INTERNATIONAL STANDARD

ISO 13959

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Water for haemodialysis and related therapies

Eaux pour hémodialyse et thérapies apparentées

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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 3.

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 International Standard may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

International Standard ISO 13959 was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants*.

Introduction

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

Haemodialysis and haemodiafiltration may expose the patient to more than 300 l of water per week across the semi-permeable membrane of the haemodialyser or haemodiafilter. Healthy individuals seldom have a weekly oral intake above 12 l. This near 30-fold increase in exposure requires control and monitoring of water quality to avoid excesses of known or suspected harmful elements. The water to be used for the preparation of dialysing fluid needs treatment to achieve the required quality. Such a water treatment system may include various components such as water softeners, sediment filters, reverse osmosis units, deionization units, ultrafilters, microfilters, carbon filters, ultraviolet disinfection units and storage tanks. The components of the system will be determined by the quality of feed water and the ability of the overall system to produce and maintain an acceptable product water.

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 being developed, this International Standard will evolve and be refined accordingly.

This International Standard contains minimum chemical and microbiological requirements for the water to be used for the preparation of dialysing fluids and the necessary steps to assure compliance. Basic criteria for feed water are included.

The physiological effects attributable to the presence of organic contaminants in product water is an important area for research. At the time of publication of this International Standard it is premature to specify threshold values below those published by various regulatory authorities. Users of this International Standard should be aware of the potential for problems if organic contaminants are present. The total concentration of organic contaminants may be monitored by measurement of the Total Organic Carbon (TOC). TOC does not indicate the concentration of a specific contaminant. Specific water treatment may be a concern for areas with known high concentrations of organic contaminants in feed water.

The final dialysing fluids are produced from concentrates manufactured, packaged and labelled according to ISO 13958, mixed with large proportions of water according to this International Standard. Operation of water treatment equipment and haemodialysis systems and handling of concentrates are the responsibility of the haemodialysis facility.

Because the final mixed dialysing fluid is not within the control of manufacturers, this International Standard cannot address those vital clinical technical processes. Haemodialysis professionals make choices about the various applications (haemodialysis, haemodiafiltration, haemofiltration) and need to understand the risks of each and the requirements for safety for fluids used for each.

Where the product water is used for the reprocessing (cleaning, testing and mixing of disinfectants) of haemodialysers, the user should ensure that the product water conforms to this International Standard. The product water should be measured at the input to the reuse equipment.

This International Standard is directed towards manufacturers 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 and dialysing fluids for haemodialysis and haemodiafiltration.

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

This International Standard is not applicable to dialysing-fluid regenerating systems.

2 Terms and definitions

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

2.1
dialysing fluid
dialysis fluid
dialysate
fluid which is intended to exchange solutes with blood during haemodialysis or haemodiafiltration

NOTE It does not include prepackaged parental fluids used in haemodiafiltration.

2.2
feed water
water supplied to a water treatment system

2.3
product water
water which has been processed completely through a water treatment system and distributed to haemodialysis equipment

cf. IEC 60601-2-16

3 Product water requirements

3.1 Product water verification and monitoring

The quality of feed water and its variation shall be determined in order to design an appropriate water treatment system to meet the needs of patients undergoing extracorporeal therapies. The feed water quality shall be periodically monitored thereafter to assure continued appropriate water treatment. The quality of the product water, as specified below, shall be verified upon installation of a water treatment system. Regular monitoring of the product water quality shall be carried out. The manufacturer shall provide instructions to the user on both methods and frequency of monitoring feed water and product water, and guidance for selecting methods and frequency of monitoring, and corrective action for deviations from requirements.

3.2 Microbiological requirements

Total viable microbial counts in product water shall not exceed 10^2 CFU/ml.

The endotoxin content in product water shall not exceed 5 IU/ml, or as required by national legislation or similar.

These measurements apply to sampling at the point of delivery to haemodialysis equipment. At the outlet of water treatment, no more than 1 IU/ml is the requirement.

When monitoring at the haemodialysis equipment, rotation among sites should assure that each is tested within a cycle of several months.

3.3 Chemical contaminants

Product water shall not contain chemical contaminants in excess of the levels specified in Table 1.

