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

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

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ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: 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.

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 document 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).

ISO draws attention to the possibility that the implementation of this document may involve the use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents. ISO shall not be held responsible for identifying any or all such patent rights.

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For an explanation of the voluntary nature of standards, 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 www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 205, *Non-active medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This fourth edition cancels and replaces the third edition (ISO 7199:2016), which has been technically revised. It also incorporates the Amendment ISO 7199:2016/Amd.1:2020.

The main changes are as follows:

— circular definitions have been corrected for platelet reduction (3.10), plasma free haemoglobin (3.11) and white blood cell reduction (3.12);

— the definition of priming volume (3.18) has been added;

— the sampling time point of 5 min has been deleted in Table 2.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

This document 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 labelling the device.

This document therefore contains procedures to be used for the evaluation of extracorporeal blood-gas exchangers (oxygenators). Type test procedures to determine 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 suits the needs of the patient.

This document also includes minimum reporting requirements that allow the user to compare performance characteristics of oxygenators of different designs in a standard way.

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

No provisions have been made for the quantification of microbubble generation or for the 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 document.

This document contains only those requirements that are specific to oxygenators. Since non-toxicity is anticipated to be the subject of a future horizontal/level 1 standard, this document does not cover non-toxicity.

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

1 Scope

This document specifies requirements for sterile, single-use, extracorporeal blood-gas exchangers (oxygenators) intended for the supply of oxygen to, and the removal of carbon dioxide from, human blood, during cardiopulmonary bypass (CPB) for up to 6 h, extracorporeal lung assist [ECLA with veno-venous (VV), veno-arterial (VA) or veno-arterial-venous (VAV) cannulation strategies], cardiopulmonary support (CPS), extracorporeal life support (ECLS with VA cannulation strategy), extracorporeal carbon dioxide removal ($ECCO_2R$), and other extracorporeal circulation techniques requiring blood-gas exchange.

This document also applies to heat exchangers and arterial filters that are integral parts of the oxygenator.

This document also applies to external equipment unique to the use of the oxygenator.

This document does not apply to

— implanted oxygenators,

— liquid oxygenators,

— extracorporeal circuits (blood tubing),

— separate heat exchangers,

— separate ancillary devices, and

— separate arterial line filters.

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 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

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

ISO 11135, *Sterilization of health-care products — Ethylene oxide — Requirements for the 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 17665, *Sterilization of health care products — Moist heat — Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 80369-7:2021, *Small-bore connectors for liquids and gases in healthcare applications — Part 7: Connectors for intravascular or hypodermic applications*

3 Terms and definitions

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

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

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

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
portion of the *oxygenator* (3.1) containing blood during intended clinical use

3.3
gas pathway
portion of the *oxygenator* (3.1) 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* (3.1) 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* (3.4) and the temperature of blood at the inlet of the oxygenator

3.6
integral arterial filter
component that is intended to filter particles such as blood clots, debris and gas emboli from the blood

3.7
filtration efficiency
ability of the filter to remove particles from the simulated blood suspension test fluid

Note 1 to entry: Filtration efficiency is expressed as a percentage.

3.8
integral part
part that is connected to the *oxygenator* (3.1) and cannot normally be separated by the user

3.9
operating variable
setting of controls that affects the function of the device

3.10
platelet reduction
decrease in platelet count in a circuit incorporating an *oxygenator* (3.1)

Note 1 to entry: Platelet reduction is expressed as a percentage.

3.11
plasma free haemoglobin
haemoglobin that is released from the red blood cells to the plasma

3.11.1
normalized index of haemolysis
NIH
mass of *plasma free haemoglobin* (3.11) released after pumping 100 l of blood

$$\mathrm{NIH} = \Delta f_{\mathrm{Hb}} \cdot V \cdot \frac{100 - \mathrm{Hct}}{100} \cdot \frac{100}{Q \cdot t}$$

where

Δf_{Hb} is the increase of plasma free haemoglobin concentration over the sampling time interval, in g/l;

V is the circuit volume, in l;

Q is the flow rate, in l/min;

Hct is the haematocrit, in %;

t is the sampling time interval, in min

Note 1 to entry: The normalized index of haemolysis is expressed in grams per hectolitre.

3.12
white blood cell reduction
decrease in white blood cell count in a circuit incorporating an *oxygenator* (3.1)

Note 1 to entry: White blood cell reduction is expressed as a percentage.

3.13
residual blood volume
difference between the priming volume of the unit and the blood volume that can be extracted

3.14
blood analogue
test solution which simulates certain blood characteristics relevant for testing, such as viscosity and salinity

3.15
subject device
device under test

3.16
comparator device
device similar to the *subject device* (3.15) that is a legally marketed device, recognized-to-be-safe and is used for the same intended clinical use

3.17
worst-case condition
operating variable (3.9) within those specified by the manufacturer for intended clinical use which represents the supposed worst-case device operation for the respective test

3.18
priming volume
amount of fluid needed to fill the blood path of 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.

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

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, a type that complies with ISO 8637-1:2017, Figure 1, or a type that complies with ISO 80369-7:2021 have been found satisfactory.

NOTE 2 Connectors with dimensions as given in Annex A and fitting to functional gauges and reference steel fittings is a way to comply with this requirement.

Performance testing of the connectors shall be performed in accordance with ISO 80369-7:2021, Clause 6. The reference fittings given in Annex A can be used in the performance testing of the connectors.

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

NOTE 3 Connectors corresponding to ISO 8637-1:2017, Figure 2 are considered as one way to comply with this requirement.

4.3 Performance characteristics

4.3.1 Oxygen 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 Integral arterial filtration efficiency

When tested in accordance with 5.4.5, filtration efficiency of any individual device should be at least 80 % when tested with particles that are 20 % larger than the nominal pore size of the filter.

4.3.4 Integral arterial filter flow rate capacity

When tested in accordance with 5.4.6, test results shall demonstrate the flow rate and pressure limitation(s) to ensure safe and effective performance, as specified by the manufacturer.

4.3.5 Integral arterial filter air handling capability

When tested in accordance with 5.4.7, test results shall demonstrate the air-handling capability, as specified by the manufacturer.

4.3.6 Blood cell damage

4.3.6.1 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.

The haemolysis results shall be reported in mg/dl and the NIH shall be given.

4.3.6.2 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.

4.3.7 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.

4.3.8 Shelf life

When tested in accordance with 5.4.4, the test results should 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 subject device prepared in accordance with the manufacturer's instructions for intended clinical use. Performing additional pre-conditioning can be required such as sterilization cycling, environmental exposure, shipping exposure and aging.

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.