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Water for haemodialysis and related therapies

Eau pour hémodialyse et thérapies apparentées

[Revision of first edition (ISO 13959:2002)]

ICS 11.040.40

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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.

ISO 13959 was prepared by Technical Committee ISO/TC 150, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition cancels and replaces the first edition, which has been technically revised.

Introduction

Assurance of adequate water quality is one of the most important aspects of ensuring a safe and effective delivery of haemodialysis, haemodiafiltration or haemofiltration.

This International Standard contains minimum requirements, chemical and microbiological, for the water to be used for preparation of dialysis fluids, concentrates, and for the reuse of haemodialyzers and the necessary steps to assure compliance with those requirements. Haemodialysis and haemodiafiltration can expose the patient to more than 500 litres of water per week across the semi-permeable membrane of the haemodialyser or haemodiafilter. Healthy individuals seldom have a weekly oral intake above 12 litres. This near 40-fold increase in exposure requires control and monitoring of water quality to avoid excesses of known or suspected harmful substances. Since knowledge of potential injury from trace elements and contaminants of microbiological origin over long periods is still growing and techniques for treating drinking water are continuously developed, this International Standard will evolve and be refined accordingly. The physiological effects attributable to the presence of organic contaminants in dialysis water are important areas for research. At the time this International Standard was published it was premature to specify threshold values for organic contaminants below those published by various regulatory authorities.

The final dialysis fluid is produced from concentrates or salts manufactured, packaged, and labelled according to ISO 13958, *Concentrates for haemodialysis and related therapies*, mixed with water meeting the requirements of this standard. Operation of water treatment equipment and haemodialysis systems, including ongoing monitoring of the quality of water used to prepare dialysis fluids, and handling of concentrates and salts are the responsibility of the haemodialysis facility or addressed in other ISO standards. Haemodialysis professionals make choices about the various applications (haemodialysis, haemodiafiltration, haemofiltration) and should understand the risks of each and the requirements for safety for fluids used for each.

This International Standard is directed towards manufacturers and providers of water treatment systems and also to haemodialysis facilities.

Water for haemodialysis and related therapies

1 Scope

This International Standard specifies minimum requirements for water to be used in the preparation of concentrates, dialysis fluids for haemodialysis, haemodiafiltration and haemofiltration and for the reprocessing of haemodialysers.

This standard does not address the operation of water treatment equipment nor the final mixing of treated water with concentrates to produce the dialysis fluids used in such therapies. That operation is the sole responsibility of dialysis professionals.

This International Standard does not apply to dialysis fluid regenerating systems.

2 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

2.1
action level
concentration of a contaminant at which steps should be taken to interrupt the trend toward higher, unacceptable levels

2.2
chlorine, total
sum of free and combined chlorine

NOTE chlorine can exist in water as dissolved molecular chlorine (free chlorine) or in chemically combined forms (combined chlorine). Where chloramine is used to disinfect water supplies, chloramine is usually the principal component of combined chlorine.

2.3
CFU
colony-forming unit
organism capable of replicating to form a distinct, visible colony on a culture plate

NOTE In practice, a colony can be formed by a group of organisms.

2.4
dialysis fluid
aqueous fluid containing electrolytes, buffer, and, usually, glucose, which is intended to exchange solutes with blood during haemodialysis

NOTE 1 The words “dialysis fluid” are used throughout this document to mean the fluid made from dialysis water and concentrates that is delivered to the dialyser by the dialysis fluid supply system. Such phrases as “dialysate” or “dialysis solution” can be used in place of dialysis fluid.

NOTE 2 In some cases, glucose is also known as dextrose.

NOTE 3 Dialysis fluid does not include prepackaged parental fluids used in haemodiafiltration.

2.5
dialysis water
water that has been treated to meet the requirements of this standard and which is suitable for use in haemodialysis applications, including the preparation of dialysis fluid, reprocessing of dialysers, preparation of concentrates and preparation of substitution fluid for online convective therapies

2.6
endotoxin
major component of the outer cell wall of gram-negative bacteria

NOTE Endotoxins are lipopolysaccharides, which consist of a polysaccharide chain covalently bound to lipid A. Endotoxins can acutely activate both humoral and cellular host defences, leading to a syndrome characterized by fever, shaking, chills, hypotension, multiple organ failure, and even death if allowed to enter the circulation in a sufficient dose (see also **pyrogen**).

2.7
EU
endotoxin units
units assayed by the *Limulus amoebocyte lysate* (LAL) method when testing for endotoxins

NOTE 1 Because the activity of endotoxins depends on the bacteria from which they are derived, their activity is referred to a standard endotoxin.

NOTE 2 In some countries, endotoxin concentrations are expressed in international units (IU). Since the 1983 harmonization of endotoxin assays, EU and IU are equivalent.

