INTERNATIONAL STANDARD

ISO 1135-4

Sixth edition
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Transfusion equipment for medical use —

Part 4: Transfusion sets for single use, gravity feed

Matériel de transfusion à usage médical —

Partie 4: Appareils de transfusion non réutilisables à alimentation par gravité

Reference number
ISO 1135-4:2015(E)

International Organization for Standardization

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

This sixth edition of ISO 1135-4, together with the first edition of ISO 1135-5, cancels and replaces the fifth edition (ISO 1135-4:2012), which has been technically revised with the following changes:

— the scope has been restricted to gravity feed applications and the whole document aligned accordingly;

— transfusion sets for single use used in conjunction with pressure infusion apparatus are now covered by ISO 1135-5;

— 3.3 "Designation examples" has been deleted;

— the Normative references and the Bibliography have been updated;

— some minor editorial changes were introduced in the whole document.

ISO 1135 consists of the following parts, under the general title *Transfusion equipment for medical use*:

— *Part 3: Blood-taking sets for single use*

— *Part 4: Transfusion sets for single use, gravity feed*

— *Part 5: Transfusion sets for single use with pressure infusion apparatus*

Transfusion equipment for medical use —

Part 4:
Transfusion sets for single use, gravity feed

1 Scope

This part of ISO 1135 specifies requirements for single use transfusion gravity sets for medical use in order to ensure their compatibility with containers for blood and blood components as well as with intravenous equipment.

Secondary aims of this part of ISO 1135 are to provide guidance on specifications relating to the quality and performance of materials used in transfusion sets, to present designations for transfusion set components, and to ensure the compatibility of sets with a range of cellular and plasma blood components.

In some countries, the national pharmacopoeia or other national regulations are legally binding and take precedence over this part of ISO 1135.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

ISO 594-2[1)], *Conical fittings with 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 2: Lock fittings*

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

ISO 3826-1:2013, *Plastics collapsible containers for human blood and blood components — Part 1: Conventional containers*

ISO 3826-2, *Plastics collapsible containers for human blood and blood components — Part 2: Graphical symbols for use on labels and instruction leaflets*

ISO 7864, *Sterile hypodermic needles for single use*

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

ISO 10993-4, *Biological evaluation of medical devices — Part 4: Selection of tests for interactions with blood*

ISO 14644-1, *Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness*

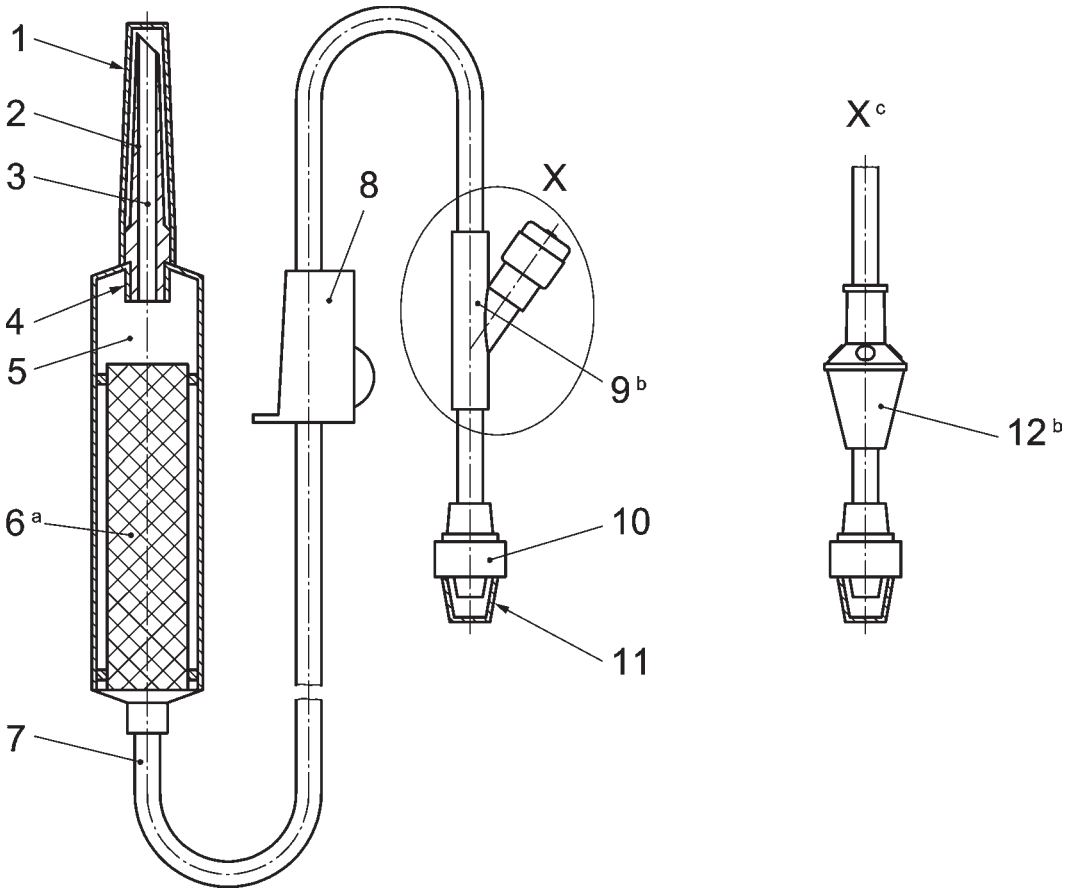
ISO 15223-1, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*

