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Cardiovascular implants and artificial organs — Hard-shell cardiotomy/venous reservoir systems (with/without filter) and soft venous reservoir bags

Implants cardiovasculaires et organes artificiels — Systèmes réservoirs de cardiotomie/veineux à paroi dure (avec/sans filtre) et sacs réservoirs veineux mous

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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 15674:2009), which has been technically revised.

Cardiovascular implants and artificial organs — Hard-shell cardiotomy/venous reservoir systems (with/without filter) and soft venous reservoir bags

1 Scope

This document specifies requirements for sterile, single-use, extracorporeal hard-shell cardiotomy/venous reservoir systems and soft venous reservoir bags intended for use as a blood reservoir during cardiopulmonary bypass (CPB) surgery.

This document applies only to the blood reservoir aspects for multifunctional systems which can have integral parts such as blood-gas exchangers (oxygenators), blood filters, defoamers, blood pumps, etc.

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

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
hard-shell cardiotomy reservoir
extracorporeal device consisting of rigid walls designed to collect, defoam and filter suctioned blood

3.2
hard-shell venous reservoir
extracorporeal device consisting of rigid walls designed to collect and defoam venous blood

3.3
soft-bag venous reservoir
extracorporeal device consisting of collapsible, pliable walls designed to collect venous blood

3.4
hard-shell cardiotomy/venous reservoir system
extracorporeal device designed to function simultaneously as both a venous reservoir and cardiotomy reservoir

3.5
blood-gas exchanger
oxygenator
extracorporeal device designed to supplement, or be a substitute for, the respiratory function of the lungs

3.6
integral part
part that is connected to the reservoir or is part of the reservoir system that cannot normally be separated by the user

3.7
operating variable
setting of controls which affects the function of the device

3.8
static volume
priming volume present in the device at zero flow

3.9
break-through volume
volume of fluid that, when added during the initial priming of the dry device (as received from the manufacturer), must be exceeded before fluid first exits the device

3.10
sealed hard-shell reservoir
hard-shell reservoir that may be operated at either positive or negative pressure

3.12
dynamic priming volume
amount of fluid volume that is contained inside the defoamer/filter compartment at a specified flow rate and, for soft bag reservoir, depending on the head pressure and the position of the compression mechanism

Note 1 to entry: The dynamic priming volume can be affected by negative pressure applied to a hard-shell reservoir.

3.13
platelet reduction
percentage reduction of platelets contained in a circuit as a function of time

3.14
plasma-free haemoglobin level
concentration of plasma-free haemoglobin in a circuit as a function of time

3.14.1
normalized index of hemolysis
NIH
grams of plasma-free hemoglobin released after pumping 100 L of blood

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

where

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

V circuit volume (L);

Q flow rate (L/min);

Hct hematocrit (%);

T sampling time interval (min)

3.15
white blood cell reduction
percentage reduction of white blood cells contained in a circuit as a function of time

3.16
predicate reservoir
similar reservoir to the test reservoir that has previously been approved and used for the same intended clinical use

3.17
filtration efficiency
ability of the filter to remove particles from the simulated blood suspension test fluid, expressed as a percentage

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

All 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 General

When tested in accordance with 5.3.1 and 5.3.2, the blood pathway shall not leak.

4.2.2 Blood volumes

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

4.2.3 Connectors

Connectors for connection to the blood pathway shall, when tested in accordance with 5.3.4, allow a secure connection.

NOTE 1 Connectors of a type that allows connection of tubes with an inner 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 used.

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

4.3 Performance characteristics

NOTE 1 Guidance for testing is given in Annex A.

NOTE 2 Some of these tests can be combined and performed at the same time.

4.3.1 Blood cell damage

4.3.1.1 Plasma-free haemoglobin

When determined in accordance with 5.3.4, the increased concentration of plasma-free haemoglobin shall be within the range of values specified by the manufacturer.

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

4.3.1.2 Platelet reduction and white blood cell reduction

When determined in accordance with 5.3.4, the percentage reduction of platelets and the percentage reduction of white blood cells shall be within the range of values specified by the manufacturer.

4.3.2 Air-handling capacity

Testing to demonstrate the air-handling characteristics shall be conducted at various flow rates and the results shall be recorded [see 6.3 p)]. The test shall be conducted according to the manufacturer's protocols.

4.3.3 Priming volume of the reservoirs in accordance with the manufacturer's quality control management system

The volume of the reservoir(s) shall be determined and the results presented in accordance with 6.3 o). Testing shall be conducted according to the manufacturer's protocols.

