SLOVENSKI STANDARD
oSIST prEN ISO 23500-3:2023

01-januar-2023

Priprava in vodenje kakovosti tekočin za hemodializo in podobne terapije - 3. del: Voda za hemodializo in podobne terapije (ISO/DIS 23500-3:2022)

Preparation and quality management of fluids for haemodialysis and related therapies - Part 3: Water for haemodialysis and related therapies (ISO/DIS 23500-3:2022)

Herstellung und Qualitätsmanagement von Flüssigkeiten für die Hämodialyse und verwandte Therapien - Teil 3: Wasser für die Hämodialyse und verwandte Therapien (ISO/DIS 23500-3:2022)

Préparation et management de la qualité des liquides d'hémodialyse et de thérapies annexes Partie 3: Eau pour hémodialyse et thérapies apparentées (ISO/DIS 23500-3:2022)

Ta slovenski standard je istoveten z: **prEN ISO 23500-3**

ICS:

11.040.40	Implantanti za kirurgijo, protetiko in ortetiko	Implants for surgery, prosthetics and orthotics

oSIST prEN ISO 23500-3:2023 **en,fr,de**

DRAFT INTERNATIONAL STANDARD
ISO/DIS 23500-3

ISO/TC **150**/SC **2** Secretariat: **ANSI**

Voting begins on:
2022-11-18

Voting terminates on:
2023-02-10

Preparation and quality management of fluids for haemodialysis and related therapies —

Part 3:
Water for haemodialysis and related therapies

Préparation et management de la qualité des liquides d'hémodialyse et de thérapies annexes —

Partie 3: Eau pour hémodialyse et thérapies apparentées

ICS: 11.040.40

This document is circulated as received from the committee secretariat.

ISO/CEN PARALLEL PROCESSING

Reference number
ISO/DIS 23500-3:2022(E)

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Published in Switzerland

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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 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 World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see 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 second edition cancels and replaces ISO 23500-3;2019, which has been technically revised. The main changes compared to the previous edition are as follows:

— The use of WHO Drinking Water Guideline as the drinking water quality reference replacing the previously used EPA Water quality requirements.

— The review on the list of chemical contaminants of other trace elements in dialysis water resulting in the removal of thallium from the list of contaminants since there are no published studies reporting that this contaminant is of particular concern in the setting of haemodialysis.

— The incorporation of alternatives to classic microbial analytical methods [endotoxin testing using rFC (tp)].

A list of all parts in the ISO 23500 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

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 document contains minimum requirements, chemical and microbiological, for the water to be used for preparation of dialysis fluids, concentrates, and for the reprocessing of haemodialysers and the necessary steps to ensure conformity with those requirements.

Haemodialysis and related therapies such as haemodiafiltration can expose the patient to more than 500 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 over 40-fold increase in exposure requires control and regular surveillance 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 document will evolve and be refined accordingly. The physiological effects attributable to the presence of organic contaminants in dialysis water are important areas for research, however, the effect of such contaminants on patients receiving regular dialysis treatment is largely unknown, consequently no threshold values for organic contaminants permitted in water used for the preparation of dialysis fluids, concentrates, and reprocessing of haemodialysers has been specified in this revised document.

Within this document, measurement techniques current at the time of publication have been cited. Other standard methods can be used, provided that such methods have been appropriately validated and are comparable to the cited methods.

The final dialysis fluid is produced from concentrates or salts manufactured, packaged, and labelled according to ISO 23500-4 mixed with water meeting the requirements of this document. Operation of water treatment equipment and haemodialysis systems, including on-going surveillance of the quality of water used to prepare dialysis fluids, and handling of concentrates and salts are the responsibility of the haemodialysis facility and are addressed in ISO 23500-1. 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 document is directed towards manufacturers and providers of water treatment systems and also to haemodialysis facilities.

The rationale for the development of this document is given in informative Annex A.

Preparation and quality management of fluids for haemodialysis and related therapies —

Part 3:
Water for haemodialysis and related therapies

1 Scope

This document specifies minimum requirements for water to be used in haemodialysis and related therapies.

This document includes water to be used in the preparation of concentrates, dialysis fluids for haemodialysis, haemodiafiltration and haemofiltration, and for the reprocessing of haemodialysers.

This document excludes the operation of water treatment equipment and the final mixing of treated water with concentrates to produce dialysis fluid. Those operations are the sole responsibility of dialysis professionals. This document does not apply to dialysis fluid regenerating systems.

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 23500-1, *Preparation and quality management of fluids for haemodialysis and related therapies — Part 1: General requirements*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 23500-1 apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

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

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

4 Requirements

4.1 Dialysis water quality requirements

The quality of the dialysis water, as specified in 4.2 and 4.3, shall be verified upon installation of a water treatment system. Regular surveillance of the dialysis water quality shall be carried out thereafter.