1) To be replaced by ISO 80369-7.

3 General requirements

3.1 Nomenclature for components of the transfusion set

The nomenclature for components of transfusion sets is given in Figure 1.



Key

1	protective cap of the closure-piercing device	9	injection site
2	closure-piercing device	10	male conical fitting
3	fluid channel	11	protective cap of the male conical fitting
4	drip tube	12	elastomeric buffer
5	drip chamber	a	Indicates alternative locations of the filter for blood and blood components. Other designs are acceptable, if the same safety aspects are ensured.
6	filter for blood and blood components	b	Injection site and elastomeric buffer are optional.
7	tubing	c	Optional design.
8	flow regulator		

Figure 1 — Example of a transfusion set

3.2 Maintenance of sterility

The transfusion set shall be provided with protective caps to maintain sterility of the internal parts of the set until the set is used.

4 Materials

The materials from which the transfusion sets given in Clause 3 are manufactured shall comply with the requirements specified in Clause 5. If components of the transfusion set come into contact with blood and blood components, they shall additionally comply with the requirements specified in Clauses 6 and 7.

5 Physical requirements

5.1 Particulate contamination

The transfusion sets shall be manufactured under conditions that minimize particulate contamination. All parts shall be smooth and clean at the fluid pathway surfaces. When tested as specified in A.1, the number of particles detected shall not exceed the contamination index limit.

5.2 Leakage

The transfusion set, when tested in accordance with A.2, shall show no signs of air leakage.

5.3 Tensile strength

Any connections between the components of the transfusion set, excluding protective caps, shall withstand a static tensile force of not less than 15 N for 15 s.

5.4 Closure-piercing device

5.4.1 The dimensions of the closure-piercing device shall conform to the dimensions shown in Figure 2.

NOTE The dimension of 15 mm in Figure 2 is a reference measurement. The cross-section of the piercing device at this site is a circle.

Dimensions in millimetres

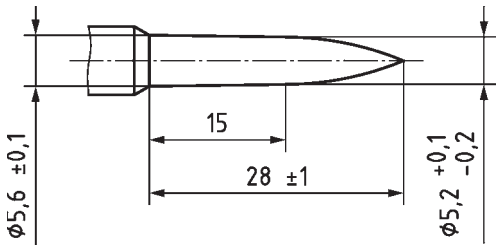


Figure 2 — Dimensions of the closure-piercing device

5.4.2 The closure-piercing device shall be capable of piercing and penetrating the closure of a container for blood and blood components without prepiercing. No coring should occur during this procedure.

NOTE 1 A carefully controlled surface treatment of the closure-piercing device (e.g. siliconization) is recommended to facilitate its insertion into the blood bag port. The same effect can be achieved by a careful selection of material for the closure-piercing device. Typical results including test equipment for penetration forces between spikes and blood bag ports have been published. See References [9] and [10].

