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Cardiovascular implants and extracorporeal systems — Centrifugal blood pumps

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National foreword

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Implants cardiovasculaires et systèmes extracorporels — Pompes sanguines centrifuges

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Foreword

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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 (see www.iso.org/directives).

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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: 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*.

Introduction

This document is intended to ensure that devices designed to provide continuous flow of blood in support of, or as a substitution for, the normal pumping function of the heart 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 centrifugal blood pumps. Test procedures for determination of the hydraulic performance, blood cell damage and other performance characteristics 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 a centrifugal blood pump 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 centrifugal blood pumps 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.

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

This document contains only those requirements that are specific to centrifugal blood pumps. Non-specific requirements are covered by references to other International Standards listed in Clause 2.

INTERNATIONAL STANDARD ISO 18242:2016(E)

Cardiovascular implants and extracorporeal systems — Centrifugal blood pumps

1 Scope

This document specifies requirements for sterile, single-use, extracorporeal centrifugal blood pumps, whether coated, non-surface modified, or surface-modified, intended for producing blood flow during extracorporeal circulation. Such blood flow is most commonly used to provide systemic perfusion during cardiopulmonary bypass, but also has applications for veno-venous bypass, kinetic-assisted venous drainage, or extracorporeal membrane oxygenation.

This document does not apply to

— centrifugal pumps used as ventricular assist devices, and

— other components of extracorporeal circuits (e.g. blood tubing, pump console/driver).

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 — Part4: Selection of tests for interactions 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 11658, *Cardiovascular implants and extracorporeal systems — Blood/tissue contact surface modifications for extracorporeal perfusion systems*

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:

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

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

3.1
centrifugal blood pump
extracorporeal device designed to produce rotational flow by means of radial force

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

3.3
operating variables
settings of controls that affect the function of the device

3.4
blood cell damage
loss or destruction of cellular components of the blood

3.5
platelet reduction
percentage reduction of platelets contained in a circuit incorporating a centrifugal pump as a function of time

3.6
plasma-free hemoglobin level
concentration of plasma-free hemoglobin in a circuit incorporating a pump, as a function of time

3.6.1
normalized index of hemolysis
NIH
grams of plasma-free hemoglobin released after pumping 100 L of blood

$$NIH\left\{g\ /\ 100L\right\} = \Delta fHb \times V \times \frac{100 - Hct}{100} \times \frac{100}{Q \times T} \quad (1)$$

where

ΔfHb is the increase of plasma free hemoglobin concentration (g/L) over the sampling time interval;

V is circuit volume (L);

Q is flow rate (L/min);

Hct is hematocrit (%);

T is sampling time interval (min).

3.7
white blood cell reduction
percentage reduction of white blood cells contained in a circuit incorporating a centrifugal pump as a function of time

3.8
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) or defined by the manufacturer based on appropriate haematocrit and temperature of the circulating blood during intended clinical use (i.e. hypothermic conditions)

3.9
predicate pump
similar pump to the test pump 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 determined in accordance with 5.3.1, the blood pathway shall not leak.

4.2.2 Prime volume

When determined in accordance with 5.3.2, the volume of the blood pathway shall be within the tolerances specified by the manufacturer (see 6.3).

4.2.3 Connector integrity

When determined in accordance with 5.3.3, the inlet and outlet ports shall allow a secure connection.

NOTE Connectors of a type that allow 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 7199.

4.3 Performance characteristics

4.3.1 Hydraulic performance

When determined in accordance with 5.4.1, the flow rates, pressure, and revolutions per minute (r/min) shall be within the range of values specified by the manufacturer (see 6.3).

4.3.2 Blood cell damage

NOTE Testing performed at the maximum rated flow specified by the manufacturer and using appropriate circuit blood volume, backpressure, pump r/min, and temperature is one way to comply with this requirement.

4.3.2.1 Plasma-free hemoglobin

When determined in accordance with 5.4.2, the rate of generation of plasma-free hemoglobin shall be within the range of values specified by the manufacturer.

The hemolysis results shall be reported as mg/dL and NIH.

4.3.2.2 Platelet reduction

When determined in accordance with 5.4.2, the percentage reduction of platelets shall be within the range of values specified by the manufacturer.

4.3.2.3 White blood cell reduction

When determined in accordance with 5.4.2, the percentage reduction of white blood cells shall be within the range of values specified by the manufacturer.

4.3.3 Bearing durability

When determined in accordance with 5.4.4, the bearing shall remain functional over the duration of the testing specified by the manufacturer, unless the device is bearingless.

4.3.4 Shelf life

When tested in accordance with 5.4.4, test results shall 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

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

5.1.2 Operating variables

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

5.1.3 Temperature

The temperature of the test liquid(s) shall be representative of a range of the intended temperatures during clinical use of the device (e.g. hypothermic, normothermic, and/or hyperthermic). Tests should be performed at multiple temperatures over the range of the intended clinical use, or justification for testing at a single temperature should be provided (e.g. why this temperature is representative of the worst case condition).

5.1.4 Relationship between variables

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

5.1.5 Procedures

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.

5.1.6 Driver/console

The specific driver(s)/console(s) used for testing of the rotary pump shall be specifically identified in the test procedure.

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 pyrogenicity 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, ISO 10993-4, ISO 10993-7, and ISO 11658, as applicable.

5.3 Physical characteristics

5.3.1 Blood pathway integrity

5.3.1.1 Test liquid

The test liquid shall be water, or other appropriate fluid.

