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Extracorporeal systems for blood purification —

Part 2: Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters

Systèmes extracorporels pour la purification du sang —

Partie 2: Circuit sanguin extracorporel pour les hémodialyseurs, les hémodiafiltres et les hémofiltres

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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 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 WTO principles in the Technical Barriers to Trade (TBT), see the following URL: Foreword - Supplementary information

This document was prepared by Technical committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This first edition of ISO 8637-2:2018 cancels and replaces the third edition (ISO 8638:2010), which has been technically revised. The following changes have been made:

— Figure 1, Figure 2, and Figure 3 have been revised.

A list of all the parts in the ISO 8637 series can be found on the ISO website.

Introduction

This document is concerned with the extracorporeal blood circuit manufactured for single use and intended for use in conjunction with haemodialysers, haemodiafilters and haemofilters. The requirements specified in this document for the extracorporeal blood circuit will help to ensure safety and satisfactory function.

It was not found practicable to specify materials of construction. This document therefore requires only that materials have been tested and that the methods and results are made available upon request.

The dimensions of the connectors intended for connecting the extracorporeal blood circuit to a haemodialyser, haemodiafilter or haemofilter have been revised and specified to ensure compatibility with these devices, as specified in ISO 8637-1. The design and dimensions have been selected in order to minimize the risk of leakage of blood and ingress of air. Connectors with either fixed or loose locking shells are permitted.

This document reflects the consensus of physicians, manufacturers and other interested parties for devices that are approved for clinical use.

Extracorporeal systems for blood purification —

Part 2: Extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters

1 Scope

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this document.

This document specifies requirements for the blood circuit for devices used in extracorporeal blood filtration therapies such as, but not limited to, haemodialysis, haemodiafiltration, haemofiltration and transducer protectors (integral and non-integral) intended for use in such circuits.

This document does not apply to:

— haemodialysers, haemodiafilters or haemofilters;

— plasmafilters;

— haemoperfusion devices;

— vascular access devices;

— blood pumps;

— pressure monitors for the extracorporeal blood circuit;

— air detection devices;

— systems to prepare, maintain or monitor dialysis fluid;

— systems or equipment intended to perform haemodialysis, haemodiafiltration, haemofiltration or haemoconcentration.

NOTE 1 Requirements for haemodialysers, haemodiafilters, haemofilters and haemoconcentrators are specified in ISO 8637-1, and requirements for plasmafilters are specified in ISO 8637-3.

NOTE 2 Extracorporeal blood tubing sets can also be used for other extracorporeal therapies such as haemoperfusion, plasmafiltration and plasma adsorption.

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 7864, *Sterile hypodermic needles for single use — Requirements and test methods*

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 80369-7, *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 terminological databases for use in standardization at the following addresses:

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

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

3.1
air capture chamber
component intended to capture air and which can provide compliance to the blood circuit or allow pressure to be monitored

Note 1 to entry: Air capture chambers are also known as drip chambers, bubble traps or venous and arterial blood chambers.

3.2
extracorporeal blood circuit
blood tubing and integral accessory tubing, including fluid and infusion tubing, for attaching the extracorporeal blood circuit to pressure monitors and integral components

EXAMPLE (Of integral components.) Air capture chambers and transducer protectors.

3.3
fluid pathway
internal surfaces of the *extracorporeal blood circuit* (3.2)

3.4
labelling
written, printed, graphic or electronic matter that is affixed to a medical device or any of its containers or wrappers, or accompanies a medical device and which is related to identification, technical description and use of that medical device, but excluding shipping documents

3.5
pump segment
portion of the *extracorporeal blood circuit* (3.2) that is acted upon by the blood pump

3.6
transducer protector
pressure-transmitting sterile barrier
component of the *extracorporeal blood circuit* (3.2) that is intended to provide an interconnection between the extracorporeal blood circuit and the haemodialysis machine while allowing the pressure within the extracorporeal blood circuit to be measured by the machine

4 Requirements

4.1 Biological safety

Parts of the device that are intended to come into direct or indirect contact with blood shall be evaluated for freedom from biological hazards, in accordance with 5.2. Attention is drawn to the need to establish whether national regulations or national standards governing toxicology and biocompatibility testing exist in the country in which the device is produced and, if applicable, in the countries in which the device is to be marketed.

