INTERNATIONAL STANDARD

ISO 8536-4

Fifth edition
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Infusion equipment for medical use —

Part 4: Infusion sets for single use, gravity feed

Matériel de perfusion à usage médical —

Partie 4: Appareils de perfusion non réutilisables, à alimentation par gravité

Reference number
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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 8536-4 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

This fifth edition cancels and replaces the fourth edition (ISO 8536-4:2007), of which it constitutes a minor revision. In detail, 7.1 was more clarified in alignment with B.2, and A.2.2 was changed in order to go back with the leakage test pressure to 20 kPa and to restrict the leakage test for (40 ± 1) °C.

ISO 8536 consists of the following parts, under the general title *Infusion equipment for medical use*:

— *Part 1: Infusion glass bottles*

— *Part 2: Closures for infusion bottles*

— *Part 3: Aluminium caps for infusion bottles*

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

— *Part 5: Burette infusion sets for single use, gravity feed*

— *Part 6: Freeze drying closures for infusion bottles*

— *Part 7: Caps made of aluminium-plastics combinations for infusion bottles*

— *Part 8: Infusion equipment for use with pressure infusion apparatus*

— *Part 9: Fluid lines for use with pressure infusion equipment*

— *Part 10: Accessories for fluid lines for use with pressure infusion equipment*

— *Part 11: Infusion filters for use with pressure infusion equipment*

— *Part 12: Check valves*

Infusion equipment for medical use —

Part 4:
Infusion sets for single use, gravity feed

1 Scope

This part of ISO 8536 specifies requirements for single use, gravity feed infusion sets for medical use in order to ensure their compatibility with containers for infusion solutions and intravenous equipment.

Secondary aims of this part of ISO 8536 are to provide guidance on specifications relating to the quality and performance of materials used in infusion sets and to present designations for infusion set components.

In some countries, the national pharmacopoeia or other national regulations are legally binding and take precedence over this part of ISO 8536.

2 Normative references

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

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

ISO 594-2, *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 7864, *Sterile hypodermic needles for single use*

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

ISO 15223-1, *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements*[2)]

3 General requirements

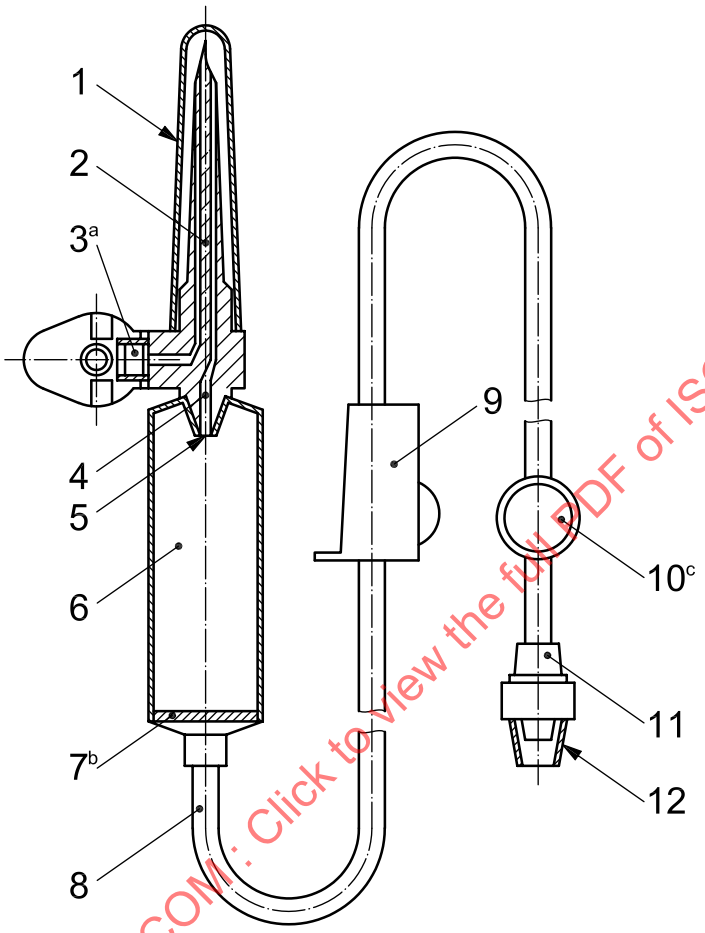
3.1 The nomenclature to be used for components of infusion sets and of a separate air-inlet device is given in Figures 1, 2 and 3. These figures illustrate examples of the configuration of infusion sets and air-inlet devices; other configurations may be used provided they lead to the same results. Infusion sets as illustrated in Figure 2 should only be used for collapsible plastic containers. Infusion sets as illustrated in Figure 2 used