NOTE 2 A central closure-piercing device tip is preferred to an asymmetric design in order to aid its insertion.

5.4.3 When inserted into a blood bag port conforming to ISO 3826-1:2013, the closure-piercing device shall resist a pull force of 15 N for 15 s.

5.4.4 When tested in accordance with ISO 3826-1:2013, 5.3, the connection between the closure-piercing device and the blood bag port shall show no evidence of leakage.

5.5 Tubing

5.5.1 The tubing, made of flexible material, shall be transparent or sufficiently translucent so that the interface of air and water during the passage of air bubbles can be observed with normal or corrected-to-normal vision.

5.5.2 The tubing from the distal end to the drip chamber shall be not less than 1 500 mm in length, including the injection site, when provided, and the male conical fitting.

5.6 Filter for blood and blood components

The transfusion set shall be provided with a filter for blood and blood components. The filter shall have uniform pores and shall cover a total area of not less than 10 cm^2. When tested in accordance with A.3[2)], the mass of solid material retained on the filter shall be not less than 80 % (mass fraction) of that retained on the reference filter.

If the filter has a confirmed thread diameter of (100 ± 10) µm and a pore size of (200 ± 20) µm, with a single warp and a single weft, a filtration performance test can be exempted.

Pore size measurement can be performed by microscopic inspection.

5.7 Drip chamber and drip tube

The drip chamber shall permit continuous observation of the fall of drops. The liquid shall enter the drip chamber through a tube which projects into the chamber. There shall be a distance of not less than 40 mm between the end of the drip tube and the outlet of the chamber, or a distance of not less than 20 mm between the drip tube and the filter for blood and blood components. The wall of the drip chamber shall not be closer than 5 mm to the end of the drip tube. The drip tube shall be such that 20 drops of distilled water at (23 ± 2) °C and at a flow rate of (50 ± 10) drops/min deliver (1 ± 0,1) ml [(1 ± 0,1) g].

The drip chamber should permit and facilitate the procedure of priming.

5.8 Flow regulator

The flow regulator shall adjust the flow of the blood and blood components between zero and maximum.

The flow regulator should be capable of continuous use throughout a transfusion without the tubing being damaged. There should be no deleterious reaction between the flow regulator and the tubing when stored in such a manner that there is contact.

5.9 Flow rate of blood and blood components

The transfusion set shall deliver not less than 1 000 ml of blood at (23 ± 2) °C in 30 min with a pressure difference of 10 kPa[2)]. The transfusion set shall also deliver not less than 500 ml of blood in 2 min under a pressure of 30 kPa above atmospheric pressure.

The blood shall be collected into a suitable anticoagulant solution and stored for not less than 2 weeks, and be free of large clots.

2) In countries where human blood is not available for testing, equivalent test methods may be established.

5.10 Injection site

When provided, the self-sealing injection site shall reseal when tested in accordance with A.4, and there shall be no leakage of more than one falling drop of water.

Sets fitted with an elastomeric buffer shall be designated “not for use at pressures above 20 kPa after perforating the elastomeric buffer”.

The injection site should be located near the male conical fitting.

NOTE The co-administration of drugs through the injection site is not permitted in some countries.

5.11 Male conical fitting

The distal end of the tubing shall terminate in a male conical fitting conforming with ISO 594-1 or ISO 594-2.

Luer lock fittings in accordance with ISO 594-2 should be used.

5.12 Protective caps

The protective caps at the end of the transfusion set shall maintain the sterility of the closure-piercing device, the male conical fitting, and the interior of the transfusion set.

Protective caps should be secure but easily removable.

6 Chemical requirements

6.1 Reducing (oxidizable) matter

When tested in accordance with B.2, the difference of volume of $Na_2S_2O_3$ solution [$c(Na_2S_2O_3)$ = 0,005 mol/l] for the extract solution, S_1, and of volume of $Na_2S_2O_3$ solution for blank solution, S_0, shall not exceed 2,0 ml.