4.2 Sterility

All fluid contacting surfaces of the device, and the mating surfaces of all connectors integral to the device, shall be sterile. Conformity shall be verified in accordance with 5.3.

4.3 Non-pyrogenicity

The blood pathway of the device shall be non-pyrogenic. Conformity shall be verified in accordance with 5.4.

4.4 Mechanical characteristics

4.4.1 Structural integrity

The device shall be capable of withstanding a positive pressure of 1,5 times the manufacturer's recommended maximum pressure above atmospheric pressure and a negative pressure not exceeding 700 mmHg (93,3 kPa below atmospheric pressure) or the highest obtainable negative pressure if at high elevation, when tested in accordance with 5.5.1.

4.4.2 Connectors to haemodialyser, haemodiafilter or haemofilter

4.4.2.1 Except where the haemodialyser, haemodiafilter or haemofilter and the extracorporeal blood circuit are designed as an integral system, the dimensions of the connectors for the haemodialyser, haemodiafilter or haemofilter shall be as given in Figure 1. Conformity shall be verified in accordance with 5.5.2.

4.4.2.2 Connectors made of semi-rigid materials shall meet the performance requirements of ISO 80369-7.

4.4.3 Connectors to vascular access device

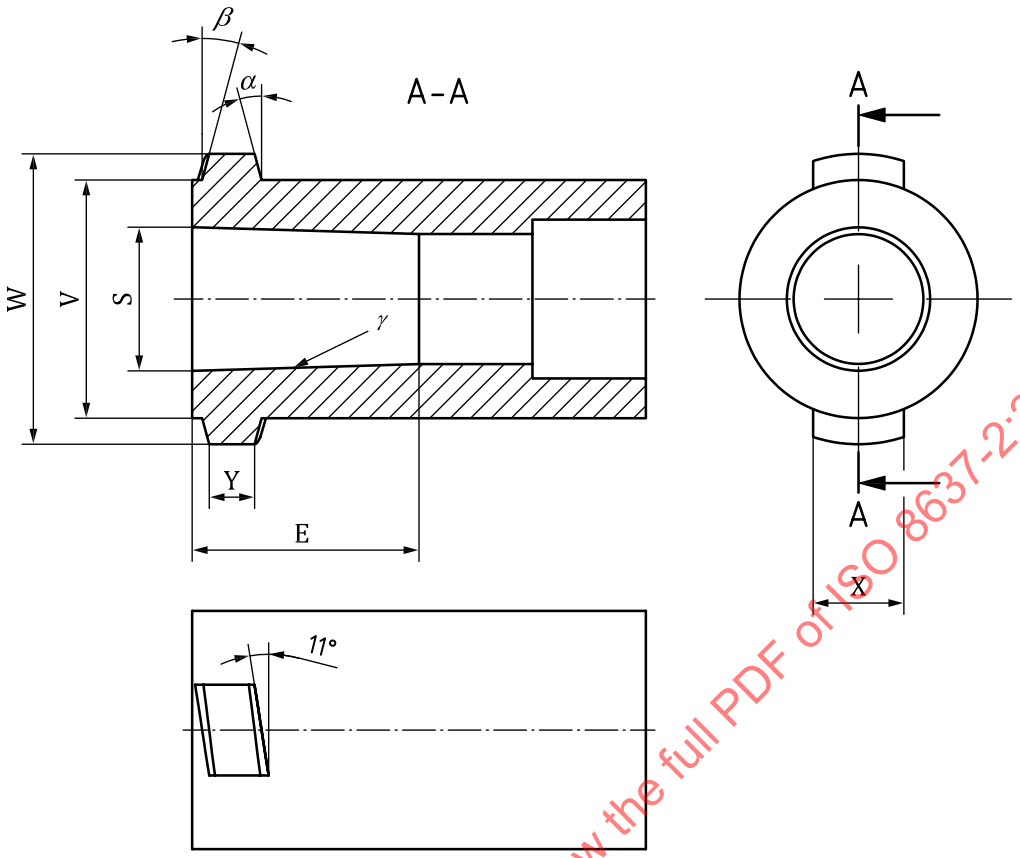
Except where the extracorporeal blood circuit and the vascular access device are an integral system, the dimensions of the connectors intended for connection to vascular access devices shall be a male 6 % (Luer) taper lock fitting (see ISO 80369-7). Connectors made of semi-rigid materials shall meet the performance requirements of ISO 80369-7. Conformity shall be verified in accordance with 5.5.3.

