FINAL DRAFT
International Standard

# ISO/FDIS 23500-2

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

## Part 2: Water treatment equipment for haemodialysis applications and related therapies

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

*Partie 2: Équipement de traitement de l'eau pour des applications en hémodialyse et thérapies apparentées*

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# Foreword

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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 document 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).

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This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems,* in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 205, *Non-active medical devices,* in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO 23500-2:2019), which has been technically revised. The main changes are as follows:



— alternative water treatment technologies (e.g. reverse osmosis pre-treatment with ultrafiltration) have been added;

— alternatives to classic microbial analytical methods [endotoxin testing using involving recombinant Factor C (rFC] have been added.

A list of all parts of 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

This document reflects the conscientious efforts of concerned physicians, clinical engineers, nurses, dialysis technicians and dialysis patients, in consultation with device manufacturers and regulatory authority representatives, to develop an International Standard for performance levels that can be reasonably achieved at the time of its publication. The term “consensus,” as applied to the development of voluntary medical device documents, does not imply unanimity of opinion, but rather reflects the compromise necessary in some instances when a variety of interests should be merged.

This document applies to individual water treatment devices and to water treatment systems assembled from one or more of these devices. In the first instance, this document is directed at the individual or company that specifies the complete water treatment system and, second, at the supplier who assembles and installs the system. Since systems can be assembled from a number of individual water treatment devices, the provisions of this document are also directed at the manufacturers of these devices, provided that the manufacturer indicates that the device is intended for use in haemodialysis applications. This document is written principally to address water treatment systems for dialysis facilities treating multiple patients. However, many of its provisions apply equally to water treatment systems used in applications where a single patient is treated, such as in a home dialysis or acute hospital dialysis setting. Specifically, requirements for the chemical and microbiological quality of water are considered to apply in all settings, regardless of whether a single patient or many patients are being treated.

Increasingly, self-contained, integrated systems designed and validated to produce water and dialysis fluid are becoming available and used clinically. The provisions included in this document apply to systems assembled from individual components. Consequently, some of the provisions in ISO 23500-1 and ISO 23500-2 do not apply to integrated systems, however such systems are required to comply with ISO 23500-3, ISO 23500-4[47] and ISO 23500-5[48].

This document helps protect haemodialysis patients from adverse effects arising from known chemical and microbial contaminants found in water supplies. However, dialysis and patient safety is ultimately dependent on the quality of the dialysis fluid. Since the manufacturer or supplier of water treatment equipment does not have control over the dialysis fluid, any reference to dialysis fluid in this document is for clarification only and not a requirement of the manufacturer. The responsibility for assuring that the dialysis fluid is not contaminated, mismatched or otherwise damaging to the patient rests with the clinical professionals caring for the patient under the supervision of the medical director. Requirements and recommendations on the preparation and handling of water and dialysis fluid in a dialysis facility are provided in ISO 23500-3 and ISO 23500-5[48] respectively. The rationale for the development of this document is given in Annex A.

Since the chemical and microbiological content of the water produced need to meet the requirements of ISO 23500-3, the maximum allowable levels of contaminants are listed in Tables B.1 and B.2. The values shown include the anticipated uncertainty associated with the analytical methodologies listed in Table B.3.

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

# Part 2:
# Water treatment equipment for haemodialysis applications and related therapies

## 1 Scope

This document specifies requirements and recommendations for individual water treatment devices and water treatment systems assembled from one or more of such devices. This document is directed at the individual or company that specifies the complete water treatment system and, the supplier who assembles and installs the system. Since systems can be assembled from a number of individual water treatment devices, the provisions of this document are also directed at the manufacturers of these devices, provided that the manufacturer indicates that the device is intended to be used to supply water for haemodialysis and related therapies.

This document is applicable to all devices, piping and fittings between the point at which water is delivered to the water purification system and the point of use of the purified water. Such components include but are not necessarily limited to water purification devices, online water quality monitors (such as conductivity monitors) and piping systems for the distribution of purified water.

This document does not apply to

— equipment used in the preparation of concentrates from powder or other highly concentrated media at a dialysis facility either for a single patient or multiple patients,

— dialysis fluid supply systems that proportion water and concentrates to produce dialysis fluid,

— sorbent dialysis fluid regeneration systems that regenerate and recirculate small volumes of the dialysis fluid,

— dialysis concentrates,

— haemodiafiltration or haemofiltration systems,

— systems that process dialysers for multiple uses, and

— peritoneal dialysis systems.

Requirements for the ongoing monitoring of water purity in terms of chemical and microbiological quality are given in ISO 23500-3.

## 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*

ISO 23500-3, *Preparation and quality management of fluids for haemodialysis and related therapies — Part 3: Water for haemodialysis and related therapies*

IEC 60601-1-11, *Medical electrical equipment — Part 1-11: General requirements for basic safety and essential performance — Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment*

## 3 Terms and definitions

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

ISO and IEC maintain terminology 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/

**3.1**
**microfilter**
filter designed to remove particles down to 0,1 µm in size

Note 1 to entry: Microfilters have an absolute size cut-off and are available in both dead-end and cross-flow configurations. Some microfilters can reduce the concentration of endotoxins by adsorption.

