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Extracorporeal systems for blood purification —

Part 1: Haemodialysers, haemodiafilters, haemofilters and haemoconcentrators

Systèmes extracorporels pour la purification du sang —

Partie 1: Hémodialyseurs, hémodiafiltres, hémofiltres et hémoconcentrateurs

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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).

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 (see 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 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 the following URL: 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*.

This first edition of ISO 8637-1:2017 cancels and replaces the third edition of ISO 8637:2010 and ISO 8637:2010/Amd1:2013, which has been technically revised. The following changes have been done:

— 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 devices intended for haemodialysis, haemodiafiltration, haemofiltration and haemoconcentration in humans. The requirements specified in this document 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 which have been used have been tested and that the methods and results are made available upon request. There is no intention to specify, or to set limits on, the performance characteristics of the devices because such restrictions are unnecessary for the qualified user and would limit the alternatives available when choosing a device for a specific application.

The dimensions of the blood ports and the dialysis fluid or filtrate ports have been specified to ensure compatibility of the device with the extracorporeal blood circuit specified in ISO 8637-2. The design and dimensions have been selected in order to minimize the risk of leakage of blood and the ingress of air.

This document reflects the consensus of physicians, manufacturers and other interested parties for devices that are approved for clinical use. Conformance with this document is voluntary and it does not supersede any national regulation.

Extracorporeal systems for blood purification —

Part 1: Haemodialysers, haemodiafilters, haemofilters and haemoconcentrators

1 Scope

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

This document specifies requirements for haemodialysers, haemodiafilters, haemofilters and haemoconcentrators, hereinafter collectively referred to as "the device", for use in humans.

This document does not apply to:

— extracorporeal blood circuits;

— 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;

— reprocessing procedures and equipment.

NOTE Requirements for the extracorporeal blood circuit for haemodialysers, haemodiafilters and haemofilters are specified in ISO 8637-2.

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 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 http://www.electropedia.org/

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

3.1
blood compartment
part of a *haemodialyser* (3.12), *haemodiafilter* (3.10), *haemofilter* (3.14) or *haemoconcentrator* (3.9) through which blood is intended to pass

Note 1 to entry: For hollow-fibre devices, the blood compartment includes the volume of the hollow fibres plus the headers.

3.2
clearance
volume of a solution from which a solute is completely removed per unit time

3.3
convection
transport of solutes across a semipermeable membrane, along with filtered fluid, caused by a pressure gradient or pressure differential across the membrane

3.4
dialysis fluid
aqueous fluid containing electrolytes and, usually, buffer and glucose, which is intended to exchange solutes with blood during *haemodialysis* (3.13) or *haemodiafiltration* (3.11)

Note 1 to entry: The term "dialysis fluid" is used throughout this document to mean the fluid (made from dialysis water and concentrates) which is delivered to the haemodialyser or haemodiafilter by a dialysis fluid delivery system. Phrases such as "dialysate", "dialysis solution" or "dialysing fluid" can be used in place of dialysis fluid.

Note 2 to entry: The dialysis fluid entering the haemodialyser or haemodiafilter is referred to as "fresh dialysis fluid", while the fluid leaving the haemodialyser or haemodiafilter is referred to as "spent dialysis fluid".

Note 3 to entry: Dialysis fluid does not include pre-packaged parenteral fluids used in some renal replacement therapies, such as haemodiafiltration and haemofiltration.

3.5
dialysis fluid compartment
part of a *haemodialyser* (3.12) or *haemodiafilter* (3.10) through which *dialysis fluid* (3.4) is intended to pass

3.6
diffusion
transport of solutes across a semipermeable membrane, caused by a concentration gradient

3.7
filtrate
fluid removed from the blood across the semipermeable membrane into the dialysis fluid or filtrate compartment of a *haemodialyser* (3.12), *haemodiafilter* (3.10), *haemofilter* (3.14) or *haemoconcentrator* (3.9), due to a pressure gradient (including the contributions of both hydrostatic and oncotic pressures) across the semipermeable membrane

3.8
haemoconcentration
process whereby plasma water and electrolytes are removed from diluted blood across a semipermeable membrane

3.9
haemoconcentrator
device intended to perform *haemoconcentration* (3.8)

3.10
haemodiafilter
device intended to perform *haemodiafiltration* (3.11)

3.11
haemodiafiltration
form of renal replacement therapy in which the waste solutes are removed from blood by a combination of diffusion and enhanced convection through a high flux or high permeability membrane

Note 1 to entry: Diffusive solute removal is achieved using a dialysis fluid stream as in haemodialysis. Enhanced convective solute removal is achieved by adding ultrafiltration in excess of that needed to achieve the desired weight loss; fluid balance is maintained by the infusion of a replacement solution into the blood circuit either before (predilution haemodiafiltration) or after (post-dilution haemodiafiltration) or a combination of the two (mixed dilution haemodiafiltration).