4.4.4 Connectors to ancillary components

All parts of the extracorporeal blood circuit intended for use with non-integral ancillary components, such as heparin lines, pressure-transducer lines, medication-administration lines and level-adjustment lines, shall terminate in fittings that meet the performance requirements of ISO 80369-7. Conformity shall be verified in accordance with 5.5.4.

4.4.5 Colour coding

The arterial patient-connection end shall be colour-coded red, and the venous patient-connection end shall be colour-coded blue. The coding shall be prominently displayed within 100 mm of the end of the tubing. Conformity to this requirement shall be verified in accordance with 5.5.5.



Symbol	Designation	Dimensions	Tolerances	Comments
α	angle of thread	15°		
β	angle of thread	15°		
γ	dimension taper rate	6:100		
δ	thread			Double thread pitch 8 mm
E	length of tapered region	10 mm or more		
S	cone diameter female	6,33 mm	+0,075 −0,0	Female connectors manufactured from soft or semi-rigid materials are not required to fulfill dimensional requirements but to comply with functional requirements.
V	core diameter	10,5 mm or less		
W	root diameter	12,8 mm	−0,20	
X	thread length	4 mm or more		
Y	thread width	2,0 mm	±0,10	

Figure 1 — Main fitting dimensions of extracorporeal blood circuit connector to blood ports of haemodialyser, haemodiafilter or haemofilter

4.4.6 Access ports

4.4.6.1 Needle access ports

Needle access ports shall not leak when tested in accordance with 5.5.6.1. The access ports shall be designed so as to minimize the risk of the needle piercing the tube completely and causing injury.

4.4.6.2 Needleless access ports

Needleless access ports shall not leak when tested in accordance with 5.5.6.2.

4.4.7 Blood pathway volume

The range of the blood pathway volume of the extracorporeal blood circuits shall be specified by the manufacturer. Conformity to this requirement shall be verified in accordance with 5.5.7.

NOTE The blood pathway volume is also known as the priming volume.

4.4.8 Air capture chamber fill level

The recommended fill level of the air capture chamber should be marked on the air capture chamber if that level is required for proper operation of some monitoring system. Conformity to this requirement shall be verified in accordance with 5.5.8.

4.4.9 Transducer protectors

4.4.9.1 Integral transducer protectors

Extracorporeal blood circuits supplied with integral transducer protectors shall be capable of preventing cross-contamination. The transducer protector shall be capable of maintaining a secure and leak-free connection to the haemodialysis machine when subjected to pressures of 1,5 times the manufacturer's recommended maximum pressure for the device. The machine side of the transducer protector shall be transparent (clear) to allow for visual inspection of blood contamination during use. Conformity to this requirement shall be in accordance with 5.5.9.

4.4.9.2 Non-integral transducer protectors

If not supplied as an integral component of the extracorporeal blood circuit, connectors shall be provided to allow the use of a transducer protector to prevent cross contamination. The transducer protector shall be capable of maintaining a secure and leak-free connection to the haemodialysis machine when subjected to pressures of 1,5 times the manufacturer's recommended maximum pressure for the device. The machine side of the transducer protector shall be transparent (clear) to allow for visual inspection of blood contamination during use. Conformity to this requirement shall be in accordance with 5.5.9.

4.4.10 Blood pathway flow dynamics

Extracorporeal blood pathways shall be designed to minimize harmful effects to the blood components. Conformity to this requirement shall be verified in accordance with 5.5.10.

4.4.11 Pump segment performance

The performance characteristics of the pump segment shall be evaluated over the range of inlet pressures (normally 0 mmHg to −250 mmHg).