6.2 Metal ions

The extract shall not contain in total more than 1 µg/ml of barium, chromium, copper, lead, and tin, and not more than 0,1 µg/ml of cadmium, when determined by atomic absorption spectroscopy (AAS) or an equivalent method.

When tested in accordance with B.3, the intensity of the colour produced in the test solution shall not exceed that of the standard matching solution containing (Pb^{2+}) = 1 µg/ml.

6.3 Titration acidity or alkalinity

When tested in accordance with B.4, not more than 1 ml of either standard volumetric solution shall be required for the indicator to change to the colour grey.

6.4 Residue on evaporation

When tested in accordance with B.5, the total amount of dry residue shall not exceed 5 mg.

6.5 UV absorption of extract solution

When tested in accordance with B.6, the extract solution, S_1, shall not show absorption greater than 0,1.

7 Biological requirements

7.1 General

The transfusion set shall not release any substances which may adversely affect the patient, see C.2.

7.2 Sterility

The transfusion set in its unit container shall have been subjected to a validated sterilization process (see References [2], [3], and [4]).

7.3 Pyrogenicity

The transfusion set shall be assessed for freedom from pyrogens using a suitable test and the results shall indicate that the transfusion set is free from pyrogenicity. Testing for pyrogenicity shall be carried out in accordance with Annex C.

7.4 Haemolysis

The transfusion set shall be assessed for freedom from haemolytic constituents and the result shall indicate that the transfusion set is free from haemolytic reactions.

NOTE Guidance on testing for haemolytic constituents is given in ISO 10993-4.

7.5 Toxicity

Materials shall be assessed for toxicity by carrying out suitable tests and the results of the tests shall indicate freedom from toxicity.

NOTE Guidance on testing for toxicity is given in ISO 10993-1.

7.6 Assessment of blood component depletion

Sets shall be assessed against the range of blood components for which they are recommended to ensure that no more than 5 % of the relevant constituent(s) of a single adult therapeutic dose of each blood component is retained by the set[3)]. The assessment should compare samples of the blood component taken prior to and after passage through the transfusion set.

NOTE For guidance, relevant constituents are typically present in the following doses or concentrations:

— red cell components: >36 g haemoglobin per unit;

— platelet concentrate: >2,4 × 10E11 platelets per unit;

— fresh frozen plasma: >0,7 IU Factor VIIIc per ml.

7.7 Assessment of damage to blood components

Transfusion sets shall be assessed against the range of blood components for which they are recommended to ensure that the relevant constituent(s) of each blood component is not significantly damaged (or where applicable, activated or inactivated) by passage through the set[3)]. The assessment should compare using a validated test method, samples of the blood component taken prior to and after passage through the transfusion set.

The clinical relevance of test results should be determined by a competent accredited laboratory.

NOTE For guidance on suitable tests:

3) In countries where human blood is not available for testing, equivalent test methods may be established.

— Red cell components: Haemolysis – supernatant (free) haemoglobin and potassium (K^+).

— Platelet concentrate: Platelet damage – pH, swirling, hypotonic shock response (HSR), morphology index under phase microscopy, supernatant lactate dehydrogenase, P-selectin expression (CD62P) on platelet surface and supernatant, Beta thromboglobulin release.

— Fresh frozen plasma: Coagulation activation – prothrombin fragment 1,2, fibrinopeptide A, Factor XIIa, thrombin-antithrombin (TAT) complexes.

8 Labelling

8.1 General

The labelling shall include the requirements as specified in 8.2 and 8.3. If graphical symbols are used, then refer to ISO 3826-2 and ISO 15223-1.

NOTE The presence of substances of interest can be indicated by using symbol 2725 of ISO 7000 by replacing the "XXX" by the abbreviation of the substance. The absence of substances of interest can be indicated by crossing the respective symbol.

8.2 Unit container

The unit container shall be labelled at least with the following information using the graphical symbols in accordance with ISO 15223-1, where appropriate:

a) name and address of the manufacturer;

b) description of the contents;

c) indication that the transfusion set is sterile;

d) lot (batch) designation;

e) year and month of expiry;

f) indication that the transfusion set is for single use only, or equivalent wording;

g) instructions for use, including warnings, e.g. about detached protective caps;

h) indication that the transfusion set is free from pyrogens, or that the transfusion set is free from bacterial endotoxins;

i) statement that 20 drops of distilled water delivered by the drip tube are equivalent to (1 ± 0,1) ml [(1 ± 0,1) g];

j) nominal dimensions of an intravenous needle, if included;

k) blood component(s) for which the set is recommended;

l) letter "G", which stands for gravity, and whose type height shall stand out clearly from surrounding text.

