INTERNATIONAL STANDARD

ISO 7199

Second edition
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Cardiovascular implants and artificial organs — Blood-gas exchangers (oxygenators)

Implants cardiovasculaires et organes artificiels — Échangeurs gaz/sang extracorporels (oxygénateurs)

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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 7199 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition cancels and replaces the first edition (ISO 7199:1996), which has been technically revised.

Introduction

This International Standard is intended to ensure that devices designed to affect the exchange of gases in support of, or as a substitution for, the normal respiratory function of the lungs have been adequately tested for both their safety and function, and that extracorporeal device characteristics are appropriately disclosed when labeling the device.

This International Standard therefore contains procedures to be used for evaluation of extracorporeal blood-gas exchangers (oxygenators). Type test procedures for determination of the gas transfer, blood cell damage and heat exchanger performance 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 an oxygenator that will suit the needs of the patient.

This International Standard also includes minimum reporting requirements, which will allow the user to compare performance characteristics of oxygenators of different designs in a standard way.

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

No provisions have been made for quantification of microbubble generation or for non-formed elements of bovine blood because there currently is no consensus regarding satisfactorily reproducible test methods.

Requirements for animal and clinical studies have not been included in this International Standard. Such studies may be parts of a manufacturer's quality system.

This International Standard contains only those requirements that are specific to oxygenators. Non-specific requirements are covered by references to other International Standards listed in the normative references section. Since non-toxicity is anticipated to be the subject of a future horizontal/level 1 standard, this International Standard does not cover non-toxicity.

Cardiovascular implants and artificial organs — Blood-gas exchangers (oxygenators)

1 Scope

This International Standard specifies requirements for sterile, single-use, extracorporeal blood-gas exchangers (oxygenators) intended for supply of oxygen to, and removal of carbon dioxide from, the blood of humans.

This International Standard also applies to heat exchangers that are integral parts of oxygenators and to external equipment unique to the use of the device.

This International Standard does not apply to:

— implanted oxygenators;

— liquid oxygenators;

— extracorporeal circuits (blood tubing);

— separate heat exchangers;

— separate ancillary devices.

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 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 11135:1994, *Medical devices — Validation and routine control of ethylene oxide sterilization*

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 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.

3.1
blood-gas exchanger
oxygenator
extracorporeal device designed to supplement, or be a substitute for, the respiratory function of the lungs

3.2
blood pathway
paths of the oxygenator containing blood during intended clinical use

3.3
gas pathway
parts of the oxygenator containing the ventilation gas during intended clinical use

3.4
heat exchanger
component that is intended to control the temperature of the circulating blood or priming solution

3.5
heat exchanger performance factor
R
ratio of the difference between the temperature of blood at the outlet of the oxygenator and the temperature of blood at the inlet of the oxygenator to the difference between the temperature of the water at the inlet of the heat exchanger and the temperature of blood at the inlet of the oxygenator

3.6
integral part
part that is connected to the oxygenator and cannot normally be separated by the user

3.7
operating variables
settings of controls that affect the function of the device

3.8
platelet reduction
percentage reduction of platelets contained in a circuit incorporating an oxygenator, less the percentage reduction in an identical control circuit without an oxygenator, as a function of time

3.9
plasma-free haemoglobin level
concentration of plasma-free haemoglobin in a circuit incorporating an oxygenator, less the concentration in an identical control circuit without an oxygenator, as a function of time

3.10
white blood cell reduction
percentage reduction of white blood cells contained in a circuit incorporating an oxygenator, less the percentage reduction in an identical control circuit without an oxygenator, as a function of time

3.11
residual blood volume
difference between the priming volume of the unit and the blood volume that can be extracted by the unit by holding it in its most advantageous drainage position for 20 s past the time that air first appears at the port being used for drainage until no remaining volume is noted in the device

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 Blood pathway integrity

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

4.2.2 Heat exchanger fluid pathway integrity

When tested in accordance with 5.3.2, the heat exchanger fluid pathway shall not leak.

4.2.3 Blood volumes

When tested in accordance with 5.3.3, the volume of the blood pathway shall be within the tolerances specified by the manufacturer (see 6.3).

4.2.4 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 Figure 1 of ISO 8637:1989, or a type that complies with ISO 594-2, have been found satisfactory.

When tested in accordance with 5.3.4, the gas inlet connection to the gas pathway shall not separate.

Connectors for the heat exchanger fluid pathway shall be capable of being connected using fast couplings.

NOTE 2 Connectors corresponding to Figure 3 of ISO 8637:1989 are considered as one way to comply with this requirement.

4.3 Performance characteristics

4.3.1 Oxygenator and carbon dioxide transfer rates

When determined in accordance with 5.4.1, the oxygen and carbon dioxide transfer rates shall be within the range of values specified by the manufacturer (see 6.3).

4.3.2 Heat exchanger performance factor

When determined in accordance with 5.4.2, the heat exchanger performance factors shall be within the range of values specified by the manufacturer (see 6.3).

4.3.3 Blood cell damage

4.3.3.1 Plasma-free haemoglobin

When determined in accordance with 5.4.3, the increased concentration of plasma-free haemoglobin shall be within the range of values specified by the manufacturer.

4.3.3.2 Platelet reduction and white blood cell reduction

When determined in accordance with 5.4.3, the percentage reduction of platelets and the percentage reduction of white blood cells shall be within the range of values specified by the manufacturer.