Conformity to this requirement shall be verified in accordance with 5.5.11.

4.5 Expiry date

If the expiry date is given, it shall be validated. Accelerated stability studies are acceptable if real time data are not available. Conformity to this requirement shall be verified in accordance with 5.6.

4.6 Tubing compliance

The blood tubing shall be capable of being occlusively clamped by the venous line clamp of the dialysis delivery system(s) with which the extracorporeal blood circuit is intended to be used, as indicated in the labelling for the blood tubing. Conformity to this requirement shall be verified in accordance with 5.7.

5 Test methods

5.1 General

The performance characteristics specified in Clause 4 shall be determined prior to marketing a new type of device and shall be re-evaluated after changes in the device that might alter its performance.

The sample of devices shall be drawn at random from the manufacturer's production and shall have passed all applicable quality control steps, as well as sterilization, if applicable. They shall be prepared according to the manufacturer's recommendations as though they are to be used for a clinical procedure.

Measurements shall be made *in vitro* at (37 ± 1) °C. When the relationship between variables is non-linear, sufficient determinations shall be made to permit interpolation between the data points. The techniques of measurement are reference tests. Other test methods may be used, provided it can be shown that they are validated and of comparable precision and reproducibility.

The test systems shown do not indicate all the necessary details of practicable test apparatus. The design and construction of actual test systems and their establishment shall also address the many factors contributing to measurement error, including, but not limited to, pressure measurement errors due to static head effects and dynamic pressure drops; parameter stabilization time; uncontrolled temperature variations at non-constant flow rates; pH; degradation of test substances due to heat, light and time; degassing of test fluids; trapped air; and system contamination by foreign material, algae and bacteria.

5.2 Biological safety

The biological safety of devices that are intended to come into direct or indirect contact with the patient's blood shall be evaluated on samples of each new type of device prior to its marketing or after any change in the materials of construction of that type of device or after any change in the method of sterilization. Testing shall be carried out in accordance with ISO 10993-1, ISO 10993-4 or ISO 10993-7, as relevant.

5.3 Sterility

Conformity to 4.2 shall be verified by inspection of the device records that show that the device has been exposed to a validated sterilization process.

5.4 Non-pyrogenicity

Conformity to 4.3 shall be verified in accordance with ISO 10993-11.

5.5 Mechanical characteristics

5.5.1 Structural integrity

5.5.1.1 Positive pressure

Conformity to 4.4.1 (positive pressure) shall be determined by either of the following tests.

a) Fill the device with water at (37 ± 1) °C. Cap all connections with applicable caps. Subject the device to a pressure of 1,5 times the manufacturer's recommended maximum pressure. Maintain pressure for a minimum of 10 min and inspect for visible signs of leakage.

b) Cap all ports with applicable caps. Submerge the device in water at (37 ± 1) °C. Subject the lumen of the device to air pressure of 1,5 times the manufacturer's recommended maximum pressure. Maintain pressure for a minimum of 10 min and inspect the device for leakage of air bubbles.

5.5.1.2 Negative pressure

Conformity to 4.4.1 (negative pressure) shall be determined by either of the following tests.

a) Cap all ports with applicable caps. Submerge the device in a water bath at (37 ± 1) °C. Subject the device to 1,5 times the manufacturer's recommended maximum negative pressure or 700 mmHg (93,3 kPa below atmospheric pressure) or the highest obtainable sub-atmospheric pressure if at high elevation. Maintain pressure for a minimum of 10 min and inspect the device for visual signs of leakage.

b) Fill the device with water at (37 ± 1) °C. Cap all ports with applicable caps. Subject the lumen of the device to 1,5 times the manufacturer's recommended maximum negative pressure or 700 mmHg (93,3 kPa below atmospheric pressure) or the highest obtainable sub-atmospheric pressure if at high elevation. Maintain pressure for a minimum of 10 min and inspect the device for leakage of air bubbles.

5.5.2 Connectors to haemodialyser, haemodiafilter or haemofilter

Conformity to 4.4.2 shall be determined by inspection (see Figures 1, 2 and 3).

