List of Titles

American National Standard

ANSI/AAMI/ISO 7199:1996/(R)2002

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

AAMI Association for the Advancement of Medical Instrumentation

List of Titles

Association for the Advancement of Medical Instrumentation
1110 N. Glebe Rd., Suite 220
Arlington, VA 22201-4795

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7199 Cardiovascular implants and artificial organs—Blood-gas exchangers

American National Standard

ANSI/AAMI/ISO 7199:1996/(R)2002

Cardiovascular implants and artificial organs— Blood-gas exchangers

Developed by

Association for the Advancement of Medical Instrumentation

Approved 8 April 1996 and reaffirmed 16 December 2002 by

American National Standards Institute, Inc.

Abstract:

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

Committee representation

Association for the Advancement of Medical Instrumentation

The adoption of ISO 7199:1996 as an American National Standard was initiated by the AAMI Blood–Gas Exchange Device Committee, which also functions as a U.S. Technical Advisory Sub-Group to the relevant work in the International Organization for Standardization (ISO).

The AAMI **Blood-Gas Exchange Device Committee** has the following members:

Cochairs: Joe R. Utley, MD
Marc Voorhees

Members: Robert H. Bartlett, MD, University of Michigan Medical Center, Ann Arbor, MI
Arthur Ciarkowski, FDA, Center for Devices and Radiological Health, Rockville, MD
Angelo Iatridis, California Pacific Medical Center, San Francisco, CA
Mark Kurusz, CCP, University of Texas Medical Branch, Galveston, TX
J. D. Mortensen, MD, Salt Lake City, UT
Suzanne Parisian, MD, Medical Device Assistance Inc., Front Royal, VA
E. Converse Peirce, MD, Hancock, ME
Donald A. Raible, Baxter Healthcare, Irvine, CA
Bruce A. Ratcliff, CCE, Riverside Methodist Hospital, Columbus, OH
Peter Richardson, PhD, Brown University, Providence, RI
Martha Rumford, Sarns 3M Health Group, Ann Arbor, MI
George Silvay, MD, Mount Sinai Hospital, New York, NY
Joe R. Utley, MD, Spartanburg, SC

Marc Voorhees, Cobe Cardiovascular, Inc., Arvada, CO
Warren Zapol, MD, Massachusetts General Hospital, Boston, MA
Alternate: Ronald A. Robinson, FDA, Office of Science and Technology, Rockville, MD

NOTE—Participation by federal agency representatives in the development of this standard does not constitute endorsement by the federal government or any of its agencies.

Background of ANSI/AAMI adoption of ISO 7199:1996

Blood-gas exchangers (oxygenators)

As indicated in the foreword to the main body of this document (page vi), the International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. The United States is one of the ISO members that took an active role in the development of the first edition of the standard for blood-gas exchangers (oxygenators).

AAMI and ANSI procedures require that standards be reviewed and, if necessary, revised every 5 years to reflect technological advances that may have occurred since publication. AAMI also encourages its committees to harmonize their work with international standards as much as possible.

This standard was prepared by ISO/TC 150/SC 2, *Implants for surgery—Cardiovascular implants, in cooperation* with CEN/TC 205, with the intention to present a document that will appear both as an International and European Standard, technically identical. The AAMI Blood-Gas Exchange Device Committee (U.S. Technical Advisory Sub-Group for ISO/TC 150/SC 2) supports such international harmonization of standards and recommended in 1995 that AAMI initiate parallel adoption of ISO 7199 in the United States as a new American National Standard.

The concepts incorporated in this standard should not be considered inflexible or static. This standard, like any other, must be reviewed and updated periodically to assimilate progressive technological developments. To remain relevant, it must be modified as technological advances are made and as new data come to light.

Suggestions for improving this standard are invited. Comments and suggested revisions should be sent to Standards Department, AAMI, 3330 Washington Boulevard, Suite 400, Arlington, VA 22201–4598.

NOTE—Beginning with the ISO foreword on page vi, this American National Standard is identical to ISO 7199:1996.

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 percent of the member bodies casting a vote.

International Standard ISO 7199 was prepared by Technical Committee ISO/TC 150, *Implants for surgery, subcommittee 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 that are technically equivalent.

Annex A of this International Standard is for information only.

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 labeling 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 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 nor for nonformed 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. 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.

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.

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

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

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

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

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

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

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

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

3 Definitions

For the 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: The ratio R 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 at the inlet of the oxygenator, expressed 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 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 that 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 hemoglobin generation: Concentration of plasma–free hemoglobin 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.

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, 6.3, 9.5, 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 hemoglobin 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 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.

5.1 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 ISO 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 that 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 hours (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 that 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 seconds (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 known 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:

– oxyhemoglobin percentage: (65 ± 5)%

– hemoglobin: (12 ± 1) g/dl

– base excess: (0 ± 5) mmol/l

– pco_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 test *in vitro* under the following:

– 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).

5.3.3 Blood cell damage

5.3.3.1 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 suitable oxygen, nitrogen, and carbon dioxide concentrations.