2.8
feed water
water supplied to a water treatment system or an individual component of the system

2.9
LAL
***Limulus* amoebocyte lysate test**
assay used to detect endotoxin

NOTE The detection method uses the chemical specific response of the horseshoe crab (*Limulus polyphemus*) to endotoxin.

2.10
microbial
referring to microscopic organisms, bacteria, fungi, and so forth

2.11
microbial contamination
contamination with any form of microorganism (e.g. bacteria, yeast, fungi, and algae) or with the by-products of living or dead organisms such as endotoxins, exotoxins, and microcystin (derived from blue-green algae)

2.12
pyrogen
fever-producing substance.

NOTE Pyrogens are most often lipopolysaccharides of gram-negative bacterial origin (see also **endotoxin**).

3 Dialysis water requirements

3.1 Dialysis water verification and monitoring

The quality of the dialysis water, as specified below, shall be verified upon installation of a water treatment system. Monitoring of the dialysis water quality shall be carried out thereafter.

3.2 Microbiological requirements

Total viable microbial counts in dialysis water shall be less than 100 CFU/ml, or as required by national legislation or similar. An action level shall be set based on knowledge of the microbial dynamics of the system. Typically, the action level will be 50 % of the maximum allowable level.

Endotoxin content in dialysis water shall be less than 0,25 EU/mL, or as required by national legislation or similar.

NOTE See A.1 for a history of these requirements.

3.3 Chemical contaminants

Dialysis water shall not contain chemicals at concentrations in excess of those in Tables 1 and 2, or as required by national legislation or similar.

NOTE See A.2 for explanation of values supplied.

Where the dialysis water is used for the reprocessing of haemodialysers, (cleaning, testing and mixing of disinfectants) the user is cautioned that the dialysis water shall meet this standard. The dialysis water should be measured at the input to the dialyser reprocessing equipment.

Table 1 — Maximum allowable levels of toxic chemicals and dialysis fluid electrolytes in dialysis water

	Contaminant	**Maximum Concentration (mg/L)**[b)]
Contaminants with documented toxicity in haemodialysis		
	Aluminium	0,01
	Total chlorine	0,1
	Copper	0,1
	Fluoride	0,2
	Lead	0,005
	Nitrate (as N)	2
	Sulphate	100
	Zinc	0,1
Electrolytes normally included in dialysis fluid		
	Calcium	2 (0,05 mmol/L)
	Magnesium	4 (0,15mmol/L)
	Potassium	8 (0,2 mmol/L)
	Sodium	70 (3,0 mmol/L)

[a)] The physician has the ultimate responsibility for ensuring the quality of water used for dialysis.

[b)] Unless otherwise noted.

Table 2 — Maximum allowable levels of trace elements in dialysis water

Contaminant	Maximum Concentration (mg/L)
Antimony	0,006
Arsenic	0,005
Barium	0,1
Beryllium	0,0004
Cadmium	0,001
Chromium	0,014
Mercury	0,0002
Selenium	0,09
Silver	0,005
Thallium	0,002

4 Tests for compliance with chemical and microbiological requirements

4.1 Microbiology of dialysis water

Samples shall be collected where a dialysis machine connects to the water distribution loop, from a sample point in the distal segment of the loop, or where water enters into a mixing tank.

Samples shall be assayed within 4 h of collection, or be immediately refrigerated and assayed within 24 h of collection on a regular schedule. Total viable counts (standard plate counts) shall be obtained using conventional microbiological assay procedures (pour plate, spread plate, membrane filter techniques). Membrane filtration is the preferred method for this test. The calibrated loop technique is not accepted.

Culture media should be tryptone glucose extract agar (TGEA), Reasoners 2A (R2A), or other media that can be demonstrated to provide equivalent results. Blood agar and chocolate agar shall not be used. Incubation temperatures of 17° C – 23° C and incubation time of 168 h (7 days) are recommended. Other incubation times and temperatures may be used if it can be demonstrated that they provide equivalent results. No method will give a total microbial count.

The presence of pyrogens shall be determined by the *Limulus* amoebocyte lysate (LAL) assay for endotoxins. Other test methods may be used if it can be demonstrated that they provide equivalent results.

4.2 Chemical contaminants test methods

Compliance with the requirements listed in Table 1 can be shown by using chemical analysis methods referenced in the American Public Health Association's *Standard methods for the examination of water and wastewater*, methods referenced in the U.S. Environmental Protection Agency's *Methods for the Determination of metals in environmental samples*, and/or other equivalent analytical methods.

Compliance with the requirements listed in Table 2 can be shown in one of three ways:

— Where such testing is available, the individual contaminants in Table 2 can be determined using chemical analysis methods referenced in the American Public Health Association's *Standard methods for the examination of water and wastewater*, methods referenced in the U.S. Environmental Protection Agency's *Methods for the Determination of metals in environmental samples*, and/or other equivalent analytical methods.

