INTERNATIONAL STANDARD

ISO 15675

Third edition
2016-08-15

Cardiovascular implants and artificial organs — Cardiopulmonary bypass systems — Arterial blood line filters

Implants cardiovasculaires et organes artificiels — Systèmes de pontage cardio-pulmonaire — Filtres en ligne pour sang artériel

Reference number
ISO 15675:2016(E)

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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.

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).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

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 World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

The committee responsible for this document is ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This third edition cancels and replaces the second edition (ISO 15675:2009), which has been technically revised.

Cardiovascular implants and artificial organs — Cardiopulmonary bypass systems — Arterial blood line filters

1 Scope

This document specifies requirements for sterile, single-use, arterial blood line filters intended to filter and remove emboli, debris, blood clots and other potentially hazardous solid and gaseous material from the blood of humans during cardiopulmonary bypass surgery.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 594-2, *Conical fittings with 6 % (Luer) taper for syringes, needles and certain other medical equipment — Part 2: Lock fittings*

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 interaction with blood*

ISO 10993-7, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*

ISO 10993-11, *Biological evaluation of medical devices — Part 11: Tests for systemic toxicity*

ISO 11135, *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 11137-1, *Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

ISO 11607-1, *Packaging for terminally sterilized medical devices — Part 1: Requirements for materials, sterile barrier systems and packaging systems*

ISO 11607-2, *Packaging for terminally sterilized medical devices — Part 2: Validation requirements for forming, sealing and assembly processes*

ISO 14937, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

ISO 17665-1, *Sterilization of health care products — Moist heat — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at http://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
arterial blood line filter
accessory device used as part of the cardiopulmonary bypass system in the arterial blood return line for filtering particles such as blood clots, debris and gas emboli from the blood

3.2
blood pathway
paths of the *arterial blood line filter* (3.1) containing blood during its intended clinical use

3.3
blood cell damage
loss or destruction of cellular components of the blood components

3.4
platelet reduction
percentage reduction of platelets contained in a circuit, as a function of time

3.5
plasma-free haemoglobin level
difference between the concentration of plasma-free haemoglobin in a circuit, as a function of time

3.5.1
normalized index of hemolysis
NIH
grams of plasma-free hemoglobin released after pumping 100 l of blood

$$NIH\left\{g\ /\ 100\ L\right\} = \Delta fHb \times V \times \frac{100 - Hct}{100} \times \frac{100}{Q \times T}$$

where

ΔfHb is the increase of plasma free hemoglobin concentration (g/L) over the sampling time interval;

V is the circuit volume (L);

Q is the flow rate (L/min);

Hct is the hematocrit (%);

T is the sampling time interval (min)

3.6
white blood cell reduction
percentage reduction of white blood cells contained in a circuit, as a function of time

3.7
filtration efficiency
ability of the filter to remove particles from the simulated blood suspension test fluid, expressed as a percentage

3.8
blood analogue
test solution which simulates blood viscosity between $2{,}0 \times 10^{-3}$ Pa·s (2,0 cP), to $3{,}5 \times 10^{-3}$ Pa·s (3,5 cP)

3.9
bubble eliminator
device that can remove bubbles

3.10
predicate arterial filter
similar arterial filter to the test arterial filter that has previously been approved and used for the same intended clinical use

4 Requirements

4.1 Biological characteristics

4.1.1 Sterility and non-pyrogenicity

The blood pathway shall be sterile and non-pyrogenic. Compliance shall be verified in accordance with 5.2.1.

4.1.2 Biocompatibility

The parts of the blood pathway shall be biocompatible with respect to their intended use. Compliance shall be verified in accordance with 5.2.2.

4.2 Physical characteristics

4.2.1 Blood pathway integrity

When tested in accordance with 5.3.1, the blood pathway shall not leak.

4.2.2 Blood volume

The volume of the blood pathway shall be within the tolerances specified by the manufacturer (see 6.3).

4.2.3 Connectors

Connectors for connection to the blood pathway shall, when tested in accordance with 5.3.3, allow a secure connection. Connection for accessory ports shall meet the requirements of ISO 594-2.

NOTE 1 Connectors of a type that allows connection of tubes with an inside diameter of 4,8 mm, 6,3 mm, 9,5 mm or 12,7 mm, or a type that complies with ISO 8637:2010, Figure 1, or a type that complies with ISO 594-2, have been found satisfactory.