If the available space is too small to give all this information in legible characters and/or symbols, the information may be reduced to d) and e). In this case, the information as required in this subclause shall be given on the label of the next bigger shelf or multi-unit container.

8.3 Shelf or multi-unit container

The shelf or multi-unit container, when used, shall be labelled at least with the following information using the graphical symbols in accordance with ISO 15223-1, where appropriate:

a) name and address of the manufacturer;

b) description of the contents;

c) indication that the transfusion sets are sterile;

d) lot (batch) designation;

e) year and month of expiry;

f) recommended storage conditions, if any;

g) number of transfusion sets.

9 Packaging

9.1 The transfusion sets shall be individually packed so that they remain sterile during storage.

The unit container shall be sealed in a tamper-evident manner.

9.2 The transfusion sets shall be packed and sterilized in such a way that there are no flattened portions or kinks when they are ready for use.

10 Disposal

Information for a secure and environmentally sound disposal of single-use transfusion sets should be given.

EXAMPLE "Always dispose of blood contaminated products in a manner consistent with established biohazard procedures."

Annex A
(normative)

Physical tests

A.1 Test for particulate contamination

A.1.1 Principle

The particles are rinsed from the inner fluid pathway surfaces of the transfusion set, collected on a membrane filter, and microscopically counted.

A.1.2 Reagents and materials

A.1.2.1 Distilled water, filtered through membrane of pore size 0,2 µm.

A.1.2.2 Non-powdered gloves.

A.1.2.3 Vacuum filter, single-membrane type of pore size 0,45 µm.

A.1.3 Procedure

The filter unit, filter, and all other equipment shall be thoroughly cleaned before the test using distilled water (A.1.2.1).

Flush through each of 10 ready-to-use transfusion appliances, under laminar flow conditions (clean-air work station class N5 in accordance with ISO 14644-1), with 500 ml of distilled water (A.1.2.1). The total volume is subsequently vacuum filtered (A.1.2.3). Place the particles on the membrane screen filter under a microscope at 50× magnification using diagonally incident illumination, and measure and count them in accordance with the size categories given in Table A.1.

Table A.1 — Evaluation of contamination by particles

Particle parameters	Size category		
	1	2	3
Particle size in µm	25 to 50	51 to 100	over 100
Number of particles in 10 transfusion appliances	n_{a1}	n_{a2}	n_{a3}
Number of particles in the blank control sample	n_{b1}	n_{b2}	n_{b3}
Evaluation coefficient	0,1	0,2	5

A.1.4 Determination of results

A.1.4.1 General

An appropriate total number of single transfusion sets (minimum of 10) are tested. The number of particles per 10 transfusion sets tested in each of the three size categories is the assay result.

A.1.4.2 Particle counts

The values obtained from a blank control sample shall be recorded in a test report and taken into account when calculating the contamination index limit.

The blank control sample is the number and size of particles obtained from 10 equivalent 500 ml water samples classified in accordance with the three size categories set out in Table A.1, using the same test equipment but not passed through the appliances under test.

The number of particles in the blank, N_b, shall not exceed the value of 9. Otherwise, the test apparatus shall be disassembled and re-cleaned, and the background test performed again. Values of the blank determination shall be noted in the test report.

The contamination index limit is calculated as follows.

For each of the three size categories, multiply the number of particles in 10 transfusion appliances by the evaluation coefficients, and add the results to obtain the number of particles in the transfusion appliances (test pieces), N_a. Then, for each of the size categories, multiply the number of particles in the blank control sample by the evaluation coefficients and add the results to obtain the number of particles in the blank sample, N_b.

Subtract N_b from N_a to obtain the contamination index limit.

