INTERNATIONAL STANDARD

ISO 13960

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Cardiovascular implants and artificial organs — Plasmafilters

Implants cardio-vasculaires et organes artificiels — Filtres de plasma

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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 13960 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants*.

Introduction

This International Standard contains requirements and acceptance criteria (including test methods) for safety-related parameters for plasmafilters. Only those requirements that are specific to plasmafilters have been included. Non-specific requirements are covered by references to other International Standards, listed in the Normative references clause. This International Standard does not address matters related to toxicity. Such issues are covered in the relevant part of ISO 10993. The reader is advised to review the normative references.

Cardiovascular implants and artificial organs — Plasmafilters

1 Scope

This International Standard specifies requirements for sterile, single-use plasmafilters, intended for use on humans.

This International Standard is not applicable to the extracorporeal circuits used for plasmapheresis or other extracorporeal blood exchange devices, such as haemodialysers, haemodiafilters, haemofilters, haemoperfusion devices, vascular access devices, oxygenators or active medical devices.

This International Standard does not address the replacement fluid.

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

ISO 8637, *Cardiovascular implants and artificial organs — Haemodialysers, haemodiafilters, haemofilters and haemoconcentrators*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing*

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 11134, *Sterilization of health care products — Requirements for validation and routine control — Industrial moist heat sterilization*

ISO 11135, *Medical devices — Validation and routine control of ethylene oxide sterilization*

ISO 11137, *Sterilization of health care products — Requirements for validation and routine control — Radiation sterilization*

ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

ISO 13488, *Quality systems — Medical devices — Particular requirements for the application of ISO 9002*

3 Terms and definitions

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

3.1
blood compartment
part of a plasmafilter through which blood is intended to pass

3.2
filtration rate
rate at which fluid is removed from the blood compartment across the semi-permeable membrane into the filtrate compartment of a plasmafilter

3.3
plasmapheresis
plasma separation
separation of a portion of the whole plasma from formed elements of blood by means of a semi-permeable membrane

NOTE Plasmapheresis can also be accomplished through the use of differential centrifugation, but this method is not addressed in this International Standard.

3.4
plasmafilter
device intended to perform membrane plasmapheresis

3.5
transmembrane pressure
p_{TM}
the mean pressure across the semipermeable membrane

$$p_{TM} = \frac{p_{inlet} + p_{outlet}}{2} - p_{filtrate}$$

3.6
sieving coefficient
ratio of a solute concentration in the filtrate to the simultaneous concentration of the same solute in blood

4 Requirements

4.1 Biological characteristics

4.1.1 Biocompatibility

Parts of plasmafilters that will come into direct or indirect contact with blood during their intended clinical use shall be biocompatible with respect to their intended clinical use.

Compliance shall be verified in accordance with 5.2.1.

4.1.2 Sterility and non-pyrogenicity

Blood and filtrate compartments shall be sterile and non-pyrogenic.

Compliance shall be verified in accordance with 5.2.2.

4.2 Physical characteristics

4.2.1 Structural integrity

When tested in accordance with 5.3.1, plasmafilters shall not leak.

NOTE This requirement refers to the external integrity of the devices.

4.2.2 Blood compartment integrity

When tested in accordance with 5.3.2, plasmafilters shall not leak.

4.2.3 Connectors and ports

4.2.3.1 Connections to the blood compartment

Except when plasmafilters and the extracorporeal circuits are designed as an integral system, the dimensions of the blood inlet and outlet connectors of plasmafilters shall be in accordance with ISO 8637.

Compliance shall be verified by inspection.

4.2.3.2 Connection to the filtrate compartment

Except when plasmafilters and their extracorporeal circuits are designed as an integral system, the filtrate ports shall be male 6 % (Luer) taper lock fittings with dimensions in accordance with ISO 594-2 or dialysing fluid inlet and outlet ports in accordance with ISO 8637.

Compliance shall be verified by inspection.

