spectrum of the extract in a spectrophotometer (F.4.2), using silica cells of path length 1 cm, over the range of wavelengths 200 nm to 450 nm.

F.6.4.1.3 Repeat F.6.4.1.2 using test fluid A and test fluid B in place of the syringe extract.

F.6.4.1.4 Examine the control spectrum and the test spectrum of each of the eight different extraction conditions and record differences.

F.6.4.2 Proposed compliance criterion

The proposed criterion is that there shall be no difference in optical density greater than 0,3 between the spectra of the syringe extract and the corresponding test fluid.

F.6.5 Resistivity

F.6.5.1 Procedure

F.6.5.1.1 Prepare extracts of groups of syringes using test fluid D (F.3.4) as described in F.5.

F.6.5.1.2 Measure and record the resistivity of the extract using the resistivity meter (F.4.3).

F.6.5.1.3 Repeat F.6.5.1.2 using test fluid D in place of the syringe extract.

F.6.5.2 Proposed compliance criterion

The proposed criterion is that the resistivity of the syringe extract shall be at least 60 % of that of test fluid D.

F.6.6 Ease of plunger movement

F.6.6.1 Procedure

F.6.6.1.1 Fill the requisite number of syringes to the nominal capacity graduation line with test fluid A (F.3.1). Move each plunger to and fro by small amounts so as to ensure it is not adhering to the barrel. Refill each syringe to the nominal capacity graduation line.

F.6.6.1.2 Clamp (F.4.15) each syringe in a vertical position with the tip downwards. After (300 ± 15) s have elapsed since first filling the syringe, apply a force (F.4.4) to the plunger so that the piston ejects the contents. By trial and error, determine the value of the force necessary to eject the contents in a time of (5 ± 2) s.

F.6.6.1.3 Repeat F.6.6.1.1 and F.6.6.1.2 on a total of 10 syringes, and calculate the mean force.

F.6.6.1.4 Repeat F.6.6.1.1 for the requisite number of syringes, using test fluid C (F.3.3) in place of test fluid A.

F.6.6.1.5 Clamp each syringe as described in F.6.6.1.2 and, after (300 ± 15) s have elapsed since first filling, apply to the plunger a force of the mean value determined in F.6.6.1.3. Measure (F.4.5) the time taken for the syringe contents to be ejected.

F.6.6.1.6 Repeat F.6.6.1.5 on a total of 10 syringes and calculate the mean time taken.

F.6.6.1.7 Repeat F.6.6.1.4 to F.6.6.1.6 on syringes that have been filled with test fluid C for a period of (60 ± 3) min.

F.6.6.2 Proposed compliance criterion

The proposed criterion is that the mean time required to expel test fluid A using the force in F.6.6.1.3 shall be at least 50 % of that required to expel test fluid C.

F.7 Test report

Report the following:

a) identity of syringe, including nominal capacity;

b) the date of testing;

c) the observations and/or results of each test performed.

Annex G
(informative)

Test method for forces required to operate plunger

G.1 Principle

A mechanical testing machine such as in figure G.1 is used to move the syringe plunger and to aspirate and expel water, whilst the force exerted and the plunger travel are recorded.

G.2 Apparatus and reagents

G.2.1 Mechanical testing machine, capable of measuring and continuously recording force and travel with an accuracy of 1 % of full scale reading, and having means for attaching the syringe to be tested.

G.2.2 Reservoir, open to the atmosphere, and having tubing of inside diameter (2,7 ± 0,1) mm for connecting it to the syringe to be tested.

G.2.3 Water.

G.3 Procedure

G.3.1 Remove the syringe from the package and mount it in the testing machine (G.2.1) as shown in figure G.1. Move the syringe plunger once until the fiducial line reaches the total graduated capacity graduation line, and then return it so that the fiducial line reaches the zero graduation line.