5.5.3 Connector to vascular access device

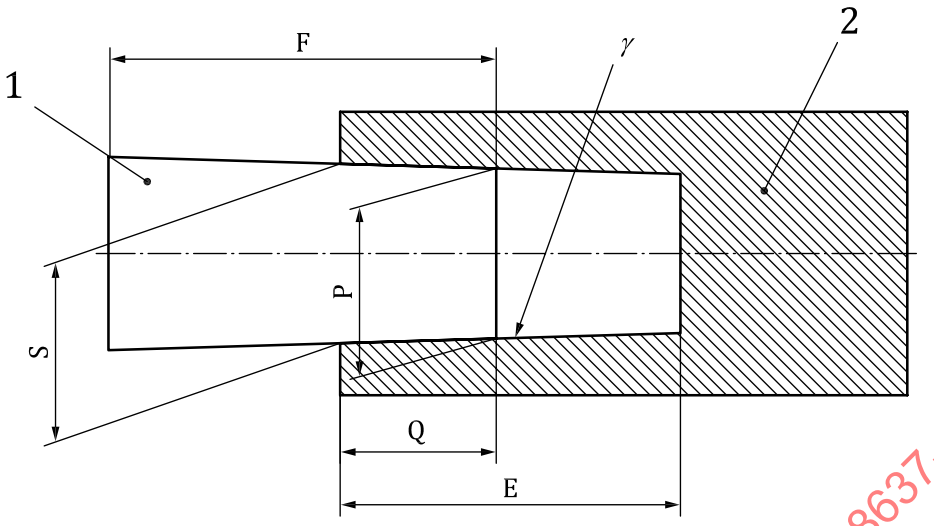
Conformity to 4.4.3 shall be determined by inspection (see ISO 80369-7).

5.5.4 Connectors to ancillary components

Conformity to 4.4.4 shall be determined by inspection (see ISO 80369-7).

5.5.5 Colour coding

Conformity to 4.4.5 shall be determined by inspection.



Symbol	Designation	Dimensions	Tolerances	Comments
1	outer cone			
2	inner cone			
γ	dimension taper rate	6:100		
P	cone diameter male	6 mm	±0,03	
S	cone diameter female	6,33 mm	+0,075 -0, 0	Female connectors manufactured from soft or semi-rigid materials need not fulfill dimensional requirements but comply with functional requirements.
Q	overlap	5 mm or more 7,26 mm or less		Based on values for P
E	length of thread	10 or more		
F	length of taper	9 or more		

Figure 2 — Gauge for measuring length of engagement of the male cone of blood inlet and outlet ports

5.5.6 Access ports

5.5.6.1 Needle access ports

Conformity to 4.4.6.1 shall be determined by the following procedure.

— Fill the portion of the extracorporeal blood circuit that contains the access port with water at (37 ± 1) °C and apply a pressure 1,5 times the maximum stated by the manufacturer [see 6.4 f) 1)]. Puncture the access port with a hypodermic needle, as stated by the manufacturer or, if no details are given, of outside diameter 0,8 mm (21 gauge) and in accordance with ISO 7864. Insert and withdraw the needle five times through the access port. Maintain the pressure for 6 h and visually inspect the device for the emergence of water.

— Using the same circuit, completely fill the device with degassed water at (37 ± 1) °C. Seal all ports except the port to which pressure is applied. Put the device under sub-atmospheric pressure, 1,5 times the manufacturer's recommended maximum negative pressure, unless that sub-atmospheric pressure

exceeds 700 mmHg or is not specified; in that case, apply a sub-atmospheric pressure of 700 mmHg and seal the apparatus. Access the port in accordance with the manufacturer's instructions. Access the port an additional 10 times over a 10 min period. Maintain the pressure for 6 h and visually inspect the device for the leakage of air into the tubing. The water may be circulated through the device.

5.5.6.2 Needleless access ports

Conformity to 4.4.6.2 shall be determined by the following procedure.

— Fill the portion of the extracorporeal blood circuit that contains the access port with water at (37 ± 1) °C and apply a pressure 1,5 times the maximum stated by the manufacturer [see 6.4 f) 1)]. Access the port in accordance with the manufacturer's instructions. Access the port an additional 10 times over a 10 min period. Maintain the pressure for 6 h and visually inspect the device for the emergence of water.