1) Under preparation. (Revision of ISO 14644-1:1999)

2) To be published. (Revision of ISO 15223-1:2007)

with separate air-inlet devices as illustrated in Figure 3, or infusion sets as illustrated in Figure 1, shall be used for rigid containers.

3.2 The infusion set shall be provided with protective caps to maintain sterility of the internal parts of the set until the set is used. The air-inlet device shall be provided with a protective cap over the closure-piercing device or needle.



Key

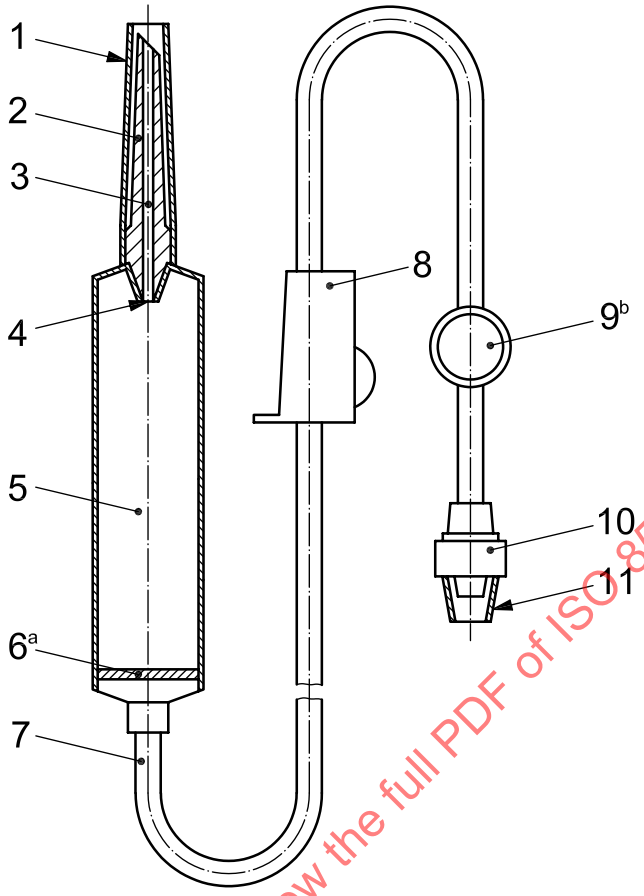
1	protective cap of closure-piercing device	7	fluid filter
2	closure-piercing device	8	tubing
3	air inlet with air filter and closure	9	flow regulator
4	fluid channel	10	injection site
5	drip tube	11	male conical fitting
6	drip chamber	12	protective cap of male conical fitting

a Closure of the air inlet is optional.

b The fluid filter may be positioned at other sites, preferably near the patient access. Generally, the fluid filter used has a nominal pore size of 15 µm.

c The injection site is optional.