3.12
haemodialyser
device intended to perform *haemodialysis* (3.13)

3.13
haemodialysis
form of renal replacement therapy in which waste solutes from the blood are removed primarily by diffusion across a semi permeable membrane contained in a haemodialyser in which the blood flows on one side of the membrane and dialysis fluid flowing on the other

Note 1 to entry: Fluid removal that is sufficient to achieve the desired weight loss is achieved by a hydrostatic pressure gradient across the membrane. This fluid removal provides some additional solute removal particularly for higher molecular weight compounds.

3.14
haemofilter
device intended to perform *haemofiltration* (3.15)

3.15
haemofiltration
a form of renal replacement therapy in which waste solutes are removed from the blood by convection

Note 1 to entry: Convective transport is achieved by ultrafiltration across a high flux membrane. Fluid balance is maintained by the infusion of a replacement solution into the blood either before the haemofilter (predilution haemofiltration) or after the haemofilter (post-dilution haemofiltration) or a combination of the two (mixed dilution haemofiltration).

Note 2 to entry: In haemofiltration there is no dialysis fluid stream.

3.16
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

3.17
sieving coefficient
ratio of a solute concentration in the filtrate to the simultaneous concentration of the same solute in the plasma

3.18
transmembrane pressure
TMP
p_{TM}
mean pressure exerted across a semipermeable membrane

Note 1 to entry: For practical reasons, the mean TMP is generally expressed as either:

— the difference between arithmetic means of inlet and outlet pressures of the blood and dialysis fluid compartments of a haemodialyser or a haemodiafilter

or

— the difference between the arithmetic mean of the inlet and outlet pressures of the blood compartment and the filtrate pressure of a haemofilter or a haemoconcentrator

3.19
ultrafiltration coefficient
permeability of membrane to water, generally expressed in millilitres per hour per millimetre of mercury

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. If the device is labelled for reuse, testing shall be performed after reprocessing following the manufacturer's instructions for use.

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

The blood pathway of the device shall be sterile. Compliance shall be verified in accordance with 5.3.

4.3 Non-pyrogenicity

The blood pathway of the device shall be non-pyrogenic. Compliance 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, when tested according to 5.5.1.

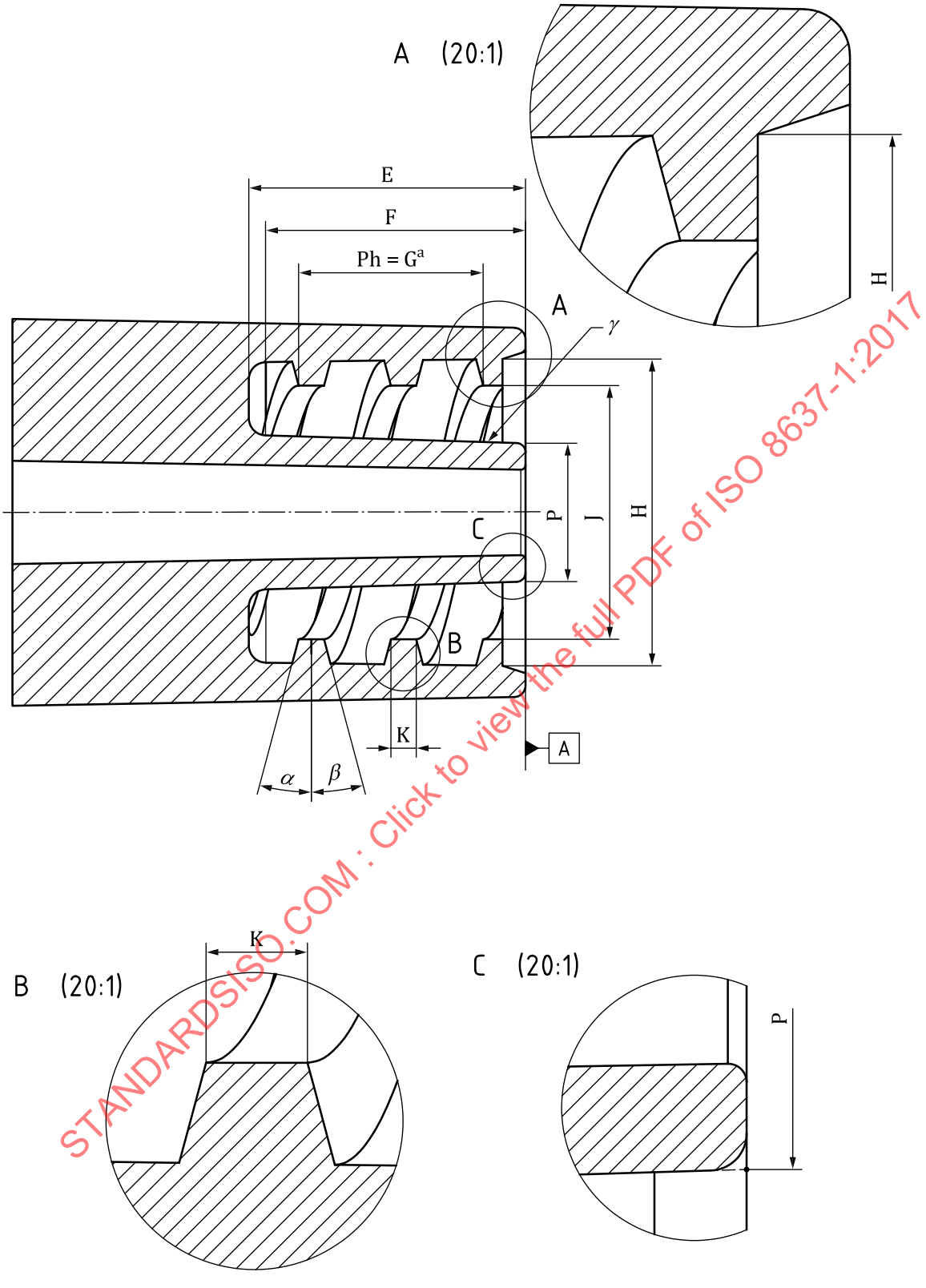
NOTE This requirement refers to the external case integrity of the device.