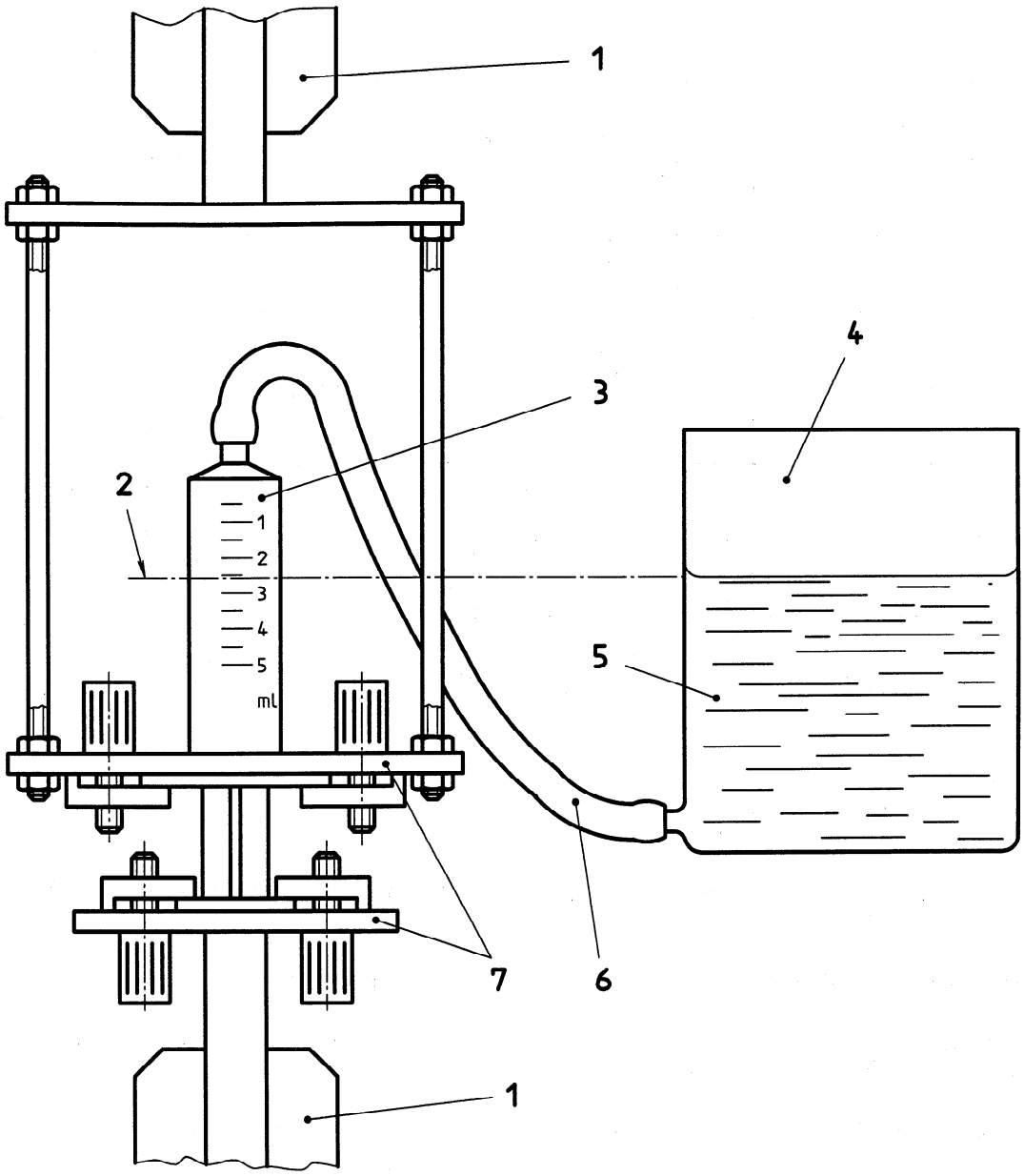
G.3.2 Connect the nozzle of the syringe to the tubing of the reservoir (G.2.2). Add to the reservoir water (G.2.3) at (23 ± 2) °C and displace any air from the tubing. Maintain the water and the syringe at this temperature. Adjust the relative positions of the syringe and reservoir so that the water level in the reservoir is approximately level with the mid-point of the syringe barrel (see figure G.1).

G.3.3 Zero the recorder and set the testing machine (G.2.1) so that it can apply compressive and tensile forces without re-setting.

G.3.4 Start the testing machine so that it withdraws the syringe plunger, at a rate of (100 ± 5) mm/min, to the graduation line that indicates the nominal capacity, thereby drawing water from the reservoir to the syringe.

