(Translator's reminder: There is 1 Amendment included)

Legend / Track Changes:

Text in BLACK: Translated from the original Chinese text.

Text in BLUE: Note / Reminder added by reviewer Wayne Zheng.

Text in RED: Integrated / Modified / Digested according to the "No. 1 Amendment [2003]".

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NATIONAL STANDARD OF THE

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Sterile Hypodermic Syringes for Single Use

Issued on: September 18, 2001 **Implemented on: February 1, 2002**

Issued by: General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China

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Foreword

This Standard equivalently adopts ISO 7886-1:1993 "Sterile Hypodermic Syringes for Single Use - Part 1: Syringes for Manual Use". this Standard is the revision of GB 15810-1995.

Compared with ISO 7886-1:1993, the main technical differences in this Standard are as follows:

In this Standard, cytoxicity, sensitization, irritation, hemolysis and acute systemic toxicity were supplemented in sterile, pyrogen and biological evaluation of biological performance; requirements on reducing substances (oxidizable substances) in chemical performance were changed from part of Appendix F (Informative) of ISO 7886-1:1993 into an indispensable part of this Standard; Appendix G (Informative) of ISO 7886-1:1993 was changed into an indispensable part of this Standard; add the residue content of epoxy ethane; add Appendix C Inspection Rules. In this Standard, editorial changes had been made on Appendixes A to J of ISO 7886-1:1993; and the Guideline of Material and Bibliography were reserved.

Compared with GB/T 15810-1995, the main technical differences of this Standard are as follows:

In this Standard, according to the requirements of GB/T 16886.1-1997, the provisions of acute systemic toxicity was add in biological performance; abnormal toxicity was deleted; sterile, pyrogen free, hemolysis and intracutaneous irritation in former national standard were reserved; cytoxicity and sensitization were supplemented. Requirements on residue content of epoxy ethane were supplemented in chemical performance. Capacity permissible error is in accordance with international standards.

This Standard replaces GB 15810-1995, from the implementation date.

Appendixes A, B, C and D of this Standard are normative.

Appendixes E and F of this Standard are informative.

This Standard was proposed by the State Drug Administration (SDA).

This Standard shall be under the jurisdiction of National Technical Committee 95 on Injector for Medical Purpose of Standardization Administration of China.

Drafting organization of this Standard: SDA-Shanghai Quality Supervision and Inspection Center for Medical Devices.

Main drafters of this Standard: Fu Guobao, and Zhao Jing.

This Standard was first-time issued in 1987, and first-revised in 1995.

Sterile Hypodermic Syringes for Single Use

1 Scope

This Standard specifies classification and nomenclature, requirements, test methods, inspection rules, packing and labeling of sterile hypodermic syringes (hereinafter referred to as "syringes") for single use.

This Standard is applicable to the manual syringes intended for the aspiration of fluids or for the injection of fluids immediately after filling.

This Standard is not applicable to syringes for use with insulin, 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.

2 Normative References

The following standards contain provisions which, through reference in this text, constitute provisions of this Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below.

GB/T 1962.1-2001 Conical Fittings with a 6 % (Luer) Taper for Syringes, Needles and Certain other Medical Equipment - Part 1: General Requirements (idt ISO 594-1:1986)

GB/T 1962.2-2001 Conical Fittings with a 6 % (Luer) Taper for Syringes, Needles and Certain other Medical Equipment - Part 2: Lock Fittings (idt ISO 594-2:1998)

GB 2828-1987 Sampling Procedures and Tables for Lot-by-lot Inspection by Attributes (Apply to Inspection of Successive Lots or Batches)

GB 2829-1987 Sampling Procedures and Tables for Periodic Inspection by Attributes (Apply to Inspection of Process Stability)

GB 6682-1992 Water for Analytical Laboratory Use - Specification and Test Methods

GB/T 14233.1-1998 Test Methods for Infusion Transfusion Injection Equipment for Medical Use - Part 1: Chemical Analysis Methods

5 Requirements

5.1 Appearance

5.1.1 When inspected by vision under an illumination of 300 lx to 700 lx, the hypodermic syringes shall be clean, free from particles and extraneous matter.

5.1.2 Hypodermic syringes shall be free from any defect of rough selvedge, burrs, creeping and breakage.

5.1.3 The barrel of hypodermic syringe shall be with adequate transparency and able to see the fiducial line clear.

5.1.4 The interior surface (including rubber piston) of hypodermic syringe shall be free from any obvious lubricant droplets or particles.

