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Cardiovascular implants and artificial organs — Requirements for single-use tubing packs for cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO)

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National foreword

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Cardiovascular implants and artificial organs — Requirements for single-use tubing packs for cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO)

Implants cardiovasculaires et organes artificiels — Exigences pour les paquets de tubes à usage unique pour pontage cardiopulmonaire et oxygénation des membranes extracorporelles

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

This second edition cancels and replaces the first edition (ISO 15676:2005), which has been technically revised.

Introduction

The intent of this document is to ensure that medical grade tubing in single-use tubing packs for the transfer of blood and fluid during the period of cardiopulmonary bypass (CPB) and extracorporeal membrane oxygenation (ECMO) is adequately tested for both safety and function. The user commonly provides the specifications for the tubing pack. Furthermore, the purpose of this document is to ensure that the tubing pack characteristics be appropriately disclosed in the labelling and manufacturing information package. Tubing performance characteristics are specifically addressed within the context of this document as a component part of a single-use tubing pack.

This document therefore contains recommended procedures to evaluate such medical grade tubing intended for use during CPB procedures and ECMO. Test procedures to determine the material characteristics, the useful life of the tubing when used in a roller pump, and cleanliness are described. The limits for these characteristics are not specified.

This document also includes minimum reporting requirements. Ready identification of the performance characteristics should assist the user in the selection of such medical grade tubing for the procedure appropriate to the patient and procedure. This information may be useful in a clinic's quality control process that aims to improve the safety of CPB and ECMO procedures.

This document makes reference to other International Standards, which references methods for the determination of characteristics common to medical devices.

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

This document contains only those requirements that are specific to such medical grade tubing for use during CPB and ECMO. Non-specific requirements are covered by reference to other International Standards listed in the Normative References section.

INTERNATIONAL STANDARD ISO 15676:2016(E)

Cardiovascular implants and artificial organs — Requirements for single-use tubing packs for cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO)

1 Scope

This document specifies requirements for single-use tubing packs for cardiopulmonary bypass and extracorporeal membrane oxygenation (ECMO). This document is applicable to all medical tubing intended for cardiopulmonary bypass (CPB) and/or extracorporeal membrane oxygenation (ECMO), but specific requirements and tests are included for tubing intended for use with peristaltic pumps during (short-term, i.e. <6 h duration) CPB surgery or (long-term, i.e. >24 h) ECMO procedures. The sterility and non-pyrogenicity provisions of this document are applicable to tubing packs labelled as "sterile".

This document is applicable only to the tubing aspects for multifunctional systems that may have integral components such as blood gas exchangers (oxygenators), reservoirs, blood filters, defoamers, blood pumps, etc.

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 34-1, *Rubber, vulcanized or thermoplastic — Determination of tear strength — Part 1: Trouser, angle and crescent test pieces*

ISO 527-1, *Plastics — Determination of tensile properties — Part 1: General principles*

ISO 9352, *Plastics — Determination of resistance to wear by abrasive wheels*

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

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 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 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 11137-2, *Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose*

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*

ASTM D792-00, *Standard test methods for density and specific gravity (relatively density) of plastics by displacement*

ASTM D2240-04, *Standard test method for rubber property — Durometer hardness*

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
durometer hardness
measure of hardness of elastic materials by Shore A range

3.2
elongation
increase in linear dimension

3.3
tensile strength
force per unit of original cross section on *elongation* (3.2) to rupture

3.4
tear strength
measure of stress needed to continue rupturing a sheet of rubber or plastic, usually after an initial cut

3.5
tubing pack
consists of tubing sections joined by extracorporeal connectors and/or connected to extracorporeal devices intended for CPB or ECMO applications

3.6
specific gravity
ratio of the mass of a body to the mass of an equal volume of water at 4 °C

3.7
spallation
phenomenon whereby particles dislodge from a surface under cyclical stress

3.8
brittle point
temperature at which 50 % of test samples exhibit cracking or breakage after linear impact at a specified speed

3.9
blood analogue
test solution which simulates blood viscosity between $2{,}0 \times 10^{-3}$ Pa·s (2,0 cP) to $5{,}0 \times 10^{-3}$ Pa·s (5,0 cP)

Note 1 to entry: The higher viscosity specified addresses conditions encountered during a range of clinical procedures specific to the tubing pack.

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 tubing pack that may come in direct contact with the patient's 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 General

When tested in accordance with 5.3.1, the blood pathway shall not leak.

4.2.2 Dimensions

The dimensions of the tubing (e.g. inner diameter, wall thickness, segment lengths) shall conform to the specifications of the user.

4.2.3 Material properties

The tubing material shall be tested or specified by the manufacturer or extruder to determine that the material properties listed in this subclause conform to the manufacturer's specifications as reported in 6.4 b). Upon request, the manufacturer should make them available in a technical data sheet. The material properties include the following:

a) durometer hardness;

b) ultimate elongation;

c) tensile strength;

d) brittle point;

e) specific gravity;

f) tear strength.

4.3 Performance characteristics

4.3.1 Priming volume

The priming volume shall be measured or calculated and reported in 6.2 e). Results shall indicate the priming volume over the entire range of tubing size provided by the manufacturer. Testing shall be performed according to the manufacturer's protocol.

Some of these tests may be combined and performed at the same time.

4.3.2 Life to failure testing

The labelled anticipated lifetime of the roller pump boot tubing should be a figure not exceeding the lifetime of tubing as determined using the test specified in 5.4.1. The tubing shall be tested under the operating variables specified by the manufacturer in 6.2 c) for each available size and wall thicknesses of tubing. The results of these tests shall be reported as mean and standard deviation in 6.3 d).

4.3.3 Spallation

When tubing intended for use in a peristaltic pump is tested in accordance with 5.4.2, the spalled particles shall not exceed the level specified by the manufacturer.