Table 1 — Maximum product water chemical contaminant levels

Contaminant	Maximum level mg/l
Aluminium	0,01
Arsenic	0,005
Barium	0,1
Cadmium	0,001
Calcium	2 (0,05 mmol/l)
Chloramines	0,1
Chlorine	0,5
Chromium	0,014
Copper	0,1
Fluoride	0,2
Lead	0,005
Magnesium	4 (0,16 mmol/l)
Mercury	0,000 2
Nitrate (N)	2
Potassium	8 (0,2 mmol/l)
Selenium	0,09
Silver	0,005
Sodium	70 (2,8 mmol/l)
Sulfate	100
Tin	0,1
Zinc	0,1

4 Tests for compliance with chemical and microbiological requirements

4.1 Microbiology of product water

Samples shall be collected where product water enters the dialysing fluid proportioning system(s) or where it enters into a mixing tank.

Samples shall be assayed within 30 min of collection, or be immediately stored at a temperature between 1 °C and 5 °C and assayed within 24 h of collection on a regular schedule; not less than monthly is suggested. Total viable

counts (standard plate counts) shall be obtained using conventional microbiological assay procedures (pour plate, spread plate membrane filter techniques, commercial samplers including dip test devices, etc.). The calibrated loop technique is not accepted. Culture media shall be tryptic soy agar or equivalent. Blood culture media are not appropriate. Colonies shall be counted after 48 h incubation at 35 °C to 37 °C. Recheck at 72 h if negative after 48 h.

The above method has proved effective in assuring safety for many years, and is the standard practice. Other authorities believe that a different method designed to detect water-borne organisms using a membrane filtration technique, filtering 500 ml to 1 000 ml of water and culturing on low-nutrient medium such as R2A agar and incubating for 5 days or longer at 28 °C to 32 °C is preferable and more appropriate. This technique is rational and also acceptable.

The presence of pyrogens shall be determined by the Limulus Amoebocyte Lysate (LAL) assay for endotoxins.

4.2 Chemical contaminants

Chemical analysis of product water for contaminants listed in Table 1 shall be obtained by using validated chemical analytical methods such as those referenced in the American Public Health Association's *Standard methods for the examination of water and wastewater* and/or the US Environmental Protection Agency's *Methods for chemical analysis of water and wastes* or elsewhere. Appropriate containers and pH adjustments shall be used to ensure accurate determinations. Table 2 lists the tests for each contaminant. Other test methods may be used provided they have been shown to be of comparable precision and reproducibility.

NOTE For the purpose of testing of chemical contaminants, it may be sufficient to collect sample(s) at a point chosen so that the effects of the water treatment system and the piping are completely included.

Table 2 — Contaminant tests

Contaminant	Test name
Aluminium	LeGendre and Alfrey (1976)
Arsenic	Atomic absorption (gaseous hydride)
Barium	Atomic absorption (graphite furnace)
Cadmium	Atomic absorption (graphite furnace)
Calcium	EDTA titrimetric method or atomic absorption (direct aspiration) or ion-specific electrode
Chlorine and chloramines	DPD ferrous titrimetric DPD calorimetric methods
Chromium	Atomic absorption (graphite furnace)
Copper	Atomic absorption (direct aspiration) Neocuprocine method
Fluoride	Electrode method SPADNS method
Lead	Atomic absorption (graphite furnace)
Magnesium	Atomic absorption (direct aspiration)
Mercury	Flameless cold vapour technique (atomic absorption)
Nitrate (N)	Brucine method or cadmium reduction method
Potassium	Atomic absorption (direct aspiration) or flame photometric method or ion-specific electrode
Selenium	Atomic absorption (gaseous hydride) or Atomic absorption (graphite furnace)
Silver	Atomic absorption (graphite furnace)
Sodium	Atomic absorption (direct aspiration or flame photometric method or ion-specific method
Sulfate	Turbidimetric method
Tin	Atomic absorption (graphite furnace)
Zinc	Atomic absorption (direct aspiration) dithizone method

Bibliography

[1] ISO 13958, *Concentrates for haemodialysis and related therapies*

[2] IEC 60601-2-16, *Medical electrical equipment — Part 2-16: Particular requirements for the safety of haemodialysis, haemodiafiltration and haemofiltration equipment*