4.2.3.3 Volume

When measured in accordance with 5.3.3, the volumes of the blood compartments of plasmafilters shall be within the range of values stated by the manufacturer [see 7.2.1 b)].

4.2.3.4 Pressure drop

When measured in accordance with 5.3.4, the pressure drop across the blood compartment of the plasmafilter shall be within the range of values stated by the manufacturer [see 7.2.1 f)].

4.3 Performance characteristics

4.3.1 Filtration rate

When measured in accordance with 5.4.1, the filtration rate shall be within the range of values stated by the manufacturer [see 7.2.1 e) 1)].

4.3.2 Sieving coefficient

When measured in accordance with 5.4.2, the sieving coefficients for albumin, immunoglobulin (IgM) and beta-lipoprotein or equivalent indicators shall be within the range of values stated by the manufacturer [see 7.2.1 e) 2)].

4.3.3 Nonhaemolytic characteristics

The device shall not cause haemolysis that represents a safety hazard to patients when tested at the maximum specified operating conditions. Testing shall be in accordance with 5.4.3.

5 Test methods

5.1 General

Carry out the tests and measurements below with the device under test prepared according to the manufacturer's instructions for the intended clinical use.

Unless otherwise stated below, use the pressures and flowrates stated by the manufacturer for the intended clinical use and conduct tests with the test liquids at $(37 \pm 1)\,^{\circ}\mathrm{C}$. If the relationship between variables is nonlinear, make sufficient determinations to permit valid interpolation between data points.

The test systems shown do not indicate all the necessary details of practicable test apparatus. The design and construction of actual test systems and the establishment of actual test systems shall also address the many factors contributing to measurement error, including, but not limited to, pressure measurement errors due to static head effects and dynamic pressure drops, parameter stabilization time, uncontrolled temperature variations at nonconstant flowrates, pH, degradation of test substances due to heat, light and time, degassing of test fluids, trapped air, and system contamination by foreign material, algae and bacteria.

The test methods below are reference methods. Other methods may be used provided they have been shown to be of comparable precision and reproducibility.

5.2 Methods for assessment of biological characteristics

5.2.1 Biocompatibility

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

5.2.2 Sterility and non-pyrogenicity

Verify compliance, as relevant, by the methods in accordance with ISO 11134, ISO 11135, ISO 11137 and ISO 10993-11.

5.3 Methods for assessment of physical characteristics

5.3.1 Structural integrity

Fill the device under test with water and raise the pressure to 1,5 times the maximum stated by the manufacturer [see 7.2.1 a)]. Maintain this pressure for approximately 10 min, and visually inspect the device for any emergence of water.

5.3.2 Blood compartment integrity

Set up the filter in the vertical position. Close off the bottom filtrate and blood ports. Wet the membrane with water and fill the filtrate compartment, if appropriate. Pressurize the blood compartment with air to 1,5 times the maximum specified by the manufacturer for a period of 10 min. If no bubbles exit the filtrate compartment through the open filtrate port, the blood compartment is intact.

5.3.3 Volume

The volume of the blood compartment shall be calculated from geometrical data (volume of case, fibre dimensions and the number of fibres). Compliance is checked by inspection of the manufacturer's documentation.

NOTE The volume is calculated since it may prove difficult to find a liquid that will not be filtered through a plasmafilter membrane.

5.3.4 Pressure drop

5.3.4.1 Test liquid

The test liquid shall be anticoagulated bovine or human blood, with sustained levels of haematocrit value (32 ± 2) % and protein content (60 ± 5) g/l.

5.3.4.2 Procedure

Fill the dialysate compartment with water or plasma and the blood compartment with the test fluid. Measure the pressure drop across the blood compartment over the manufacturer's stated range of blood flowrates.

5.4 Performance characteristics

5.4.1 Filtration rate

5.4.1.1 Test liquid

The test liquid shall be anticoagulated bovine or human blood, with sustained levels of haematocrit value of (32 ± 2) % and protein content of (60 ± 5) g/l.