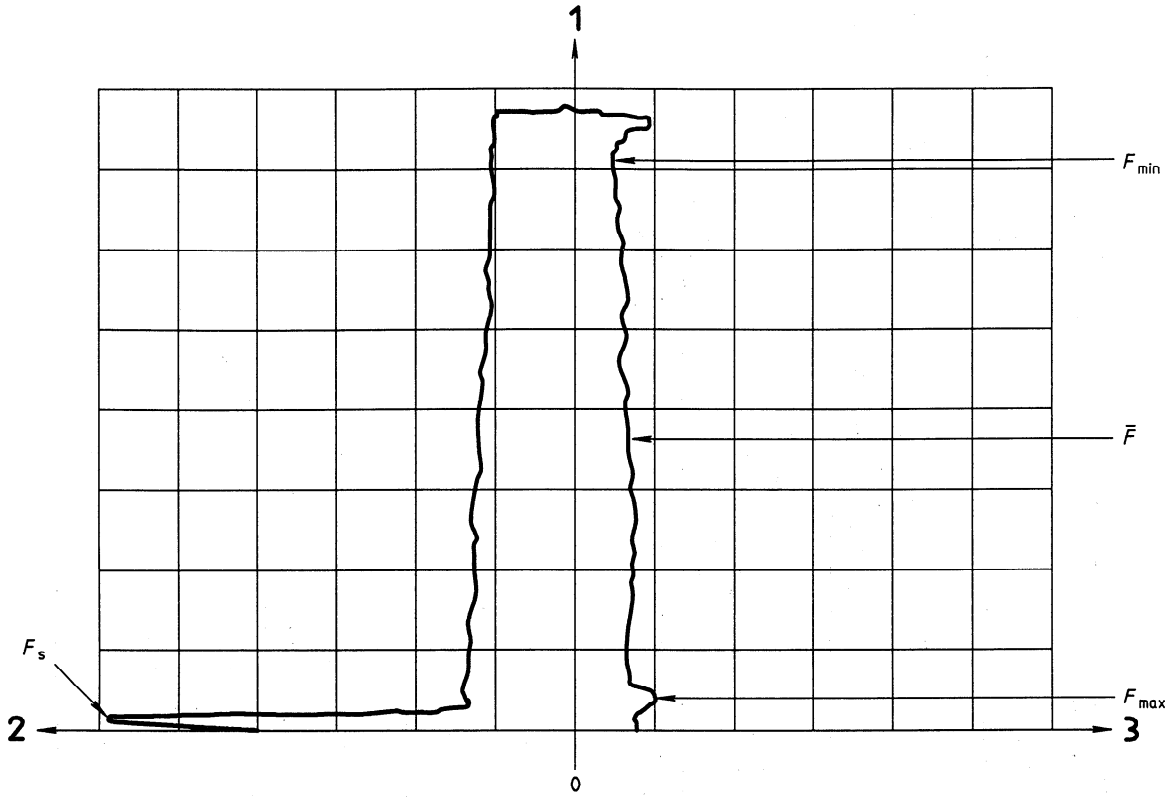
NOTE 9 The presence of air in the syringe nozzle will not affect the results of the test.

G.3.5 Withdraw the syringe plunger until the fiducial line has reached the nominal capacity graduation line. Stop the plunger travel and readjust the recorder to zero. Wait 30 s. Reverse the testing machine and return the plunger to its original position, thereby expelling the water from the syringe into the reservoir.



1. Jaw of mechanical testing machine (G.2.1)
2. Water level at approximately the mid-point of the syringe
3. Syringe being tested
4. Reservoir (G.2.2)
5. Water (G.2.3)
6. Connecting tubing (G.2.2)
7. Adjustable mounts to accommodate different nominal capacities of syringe

Figure G.1 — Apparatus for determining forces to operate plunger



1. Plunger travel
2. Force (newtons) during withdrawal of plunger
3. Force (newtons) during return of plunger

Figure G.2 — Examples of graph of forces required to operate plunger

G.4 Calculation of results

G.4.1 From the recording of plunger travel and force applied (see figure G.2), determine the following:

a) the force required (F_s) to initiate movement of the plunger i.e. the peak force recorded when the testing machine starts to withdraw the plunger (see G.3.4);

b) the mean force ($\bar{F}$) during return of the plunger (i.e. the estimated or integrated mean value while the testing machine is returning the plunger (see G.3.5);

c) the maximum force (F_{max}) during return of the plunger (see G.3.5);

d) the minimum force (F_{min}) during return of the plunger (see G.3.5).

G.4.2 Proposed values for the forces required to operate the plunger are given in table G.1.

G.5 Test report

The test report shall contain at least the following information:

a) the identity and nominal capacity of syringe;

b) the force (F_s) required to initiate movement of the plunger, expressed in newtons;

c) the mean force ($\bar{F}$) during return of the plunger, expressed in newtons;

d) the maximum force (F_{max}) during return of the plunger, expressed in newtons;

e) the minimum force (F_{min}) during return of the plunger, expressed in newtons;

f) the date of testing.