4.3.4 Defoaming characteristics

Where applicable, the defoaming characteristics shall be determined and the results shall be recorded [see 6.3 p)]. The testing shall be conducted according to the manufacturer's protocols.

4.3.5 Volume calibration

Where applicable, the accuracy of the volume markings shall be measured and tolerances shall be presented as required in 6.3 n). The testing shall be conducted according to the manufacturer's protocols.

4.3.6 Filtration efficiency

The efficiency of the filter shall be determined by the manufacturer according to their protocol. The filter efficiency results shall be recorded [see 6.3 p)]. The testing shall be performed around the anticipated flow range of the filter.

4.3.7 Break-through volume

Where applicable, the break-through volume shall be measured and the results shall be recorded [see 6.3 p)]. The testing shall be performed according to the manufacturer's protocols.

4.3.8 Dynamic priming volume

Where applicable, the dynamic priming volume applies to hard-shell cardiotomy/venous reservoir systems (with/without filter) and shall be measured and reported as in 6.3 k). Results shall indicate the priming volume over the entire range of flows specified by the manufacturer and operational volume used for the test. Testing shall be performed according to the manufacturer's protocols.

4.3.9 Minimum and maximum volumes

The minimum and maximum volumes shall be specified by the manufacturers in the testing protocols.

4.3.10 Shelf life

When tested in accordance with 5.3.4, test results shall demonstrate the rated shelf life, 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 under test 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 ± 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 are to 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 inspection of the manufacturer's documentation on biocompatibility for the finished device in accordance with ISO 10993-1 and ISO 10993-7.

5.3 Physical characteristics

5.3.1 Blood pathway integrity for soft venous reservoir bags

Subject the blood pathway of the device, filled with water, 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 this 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 pathway integrity for sealed hard-shell reservoirs

5.3.2.1 Perform the test with air or water at the appropriate pressures.

5.3.2.2 Subject the blood pathway of the device to a negative or positive pressure of 1,5 × the manufacturer's rated pressure and maintain this pressure for 6 h or for the intended time of use specified by the manufacturer. Using air pressure decay or visual inspection, check for evidence of leakage.

NOTE If the hard-shell reservoirs are only operated at atmospheric pressure, the test for blood pathway integrity needs to be performed at atmospheric pressure on these units.

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.

5.3.4 Blood cell damage

5.3.4.1 Test media

The test liquid for the blood pathway shall be anticoagulated whole blood.

5.3.4.2 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 reservoir should be tested under the same conditions.

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			
Activated clotting time	X	X	X	X
Temperature	X	X	X	X
Flow rates	X	X	X	X

5.3.5 Filtration efficiency

5.3.5.1 Test liquid

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

5.3.5.2 Procedure

Pass 500 ml of the test liquid at room temperature (20 °C to 22 °C) through the reservoir 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.

5.3.6 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.

6 Information supplied by the manufacturer

6.1 Information on the reservoir (labelling)

The following shall be provided on the reservoir:

a) the manufacturer's identity;

b) batch, lot or serial number designation;

c) model designation;

d) the direction of blood flow, if necessary.

6.2 Information on the packaging

6.2.1 Information on the unit container

The following shall be given on the unit container:

a) the manufacturer's name and address;

b) description of contents;

c) model designation;

d) statement on sterility and non-pyrogenicity;

e) batch, lot or serial number designation;

f) the statement "Read instructions before use" or equivalent symbol;

g) special handling or storage conditions;

h) statement on single-use;

i) expiry date.

6.2.2 Information on the shipping container

The following shall be provided on the shipping container:

a) the manufacturer's name and address;

b) description of contents, including number of units;

c) model designation;

d) statement on sterility and non-pyrogenicity;

e) special handling, storage or unpacking instructions;

f) lot number or serial number.

6.3 Information in the accompanying documents

Each shipping container shall contain an "Instructions for Use" leaflet with the following information:

a) the manufacturer's address and telephone and fax number;

b) model designation;

c) required ancillary equipment;

d) instructions on necessary, special or unique procedures applicable;

e) placement, type and securing of tubing connections;

f) location and purpose of additional entry or exit ports;

g) direction of blood flow;

h) general operating procedures for normal use;

i) a recommended procedure for intraoperative replacement of a reservoir system;

j) maximum and minimum recommended blood flow rates;