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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.

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 documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2. www.iso.org/directives

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received. www.iso.org/patents

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on 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 the following URL: http://www.iso.org/iso/foreword.html



The committee responsible for this document is ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.



This third edition cancels and replaces the second edition (ISO 7199:2009), which has been technically revised.

It also incorporates the Amendment ISO 7199:2009/Amd.1:2012.

 

# 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 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 document also includes minimum reporting requirements, which will 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 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 document. Such studies may be parts of a manufacturer's quality system.



This document 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 clause. 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 supply of oxygen to, and removal of carbon dioxide from, the blood of humans.

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 filter.



## 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 10993-4, *Biological evaluation of medical devices — Part 4: Selection of tests for interaction with blood*

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, *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 15675, *Cardiovascular implants and artificial organs — Cardiopulmonary bypass systems — Arterial blood line filters*

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.

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

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

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

**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 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, expressed as a percentage

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

**3.9**
**operating variables**
settings of controls that affect the function of the device

**3.10**
**platelet reduction**
percentage reduction of platelets contained in a circuit incorporating an oxygenator, as a function of time

**3.11**
**plasma-free haemoglobin level**
concentration of plasma-free haemoglobin in a circuit incorporating an oxygenator, as a function of time

**3.11.1**
**normalized index of hemolysis**
**NIH**
grams of plasma-free hemoglobin released after pumping 100 l of blood

$$\mathrm{NIH\,(g\,/\,100\ l)} = \Delta f_{\mathrm{Hb}} \cdot V \cdot \frac{100 - \mathrm{Hct}}{100} \cdot \frac{100}{Q \cdot t} \tag{1}$$

where

$\Delta f_{\mathrm{Hb}}$ is the increase of plasma free hemoglobin concentration (g/l) over the sampling time interval;

$V$ is the circuit volume (l);

$Q$ is the flow rate (l/min);

Hct is the hematocrit (%);

$t$ is the sampling time interval (min)

**3.12**
**white blood cell reduction**
percentage reduction of white blood cells contained in a circuit incorporating an oxygenator, as a function of time



**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 blood viscosity between $2{,}0 \times 10^{-3}$ Pa·s (2,0 cP), to $3{,}5 \times 10^{-3}$ Pa·s (3,5 cP)

**3.15**
**predicate oxygenator**
similar oxygenator to the test oxygenator that has previously been approved and used for the same intended clinical use

## 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 ISO 8637:2010, Figure 1, 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 ISO 8637:2010, Figure 3 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 will 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 as mg/dl and NIH.

##### 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, 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 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 nonlinear, 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.