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Cardiovascular implants and extracorporeal systems — Cardiopulmonary bypass systems — Venous bubble traps

Implants cardiovasculaires et systèmes extracorporels — Systèmes de pontage cardiopulmonaire — Pièges à bulles veineuses

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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*.

Introduction

This document is intended to ensure that devices designed to remove air entering the venous line during surgical procedures requiring extracorporeal circulatory support have been adequately tested for both their safety and function, and that extracorporeal device characteristics are appropriately disclosed when labeling the device.

This document therefore contains procedures to be used for evaluation of extracorporeal venous bubble traps. Test procedures for determination of the air removal efficiency, blood cell damage and other performance characteristics are described, although limits for these characteristics are not specified. Ready identification of the performance characteristics should, however, assist the user in the selection of a venous bubble trap that will suit the needs of the patient.

This document also includes minimum reporting requirements, which will allow the user to compare performance characteristics of venous bubble traps of different designs in a standard way.

This document makes reference to other International Standards in which methods for determination of characteristics common to medical devices can be found.

Requirements for animal and clinical studies have not been included in this document.

Such studies may be part of a manufacturer's quality system.

This document contains only those requirements that are specific to venous bubble traps. Nonspecific requirements are covered by references to other International Standards listed in the normative references section.

Cardiovascular implants and extracorporeal systems — Cardiopulmonary bypass systems — Venous bubble traps

1 Scope

This document specifies requirements for sterile, single-use, venous bubble traps intended to remove air entering the venous line during surgical procedures requiring extracorporeal circulatory support, which may include cardiopulmonary bypass (CPB), extracorporeal membrane oxygenation (ECMO), or venovenous bypass for liver transplantation.

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 11135-1, *Sterilization of health care products — Ethylene oxide — Part 1: Requirements for 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 https://www.iso.org/obp/

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

3.1
venous bubble trap
device for removing air from the venous line of an extracorporeal circuit

3.2
blood pathway
blood-contacting surfaces of the venous bubble trap during its intended clinical use

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

3.4
platelet reduction
percentage reduction of platelets contained in a circuit incorporating a venous bubble trap, as a function of time

3.5
plasma-free hemoglobin level
difference between the concentration of plasma-free hemoglobin in a circuit incorporating a venous bubble trap, 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 incorporating a venous bubble trap, as a function of time

3.7
air removal efficiency
ability of the venous bubble trap to remove air from the blood, 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
predicate venous bubble trap
similar venous bubble trap to the test venous bubble trap 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 Prime 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.

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.

Connection for accessory ports shall meet the requirements of ISO 594-2.

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 hemoglobin, 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 Air removal efficiency

When tested in accordance with 5.4.2, the air removal efficiency shall be as expressed as a percentage. The manufacturer should specify the air challenge conditions. The test methodology should account for and measure gaseous microemboli for size and number and a second measurement of gross air volume.

4.3.3 Flow rate capacity

When tested in accordance with 5.4.3, the test results shall demonstrate the flow rate and pressure limitation(s), as specified by the manufacturer.

4.3.4 Shelf life

When tested in accordance with 5.4.4, the 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 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 non-linear, 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 10993-11, ISO 11135-1, ISO 11137-1, ISO 14937 or ISO 17665-1, 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

Fill the blood pathway of the device with water and subject it to a negative pressure of 1,5 × the manufacturer's rated negative pressure 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 air entrainment.

5.3.2 Prime 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 liquid

The test liquid for the blood pathway shall be anticoagulated whole 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 means of controlling temperature, shall be assembled. The device under test shall be placed in one of the circuits between the inflow of a blood pump and the outlet of a patient simulating reservoir per the manufacturer's instructions for use. 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. If the instructions for use call for connection to ancillary devices, these should be connected and operated at the worst case conditions allowed per the manufacturer's instructions for use. A sufficient number of paired tests should be performed to support a statistical analysis. The predicate venous bubble trap 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
Hemoglobin	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 hemoglobin	X	X	X	X
White blood cell	X	X	X	X
Platelets	X	X	X	X
Hemoglobin	X	X	X	X
Glucose	X			
Activated clotting time	X	X	X	X
Temperature	X	X	X	X
Flow rates	X	X	X	X

5.4.2 Air removal efficiency

5.4.2.1 Test liquid

The test liquid shall be anticoagulated whole blood with a hemoglobin content of (12 ± 1) g/dl.

5.4.2.2 Procedure

Prepare a test set up which places the venous bubble trap, per the manufacturer's instructions for use, between the inflow of a blood pump and the outlet of a patient simulating reservoir. (If the instructions for use call for connection to ancillary devices such as active air removal systems, these should be connected per the instructions for use.)

The inflow tubing between the venous bubble trap and the reservoir should include an access connector located upstream of the venous bubble trap for injecting the air challenge and an inline micro bubble detector upstream from this connector. Another inline micro bubble detector should be located after the venous bubble trap and the pump.

The test liquid should have a baseline micro bubble value of <1% of the air challenge bolus volume.

After the baseline is stabilized, introduce air at the injected site. The volume of air injected and the method of injection must be defined in the test procedure. In addition, a bubble volume collection chamber placed before the micro bubble detector may be used as an adjunctive method to determine air removal efficiency. The test should be performed at the minimum and maximum flow rates recommended by the manufacturer as well at one flow rate midway between the minimum and maximum.

NOTE This procedure will produce bubbles of different sizes.

The total volume of air downstream of the venous bubble trap should be measured by the micro bubble detector placed between the venous bubble trap and the pump. If a bubble volume collection chamber is used, the volume of air collected should be measured and added to the volume of air measured by the micro bubble detector to document total volume of air downstream of the venous bubble trap. The volume of air collected should be measured and the bigger between the volume provided by the micro bubble detector and the air collected will be considered the total volume of air downstream of the venous bubble trap

5.4.2.3 Results

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

EFF = (BOLUS VOLUME – DOWNSTREAM VOLUME) / BOLUS VOLUME

NOTE The downstream volume is the sum of the volume measured by the microbubble detector plus the volume collected by the collection chamber.

5.4.3 Flow rate and pressure drop

5.4.3.1 Test liquid

The test liquid shall be anticoagulated whole blood with a hemoglobin content of (12 ± 1) g/dl or blood analogue.

NOTE This test may be performed concurrently with the blood trauma test (see 5.4.1).

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 venous bubble trap for 6 h or greater according