4.4.2 Blood compartment integrity

When exposing the blood compartment to a validated test procedure performed at 1,5 times the manufacturer's maximum recommended transmembrane pressure, the blood compartment shall not leak. Compliance with this requirement shall be verified in accordance with 5.5.2.

4.4.3 Haemodialyser, haemodiafilter and haemofilter blood compartment ports

Except where the haemodialyser, haemodiafilter or haemofilter and the extracorporeal blood circuit are designed as an integral system, the dimensions of the blood ports shall be as given in Figure 1. Compliance with this requirement shall be verified in accordance with 5.5.3.



Key

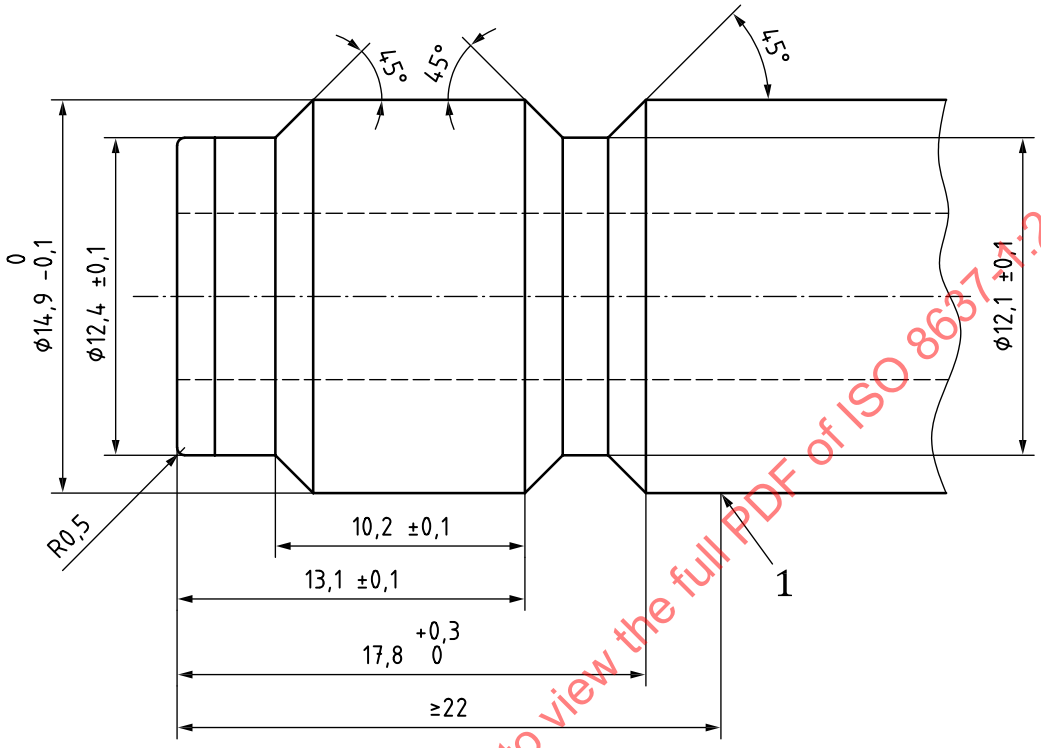
Symbol	Designation	Dimension in mm	Comments
α	Angle of thread	15°	—
β	Angle of thread	15°	—
γ	Dimension taper rate	6:100	—
E	Length of thread	10 or more	—
F	Length of tapered region	9 or more	—
G^a	Thread pitch	8	The superscript “a” of G^a means double thread.
H	Root diameter	13 or more	—
J	Crest diameter	11 +0,3 -0,2	Altered upper tolerance to accommodate different components and materials.
K	Thread crest width	1,1 ±0,25	Revised dimension and tolerances based on existing manufacturing practice.
P	cone diameter male plane of reference"A square"	6 ±0,03	This dimension to be measured as a projection on the front face. See Figure 1 (C).