4.3.4 Shelf life

When tested in accordance with 5.4.3, test results shall demonstrate the rated shelf life as specified by the manufacturer.

5 Tests and measurements

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 According to the intended clinical use of the tubing, the temperature of test liquids shall be 4 °C, 30 °C and 39 °C, or other temperatures to reflect typical and extreme use conditions.

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

Sterility and non-pyrogenicity shall be determined in accordance with the requirements of ISO 17665-1, ISO 11135, ISO 11137-1, ISO 11137-2 and ISO 14937, as applicable.

5.2.2 Biocompatibility

Biocompatibility shall be determined in accordance with the requirements of ISO 10993-1 and ISO 10993-11. If the product is sterilized with ethylene oxide, biocompatibility shall also be tested in accordance with the requirements of ISO 10993-7.

5.3 Physical characteristics

5.3.1 Blood pathway integrity

5.3.1.1 The test shall be performed at 37 °C with air or water at the appropriate pressures. The test shall be performed to ensure freedom from leaking.

5.3.1.2 Subject the tubing to a positive pressure of 1,5 times the manufacturer's rated pressure or, if no maximum pressure is specified, the test shall be performed at 152 kPa for 6 h or as long as it is specified by the manufacturer for clinical use. Using air pressure decay or visual inspection, check for leakage.

5.3.2 Connections

The connections shall withstand a pull force of 15 N for 15 s without separating. Testing shall be performed as specified in the manufacturer's protocol.

5.3.3 Tubing material property testing

Tubing material property testing shall be determined in accordance with the requirements of ISO 34-1, ISO 527-1, ISO 9352, ASTM D792-00, and ASTM D2240-04, as applicable or consistent with the requirements of the end user.

5.4 Performance characteristics

5.4.1 Tubing life

5.4.1.1 The test liquid shall be a blood analogue to simulate blood viscosity.

5.4.1.2 The manufacturer shall conduct the test with a conventional dual-roller pump, reservoir, tubing, measurement and control equipment specified by the manufacturer. Tubing of each internal diameter and wall thickness shall be tested. The operating variables of pump speed, back pressure, liquid temperature, and method of setting pump occlusion shall be described, monitored and kept constant over the course of the test.

5.4.1.3 A failure is a leak in the tubing wall.

5.4.2 Spallation in tubing used in roller pumps

5.4.2.1 The test circuit should incorporate two Y-connectors to accommodate a bypass that includes a fine filter to collect particles by circulating the entire test circuit volume in such a manner that all fluid is diverted through the filter.

5.4.2.2 The test liquid shall be glycerine solution to simulate blood viscosity and the test shall be conducted at temperatures intended for clinical use, pre-filtered through a 5 µm filter.

5.4.2.3 The minimum volume of fluid in the circuit shall be provided and actual volume contained at test onset shall be reported.

5.4.2.4 The flow rate(s) shall be reported, so that the volume/hour of fluid contacting the tubing wall can be estimated, as in accepted methods for quantifying wear debris generation.

5.4.2.5 The filter should be removed at the appropriate time point (e.g. 1 h, 2 h, or longer depending on specific application such as CPB or ECMO as described in 5.4.2.7) assuring that all the liquid contained in the circuit has passed through the filter at least once and a new filter inserted for the next time period.

Removed filters shall be dried and weighed and values recorded. In this manner, there will be minimal volume depletion of the total circulating volume.

5.4.2.6 The manufacturer shall test tubing of each internal diameter and wall thickness with the test equipment described in 5.4.1.2.

5.4.2.7 The circuit shall be run for 1 h intervals with the longest test lasting 6 h. For CPB, the circuit shall be sampled at 1 h, 2 h, 4 h, 6 h and for ECMO circuits, at least every 24 h thereafter for the length of time specified by the manufacturer.

5.4.2.8 The cumulative mass of spall particles shall be reported in milligrams recovered for each time point.

5.4.3 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 tubing pack

6.1.1 Information on the unit container

The following shall be given on the unit container:

a) the manufacturer's name and address;

b) the description of contents;

c) the model designation;

d) the statement on sterility and non-pyrogenicity;

e) the batch, lot or serial number designation;

f) the statement "read instructions before use" or equivalent symbol;

g) the special handling or storage conditions;

h) the statement on single-use;

i) the expiry date.

6.1.2 Information on the shipping container

The following shall be provided on the shipping container:

a) the manufacturer's name and address;

b) the description of contents, including number of units;

c) the model designation;

d) the statement on sterility and non-pyrogenicity;

e) the special handling, storage or unpacking instructions;

f) the batch, lot or serial number.

6.2 Information on the accompanying documents

Each shipping container shall contain an "Instructions for use" leaflet with the following information:

a) the manufacturer's address and telephone number (fax number and internet site address optional);

b) the model designation;

c) the operating instructions;

d) the placement, type and securing of tubing connections;

e) the volume per length for all sizes of tubing;

f) the pressure limitations for blood pathways;

g) the statement that the following are available upon request:

   1) sterilization method;

   2) list of the materials of the blood pathway.

6.3 Information in the accompanying documents in a prominent form

The following information shall be provided in a prominent form in the accompanying documents:

a) the inner diameter and wall thickness;

b) the pressure limitations;

c) the flow rate limitations;

d) the expected life under manufacturer's operating conditions, reported as mean and standard deviation;

e) the other device limitations, e.g. material incompatibility with known volatile anaesthetic agents, solvents, or disinfectants.

6.4 Information to be provided by manufacturer upon request

The following information shall be provided by the manufacturer upon request:

a) the results of the testing conducted under 5.3.3;

b) the physical characteristics (cited in 4.2.3);

c) the spallation data.

7 Packaging

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

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