Table G.1 — Proposed values for forces required to operate plunger

Nominal capacity of syringe, V ml	**Initial force,** F_s max. N	**Mean force,** $\overline{F}$ max. N	**Maximum force,** F_{max} N	**Minimum force,** F_{min} N
$V < 2$	10	5	$\not>$ (2,0 × measured $\overline{F}$) or (measured $\overline{F}$ + 1,5 N), whichever is the higher	$\not<$ (0,5 × measured $\overline{F}$) or (measured $\overline{F}$ – 1,5 N), whichever is the lower
$2 \leqslant V < 50$	25	10	$\not>$ (2,0 × measured $\overline{F}$) or (measured $\overline{F}$ + 1,5 N), whichever is the higher	$\not<$ (0,5 × measured $\overline{F}$) or (measured $\overline{F}$ – 1,5 N), whichever is the lower
$50 \leqslant V$	30	15	$\not>$ (2,0 × measured $\overline{F}$) or (measured $\overline{F}$ + 1,5 N), whichever is the higher	$\not<$ (0,5 × measured $\overline{F}$) or (measured $\overline{F}$ – 1,5 N), whichever is the lower

Annex H
(informative)

Symbol for "do not re-use"

H.1 General

The ISO symbol to denote equipment intended for single use is ISO symbol registration number ISO 7000/1051, given in ISO 7000.

NOTE 10 Further information on design, dimensions and application of ISO symbols is given in ISO 3461.

H.2 Original design

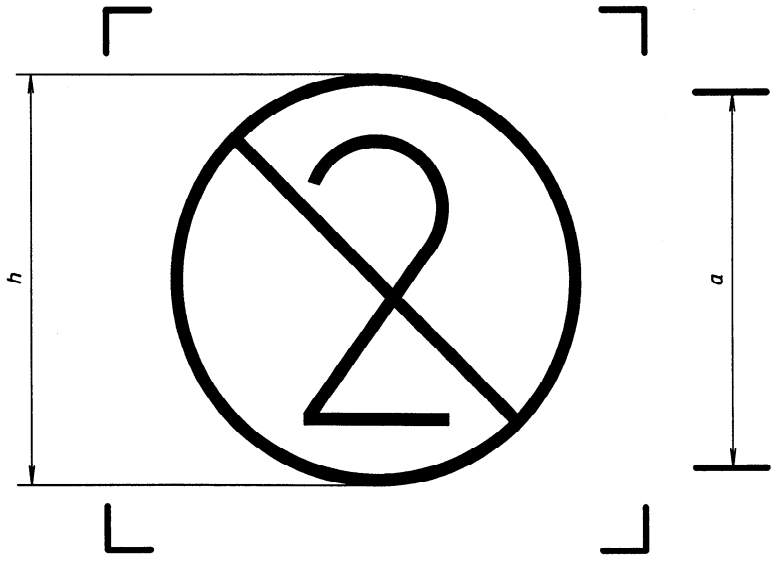
Symbol ISO 7000/1051 is shown in figure H.1.

The thickness of the lines is 2 mm. Dimension *a* is the nominal size of the original design of all ISO symbols and is normally 50 mm. In many cases, including ISO 7000/1051, the actual dimension differs slightly, and the outside diameter of the circle (dimension *h*) of the original design is 1,16 *a*, i.e. 58 mm.

No colour is specified in ISO 7000 or in this part of ISO 7886 for symbol 1051.

H.3 Reduction and enlargement of original design

For the application of the symbol it may be necessary to reduce or enlarge the size of the original to a suitable size at which it will actually appear. The nominal dimension *a* should be used as a gauge. Practice has shown that dimension *a* may be reduced to 3 mm without the symbol losing its legibility. However, the legibility of the symbol when reduced in size should be checked.



$h = 1{,}16\ a$

NOTE — The visual centring lines do not form part of the symbol.

Figure H.1 — ISO symbol for "do not re-use", number ISO 7000/1051

Annex J
(informative)

Bibliography

[1] ISO 384:1978, *Laboratory glassware — Principles of design and construction of volumetric glassware.*

[2] ISO 3461-1:1988, *General principles for the creation of graphical symbols — Part 1: Graphical symbols for use on equipment.*

[3] ISO 3461-2:1987, *General principles for the creation of graphical symbols — Part 2: Graphical symbols for use in technical product documentation.*

[4] ISO 7000:1989, *Graphical symbols for use on equipment — Index and synopsis.*

[5] ISO 7864:1993, *Sterile hypodermic needles for single use.*

[6] ISO 8537:1991, *Sterile single-use syringes, with or without needle, for insulin.*

[7] ISO 10993-1:1992, *Biological evaluation of medical devices — Part 1: Guidance on selection of tests.*

This page intentionally left blank

This page intentionally left blank

UDC 615.473.3.014.45

Descriptors: medical equipment, disposable equipment, syringes, specifications, dimensions, tests, packaging, labelling.

Price based on 23 pages