Figure 1 — Example of a vented infusion set



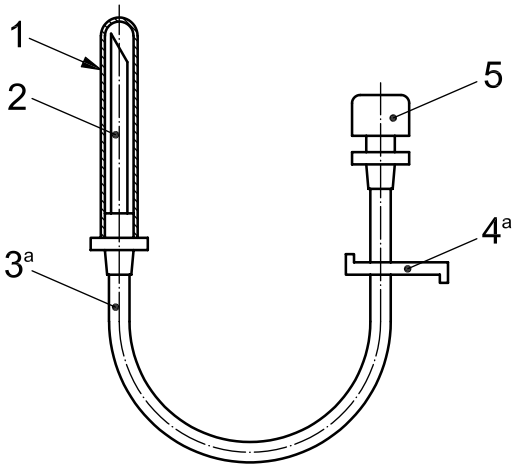
Key

1 protective cap of closure-piercing device
2 closure-piercing device
3 fluid channel
4 drip tube
5 drip chamber
6 fluid filter
7 tubing
8 flow regulator
9 injection site
10 male conical fitting
11 protective cap of the male conical fitting

[a] The fluid filter may be positioned at other sites, preferably near the patient access. Generally, the fluid filter used has a nominal pore size of 15 µm.

[b] The injection site is optional.

Figure 2 — Example of a non-vented infusion set



Key

1	protective cap	4	clamp
2	closure-piercing device or needle	5	air-inlet with air filter
3	tubing		

a Other designs are acceptable if the same safety aspects are ensured.

Figure 3 — Example of an air-inlet device

4 Designation

4.1 Infusion set

Infusion sets complying with the requirements specified in this part of ISO 8536 shall be designated by the descriptor words, followed by a reference to this part of ISO 8536, followed by the letters IS, followed by the letter G:

Infusion set ISO 8536-4 - IS - G

4.2 Air-inlet device

Air-inlet devices complying with the requirements specified in this part of ISO 8536 shall be designated by the descriptor words, followed by a reference to this part of ISO 8536, followed by the letters IS, followed by the letters AD:

Air-inlet device ISO 8536-4 - IS - AD

5 Materials

The materials from which the infusion set and its components are manufactured (as described in Clause 3) shall comply with the requirements specified in Clause 6. Where components of the infusion set come into contact with solutions, the materials shall also comply with the requirements specified in Clauses 7 and 8.

6 Physical requirements

6.1 Particulate contamination

The infusion 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 shall not exceed the contamination index limit.

6.2 Leakage

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

6.3 Tensile strength

When tested as specified in A.3, the infusion set, excluding protective caps, shall withstand a static tensile force of not less than 15 N for 15 s.

6.4 Closure-piercing device

The dimensions of the closure-piercing device shall conform to the dimensions shown in Figure 4.

NOTE The dimension of 15 mm in Figure 4 is a reference measurement. The cross-section of the piercing device at this site is a circle.

The closure-piercing device shall be capable of piercing and penetrating the closure of a fluid container without pre-piercing. No coring should occur during this procedure.

Dimensions in millimetres

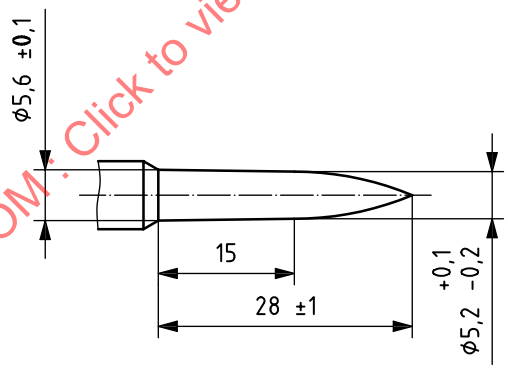


Figure 4 — Dimensions of the closure-piercing device

6.5 Air-inlet device

The air-inlet device shall conform to 3.2 and 8.2.

The air-inlet device shall be provided with an air filter to prevent the ingress of microorganisms into the container into which the device is to be inserted.

The air-inlet device shall be separate from, or integral with, the closure-piercing device.

When the air-inlet device is inserted into a rigid infusion container, the air admitted into the container shall not become entrained in the liquid outflow.

