INTERNATIONAL STANDARD

ISO 7199

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

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

Reference number
ISO 7199:1996(E)

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.

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.

International Standard ISO 7199 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, subcommittee SC 2, *Cardiovascular implants* in collaboration with the European Committee for Standardization (CEN), TC 205, with the intention to publish both an International Standard and a European Standard which are technically equivalent.

Annex A of this International Standard is for information only.

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Introduction

This International Standard is intended to ensure that devices designed to effect 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 labelling the device.

This International Standard therefore contains recommended 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 of such devices 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 which 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 nor for nonformed elements of bovine blood, due to the fact that there is currently 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. Nonspecific requirements are covered by references to other International Standards listed in the normative references section. Since nontoxicity is anticipated to be the subject of a future horizontal/level 1 standard, this International Standard does not cover nontoxicity.

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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 standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 10993-1:1992, *Biological evaluation of medical devices — Part 1: Evaluation and testing.*

ISO 10993-7:1995, *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals.*

ISO 10993-11:1993, *Biological evaluation of medical devices — Part 11: Test for systemic toxicity.*

ISO 11134:1994, *Sterilization of health care products — Requirements for validation and routine control — Industrial moist heat sterilization.*

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

ISO 11137:1995, *Sterilization of health care products — Requirements for validation and routine control — Radiation sterilization.*

ISO 13485:—[1], *Quality systems — Medical devices: Particular requirements for the application of ISO 9001.*

ISO 13488:—[1], *Quality systems — Medical devices: Particular requirements for the application of ISO 9002.*

3 Definitions

For purposes of this International Standard, the following definitions apply:

3.1 blood-gas exchanger (oxygenator): Extracorporeal device designed to supplement, or be a substitute for, the respiratory function of the lung.

3.2 blood pathway: Paths of the oxygenator containing blood during intended clinical use.

3.3 bovine blood: Heparinized bovine blood, whole, or diluted with physiological saline solution.

3.4 gas pathway: Parts of the oxygenator containing the ventilation gas during intended clinical use.

3.5 heat exchanger: Component that is intended to control the temperature of the circulating blood or priming solution.

3.6 heat exchanger performance factor, R: Ratio of the difference between the temperature of blood at the outlet and inlet of the oxygenator, to the difference between the temperature of the water at the inlet of the heat exchanger and the temperature of the blood at the inlet of the oxygenator, expressed by the following equation:

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

where

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

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

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

3.7 integral part: Part that is connected to the oxygenator and cannot normally be separated by the user.

3.8 operating variables: Settings of controls which affect the function of the device.

3.9 platelet percentage 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.

3.10 plasma-free haemoglobin generation: 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.

3.11 white blood cell percentage 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.

4 Requirements

4.1 Biological characteristics

4.1.1 Sterility and nonpyrogenicity

The blood pathway shall be sterile and nonpyrogenic.

Compliance shall be verified in accordance with 5.1.1.

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1) To be published.

4.1.2 Biocompatibility

Parts of the blood pathway shall be biocompatible with respect to their intended use.

Compliance shall be verified in accordance with 5.1.2.

4.2 Physical characteristics

4.2.1 Blood pathway integrity

When tested in accordance with 5.2.1, the blood pathway shall not leak.

4.2.2 Heat-exchanger fluid pathway integrity

When tested in accordance with 5.2.2, the heat-exchanger fluid pathway shall not leak.

4.2.3 Blood volumes

When tested in accordance with 5.2.3, the volume of the blood pathway shall be within the tolerance specified by the manufacturer (see 6.3).

4.2.4 Connectors

Connectors for connection to the blood pathway shall, when tested in accordance with 5.2.4, allow a secure connection.

NOTE — 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 594-2:1991, have been found satisfactory.

When tested in accordance with 5.2.4, 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 — 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 5.3.1, 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 5.3.2, 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

When determined in accordance with 5.3.3, the increased concentration of plasma-free haemoglobin and the percentage reduction of platelets and white blood cells shall be within the range of values specified by the manufacturer (see 6.3).

4.3.4 Time-dependent performance changes

When determined in accordance with 5.3.1, the oxygen and carbon dioxide transfer rates shall be within the range of values specified by the manufacturer (see 6.3).

5 Tests and measurements to determine compliance with this International Standard

Tests and measurements shall be performed with the device under test prepared according to the manufacturer's instructions for intended clinical use.

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

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

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

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 and reproducibility.

5.1 Biological characteristics

5.1.1 Sterility and nonpyrogenicity

Compliance shall be verified by inspection of the manufacturer's documentation on sterilization and pyrogen testing, in accordance with ISO 11134, 11135, 11137 and 10993-11, as applicable.

5.1.2 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 10993-7, as applicable.

5.2 Physical characteristics

5.2.1 Determination of blood pathway integrity

5.2.1.1 Test liquid

The test liquid shall be water.

5.2.1.2 Procedure

Place the device under test in an appropriate test circuit. Subject the blood pathway of the device to a pressure which is 1,5 times the maximum pressure or flow specified by the manufacturer for intended clinical use (see 6.3). If no maximum pressure or flow is specified, the test shall be performed at 40 kPa. Maintain this pressure for 6 h, or as long as is specified by the manufacturer for intended clinical use (see 6.3), and visually inspect the device for leakage of water.

5.2.2 Determination of heat-exchanger fluid pathway integrity

5.2.2.1 Test liquid

The test liquid shall be water.

5.2.2.2 Procedure

Place the device under test in an appropriate test circuit. Subject the heat exchanger fluid pathway to a pressure 1,5 times specified by the manufacturer for intended clinical use (see 6.3). 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 (see 6.3), and visually inspect the device for leakage of water.

5.2.3 Blood volumes

5.2.3.1 Test liquid

The test liquid shall be heparinized bovine blood or water.

5.2.3.2 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).

5.2.4 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.

5.3 Performance characteristics

5.3.1 Oxygen and carbon dioxide transfer rates

5.3.1.1 Test media

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

5.3.1.2 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

— 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, 3 and 6 h after the start of the test. As applicable, further determinations shall be made at 6-h intervals.

NOTES

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

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

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

5.3.2 Heat-exchanger performance factor

5.3.2.1 Test liquid

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

5.3.2.2 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.