Figure 1 — Main fitting dimensions of blood inlet and outlet ports

4.4.4 Haemodialyser and haemodiafilter dialysis fluid compartment ports

Except where the haemodialyser or haemodiafilter and the dialysis fluid circuit are designed as an integral system, the dimensions of the dialysis fluid compartment ports shall be as given in Figure 2. Compliance with this requirement shall be verified in accordance with 5.5.4.

Dimensions in millimetres



Key

1 necessary length and diameter for engagement with female connectors of dialysis fluid circuit

Figure 2 — Main fitting dimensions of dialysis fluid inlet and outlet ports

4.4.5 Haemofilter filtrate ports

Except where the haemofilter and the filtrate circuit are designed as an integral system, the filtrate ports of haemofilters shall comply either with Figure 2 or with the requirements of the Luer lock fitting of ISO 80369-7. Compliance with this requirement shall be verified in accordance with 5.5.5.

4.4.6 Haemoconcentrator blood and filtrate ports

The blood and filtrate ports of haemoconcentrators shall allow for a secure connection to the tubing which is to be used with the device. Compliance with this requirement shall be verified in accordance with 5.5.6.

4.5 Performance characteristics

4.5.1 Solute clearance of haemodialysers and haemodiafilters

The clearance of urea, creatinine, phosphate and vitamin B_{12} shall be determined in accordance with 5.6.1. Blood and dialysis fluid flow rates shall cover the manufacturer's specified range.

NOTE As a supplement, urea mass transfer area coefficent (*KoA*) results are included.

4.5.2 Sieving coefficient of haemodiafilters, haemofilters and haemoconcentrators

For haemodiafilters and haemofilters the sieving coefficient for albumin, inulin and β_2-microglobulin or myoglobin shall be determined in accordance with 5.6.2.

For haemoconcentrators the sieving coefficient for albumin shall be determined in accordance with 5.6.2

4.5.3 Ultrafiltration coefficient

The ultrafiltration coefficient shall be determined in accordance with 5.6.3. Testing shall be conducted over the manufacturer's specified range of transmembrane pressures and blood flow rates.

4.5.4 Volume of the blood compartment

The volume of the blood compartment shall be determined in accordance with 5.6.4.

If the blood compartment volume is stable or constant over the clinical range of pressures, a single measurement is sufficient. If the blood compartment volume varies with pressure, the blood compartment volume over the clinical range of pressures shall be established.

4.5.5 Pressure drop of the blood compartment

The pressure drop of the blood compartment shall be determined in accordance with 5.6.5.

4.6 Expiry date

The biological safety, sterility, performance data and mechanical integrity of the device shall be proven after storage for a period corresponding to the expiry date. Compliance shall be in accordance with 5.7.

5 Test methods

5.1 General

The performance characteristics specified in 4.5 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. If labelled for multiple uses, devices shall be tested for clearances and ultrafiltration coefficient after reprocessing according to the manufacturer's instructions to characterize the effects of the recommended cleaning agent and germicide on membrane 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 given in this document are reference tests. Other test methods may be used, provided they have been validated and shown to be precise and reproducible.

The test systems shown do not indicate all the necessary details of practicable test apparatus. The design and construction of actual test systems and the establishment of actual test systems 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 the 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.

NOTE Clause 5 contains tests that are of a type-testing nature, such as the ones described in 5.5.1, 5.5.3, 5.5.4, 5.6.1, 5.6.2, 5.6.3 and 5.6.4, which are carried out prior to marketing of a new device or when changes are made to the device or its manufacturing processes. Others are of a quality control nature, such as the ones described in 5.3, 5.4 and 5.5.2, which are repeated on a regular basis in accordance with quality management system requirements.

5.2 Biological safety

The biological safety of haemodialysers, haemodiafilters, haemofilters and haemoconcentrators 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. If labelled for multiple use, testing shall demonstrate the safety of the device before first use and after reprocessing according to the manufacturer's instructions. Testing shall be carried out in accordance with ISO 10993-1, ISO 10993-4, ISO 10993-7 or ISO 10993-11, as relevant.

5.3 Sterility

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

5.4 Non-pyrogenicity

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

5.5 Mechanical characteristics

5.5.1 Structural integrity

5.5.1.1 General

The requirements of 4.4.1 shall be verified by the following test methods.

5.5.1.2 Positive-pressure test

Completely fill the device with degassed water at (37 ± 1) °C. Seal all ports except the port to which pressure is applied. Apply a positive air pressure 1,5 times the manufacturer's recommended maximum pressure and seal the apparatus. After 10 min, record the pressure and visually examine the device for leaks.