NOTE 2 Connectors corresponding to ISO 8637:2010, Figure 3 are considered as one way to comply with this requirement.

4.3 Performance characteristics

4.3.1 Blood cell damage

When determined in accordance with 5.4.1, the percentage change (positive or negative) of plasma-free haemoglobin, platelets, and white blood cells, shall be within the range of values specified by the manufacturer.

The hemolysis results shall be reported as mg/dL and NIH.

4.3.2 Filtration efficiency

When tested in accordance with 5.4.2, the filtration efficiency of any individual filter shall be at least 80 % when tested with particles that are 20 % larger than the nominal pore size of the filter.

4.3.3 Flow rate capacity

When tested in accordance with 5.4.3, test results will demonstrate the flow rate and pressure limitation(s) to ensure safe and effective performance, as specified by the manufacturer.

4.3.4 Shelf life

When tested in accordance with 5.4.4, test results shall demonstrate the rated shelf life, as specified by the manufacturer.

4.3.5 Air-handling capability

When tested in accordance with 5.4.5, test results shall demonstrate the air-handling capability, as specified by the manufacturer.

5 Tests and measurements to determine compliance with this document

5.1 General

5.1.1 Tests and measurements shall be performed with the device in its terminally sterilized form and prepared according to the manufacturer's instructions for intended clinical use.

5.1.2 Operating variables shall be those specified by the manufacturer for intended clinical use, unless otherwise specified.

5.1.3 Unless otherwise stated, the temperature of test liquids shall be 37 °C ± 1 °C.

5.1.4 If the relationship between variables is nonlinear, sufficient determinations shall be made to permit valid interpolation between data points.

5.1.5 The test or measurement procedures shall be regarded as reference procedures. Other procedures can be accepted, provided that the alternative procedure has been shown to be of comparable precision.

5.2 Biological characteristics

5.2.1 Sterility and non-pyrogenicity

Compliance shall be verified by inspection of the manufacturer's documentation on sterilization and pyrogen testing, in accordance with ISO 17665-1, ISO 11135, ISO 11137-1, ISO 14937 or ISO 10993-11, as applicable.

5.2.2 Biocompatibility

Compliance shall be verified by test or by inspection of the manufacturer's documentation on biocompatibility for the finished device, in accordance with ISO 10993-1 and ISO 10993-7, as applicable.

5.3 Physical characteristics

5.3.1 Blood pathway integrity (sterile final assembly)

Fill the blood pathway of the device with water and subject it to a positive pressure of 1,5 × the manufacturer's rated pressure or, if none is given, to a pressure of 152 kPa (22 psi) gauge and maintain the pressure for 6 h or for the intended time of use specified by the manufacturer. Visually inspect the device for evidence of water leakage.

5.3.2 Blood volume

The test liquid shall be anticoagulated whole blood or water.

The volume of the blood pathway shall be determined as specified by the manufacturer.

5.3.3 Connectors

The connection shall be made in accordance with the manufacturer's instructions for use.

The connection shall withstand a pull force of 15 N for 15 s without separating.

5.4 Performance characteristics

5.4.1 Blood cell damage

5.4.1.1 Test media

The test liquid for the blood pathway shall be heparinized blood.

5.4.1.2 Procedure

Two sets of appropriate, identical circuit components, including a pump, connecting tubing, a reservoir (as specified by the manufacturer and of suitable size relative to the device under test), and a heat exchanger, shall be assembled. The device under test shall be placed in one of the circuits. A predicate device shall be placed in the second test circuit. Priming and debubbling of the circuits by recirculating with an appropriate solution is recommended before blood is added. The blood pathway test-liquid volumes shall, at the initiation of the test, be within 1 % of each other. Perform the test *in vitro* using the conditions given in Table 1. A sufficient number of paired tests should be performed to support a statistical analysis. The predicate filter should be tested under the same conditions. Compliance shall be verified by test or by inspection of the manufacturer's documentation on blood cell damage for the finished device, in accordance with ISO 10993-4, as applicable.

