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Cardiovascular implants and artificial organs — Cannulae for extracorporeal circulation

Implants cardiovasculaires et organes artificiels — Canules pour circulation extracorporelle

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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 (see www.iso.org/directives).

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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*.

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 cannulae designed to enable extracorporeal circulation (ECC) have been adequately tested for both their safety and function, and that cannulae characteristics are appropriately disclosed when labelling the device.

This document therefore contains procedures to be used for the evaluation of ECC cannulae. Type test procedures for determination of the cannulae performance and blood cell damage 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 cannulae that suits the needs of the patient.

This document also includes minimum reporting requirements, which allows the user to compare performance characteristics of cannulae 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 can be necessary for regulatory submissions and/or be parts of a manufacturer's quality system.

This document contains only those requirements that are specific to cannulae. Non-specific requirements are covered by references to other International Standards listed in Clause 2. 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 — Cannulae for extracorporeal circulation

1 Scope

This document specifies requirements for sterile, single-use cannulae for removal and delivery of patients' blood during cardiopulmonary bypass (CPB) up to 6 h duration, extracorporeal lung assist (ECLA with VV, VAV, or AV cannulation strategies), left or right heart bypass (LHB, RHB), cardiopulmonary support (CPS), extracorporeal life support (ECLS with VA cannulation strategy), extracorporeal carbon dioxide removal ($ECCO_2R$), and other extracorporeal circulation techniques. This standard does not apply to:

— introducers (e.g., guidewires) as addressed in ISO 11070,

— isolated organ perfusion cannulae, and

— intravascular catheters as addressed in ISO 10555-3.

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 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 14937, *Sterilization of health care products — General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*

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*

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

ASTM F640-12, *Standard Test Methods For Determining Radiopacity For Medical Use*

DIN 13273-7, *Catheters for medical use — Part 7: Determination of the x-ray attenuation of catheters; Requirements and testing*

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 https://www.iso.org/obp

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

3.1
extracorporeal circulation
blood circulation through an extracorporeal circuit used to support or replace a subject's circulatory and/or gas exchange requirements when the heart and/or lungs are temporarily not capable of functioning normally (e.g. due to lung and/or heart disease) incorporating cannulae, oxygenators, tubing, and/or other devices such as blood pump, arterial filter, reservoir

3.2
cannula
tubular device, single-lumen (3.4) or dual-lumen (3.5), designed to be partially inserted into the cardiovascular system for connection of the patient to the extracorporeal circuit

3.3
blood pathway
portions of the *cannula* (3.2) in contact with blood during the intended clinical use

3.4
single-lumen
cannula (3.2) with one inner lumen used to draw blood from the patient or to return blood to the patient

3.5
dual-lumen
cannula (3.2) with two inner lumens, separated from each other, used to draw blood from and to return blood to the patient

3.6
integral part
part that is connected to the *cannula* (3.2) and that cannot normally be separated by the user

3.7
operating variable
setting of controls that affects the function of the device

3.8
platelet reduction
percentage reduction of platelets contained in a circuit incorporating a *cannula* (3.2)

3.9
plasma free haemoglobin level
concentration of plasma free haemoglobin in a circuit incorporating a *cannula* (3.2)

3.9.1
NIH
normalized index of haemolysis

grams of plasma free haemoglobin released after pumping 100 l of blood

$$N_{ih}\,(g/100\ l) = \Delta f_{Hb} \cdot V \cdot \frac{100 - Hct}{100} \cdot \frac{100}{Q \cdot t} \quad (1)$$

where

N_{ih} is NIH;

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

V is the circuit volume (l);

Q is the flow rate (l/min);

Hct is the haematocrit (%);

t is the sampling time interval (min).

3.10
white blood cell reduction
percentage reduction of white blood cells contained in a circuit incorporating a *cannula* (3.2)

3.11
blood analogue
test solution which simulates certain blood characteristics relevant for testing, such as viscosity and salinity

3.12
predicate cannula
similar *cannula* (3.2) to the test cannula that is a legally marketed device, recognized-to-be-safe and is used for the same intended clinical use

3.13
distal end
end of the *cannula* (3.2) inserted furthest into the patient

3.14
proximal end
end(s) of the *cannula* (3.2) furthest away from the patient to which connection(s) can be made

3.15
inside diameter
inner diameter of the *cannula* (3.2), measured at the smallest part of the *cannula*

Note 1 to entry: The inside diameter is given in millimetres.

3.16
outside diameter
outer diameter of the *cannula* (3.2), measured at the biggest part of the *cannula* intended for insertion

Note 1 to entry: The outside diameter is given in millimetres.

3.17
effective length
length of the *cannula* (3.2), that can be inserted into the body

Note 1 to entry: The effective length is given in millimetres.

3.18
French size
diameter, D_{fr}, that is three times the normal diameter, D, in millimetres, $D_{fr} = 3D$

3.19
primary packaging
packaging which has direct contact with the device and/or maintains the sterility of the product

3.20
simulated use
use similar to the intended clinical use in an appropriate in-vitro test circuit with a *blood analogue* (3.11) at maximum flow rate as specified by the manufacturer and for the duration specified by the manufacturer for intended clinical use

3.21
vascular model
<single-lumen cannulae> tubular structure of diameter two times the outer diameter of the device under test

3.22
vascular model
<dual-lumen cannulae> simplified vascular model of superior vena cava, right atrium, and inferior vena cava for testing dual-lumen cannulae intended for use as a single *cannula* (3.2), for both venous drainage and return of blood via cannulation of the internal jugular vein

Note 1 to entry: See Annex C.

4 Requirements

4.1 Biological characteristics

4.1.1 Sterility and non-pyrogenicity

The cannula shall be sterile and non-pyrogenic.