Alternately a constant air pressure (1,5 times the manufacturer's recommended maximum pressure) can be applied and the device submerged in water to test for air leakage.

5.5.1.3 Negative pressure test

Completely fill the device with degassed water at (37 ± 1) °C. Seal all ports except the port to which pressure is applied. Place the device under sub-atmospheric pressure of 1,5 times the manufacturer's recommended maximum pressure, unless that sub-atmospheric pressure exceeds 700 mmHg or is not specified. In that case, apply a sub-atmospheric pressure of 700 mmHg (93,3 kPa) or the highest obtainable negative pressure if at high elevation.

Seal the apparatus and after 10 min, record the pressure and visually examine the device for leaks.

5.5.2 Blood compartment integrity

Compliance shall be determined by review of the validation records for the test procedure.

5.5.3 Haemodialyser, haemodiafilter and haemofilter blood compartment ports

Compliance with 4.4.3 shall be determined by inspection. See Figure 1 and Figure 3.

5.5.4 Haemodialyser and haemodiafilter dialysis fluid compartment ports

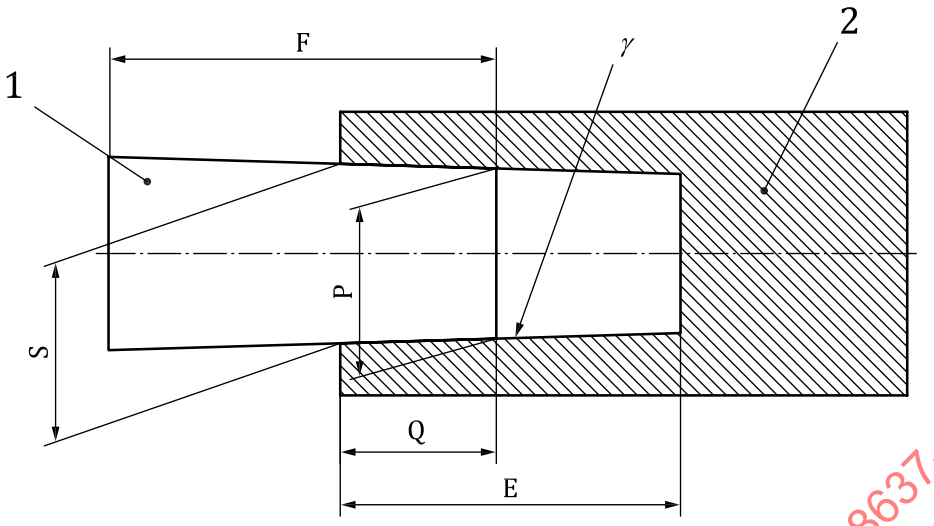
Compliance with 4.4.4 shall be determined by inspection. See Figure 2.

5.5.5 Haemofilter filtrate ports

Compliance with 4.4.5 shall be determined by inspection and shall meet the requirements of Figure 2 or the requirements of ISO 80369-7.

5.5.6 Haemoconcentrator blood and filtrate ports

Compliance with 4.4.6 shall be determined by inspection. Non locking connections shall not separate under an axial force of 15 N. For locking connections test method from small bore connections to be inserted.



Key

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 taper inner cone	10 or more		
F	length of taper	9 or more		

Figure 3 — Gauge for measuring length of engagement of the male cone of blood inlet and outlet ports

5.6 Performance characteristics

5.6.1 Clearance

5.6.1.1 General

Compliance with 4.5.1 shall be determined as stated below.

5.6.1.2 Test solutions

Perfuse the blood compartment with dialysis fluid, saline, phosphate-buffered saline or water containing one or more of the test substances listed in Table 1.

Perfuse the dialysis fluid compartment of haemodialysers and haemodiafilters with dialysis fluid, saline, phosphate-buffered saline or water.

NOTE The solutions used to perfuse the blood and dialysis fluid compartments are intended to be of similar ionic strength.