5.2 Graduated scale of hypodermic syringes

5.2.1 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.

5.2.2 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.

5.3 Graduation lines of graduated scale

5.3.1 The graduation lines shall be numbered at the volume increments given in ~~Table 2~~ Table 1.

5.3.2 The graduation lines shall be laid in planes at right angles to the axis of the barrel. 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.

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

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

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

5.4 Numbering of scale

5.4.1 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.

5.4.2 The numbers shall be close to, but shall not touch, the ends of the graduation lines to which they relate.

5.4.3 Sequence of numbering of scale shall be started from the zero graduation line (the word “zero” may be omitted) on the bottom of barrel. Examples of scales and the numbering of graduation lines are shown in Figure 2.

5.11.3 Oxidizable substances [1]: compare extracts of groups of syringes with the same volume and batch of blank control liquid, the difference of consumption of potassium permanganate solution [c($KMnO_4$) = 0.002 mol/L] shall be ≤0.5 mL.

5.11.4 Residue content of epoxy ethane [2]: Residue content of epoxy ethane shall be ≤10 μg/g.

5.12 Biological performance [3]

5.12.1 Syringes shall be sterile.

5.12.2 Syringes shall be free from pyrogen.

5.12.3 Hemolysis: syringes shall be free from hemolytic reaction (hemolysis rate ≤ 5%).

5.12.4 Acute systemic toxicity: syringes shall be free from acute systemic toxicity.

6 Test Methods

6.1 Appearance

Visual inspection shall meet the requirements of 5.1, 5.2.2, 5.3, 5.4, 5.5, 5.8 and 5.9.3.

6.2 Dimension

Measurement with general or special measuring tools shall meet the requirements of 5.2.1, 5.6.1, 5.7, 5.9.1 and 5.9.4.

6.3 Crimping

Tested syringe is placed on a flat surface at an angle of 10° to the horizontal; the result shall meet the requirements of 5.6.2.

6.4 Sliding performance

In accordance with Appendix A, the result shall meet the requirements of 5.10.1.

6.5 Outer cone joint test

Test in accordance with GB/T 1962.1 or GB/T 1962.2; the result shall meet the requirements of 5.9.2.

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1 This provision in ISO 7886-1:1993 is part of Appendix F (Informative).

2 ISO 7886-1:1993 has no technical indexes on this provision.

3 ISO 7886-1:1993 has no technical indexes on this provision, only explained in Introduction.

6.6 Pressurizing of syringe

Draw into the syringe a volume of water exceeding the nominal capacity of the syringe. Apply an axial force 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 s. Examine the syringe for leakage of water past the piston seals.

Draw into the syringe a volume of water of not less than 25 % of the nominal capacity. With the nozzle uppermost, withdraw the plunger axially, so that the fiducial line piston coincides with nominal capacity line; suck-out the air from nozzle-hole; when it reaches 88 kPa below ambient atmospheric pressure, maintain for 60 s ± 5 s; inspect visually; the result shall meet the requirements of 5.10.2.

6.7 Capacity permissible error test

Weigh the weight of empty glass cylinder with a balance to the precision of 0.1 mg; then extract distilled water (20°C ± 5°C) by syringe to the scale capacity [V_0, elective value from the range between ~~greater than~~ greater than (or equal to) half of nominal capacity and less than half of nominal capacity]. Vent gas bubble to ensure that the water surface is flushed with the termination of conical fitting, and the top edge of fiducial line is tangential to the graduated line of lower edge. Transfer the distilled water into empty glass cylinder; and weigh the weight; the difference between two weights is the ~~actual capacity~~ displaced volume (V_i, water density is 1000 kg/m^3).

Calculation equation of capacity permissible error (%) that is greater than or equal to nominal capacity is: $\frac{V_0 - V_i}{V_i} \times 100\%$

Where: V_0 — Scale capacity;

V_i — ~~Actual capacity~~ Displaced volume.

~~It may also adopt standard capacity ball test method, and comply with the provisions of 5.10.3. Weighing method is the arbitration method.~~

In addition, capacity permissible error (V_0 - V_i) of less than half of nominal capacity shall meet the requirements of 5.10.3.

6.8 Residual capacity test

Weigh the mass of empty syringe with a balance to the precision of 0.1 mg; then extract distilled water (20°C ± 5°C) by syringe to the scale line of nominal capacity. Vent the gas bubble to ensure that the water surface is flushed with the termination of conical fitting. Depress the plunger completely to discharge water, and dry up the external surface of syringe. Weigh the syringe again. The mass of syringe after discharged water is deducted by the mass of empty syringe to obtain the mass of residual water (in g) within syringe. Residual water can be expressed in milliliters (mL),

water density is 1000 kg/m^3. Test result shall meet the requirements of 5.10.4.