Conformity shall be verified in accordance with 5.2.1.

4.1.2 Biocompatibility

All parts of the blood pathway and all tissue contacting parts of the cannula shall be biocompatible with respect to their intended use.

Conformity 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(s) shall not leak.

4.2.2 Connectors

Connectors for connection to the blood pathway shall, when tested in accordance with 5.3.2, allow a secure connection.

Connectors with dimensions as given in the Annex A and fitting to functional gauges and reference steel fittings are a way to comply with this requirement. Performance testing of the connectors shall be performed according to ISO 80369-7:2021, Clause 6, using the reference fittings given in Annex A.

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

4.2.3 Kink resistance

When tested in accordance with 5.3.3 the cannula shall not kink. Kinking is defined as a deformation of lumen of the device when the bending causes a decrease in flow such that the initial flow through the straight cannula is reduced by more than 50 %.

4.2.4 Pull strength

When tested in accordance with 5.3.4, each cannula shall withstand without disintegration an axial tensile force of a minimum of 15 N or 1,5 times the force possibly occurring during the intended use as determined by the risk assessment of the manufacturer for a duration of 30 s.

4.2.5 External surface

When examined by normal or corrected to normal vision, with a minimum ×2 magnification the external surface of the effective length of the cannula shall appear free from extraneous matter per manufacturer's specification.

The external surface of the effective length of the cannula, including the distal end, shall be free from process and surface defects which could cause trauma to vessels during use or obstruct flow, per manufacturer's specification.

4.2.6 Integrity (corrosion, abrasion, degradation)

When examined in accordance with 5.3.5 by normal or corrected to normal vision, with a minimum ×2 magnification the surface of the cannula shall appear free from corrosion, abrasion, and degradation per manufacturer's specifications.

4.2.7 Radio-detectability

When examined in accordance with 5.3.6 parts of the cannula shall be radio-detectable, if required as determined by the risk assessment.

4.2.8 Distance markings

If the cannula is provided with distance markings, the marking system shall indicate distance from the distal end. From the first mark, the distance between marks should not exceed 50 mm or a distance determined by risk management.

It is recommended that the distance marks be 10 mm or less apart on that portion of the cannula likely to be of importance to the user in positioning the cannula and monitoring cannula migration.

4.2.9 Lumen markings

If the cannula is not axially symmetric, the position of any side outlets shall be identifiable by the user on the proximal end when the cannula is inserted as defined by the information given by the manufacturer.

For dual-lumen cannulae, the direction of blood flow of each lumen shall be visually identifiable by the user.

4.3 Performance characteristics

4.3.1 Pressure drop

When determined in accordance with 5.4.1, the cannula pressure drop shall be within the range of values specified by the manufacturer.

4.3.2 Collapse resistance

For drainage cannula, when determined in accordance with 5.4.2, the cannula-induced pressure drop shall not increase by more than 50 %.

4.3.3 Recirculation

For dual-lumen cannulae, the percentage of recirculated blood in relation to the blood flow through the extracorporeal circuit shall be within the range of values specified by the manufacturer, when determined in accordance with 5.4.3.

4.3.4 Blood cell damage

4.3.4.1 Plasma-free haemoglobin

When determined in accordance with 5.4.4, 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.

4.3.4.2 Platelet and white blood cell reduction

When determined in accordance with 5.4.4, the platelet reduction and the white blood cell reduction shall be within the range of values specified by the manufacturer.

4.3.5 Shelf life

Test results should demonstrate the rated shelf life, as specified by the manufacturer.

5 Tests and measurements for conformity to this document

5.1 General

5.1.1 Tests and measurements shall be performed with final, finished, sterilized devices that are 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 ± 2) °C.

5.1.4 If the relationship between variables is non-linear, 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.

5.1.6 Unless otherwise justified, each test shall be performed using a sufficient number of samples to support a statistical analysis.

5.2 Biological characteristics

5.2.1 Sterility and non-pyrogenicity

Conformity 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, ISO 14937 and ISO 10993-11, as applicable.

5.2.2 Biocompatibility

Conformity 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, and ISO 10993-7, 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

Using an appropriate test circuit, subject the blood pathway of the device (test both lumens at the same time for dual-lumen cannulae) to a pressure that is 1,5 times the maximum pressure specified by the manufacturer for intended clinical use for the duration specified by the manufacturer for clinical use. Visually inspect the device for leakage of test liquid.

For dual-lumen cannulae, perform an additional test using an appropriate test circuit, subject only the lumen which is intended for the return of blood to the patient, to a pressure that is 1,5 times the maximum pressure specified for this pathway by the manufacturer for intended clinical use for the duration specified by the manufacturer for clinical use. Visually inspect the device for leakage of test liquid.

5.3.2 Connectors

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

Each connection shall withstand a pull force of 15 N for 15 s without separating.

5.3.3 Kink resistance

5.3.3.1 Test liquid

The test liquid for the blood pathway shall be blood or blood analogue with a viscosity of $2{,}0 \times 10^{-3}$ Pa·s (2,0 cP), to $3{,}5 \times 10^{-3}$ Pa·s (3,5 cP).

5.3.3.2 Procedure

Insert device under test into a suitable fluid reservoir in such a way that it allows for unrestricted blood flow through the cannula and for full immersion of the inserted part of the cannula at a worst-case temperature that simulates intended clinical use. For examples of test set-ups, see Annex B. De-air the circuit. Subject the blood pathway to the maximum blood flow rate as specified by the manufacturer while the cannula is completely straight. Set flow direction as specified by the manufacturer. Now bend the cannula around a radius template with a diameter of 4 times the outer diameter of the cannula under test, until minimum 180° enlacement is reached. Alternatively, based on the risk assessment, a