4.3.4 Time-dependent performance changes

When determined in accordance with 5.4.1, the oxygen and carbon dioxide transfer rates shall remain consistent within the range of values over the duration of the testing specified by the manufacturer.

5 Tests and measurements to determine compliance with this International Standard

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 non-linear, 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 and reproducibility.

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 and 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 Determination of blood pathway integrity

5.3.1.1 Test liquid

The test liquid shall be water.

5.3.1.2 Procedure

Place the device under test in an appropriate test circuit. Subject the blood pathway of the device to a pressure that is 1,5 × the maximum pressure specified by the manufacturer for intended clinical use. If no maximum pressure is specified, the test shall be performed at 40 kPa. Visually inspect the device for leakage of water.

5.3.2 Determination of heat exchanger water pathway integrity

5.3.2.1 Test liquid

The test liquid shall be water.

5.3.2.2 Procedure

Place the device under test in an appropriate test circuit. Subject the heat exchanger fluid pathway to a pressure 1,5 × that specified by the manufacturer for intended clinical use. If no maximum pressure is specified, the test shall be performed at 350 kPa. Maintain this pressure for 6 h or as long as is specified by the manufacturer for intended clinical use and visually inspect the device for leakage of water.

5.3.3 Blood volumes

5.3.3.1 Test liquid

The test liquid shall be heparinized blood or water.

5.3.3.2 Procedure

The volume of the blood pathway shall be determined over the range of operating variables specified by the manufacturer for intended clinical use (see 6.3).

5.3.4 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 Oxygen and carbon dioxide transfer rates

5.4.1.1 Test media

The test liquid for the blood pathway shall be heparinized bovine, porcine or ovine blood. The test medium for the gas pathway shall be gas of known oxygen, nitrogen and carbon dioxide concentrations.

5.4.1.2 Procedure

Place the device under test in an appropriate test circuit. Perform tests using the following blood inlet conditions during determination of oxygen and carbon dioxide transfer rates:

— oxyhaemoglobin percentage: (65 ± 5);

— haemoglobin: (12 ± 1) g/dl;

— base excess: (0 ± 5) mmol/l;

— partial pressure of carbon dioxide in blood, p_{CO_2}: (6,0 ± 0,7) kPa.

Oxygen and carbon dioxide transfer rates shall be determined over the manufacturer's specified range of operating variables (see 6.3).

Between each set of measurements, the blood flow shall be kept at the maximum specified by the manufacturer for intended clinical use (see 6.3).

Determination of oxygen and carbon dioxide transfer rates shall be made at the initiation of the test. For dependent determinations, measurements shall be performed at initiation of the test and then at 1 h, 3 h and 6 h after the start of the test. As applicable, further determinations shall be made at 6 h intervals.

In vitro tests as well as tests using cattle are acceptable.

The blood may be exchanged for fresh blood as required in oxygen and carbon dioxide transfer measurements.

Data need not be collected at the precise conditions specified. Approximations obtained by reasonable interpolation are acceptable.

5.4.2 Heat exchanger performance factor

5.4.2.1 Test liquid

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

5.4.2.2 Procedure

Place the device under test in an appropriate test circuit. Perform the test *in vitro* under the following conditions:

— blood inlet temperature, B_{Ti}: (30 ± 1) °C;

— water inlet temperature, W_{Ti}: (40 ± 1) °C.

The determination of heat exchanger performance factors shall be made over the manufacturer's specified range of operating variables (see 6.3).

5.4.2.3 Equation

The heat exchanger performance factor is given by the following equation:

$$R = \frac{B_{To} - B_{Ti}}{W_{Ti} - B_{Ti}}$$

where

B_{To} is the temperature of the blood at the outlet of the oxygenator, in degrees centigrade;

B_{Ti} is the temperature of the blood at the inlet of the oxygenator, in degrees centigrade;

W_{Ti} is the temperature of the water at the inlet of the heat exchanger, in degrees centigrade.

5.4.3 Blood cell damage

5.4.3.1 Test media

The test liquid for the blood pathway shall be heparinized bovine, ovine or porcine blood. The test medium for the gas pathway shall be gas of suitable oxygen, nitrogen and carbon dioxide concentrations.

5.4.3.2 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. 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.

The sampling schedule shall be in accordance with Table 2.

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 %
Gas flow rate	The maximum specified by the manufacturer for intended clinical use (see 6.3)	± 5 %
p_{CO_2}	5,3 kPa	± 0,7 kPa
Base excess	0	± 5 mmol/dl
Blood glucose	10 mmol/dl	± 5 mmol/dl
Haemoglobin	12 g/dl	± 1 g/dl

Table 2 — Sampling schedule

Parameter	Prior to test	Time, after initiation of test min			
		10	30	180	360
Plasma-free haemoglobin	X		X	X	X
White blood cell	X		X	X	X
Platelets	X		X	X	X
Blood gas values p_{CO_2} p_{O_2} pH Base excess		X	X	X	X
Haemoglobin	X	X	X	X	X
Glucose	X				
Activated clotting time	X				
Temperature	X	X	X	X	X
Flow rates	X	X	X	X	X

6 Information supplied by the manufacturer

6.1 Information to be given on the oxygenator

The following information shall be given on the oxygenator:

a) the manufacturer's identification;

b) batch, lot or serial number designation;

c) model designation;

d) the direction of blood and/or gas and/or water flows, if necessary;

e) the minimum and operating reservoir levels, where appropriate.

6.2 Information to be given on the packaging

6.2.1 Unit container

The following shall be visible through or 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) expiry date;