6.9 Chemical performance

6.9.1 Preparation of control fluid

Prepare in accordance with No. 4 method specified in Table 1 of GB/T 14233.1-1993.

6.9.2 Extractable metals content

Prepare the test solution in accordance with the method of 6.9.1 and immersion for 8 h. Test in accordance with the method specified in 5.6 of GB/T 14233.1-1998; the result shall meet the requirements of 5.11.1. Cadmium content shall be tested in accordance with the method specified in 5.9.1 of GB/T 14233.1-1998; the result shall meet the requirements of 5.11.1 [Newly-added. See No. 1 Amendment].

6.9.3 Acidity or alkalinity

Prepare the test solution in accordance with the method of 6.9.1 and immersion for 8 h. Test in accordance with the method specified in ~~5.4~~ 5.4.1 of GB/T 14233.1-1998; the result shall meet the requirements of 5.11.2.

6.9.4 Oxidizable substances

Use the method of 6.9.1; 20 mL of test solution obtained after immersion for 1 h shall be conducted in accordance with the method specified in ~~5.2~~ 5.2.2 of GB/T 14233.1-1998; the result shall meet the requirements of 5.11.3.

6.9.5 Residue content of epoxy ethane

Preparation of control fluid: accurate weigh the mass of syringe (m_0); inject Grade 3 water (in conformity with GB 6682-1992) into syringe to nominal capacity (V); keep constant temperature at 37°C ± 1°C for 1 h. Take a given amount of extracting solution to test according to Chapter 9 Gas Chromatographic Method of GB/T 14233.1-1998. Epoxy ethane content W (W shall meet the requirements of 5.11.4) in the syringe can be calculated by following equation:

$$W(\mu g / g) = \frac{c \times V}{m_0}$$

6.10 Biological performance

6.10.1 Sterility test

Test shall be carried out at disinfection chamber. Take 6 syringes and extract 0.9% sodium chloride solution to total scale capacity; reversely draw the plunger to make the piston a little separated from liquid level; then shake for 5 times. Carry out test in accordance with the Sterility Test Method specified in GB/T 14233.2-1993; the result

b) the word “STERILE”;

c) the words “FOR SINGLE USE” or equivalent;

d) the lot number, prefixed by the word “LOT”;

e) the date (year and month) of invalidation;

f) the name and address of the manufacturer or supplier.

g) the size of syringe, if any.

8.3 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 8.2 a);

b) the lot number, prefixed by the word “LOT”;

c) the word “STERILE”;

d) the date (year and month) of invalidation;

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

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

8.4 Transport wrapping

If a storage container is not used but the secondary containers are wrapped for transportation, the information required by 8.3 shall either be marked on the wrapping or shall be visible through the wrapping.

9 Storage

Sterile hypodermic syringes shall be stored in a well ventilated storehouse with a relative humidity not exceed 80 % and free from corrosive gas. Hypodermic syringes shall be provided with sufficient protective measures.

attaching the syringe to be tested.

A2.2 Reservoir, open to the atmosphere, and having tubing of inside diameter 2.7 mm ± 0.1 mm for connecting it to the syringe to be tested.

A2.3 Water

A3 Procedures

A3.1 Remove the syringe from the package and mount it in the testing machine (A2.1) as shown in Figure A1. Move the syringe plunger once until the fiducial line reaches the total graduated capacity graduation line; then return it so that the fiducial line reaches the zero graduation line [1)].

A3.2 Connect the nozzle of the syringe to the tubing of the reservoir (G.2.2). Add water (A2.3) at (23 ± 2)°C to the reservoir; at the same time, 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 A1).

A3.3 Zero the recorder and set the testing machine (A2.1) so that it can apply compressive and tensile forces without re-setting.

A3.4 Start the testing machine so that it withdraws the syringe plunger, at a rate of 100 mm/min ± 5 mm/min, to the graduation line that indicates the nominal capacity, thereby drawing water from the reservoir to the syringe.

Note: The presence of air in the syringe nozzle will not affect the results of the test.

A3.5 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 for 30 s. Reverse the testing machine and return the plunger to its original position, thereby expelling the water from the syringe into the reservoir.