5.3.1.2 Procedure

Place the device under test in an appropriate test circuit including the connector and tubing. 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 152 kPa. Visually inspect the device for leakage of water for a minimum of 6 h.

5.3.2 Prime volume

5.3.2.1 Test liquid

The test liquid shall be water, or other appropriate fluid.

5.3.2.2 Procedure

The volume of the blood pathway shall be determined, from the tip of the inlet port to the tip of the outlet port, over the range of operating variables specified by the manufacturer for intended clinical use (see 6.3).

5.3.3 Connectors

The connection shall be made in accordance with the manufacturer's instructions for use.

5.3.3.1 Procedure

The connection shall withstand a pull force in the same orientation of the tubing/connector at 15 N for 15 s without separating.

5.4 Performance characteristics

5.4.1 Hydraulic performance

5.4.1.1 Test liquid

The test liquid shall be a blood analogue or anticoagulated blood, and its composition and viscosity (measured at the same temperature as the hydraulic performance testing) shall be indicated.

5.4.1.2 Procedure

Place the device under test in an appropriate test circuit. Perform the testing at 37 °C ± 1 °C or at typical temperature, viscosity, and hematocrit of blood during intended clinical use. Set the r/min of the pump. By varying the restriction on the outlet tubing, measure the pressure differential between the inlet and outlet and the corresponding flow rate. Construct a plot showing the pressure differential versus flow rate for multiple r/min settings over the entire rated operating range of the pump (up to the maximum r/min).

5.4.2 Blood cell damage

5.4.2.1 Test liquid

The test liquid shall be anticoagulated whole blood, and the method of collection and species should be described.

5.4.2.2 Procedure

Two sets of appropriate circuit components (including a pump in the test circuit and a predicate pump in the control circuit), connecting tubing, and a reservoir (as specified by the manufacturer and of suitable size relative to the device under test) shall be assembled. Priming and debubbling of the circuits by recirculating with an appropriate solution is recommended before blood is added. The test liquid volumes shall, at the initiation of the test, be within 1 % of each other. Perform the test using the maximum rated flow rate of the device and obtain blood samples at least at the following time points: prior to test, 30 min, 180 min, and 360 min. More frequent sampling times are optional. For each sample, measure the following: plasma-free hemoglobin, white blood cell, platelet counts, activated clotting time, temperature, and flow rate. Glucose should also be measured prior to the test. A sufficient number of paired tests should be performed to support a statistical analysis. The predicate pump should be tested under the same conditions regarding flow rate, preload, and afterload.

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 %
Blood glucose	10 mmol/L	±5 mmol/L
Hemoglobin	12 g/dl	±1 g/dl

The sampling schedule shall be in accordance with Table 2.

Table 2 — Sampling schedule

Parameter	Time, after initiation of test min			
	Prior to test	**30**	**180**	**360**
Plasma-free hemoglobin	X	X	X	X
White blood cell	X	X	X	X
Platelets	X	X	X	X
Hemoglobin	X	X	X	X
Glucose	X			
Activated clotting time	X	X	X	X
Temperature	X	X	X	X
Flow rates	X	X	X	X

5.4.3 Bearing wear

5.4.3.1 Test liquid

The test liquid shall be a blood analogue or anticoagulated whole blood.

5.4.3.2 Procedure

The worst case conditions for bearing wear should be identified. Set the pump speed at the maximum r/min at a clinical relevant back pressure. Operate the pump for a minimum of 6 h or as specified by the manufacturer's instructions for use and measure the flow output of the pump for the duration of the test. Assess the extent of wear on the bearing.

5.4.4 Shelf life

Using a validated method, ageing should be performed on final, finished, sterilized devices in primary packaging in order to determine nominal shelf life.

6 Information supplied by the manufacturer

6.1 Information on the device

The following information shall be given on the pump:

a) the manufacturer's identification;

b) batch, lot or serial number designation;

c) model designation;

d) the direction of blood flow, if necessary.

A bar code or other system of identification may be used; considerations for visibility of the blood flow pathway should be considered.

6.2 Information 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;

f) batch, lot or serial number designation;

g) the words "Read instructions before use;"

NOTE 1 The approved symbol can be added before "Read instructions before use."

h) any special handling or storage conditions;

i) statement on single use.

NOTE 2 The approved symbol can be added before the words "Do not re-use," "Single use," or "Use only once."

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 non-pyrogenicity;

e) expiry date;

f) any special handling, storage or unpacking instructions.

6.3 Information 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 fax number;

b) model designation;

c) required ancillary equipment;

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

e) directions for placing the device 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) priming procedure;

i) direction of blood flow;

j) general operating procedures for normal use;

k) a recommended procedure for intraoperative replacement of the device;

l) maximum and minimum recommended blood flow rates;

m) pressure limitations for the blood pathway;

n) pressure/flow curves over r/min specified by the manufacturer for intended clinical use;

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

   1) sterilization method;

   2) a list of materials in contact with the blood pathway;

   3) data related to blood cell damage;

   4) relevant tolerances for data presented.

6.4 Information 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) other device limitations;

d) pressure/flow curve.

7 Packaging

Packaging shall comply with the appropriate requirements of ISO 11607-1 and ISO 11607-2.

Bibliography

[1] ASTM F1830, *Standard practice for selection of blood for in vitro evaluation of blood pumps*

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