Table 1 — Conditions for *in vitro* testing of blood cell damage

Item	Level	Maximum variation
Blood flow rate	The maximum specified by the manufacturer for intended clinical use (see 6.3)	±5 %
Blood glucose	10 mmol/l	±5 mmol/l
Haemoglobin	12 g/dl	±1 g/dl

The sampling schedule shall be in accordance with Table 2. More frequent sampling times are optional.

Table 2 — Sampling schedule

Parameter	Time, after initiation of test (min)			
	Prior to test	30	180	360
Plasma-free haemoglobin	X	X	X	X
White blood cell	X	X	X	X
Platelets	X	X	X	X
Haemoglobin	X	X	X	X
Glucose	X			

Table 2 *(continued)*

Parameter	Time, after initiation of test (min)			
	Prior to test	30	180	360
Activated clotting time	X	X	X	X
Temperature	X	X	X	X
Flow rates	X	X	X	X

5.4.2 Filtration efficiency

5.4.2.1 Test liquid

The test liquid shall be a glycerin solution or water. The test liquid shall contain 350 to 5 000 particles per ml that are 15 % to 25 % larger than the nominal pore size of the filter.

5.4.2.2 Procedure

Pass 500 ml of the test liquid at room temperature (20 °C to 22 °C) through the arterial blood line filter at a flow rate of no less than 100 ml/min and a pressure not exceeding 152 kPa (22 psi) gauge. Determine the pre- and post-filtration mean number of particles. The test shall be performed at the manufacturer's recommended flow rates. Calculate the filtration efficiency, using the readings from the size range of the test particles used for each test sample, by subtracting the post-filtration mean number of particles from the pre-filtration mean, dividing the quotient by the pre-filtration mean number of particles, and multiplying by 100 to obtain a percentage.

5.4.3 Filter flow rate

5.4.3.1 Test liquid

The test liquid shall be anticoagulated whole blood or a blood analogue.

5.4.3.2 Procedure

Place the device under test in an appropriate test circuit. Set the flow rate at the maximum rated flow and monitor the inlet and outlet pressures across the filter for 6 h. Measure the flow rate using a calibrated flowmeter. Note any pressure changes during the test.

If anticoagulated whole blood is used, this test shall not take into account the effects of formed elements or proteinaceous aggregates.

5.4.4 Shelf life

Using a validated method, ageing should be performed on final, finished, sterilized, devices in primary packaging in order to determine nominal shelf life.

5.4.5 Air-handling capability

5.4.5.1 Test liquid

The test liquid shall be heparinized blood with a haemoglobin content of (12 ± 1) g/dl.

5.4.5.2 Procedure

Use filter vent tubing as specified in the IFU. The length and internal diameter of the vent tubing shall be specified. The back pressure at the maximum test flow shall be 26,6 kPa (3,9 psi) ± 5 %. Use a bubble

eliminator to measure any air downstream of the filter accumulated over a period of 5 min from bolus injection.

At flow rates of 33 %, 67 %, and 100 % of the specified maximum rated flow rate, 30 ml (for paediatric or infant arterial filter with a maximum flow rate of less than 500 ml/min, the bolus shall be 2,5 ml and for maximum flow rates higher than 500 ml/min, the bolus shall be increased by 2,5 ml for every 500 ml/min maximum flow rate; the maximum bolus shall be 10 ml) shall be injected as a single bolus. Indication of the air bolus injection point in the test circuit, rate of injection, and type of pump utilized to circulate test liquid should be provided in the test protocol.

5.4.5.3 Test results

The results shall be reported as the percentage efficiency of gross air removal.

6 Information supplied by the manufacturer

6.1 Information on the arterial blood line filter

The following information shall be given on the arterial blood line filter:

a) the manufacturer's identity;

b) the model designation;

c) the direction of blood flow.

6.2 Information on the packaging

6.2.1 Information on the unit container

The following shall be visible through or given on the unit container:

a) the manufacturer's name and address;

b) the description of contents;

c) the model designation;

d) the statement on sterility and method of sterilization and non-pyrogenicity;

e) the expiry date;

f) the batch, lot or serial number designation;

g) the words, "Read instructions before use" or equivalent symbol;

h) any special handling or storage conditions;

i) the statement on single-use.

6.2.2 Information on the shipping container

The following information shall appear on the shipping container:

a) the manufacturer's name and address;

b) the description of contents, including number of units;

c) the model designation;

d) the expiry date;