A4 Calculation of results: Based on the recording of plunger travel and force applied (see figure A2), determine the following:

a) the force required (F_s) to initiate movement of the plunger, expressed in N;

b) the mean force ($\overline{F}$) during return of the plunger, expressed in N;

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

d) the minimum force (F_{min}) during return of the plunger, expressed in N.

1) For two-piecec syringes, fiducial line shall be shifted down 2 division values.

Appendix B

(Normative)

Hemolytic Test

B1 Principle

Red blood cell may be dissolved by the action of medicine or toxic substances, and the hemoglobin may be produced. The purpose of this test is to make the direct contact of test solution of syringe and blood diluent, and determine the quantity of hemoglobin produced by the dissolution of red blood cell, in order to determine the extracorporeal hemolysis degree of syringes.

B2 Test apparatuses

Spectrophotometer, centrifuge, incubator for water bath.

B3 Reagents

a) Distilled water;

b) 0.9 % sodium chloride injection.

B4 Test procedure

B4.1 Preparation of whole blood diluent

a) Preparation of 2% whole blood diluent

Take 2 mL of human blood or rabbit blood, dilute to 100 mL with 0.9 sodium chloride injection, mix uniformly (no hemolysis and coagulum).

b) Preparation of 1% whole blood diluent

Take part of 2% whole blood diluent, add isometric 0.9 % sodium chloride injection.

B4.2 Operation procedures

B4.2.1 Take at least 3 syringes and add 1% whole blood diluent to full scale capacity (test solution A).

B4.2.2 Take 3 test tubes and add 10 mL of 1% whole blood diluent (negative control fluid B).

B4.2.3 Take 3 test tubes, add 5 mL of distilled water and 5 mL of 2% whole blood diluent (positive control fluid C).

B4.2.4 Place aforesaid test solution A, B and C into an incubator (37°C ± 1°C) and maintain for 60 min + 5 min. Transfer test solution A into 3 test tubes (10 mL for each test tube); then process centrifugation (1500 r/min) for 5 min respectively. Take supernatant fluid and determine the absorbance by spectrophotometer at wavelength of 545 nm. Take the average value of 3 test tubes; the hemolysis rate can be calculated by following equation:

$$\text{Hemolysis rate} = \frac{A - B}{C - B} \times 100$$

Where: A — Absorbance of test solution;

B — Absorbance of negative control fluid;

C — Absorbance of positive control fluid.

Appendix D

(Normative)

Biological Evaluation

When new product is launched, or there is significant change of material source or manufacturing process, biological evaluation shall be carried out on material and final product according to the requirements of GB 16886.1. Basic evaluation tests are as follows:

a) Cytoxicity;

b) Sensitization;

c) Irritation;

d) Hemolysis;

e) Acute systemic toxicity.

Appendix 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.

No.1 Amendment of GB 15810-2001

"Sterile Hypodermic Syringes for Single Use"

This amendment was approved in the document GBWNQH [2003] No.11 by Standardization Administration of China on February 10, 2003, and was implemented on July 1, 2003.

1. "Appendix D" in 4.3 was changed into "Appendix E" (Page 2).

2. "Table 2" in 5.3.1 was changed into "Table 1" (Page 3).

3. "Table 2" in 5.10.3 was changed into "Table 1", and "greater than" was changed into "greater than (or equal to)" (Page 5).

4. Chinese character "隔" in 5.11.1 was changed into “cadmium" (Page 5).

5. Add (hemolysis rate ≤5%) in 5.12.3 (Page 6).

6. "5.4" in 6.9.3 was changed into "5.4.1" (Page 7).

7. "Take test solution prepared in accordance with 6.10.1" was deleted from item a) of 6.10.2 (Page 7).

8. "ATC9372" in Note 2 of Table C2 was changed into "ATCC9372" (Page 12).

9. 6.7 (Page 6) was changed into: Capacity permissible error test

Weigh the weight of empty glass cylinder with a balance to the precision of 0.1 mg; then extract distilled water (20°C ± 5°C) by syringe to the scale capacity [V_0, elective value from the range between greater than (or equal to) half of nominal capacity and less than half of nominal capacity]. Vent gas bubble to ensure that the water surface is flushed with the termination of conical fitting, and the top edge of fiducial line is tangential to the graduated line of lower edge. Transfer the distilled water into empty glass cylinder; and weigh the weight; the difference between two weights is the displaced volume (V_i, water density is 1000 kg/m^3).

Calculation equation of capacity permissible error (%) that is greater than or equal to nominal capacity is: $\frac{V_0 - V_i}{V_i} \times 100\%$

Where: V_0 - Scale capacity;

V_i - Displaced volume.

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