Number of particles in the transfusion appliances (test pieces):

$$N_a = n_{a1}0{,}1 + n_{a2}0{,}2 + n_{a3}5 \quad \text{(A.1)}$$

Number of particles in the blank sample:

$$N_b = n_{b1}0{,}1 + n_{b2}0{,}2 + n_{b3}5 \quad \text{(A.2)}$$

Contamination index limit:

$$N = N_a - N_b \leq 90 \quad \text{(A.3)}$$

A.2 Test for leakage

A.2.1 At the beginning of the test, condition the whole system at the test temperature

A.2.2 Immerse the transfusion set, with one end blocked, in water at (40 ± 1) °C and apply an internal air pressure of 50 kPa above atmospheric pressure for 15 s

Examine the transfusion set for air leakage.

A.3 Tests for efficiency of filter for blood and blood components

A.3.1 Principle

A measured volume of pre-filtered, stored blood is passed through a test filter and a reference filter, and the mass of the material removed by each filter is compared.

A.3.2 Reference filter

The reference filter shall be of woven polyamide 66 monofilament having a thread diameter of (100 ± 10) µm with a single warp and weft, and shall have a pore size of (200 ± 20) µm.

A.3.3 Procedure

A.3.3.1 General

Prepare a 4 l pool of anti-coagulated whole human blood of the same ABO group, stored for not less than 2 weeks, by emptying the packs into a large vessel through a coarse filter with a pore size of about 2 250 µm. Mix the blood well.

Allow one 800 ml volume of the pool to flow, under gravity, through each piece of filter material. Drain excess blood from the filter and dry to approximately constant mass in an oven at (60 ± 2) °C under a pressure of approximately 0,65 kPa (6,5 mbar).

Either method A or B may be used.

A.3.3.2 Method A (for filter material)

Cut two pieces from the reference filter material and two pieces from the filter material to be tested, each having a diameter of 40 mm. During the test, hold each piece of filter material in a device such that the whole surface of each filter material is covered with blood throughout the duration of the test. Carry out the test as described in A.3.3.1.

A.3.3.3 Method B (for assembled filters)

The reference filter assembly shall consist of 32 cm^2 of reference filter material with the bottom end sealed. This shall be contained within a plastics filter chamber having an outlet at the bottom formed of a standard drip tube delivering 20 drops/ml when distilled water is used. The inlet tube shall project into the filter chamber. A suitable reference filter assembly is shown in Figure A.1. Carry out the test as described in A.3.3.1.

A.3.4 Expression of results

The percentage of solid material removed by the test filter relative to the mass removed by the reference filter is given by:

$$\frac{m_{T1} - m_{T0}}{m_{R1} - m_{R0}} \times 100\,\% \qquad \text{(A.4)}$$

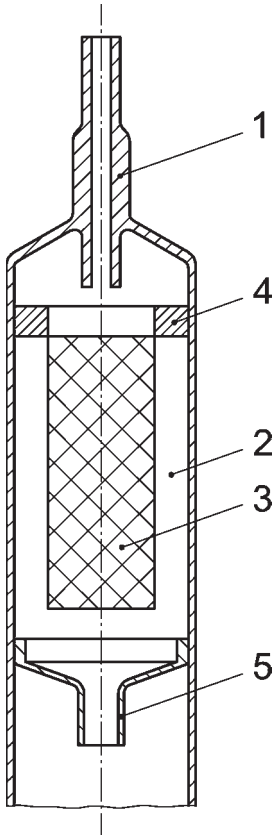
where

m_{T0} is the mass of the test filter before blood has been passed through it;

m_{T1} is the mass of the test filter after blood has been passed through it;

m_{R0} is the mass of the reference filter before blood has been passed through it;

m_{R1} is the mass of the reference filter after blood has been passed through it.



Key

1 inlet tube (internal diameter)
2 filter chamber
3 reference filter
4 fit of the filter
5 drip tube outlet from filter chamber delivering 20 drops/ml

Figure A.1 — Reference filter assembly

A.4 Test of the injection site

Place the injection site in a horizontal, stress-free position, fill with water in such a manner that no air bubbles are trapped, and apply a pressure of 50 kPa above atmospheric pressure. Perforate the injection site at the foreseen area, using a hypodermic needle with an outside diameter of 0,8 mm and conforming to ISO 7864.