Table 1 — Reference concentrations of test solutions

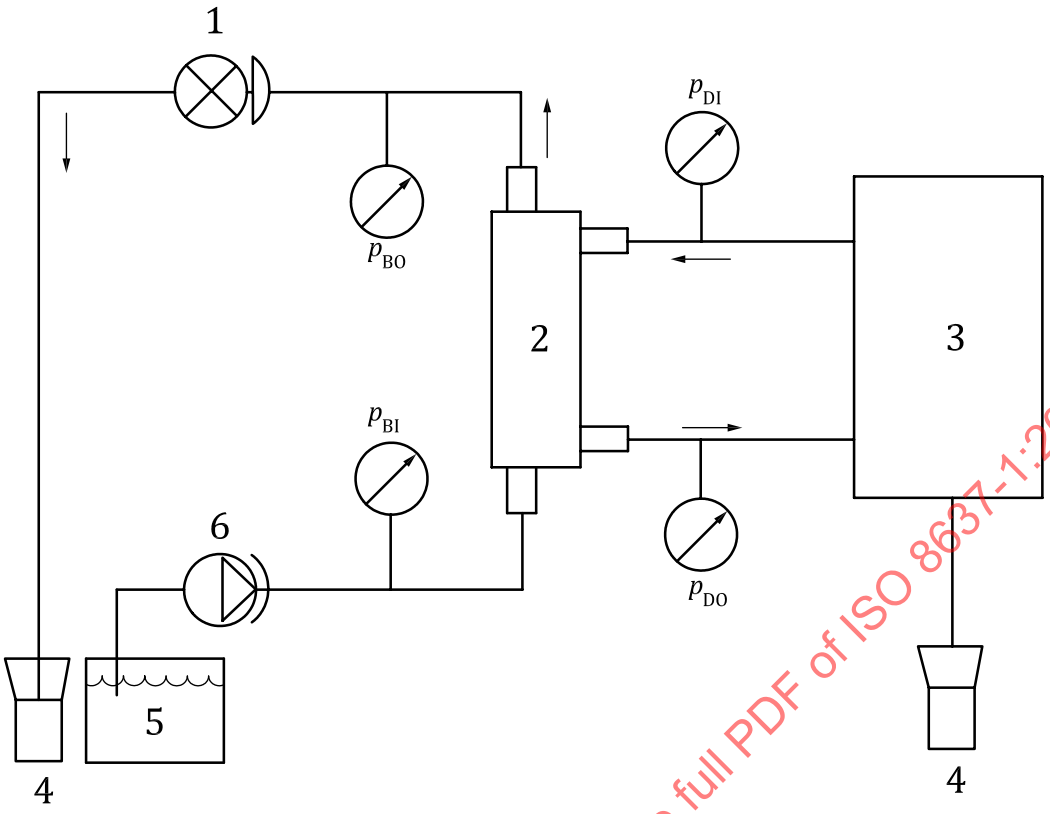
Solute	Molar concentration
Urea, mmol/L	15 to 35
Creatinine, µmol/L	500 to 1 000
Phosphate, mmol/L	1 to 5, adjusted to pH 7,4 ± 0,1
Vitamin B12, µmol/L	15 to 40
NOTE The concentrations of the solutes listed will vary based on the test procedure. The listed solutes are only given as a starting point.	

5.6.1.3 Clearance test procedure

Set up the test circuit as shown in Figure 4. Establish stable conditions (temperature, flow and pressure) for blood and filtrate flows and ensure all air is removed from the haemodialyser or haemodiafilter. Collect test samples after steady state has been reached, over the specified range of blood and dialysis fluid flow rates. The ultrafiltration rate shall be stated for each condition. Analyse samples and calculate clearance in accordance with Formula (1).

NOTE 1 Although Figure 4 shows flow entering the blood compartment at the bottom of the haemodialyser or haemodiafilter, the test can also be performed with flow entering the blood compartment at the top of the haemodialyser or haemodiafilter, provided the flows through the blood and dialysis fluid compartments remain counter-current. The test can also be performed with the haemodialyser or haemodiafilter in the horizontal position, provided that configuration has been shown to produce equivalent results to those obtained with the haemodialyser or haemodiafilter in the vertical position.

NOTE 2 A practical method of confirming the reliability of the measurement is to monitor the mass balance error.



Key

1	pressure control
2	haemodialyser or haemodiafilter
3	dialysis fluid supply system with ultrafiltration controller
4	waste
5	test solution reservoir
6	blood pump
p_{BI}	blood pressure, in
p_{BO}	blood pressure, out
P_{DI}	dialysis fluid pressure, in
P_{DO}	dialysis fluid pressure, out

Figure 4 — Diagram of open-loop system for measuring clearance of haemodialyser or haemodiafilter

5.6.1.4 Equation for calculating clearance

The clearance for haemodialysis and haemodiafiltration, K, is calculated using Formula (1).

$$K = \left(\frac{c_{BI} - c_{BO}}{c_{BI}} \right) q_{BI} + \frac{c_{BO}}{c_{BI}} q_F \quad (1)$$

In the Formula, it is necessary to use the same units of measurement for c_{BI} and c_{BO}.

where

c_{BI} is the concentration of solute on the blood inlet side of the haemodialyser or haemodiafilter;

c_{BO} is the concentration of solute on the blood outlet side of the haemodialyser or haemodiafilter;

q_{BI} is the blood flow rate at the inlet of the device;

q_F is the filtrate flow rate (ultrafiltration rate).

5.6.2 Sieving coefficient of haemodiafilters, haemofilters and haemoconcentrators

5.6.2.1 General

Compliance with 4.5.2 shall be determined in accordance with the test described below.