The air filter shall be fitted such that all air entering the rigid container passes through it, and such that the flow of fluid is not reduced by more than 20 % of that from a freely ventilated container when tested in accordance with A.4.

6.6 Tubing

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

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.

6.7 Fluid filter

The infusion set shall be provided with a fluid filter.

When tested in accordance with A.5, the retention of latex particles on the filter shall be not less than 80 %.

6.8 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 that 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 fluid filter. 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 or 60 drops of distilled water at (23 ± 2) °C at a flow rate of (50 ± 10) drops/min deliver a volume of (1 ± 0,1) ml or a mass of (1 ± 0,1) g. The drip chamber should permit and facilitate the priming procedure.

6.9 Flow regulator

The flow regulator shall adjust the flow of the infusion solution between zero and the maximum. The flow regulator should be capable of continuous use throughout an infusion without the tubing being damaged. There should be no deleterious reaction between the flow regulator and the tubing when they are stored in such a way that there is contact.

6.10 Flow rate of infusion fluid

The infusion set shall deliver not less than 1 000 ml of a sodium chloride solution [mass concentration ρ(NaCl) = 9 g/l] in 10 min under a static head of 1 m.

6.11 Injection site

When provided, the self-sealing injection site shall reseal when tested in accordance with A.6, and there shall be no leakage of more than one falling drop of water. The injection site should be located near the male conical fitting.

6.12 Male conical fitting

The distal end of the tubing shall terminate in a male conical fitting in accordance with ISO 594-1 or ISO 594-2. Luer lock fittings in accordance with ISO 594-2 should preferably be used.

6.13 Protective caps

The protective caps at the end of the infusion set shall maintain the sterility of the closure-piercing device, the male conical fitting and the interior of the infusion set. Protective caps should be secure but easily removable.

7 Chemical requirements

7.1 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.

7.2 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 with a mass concentration ρ (Pb^{2+}) = 1 µg/ml.

7.3 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.

7.4 Residue on evaporation

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

7.5 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.

8 Biological requirements

8.1 General

The infusion set shall be assessed for biological compatibility according to the guidelines given in C.2.

8.2 Sterility

The infusion set or the air-inlet device, or both, in its unit container shall have been subjected to a validated sterilization process (see ISO 11135, ISO 11137 and ISO 17665).

8.3 Pyrogenicity

The infusion set and/or the air-inlet device shall be assessed for freedom from pyrogens by using a suitable test, and the results shall indicate that the infusion set is free from pyrogens. Guidance on testing for pyrogenicity is given in C.1.

8.4 Haemolysis

The infusion set shall be assessed for freedom from haemolytic constituents and the result shall indicate that the infusion set is free from haemolytic reactions. Guidance on testing for haemolytic constituents is given in ISO 10993-4.

8.5 Toxicity

Materials shall be assessed for toxicity by carrying out suitable tests, and the results of the tests shall indicate freedom from toxicity. Guidance on testing for toxicity is given in ISO 10993-1.

9 Labelling

9.1 Unit container

The unit container shall be labelled with at least the following information:

a) a textual description of the contents, including the words “Gravity feed only”;

b) indication that the infusion set is sterile, using the graphical symbol as given in ISO 15223-1;

c) indication that the infusion set is free from pyrogens, or that the infusion set is free from bacterial endotoxins;

d) indication that the infusion set is for single use only, or equivalent wording, or using the graphical symbol in accordance with ISO 15223-1;

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

NOTE Instructions for use can also take the form of an insert.

f) the lot (batch) designation, prefixed by the word LOT, or using the graphical symbol in accordance with ISO 15223-1;

g) year and month of expiry, accompanied by appropriate wording or the graphical symbol in accordance with ISO 15223-1;

h) the manufacturer's or supplier's name and address, or both;

i) a statement that 20 drops of distilled water or 60 drops of distilled water delivered by the drip tube are equivalent to a volume of (1 ± 0,1) ml or a mass of (1 ± 0,1) g;

j) the nominal dimensions of the intravenous needle, if included.