— Using the same circuit, completely fill the device with degassed water at (37 ± 1) °C. Seal all ports except the port to which pressure is applied. Put the device under sub-atmospheric pressure, 1,5 times the manufacturer's recommended pressure, unless that sub-atmospheric pressure exceeds 700 mmHg or is not specified; in that case, apply a sub-atmospheric pressure of 700 mmHg and seal the apparatus. Access the port in accordance with the manufacturer's instructions. Access the port an additional 10 times over a 10 min period. Maintain the pressure for 6 h and visually inspect the device for the leakage of air into the tubing. The water may be circulated through the device.

5.5.7 Blood pathway volume

Conformity to the 4.4.7 shall be verified by filling the blood pathway of the device with water and measuring the volume of the water needed to fill this pathway. The air capture chambers shall be filled to their normal operating level.

5.5.8 Air capture chamber fill level

Conformity to this marking shall be by visual inspection of the existence of a marking giving the normal operating level.

5.5.9 Transducer protectors

Conformity to 4.4.9.1 and 4.4.9.2 shall be verified by testing to withstand 1,5 times the maximum pressure specified by the manufacturer according to the following.

With the machine side open, fill the extracorporeal blood circuit side with water, pressurize the extracorporeal side to 1,5 times the manufacturer's recommended maximum pressure and hold for 1 h; examine for signs of leakage. Leakage shall not occur at the Luer connector, at the housing welds or through the membrane.

Visually inspect the device component to ensure Conformity to the connection requirements of 4.4.4.

Visually inspect the transducer for transparency of the machine side.

5.5.10 Blood pathway flow dynamics

Conformity to 4.4.10 shall be verified by review of the manufacturing risk management file for the device.

5.5.11 Pump segment performance

Conformity to 4.4.11 can be determined by evaluating the flow rate changes over time with a negative inlet pressure between 0 mmHg and −250 mmHg. The testing shall be performed over the range of blood flows recommended by the manufacturer with back-pressures. The results shall be used to give the recommendations in 6.4 f) 3).