5.4.1.2 Procedure

Set up a test circuit as shown in Figure 1. Do not allow the priming pressure to exceed the maximum transmembrane pressure stated by the manufacturer [see 7.1 f)]. Make measurements of plasma flowrates with the test liquid circulating through the blood compartment of the device under test and in sequence of measurement from minimum to maximum transmembrane pressure at each blood flowrate stated by the manufacturer [see 7.2.1 a)].

5.4.2 Sieving coefficient

5.4.2.1 Test liquid

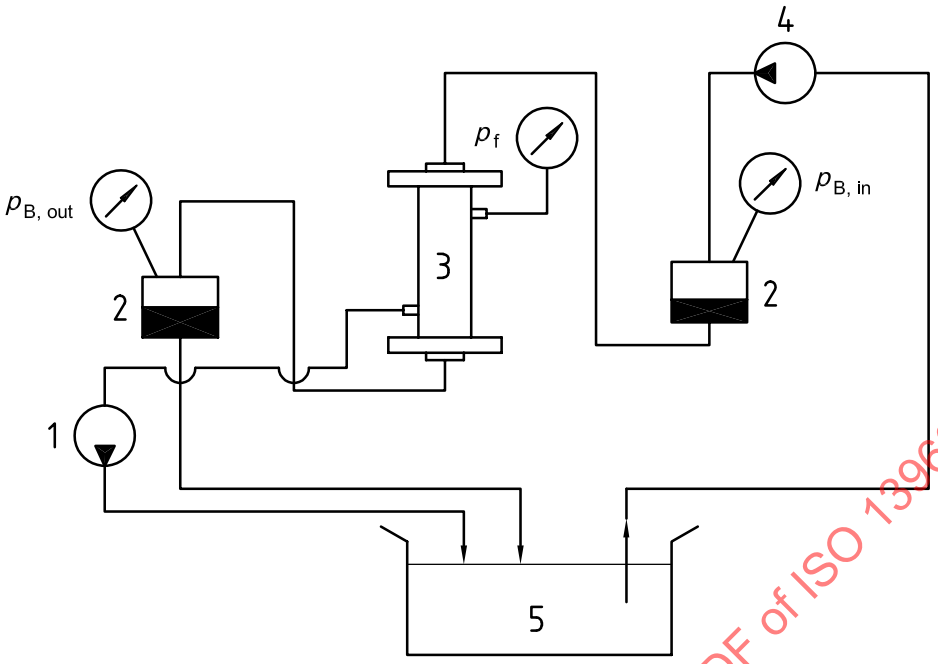
The test liquid shall be bovine or human plasma with a protein content of (60 ± 5) g/l and containing one or more of the following substances or equivalent indicators:

a) albumin (present as plasma albumin);

b) immunoglobulin (IgM);

c) beta-lipoprotein.

Further substances/indicators or whole blood may also be used.



Key

1 plasma pump
2 chamber
3 device under test
4 blood pump
5 test liquid, at $(37 \pm 1)\,^{\circ}C$

$p_{B,in}$ is the pressure of blood at the inlet of the device under test

$p_{B,out}$ is the pressure of blood at the outlet of the device under test

p_f is the pressure of the filtrate at the outlet of the device under test

Figure 1 — Schematic test circuit for determination of the filtration rate and sieving coefficient

5.4.2.2 Procedure

Set up a test circuit as shown in Figure 1. Measure the protein content of the test liquid and record this value. Set the test liquid flowrate to the maximum blood flowrate stated by the manufacturer [see 7.2.2 b)] and the filtration rate to at least 20 % of the test liquid flowrate. If, for device-related reasons, the stated test liquid flowrate cannot be achieved, use the maximum possible flowrate and record the flowrate used.

Collect test samples after steady state has been reached (30 min and 90 min following blood exposure). Measure the concentration of the protein in the filtrate.

Calculate the sieving coefficient, S, by means of the expression

$$S = \frac{c_f}{c_{in}}$$

where

c_f is the concentration of a solute in the filtrate;

c_{in} is the concentration of a solute at the inlet of the device under test.