9.2 Shelf or multi-unit container

The shelf or multi-unit container, when used, shall be labelled with at least the following information:

a) a textual description of the contents, including the words “Gravity feed only”;

b) the number of infusion sets;

c) indication that the infusion sets are sterile, using the graphical symbol as given in ISO 15223-1;

d) the lot (batch) designation, prefixed by the word LOT, or using the graphical symbol in accordance with ISO 15223-1;

e) year and month of expiry, accompanied by appropriate wording or the graphical symbol in accordance with ISO 15223-1;

f) the manufacturer's and/or supplier's name and address;

g) the recommended storage conditions, if any.

10 Packaging

10.1 The infusion set and/or the air-inlet device shall be individually packed so that they remain sterile during storage. The unit container shall be sealed in a tamper-evident manner.

10.2 The infusion sets and/or the air-inlet devices shall be packed and sterilized in such a way that there are no flattened portions or kinks when they are ready for use.

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 infusion set, collected on a membrane filter and microscopically counted.

A.1.2 Reagents and materials

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

A.1.2.2 **Non-powdered gloves**.

A.1.2.3 **Vacuum filter**, single membrane filter 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 10 ready-to-use infusion 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 in accordance with the size categories given in Table A.1.

A.1.4 Determination of results

A.1.4.1 General

An appropriate number of single infusion sets (minimum of 10) are tested. The number of particles per 10 infusion 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, re-cleaned, and the background test performed again. Values of the blank determination shall be noted in the test report.

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 infusion 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

The contamination index limit is calculated as follows.

For each of the three size categories, multiply the number of particles in 10 infusion appliances by the evaluation coefficients, and add the results in order to obtain the number of particles in the infusion 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 infusion appliances (test pieces):

$$N_a = n_{a1} \times 0{,}1 + n_{a2} \times 0{,}2 + n_{a3} \times 5$$

Number of particles in the blank sample:

$$N_b = n_{b1} \times 0{,}1 + n_{b2} \times 0{,}2 + n_{b3} \times 5$$

Contamination index limit:

$$N = N_a - N_b \leqslant 90$$

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 infusion set, with one end blocked, in water at (40 ± 1) °C and apply an internal air pressure of 20 kPa for 15 s. Examine the infusion set for air leakage.

A.2.3 Fill the infusion set with degassed, distilled water, connect it with its openings sealed to a vacuum device and subject it to an internal excess pressure of −20 kPa at (40 ± 1) °C for 15 s. Atmospheric pressure shall be the reference pressure. Excess pressure, in accordance with ISO 80000-4, can assume positive or negative values. Ascertain whether air enters the infusion set.

A.3 Test for tensile strength

Expose the infusion set to be tested to a static tensile force of 15 N applied along the longitudinal axis for 15 s. Inspect whether the infusion set withstands the test force applied.

A.4 Determination of flow rate when using an air-inlet device

A.4.1 Fill an infusion container with distilled water at (23 ± 2) °C and insert its closure. Insert the air-inlet device through the closure into the container and then insert the infusion set with the flow regulator set, such that no liquid flows. Arrange the container to give the equivalent of a pressure of 1 m head of water throughout the test. Open the flow regulator of the infusion set to maximum and measure the rate of flow of water from the set. Repeat the procedure with the filter removed from the air-inlet device.

A.4.2 For air-inlet devices integral with the closure-piercing device of the infusion set, follow the procedure given in A.4.1 but omit the insertion of the separate air-inlet device.

A.5 Test for efficiency of the fluid filter

A.5.1 Preparation of the test fluid

As a test liquid, use an aqueous suspension of latex particles with a diameter of (20 ± 1) µm and a concentration of approximately 1 000 particles per 100 ml.

A.5.2 Procedure

Assemble the fluid filter and position it so that it is equivalent to that of actual use in a suitable test apparatus in accordance with Figure A.1. Cut the tubing of the infusion set approximately 100 mm below the fluid filter.