Dimensions in millimetres

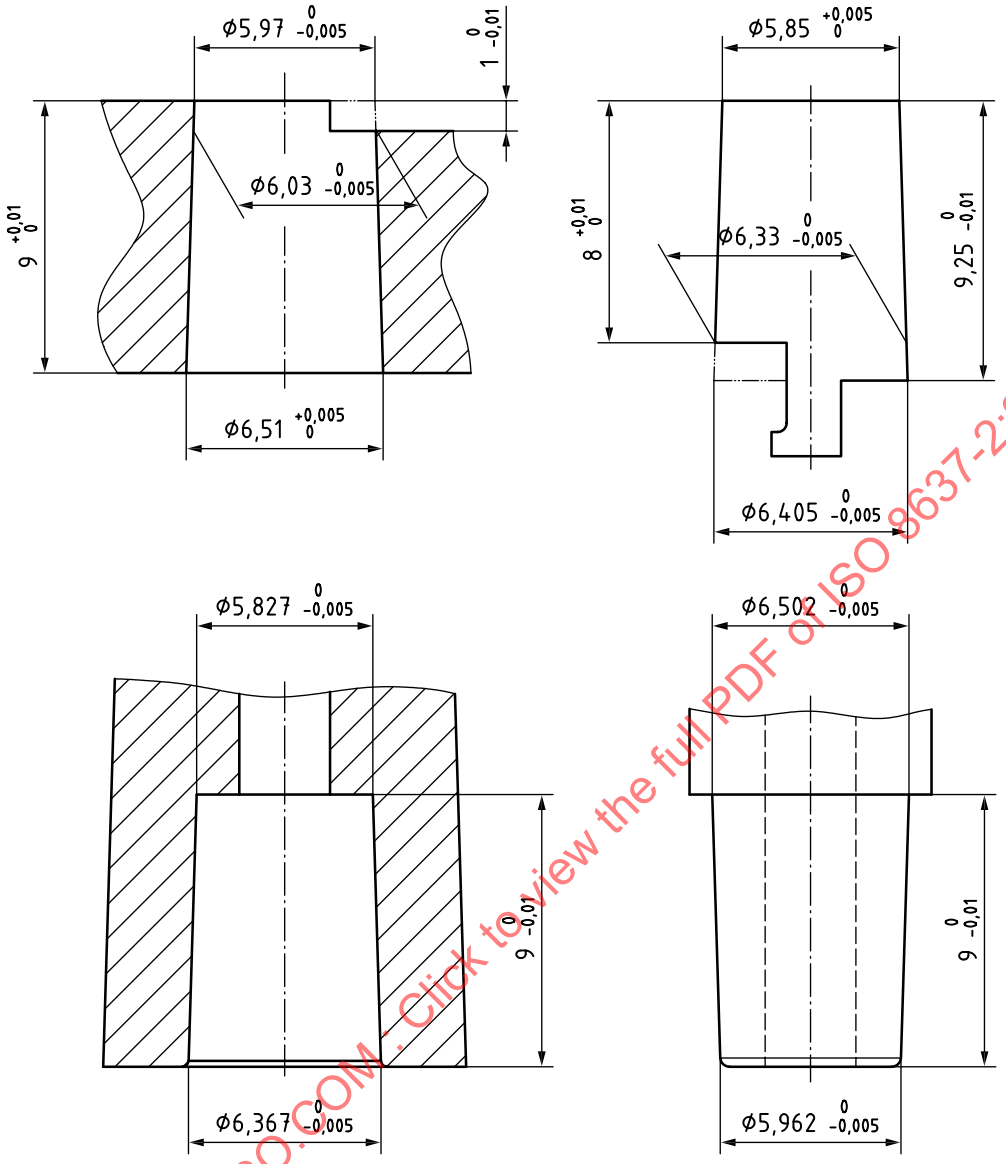


Figure 3 — Test device used for ISO blood port connectors

5.6 Expiry date

Conformity to 4.5 can be met by accelerated or real time testing of the device for biological safety, sterility and mechanical integrity after storage for a period corresponding to the expiry date.

5.7 Tubing compliance

Conformity to 4.6 can be verified by placing the tubing in the dialysis machine clamp for which the product will be labelled, and activating the clamp. The circuit shall then be pressurized to 1,5 times the manufacturer's recommended maximum pressure and observed for leakage past the clamp for 20 min. No leakage shall occur.

6 Labelling

6.1 Labelling on the device

The device shall be labelled with at least the following information:

a) red and blue markings at patient connection ends;

b) air capture chamber level markings, if appropriate.

Where symbols exist as shown in ISO 7000 and/or ISO 15223-1 these may be used as an alternative.

6.2 Labelling on unit containers

At least the following information shall be visible on or through the unit container:

a) the manufacturer's name and address;

b) the device proprietary name;

c) the manufacturer’s identifying code (such as the catalogue number or model number) for the device;

d) the batch lot or serial number designation;

e) the expiry date, stated as mm/yyyy , yyyy/mm or yyyy-mm-dd; where yyyy represents the year, mm the month, and dd the day;

f) the method of sterilization;

g) a statement of single use, if appropriate;

h) a statement of sterility and non-pyrogenicity; there are two possibilities:

   1) that the entire contents of the package are sterile;

   2) that the fluid pathways (blood and any fluid pathways connected to the blood pathway) are sterile;

i) the statement “Read the instructions before use”;

Instructions for use should include the statement or symbol “Do not use the tubing set if package is damaged.” If protective end caps are used for sterile protection, then the statement “Do not use the device if the protective end caps are not in place”;

j) if applicable and not provided as an integral part of the tubing set, a statement stating, “Caution, a transducer protector must be installed on each pressure monitoring line prior to patient use;

k) if applicable, the length and internal diameter of the pump segment.

Where symbols exist as shown in ISO 7000 and/or ISO 15223-1 these may be used as an alternative.

6.3 Labelling on the outer containers

At least the following information shall appear on the outer container which generally contains a number of devices:

a) the manufacturer's name and address;

b) the name and address of the distributor, if different from the information given under a), if applicable and in accordance with national requirements;