5.6.2.2 Test solution

The test fluid shall be anticoagulated human or bovine plasma with a protein content of (60 ± 5) g/L or anticoagulated whole blood with a haematocrit of (32 ± 3) % and a plasma protein content of (60 ± 5) g/L.

Perfuse the blood compartment with a test fluid containing one or more of the substances listed in 4.5.2.

5.6.2.3 Sieving coefficient test procedure

Set up the test circuit as shown in Figure 5. Establish stable conditions (temperature, flow and pressure) for blood and filtrate flows and ensure all air is removed from the haemodiafilter, haemofilter or haemoconcentrator. Adjust the ultrafiltration rate to cover the manufacturer's specified range. Collect paired test samples of blood and filtrate fluid flows. Calculate sieving coefficient in accordance with Formula (2).

NOTE Although Figure 5 shows flow entering the blood compartment at the bottom of the haemodiafilter, haemofilter or haemoconcentrator, the test can also be performed with flow entering the blood compartment at the top of the haemodiafilter, haemofilter or haemoconcentrator. The test can also be performed with the haemodiafilter, haemofilter or haemoconcentrator in the horizontal position, provided that configuration has been shown to produce equivalent results to those obtained with the haemodiafilter, haemofilter or haemoconcentrator in the vertical position.

5.6.2.4 Equation for sieving coefficient

The sieving coefficient, S, is calculated using Formula (2):

$$S = \frac{2c_F}{(c_{BI} + c_{BO})} \quad (2)$$

where

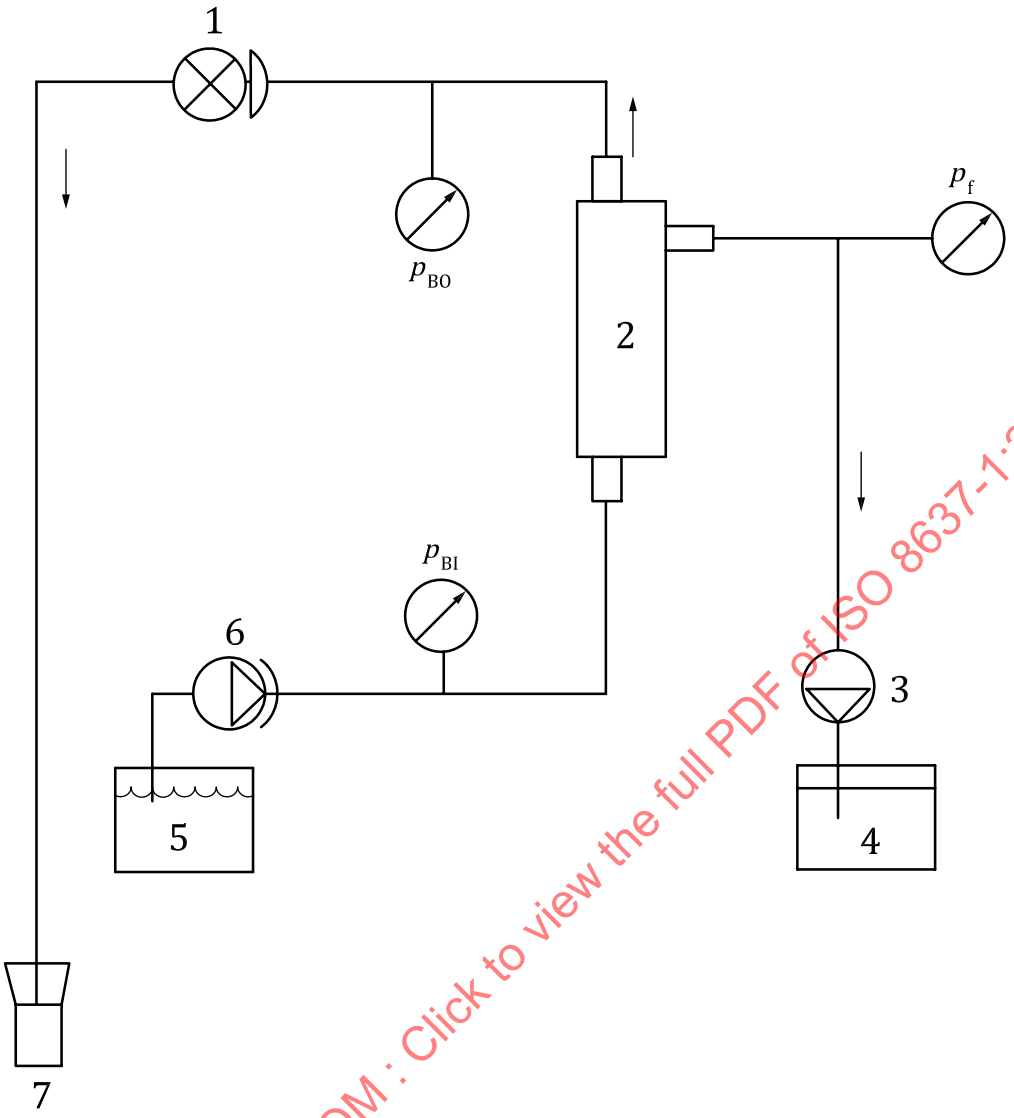
S is the sieving coefficient;

c_{BI} is the concentration of solute on the blood inlet side of the haemodiafilter, haemofilter or haemoconcentrator;

c_{BO} is the concentration of solute on the blood outlet side of the haemodiafilter, haemofilter or haemoconcentrator;