NOTE Throughout this document it is assumed that the water undergoing treatment is potable water and therefore meets the appropriate regulatory requirements for such water. If the water supply is derived from an alternate source such as a privately-owned borehole or well, contaminant levels cannot be as rigorously controlled.

4.2 Chemical contaminant requirements

4.2.1 General

Dialysis water shall not contain chemicals at concentrations in excess of those listed in Tables 1 and 2, or as required by national legislation or regulations. Table 1 does not include any recommendation in respect of organic carbon, pesticides and other chemicals such as pharmaceutical products and endocrine disruptors that can be present in feed water. It is technically difficult and costly to measure such substances on a routine basis. The effect of their presence on haemodialysis patients is difficult to define and consequences of exposure are probably of a long-term nature. Furthermore, there is an absence of evidence of their widespread presence in water although it is recognized that inadvertent discharges are possible. In view of this, it is not at present possible to define limits for their presence in water used in the preparation of dialysis fluid.

Nanofiltration and reverse osmosis are capable of significant rejection of many such compounds. Granular Activated Carbon (GAC) is also highly effective at removing majority of these chemicals. However, as Granular Activated Carbon is widely used in the removal chlorine/chloramine, their use in the removal of organic carbons, pesticides and other chemicals will be dependent upon the size of the carbon filters and/or beds and users shall be aware of appropriate dimensioning since the majority of carbon valences can be already occupied and not available for further removal activity.

NOTE 1 See A.3 for an explanation of values supplied.

NOTE 2 The maximum allowable levels of contaminants listed in Tables 1 and 2 include the anticipated uncertainty associated with the analytical methodologies listed in Table 4.

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 the requirements of this document. 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[a]

Contaminant	Maximum concentration mg/L[b]
Contaminants with documented toxicity in haemodialysis	
Aluminium	0,01
Total chlorine[1]	0,1
Copper	0,1
Fluoride	0,2
Lead	0,005
Nitrate (as N)	2
Sulfate	100
Zinc	0,1

[a] A physician in charge of dialysis has ultimate responsibility for ensuring the quality of water used for dialysis.

[b] Unless otherwise indicated.

[1] When chlorine is added to water, some of the chlorine reacts with organic materials and metals in the water and is not available for disinfection (the chlorine demand of the water). The remaining chlorine is the total chlorine, and is the sum of free or non bound chlorine and combined chlorine.

There is no direct method for the measurement of chloramine. It is generally established by measuring total and free chlorine concentrations and calculating the difference. When total chlorine tests are used as a single analysis the maximum level for both chlorine and chloramine shall not exceed 0,1 mg/L Since there is no distinction between chlorine and chloramine, this safely assumes that all chlorine present is chloramine.

Table 1 *(continued)*

Contaminant	Maximum concentration mg/L[b]
Electrolytes normally included in dialysis fluid	
Calcium	2 (0,05 mmol/L)
Magnesium	4 (0,15 mmol/L)
Potassium	8 (0,2 mmol/L)
Sodium	70 (3,0 mmol/L)

[a] A physician in charge of dialysis has ultimate responsibility for ensuring the quality of water used for dialysis.

[b] Unless otherwise indicated.

[1] When chlorine is added to water, some of the chlorine reacts with organic materials and metals in the water and is not available for disinfection (the chlorine demand of the water). The remaining chlorine is the total chlorine, and is the sum of free or non bound chlorine and combined chlorine.

There is no direct method for the measurement of chloramine. It is generally established by measuring total and free chlorine concentrations and calculating the difference. When total chlorine tests are used as a single analysis the maximum level for both chlorine and chloramine shall not exceed 0,1 mg/L Since there is no distinction between chlorine and chloramine, this safely assumes that all chlorine present is chloramine.

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

Contaminant	Maximum concentration mg/L
Antimony	0,006
Arsenic	0,005
Barium	0,1
Beryllium	0,000 4
Cadmium	0,001
Chromium	0,014
Mercury	0,000 2
Selenium	0,09
Silver	0,005

4.2.2 Organic Carbon, pesticides and other chemicals

The presence of organic compounds, such as pesticides, polycyclic aromatic hydrocarbons and other chemicals such as pharmaceutical products and endocrine disruptors in respect of haemodialysis patients are difficult to define. Consequences of exposure are probably of a long-term nature and it is technically difficult and costly to measure these substances on a routine basis. Furthermore, there is an absence of evidence of their widespread presence in water although it is recognized that inadvertent discharges are possible. In view of this, it is at present not possible to define limits for their presence in water used in the preparation of dialysis fluid.

4.3 Dialysis water microbiological requirements

Total viable microbial counts in dialysis water shall be less than 100 CFU/mL, or lower if required by national legislation or regulations. 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 lower if required by national legislation or regulations. An action level shall be set, typically at 50 % of the maximum allowable level.