5.3.3.2 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. In one of the circuits, the device under test shall be placed. 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	Max. variation
Blood flow rate	The maximum specified by the manufacturer for intended clinical use (see 6.3), or 6 1/min, whichever is smaller	±5%
Gas flow rate	The maximum specified by the manufacturer for intended clinical use (see 6.3)	±5%
pco_2	5.3 kPa	±0.7 kPa
Base excess	0	±5 mmol/dl
Blood glucose	10 mmol/dl	±5 mmol/dl
Hemoglobin	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 hemoglobin	X		X	X	X
WBC	X		X	X	X
Platelets	X		X	X	X
Blood gas values:		X	X	X	X
pco_2					
po_2					
pH					
Base excess					
Hemoglobin	X	X	X	X	X
Glucose	X				
ACT	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 nonpyrogenicity;

e) expiry date;

f) batch, lot, or serial number designation;

g) the words "Read instructions before use";

NOTE—The symbol ⚠ may be used.

h) any special handling or storage conditions;

i) statement on single-use.

NOTE—The symbol ② may be used.

6.2.2 Shipping container

The following information shall appear 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 nonpyrogenicity;

e) expiry date;

f) any special handling, storage, or unpacking instructions.

6.3 Information to be given 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 or telefax number;

b) model designation;

c) required ancillary equipment;

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

e) directions for placing the oxygenator in a support or operational fixture;

f) placement, type, and securing of tubing connections;

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

h) heat exchanger priming and operation;

i) priming procedure;

j) direction of blood, gas, and water flows;

k) general operating procedures for normal use;

l) a recommended procedure for intraoperative replacement of an oxygenator;

m) maximum and minimum recommended blood flow rates;

n) maximum and minimum operating volumes of the blood pathway, including any integral reservoir;

o) maximum and minimum specified gas flow rates;

p) heat exchanger performance factors;

q) residual blood volume;

r) oxygen and carbon dioxide transfer rates;

s) pressure limitations for blood, water, and gas pathways;

t) a statement that the following are available upon request:

– sterilization method;
– a list of materials of the blood pathway;
– data on plasma leakage across any semipermeable membrane, if applicable;
– blood pathway pressure drop at the maximum blood flow rate specified by the manufacturer for intended clinical use;
– gas pathway pressure drop at the maximum blood and gas flow rates specified by the manufacturer for intended use;
– data related to blood cell damage;
– data on particle release from the oxygenator;
– relevant tolerances for data presented.

6.4 Information to be given in the accompanying documents in a prominent form

The following information shall be given, in prominent form, in the accompanying documents:

a) pressure limitations;

b) flow rate limitations;

c) blood level limitations;

d) other device limitations.

7 Packaging

Packaging shall comply with the appropriate requirements of ISO 13485 or 13488.

Annex A
(informative)

Bibliography

[1] ISO 594-2:1991, *Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment—Part 2: Lock fittings.*

[2] ISO 8637:1989, *Haemodialysers, haemofilters and haemoconcentrators.*

Annex B
(informative)

Rationale for the development and provisions of this standard

B.1 Introduction

The routine of blood oxygenators as part of the cardiopulmonary bypass apparatus has been applied to increasing numbers of patients in recent years. The widespread use of these devices, the use of blood oxygenators with components from different manufacturers, and the need for a standard of quality in the devices justify the creation and adoption of a national and international standard for blood oxygenators. The goal of the standard is to assure the level of performance of the device and to assure that the appropriate information related to operating the device is communicated to the user.

B.2 Rationale for the biologic characteristics

The standard addresses the requirement for sterility and nonpyrogenicity of the device. The biocompatibility of the device is related to the degree of trauma to the circulating blood components. The standard relates to the biocompatibility to the intended use of the oxygenator.

B.3 Rationale for the physical characteristics

The standard ensures that there will not be leakage between the blood, gas, and heat exchanger fluid pathways to assure that blood is not contaminated from the other pathways. The volume of blood in the oxygenator is part of the standard. The connector assures that the connectors are of standard size and perform without unexpected disconnects.

B.4 Rationale for the performance characteristics

The standard for the performance characteristics requires that the oxygen and carbon dioxide transfer rates be stated. The standard also addresses the performance of the heat exchanger. The effect of the oxygenator device on plasma hemoglobin concentration, platelet counts, and white blood cell counts is also a part of the standard. These standards enable the user to assure that the oxygenator will perform within the needs of the patient.

The standard describes methods for testing the various parts of the performance characteristics to assure uniformity in testing of the devices.

B.5 Rationale for the information described by the manufacturer

The standard requires that the oxygenator be labeled with the various connections, the direction of flow, and the range of reservoir levels to increase the safety of the device. The container of the device must be labeled with the expiration date and special handling and storage conditions. The Instructions for Use document is required to contain the manufacturer’s name, telephone, and fax numbers. The instructions also must contain required ancillary equipment, support of oxygenator, connections to oxygenator, and priming procedures for heat exchanger and oxygenator. The instructions also address the range of operation for blood flow rates, operating volumes, gas flow rates, residual blood volume, and pressure limitations. Limitations of pressure, flow rates, blood levels, and other device limitations must be prominently displayed.

Annotations from 7199.pdf

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