C_F is the concentration of the solute on the filtrate side of the haemodiafilter, haemofilter or haemoconcentrator.

In Formula (2) it is necessary to use the same units of concentration for C_{BI}, C_{BO} and C_F.



Key

1	pressure control	6	blood pump
2	haemodialyser, haemodiafilter, haemofilter haemoconcentrator	or7	waste
3	filtrate pump	p_{BO}	blood pressure, out
4	filtrate	p_{BI}	blood pressure, in
5	test solution reservoir	P_F	filtrate pressure

Figure 5 — Diagram of system for measuring ultrafiltration or sieving coefficients of a haemodialyser, haemodiafilter, haemofilter or haemoconcentrator

5.6.3 Ultrafiltration coefficient

5.6.3.1 Test solution

The test solution for haemodialysers, haemodiafilters and haemofilters shall be anticoagulated bovine or human blood, with a haematocrit of (32 ± 3) % and a protein content of (60 ± 5) g/L. For haemoconcentrators, a test solution of anticoagulated bovine or human blood, with a haematocrit of (25 ± 3) % and a protein content of (50 ± 5) g/L may be used.

No fluid is to perfuse the dialysis fluid or filtrate compartment.

5.6.3.2 Ultrafiltration coefficient test procedure

Set up the test circuit as shown in Figure 5. Establish stable conditions (temperature, flow and pressure) for blood and filtrate flows and ensure all air is removed from the haemodiafilter, haemofilter or haemoconcentrator. Measure the ultrafiltration flow rate over the manufacturer's specified range. Calculate the ultrafiltration coefficient as the slope of the regression line between filtration flow rate and transmembrane pressure, taking oncotic pressure into account.

NOTE The relationship between filtration flow rate and transmembrane pressure can deviate from linearity at high transmembrane pressures and attain a constant value despite increasing transmembrane pressure. This, plateau represents the maximum filtration flow rate for the device.

5.6.4 Volume of the blood compartment

For hollow-fibre devices, the blood compartment volume can be calculated by utilizing the dimensions and the number of fibres in the bundle. If the membrane is known to significantly change dimensions after wetting, the following alternative method should be used.

Alternately, fill blood compartment volume with a liquid that is easily removable but will not pass through the membrane. Measure the volume needed to fill the blood compartment.

If the volume of the blood compartment of the device varies with pressure, perform the measurements over a specified range of transmembrane pressures, corresponding to anticipated clinical pressures.

5.6.5 Pressure drop of the blood compartment

5.6.5.1 General

Compliance with 4.5.5 shall be determined in accordance with the test described below.

5.6.5.2 Test fluids

Fill the blood compartment with a test solution of anticoagulated bovine or human blood, with a haematocrit of (32 ± 3) % and a protein content of (60 ± 5) g/L.

Fill the dialysis fluid or filtrate compartment with normal dialysis fluid or saline.

5.6.5.3 Pressure drop test procedure

Establish blood flow rate. Read the inlet and outlet pressures of the blood compartment. Determine the pressure drop. Repeat over the manufacturer's specified range of blood flow rates.

For plate dialysers, it is also necessary to establish dialysis fluid flow rates and measure pressures and blood flow rates.

5.7 Expiry date

Compliance with 4.6 can be met by accelerated or real time testing for biological safety, sterility, performance data and mechanical integrity of the device after storage for a period corresponding to the expiry date.

6 Labelling

6.1 Labelling on the device

The device label shall contain the following information:

a) the manufacturer's name;

b) the proprietary device name;

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

d) the batch, lot or serial number designation;

e) the direction of blood flow, and the dialysis fluid flow, if applicable (colour coding can be used to distinguish between inlet to the device and outlet from the device);

f) the maximum transmembrane pressure;

g) 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;

h) the method of sterilization;

i) a statement of single use, if appropriate.

NOTE Where symbols exist as shown in ISO 7000 and/or ISO 15223-1 these can 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 three possibilities:

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

   2) that the fluid pathways (blood and dialysis fluid) are sterile;

   3) that only the blood pathway is sterile;

i) the statement "Read the instructions before use";

j) if applicable, a statement that the device must be used with a dialysis machine incorporating ultrafiltration control.

NOTE 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;