Flush the fluid filter with 5 ml of the test fluid from the storage bottle and discard the filtrate. Pass 100 ml of the test fluid through the fluid filter and collect the effluent under vacuum after passing it through a black gridded membrane filter with a pore size of 5 µm to 8 µm and 47 mm diameter. Mount the membrane with any retained latex particles on a suitable microscope slide or holder and count the latex particles in a minimum of 50 % of the grid squares under a magnification of ×50 to ×100. Disregard any particles which are obviously non-latex.

Carry out the test in duplicate.

Repeat the test if the required limit value of 80 % retention rate is not met.

All procedures involved in this test should be conducted in a clean environment, if possible under laminar flow.

A.5.3 Expression of results

The retention rate of the filter, expressed as a percentage, is given by

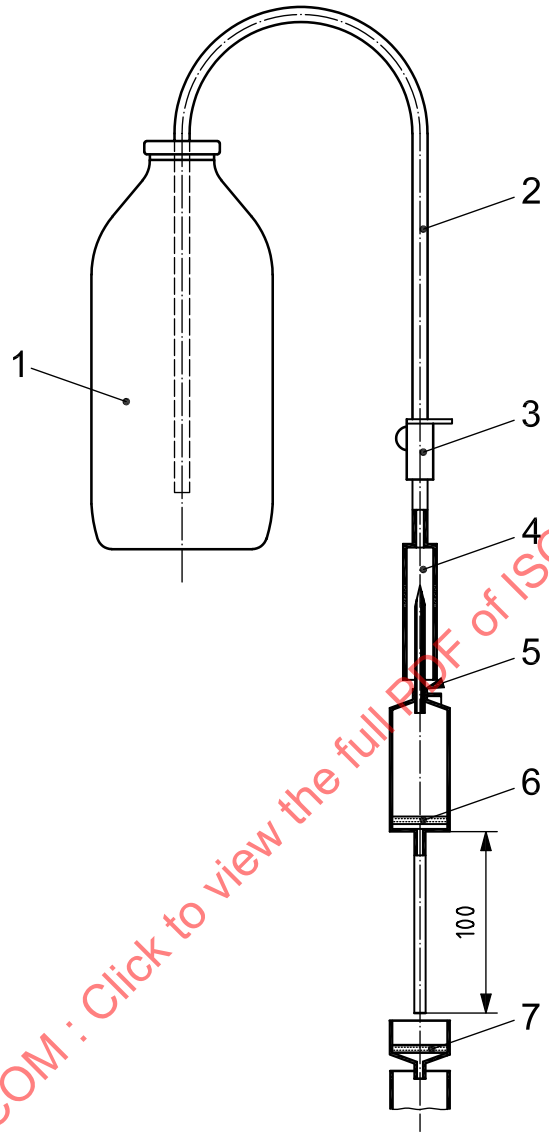
$$\left(1-\frac{n_1}{n_0}\right)\times 100 \qquad \text{(A.1)}$$

where

n_1 is the number of particles retained on the filter;

n_0 is the number of particles in the test fluid used.

Dimensions in millimetres



Key

1	storage bottle	5	piercing device
2	transfer tube	6	fluid filter
3	flow regulator	7	membrane filter
4	connecting piece		

Figure A.1 — Apparatus for testing the efficiency of the fluid filter

A.6 Test of the injection site

Place the injection site in a horizontal, stress-free position. Fill the infusion set with water in such a manner that no air bubbles are trapped and apply a pressure of 50 kPa above the atmospheric air pressure. Perforate the injection site at the foreseen area using a hypodermic needle with an outside diameter of 0,8 mm and which conforms to ISO 7864. Keep the needle in position for 15 s. Remove the needle and immediately dry the perforated site. Over a period of 1 min, observe whether there is any leakage from the injection site. In the case of an alternative injection site design, the test should be performed by injection into the site in accordance with the instructions provided by the manufacturer.