Keep the needle in position for 15 s. Remove the needle and immediately dry the perforated site. Observe during a period of 1 min in order to ascertain whether there is any leakage.

In the case of alternative injection-site designs, the test should be performed by injection into the site in accordance with the instructions provided by the manufacturer.

Annex B
(normative)

Chemical tests

B.1 Preparation of extract solution, S_1, and blank solution, S_0

B.1.1 Extract solution, S_1

Assemble a closed circulation system composed of three sterilized transfusion sets and a 300 ml borosilicate glass boiling flask. Fit to the flask a thermostat device that maintains the temperature of the liquid in the flask at (37 ± 1) °C. Circulate 250 ml of water, conforming to ISO 3696 grade 1 or 2, through the system for 2 h at a rate of 1 l/h, for example using a peristaltic pump applied to a piece of suitable silicone tubing that is as short as possible.

Collect all of the extract solution, S_1, and allow to cool.

B.1.2 Blank solution, S_0

The blank solution, S_0, is prepared as described for the extract solution, S_1, but omitting the transfusion sets from the circuit.

The extract solution, S_1, and the blank solution, S_0, shall be used for the chemical tests.

B.2 Tests for reducing (oxidizable) matter

Add 10 ml of extract solution, S_1, to 10 ml of potassium permanganate solution, $c(KMnO_4)$ = 0,002 mol/l, and 1 ml of sulfuric acid solution, $c(H_2SO_4)$ = 1 mol/l, agitate and allow to react for 15 min at (23 ± 2) °C.

After 0,1 g of potassium iodide has been added, titrate the solution against a sodium thiosulfate standard volumetric solution, $c(Na_2S_2O_3)$ = 0,005 mol/l, until it turns light brown. Add 5 drops of starch solution and continue to titrate until the blue colour has disappeared.

Carry out a blank test simultaneously using the blank solution, S_0.

Calculate the difference of the volume of 0,005 mol/l $Na_2S_20_3$ solution for the extract solution, S_1, and of the volume of $Na_2S_20_3$ solution for the blank solution, S_0.

B.3 Test for metal ions

Test 10 ml of the extract solution, S_1, for metal ions, using procedures endorsed by the national pharmacopoeia. Determine the degree of coloration.

B.4 Test for titration acidity or alkalinity

Add 0,1 ml Tashiro indicator solution to 20 ml of extract solution, S_1, in a titration flask.

If the colour of the resulting solution is violet, titrate with sodium hydroxide standard volumetric solution, c(NaOH) = 0,01 mol/l, and if green, with hydrochloric acid standard volumetric solution, c(HCl) = 0,01 mol/l, until a greyish colour appears.

Express the volume of sodium hydroxide solution or hydrochloric acid solution used in millilitres.

B.5 Test for non-volatile residue

Transfer 50 ml of the extract solution, S_1, to a tared evaporating dish, and evaporate to dryness at a temperature just below the boiling point. Dry to constant mass at 105 °C.

Treat 50 ml of the blank solution, S_0, in the same manner.

Express the difference between the residual masses obtained from the extract solution, S_1, and the blank solution, S_0, in milligrams.

B.6 Test for absorbance

Pass the extract solution, S_1, through a membrane filter with pore size of 0,45 µm in order to avoid stray light interferences. Within 5 h of preparation, place the solution in a scanning UV spectrometer contained in a 1 cm quartz cell with the blank solution, S_0, in the reference cell, and record the spectrum in the wavelength range from 250 nm to 320 nm.

Report the result as a spectrum showing the absorbance plotted versus the wavelength.

Annex C
(normative)

Biological tests

C.1 Test on pyrogenicity

The test on pyrogenicity shall be carried out as described in national pharmacopoeias or national standards.

NOTE A test for pyrogens and bacterial endotoxins is described in the European Pharmacopoeia, in the United States Pharmacopeia and in the Japanese Pharmacopoeia.

C.2 Tests for biological evaluation

The test methods for biological evaluation as described in ISO 10993-1 should be considered as guidance when assessing biological compatibility.

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