## 4 Requirements

### 4.1 Dialysis water quality requirements

#### 4.1.1 General

The requirements contained in this document apply to the dialysis water as it enters the equipment used to prepare concentrates from powder or other concentrated media at a dialysis facility, to prepare dialysis fluid, or to reprocess dialysers. As such, these requirements apply to the water treatment system as a whole including the distribution network and not only to each of the individual devices that make up the system.



#### 4.1.2 Chemical contaminant requirements

Dialysis water used to prepare dialysis fluid or concentrates from powder at a dialysis facility, or to reprocess dialysers for multiple uses, shall not contain chemical contaminants at concentrations in excess of those in ISO 23500-1:2024, Tables 1 and 2 (reproduced as Tables B.1 and B.2). The manufacturer or supplier of a complete water treatment system shall recommend a system capable of meeting the requirements of Clause 4 based on the analysis of the feed water. The system design should reflect possible seasonal variations in feed water quality. The manufacturer or supplier of a complete water treatment and distribution system shall demonstrate that the complete water treatment, storage and distribution system is capable of meeting the requirements of this document at the time of installation.

For disposable water treatment and distribution systems that have been validated to produce dialysis water meeting the quality requirements of this document for a specified time, incoming water shall be surveyed to ensure that the input to the treatment system is in the range for which the system has been validated. The manufacturer's recommendation for surveying the final dialysis water can be followed when the system is operated according to the manufacturer's instructions. Alternatively, the quality of the dialysis water can be closely observed as outlined for non-validated systems.

NOTE 1 If the manufacturer or supplier does not install the water storage and distribution system, then the responsibility of the manufacturer or supplier is limited to demonstrating that the water treatment system, excluding the water storage and distribution system, meets the requirements of this document. If individual devices of the water treatment system are provided by different manufacturers or suppliers, the person or organization specifying the devices is responsible for demonstrating that the complete system meets the requirements of this document at the time of installation.

NOTE 2 Following the installation of a water treatment, storage and distribution system, the user is responsible for continued surveillance of the levels of chemical contaminants in the water and for complying with the requirements of this document.

#### 4.1.3 Organic carbon, pesticides and other chemicals

The impact 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 specify. 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 not possible to currently specify 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 such compounds. However, as granular activated carbon is widely used in the removal of 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.

#### 4.1.4 Microbiology of dialysis water

Dialysis water used to prepare dialysis fluid or concentrates from powder at a dialysis facility, or to reprocess dialysers for multiple uses, shall comply with the requirements specified in ISO 23500-3.

The manufacturer or supplier of a complete water treatment and distribution system shall demonstrate that the complete water treatment, storage, and distribution system meets the requirements of this document, including those related to action levels at the time of installation.



For disposable water treatment systems validated by the manufacturer to produce dialysis water meeting the quality requirements of this document for a specified time, incoming feed water shall be surveyed to ensure that the input to the treatment system is in the range for which the system has been validated. The manufacturer's recommendations for surveying the dialysis water can be followed when the system is operated according to the manufacturer's instructions. Alternatively, the quality of the dialysis water can be observed as outlined for non-validated systems.



NOTE 1 If the manufacturer or supplier does not install the water storage and distribution system, then the responsibility of the manufacturer or supplier is limited to demonstrating that the water treatment system, excluding the water storage and distribution system, meets the requirements of this document. If individual devices of the water treatment system are provided by different manufacturers or suppliers, the person or organization specifying the devices is responsible for demonstrating that the complete system meets the requirements of this document at the time of installation.

NOTE 2 Following installation of a water treatment, storage, and distribution system, the user is responsible for continued surveillance of the water bacteriology of the system and for complying with the requirements of this document, including those requirements related to action levels.

### 4.2 Water treatment equipment requirements

#### 4.2.1 General

##### 4.2.1.1 Water treatment system

The supplier of the feed water or the supplier of the water treatment system or a laboratory specified by the user shall perform chemical analyses on feed water to determine the compatibility of the system with the feed water and the suitability of the system for providing dialysis water meeting the requirements of 4.1.2. The result of the chemical analyses shall be available to the user in charge of dialysis. In the case of an individual device, the person incorporating the device into the water treatment system is responsible for

ensuring that incorporation of the device does not compromise the ability of the overall system to deliver dialysis water capable of meeting the requirements of 4.1.2 and 4.1.4.

The water treatment and distribution system should include appropriate pressure gauges, flow meters, sample ports, and other ancillary equipment necessary to allow surveillance of the performance of individual system devices and the system as a whole.

Valves can be included in the water treatment system to allow individual devices to be bypassed when there is device failure or to facilitate replacement of a device. Bypass valves should have a physical lockout installed and be labelled with a warning notifying the user of the result of its removal.

If it is possible to bypass a device of the water treatment system, then the manufacturer or installer of that component shall inform the user of the risks associated with bypassing that device and the need for clearly defining the responsibility for operating the bypass. Where such valves are installed, however, a means should be included to minimize the likelihood that the device will be inadvertently bypassed during normal operation of the system.

Bypass valves should not be used to bypass deionization tanks, carbons and other critical components e.g. reverse osmosis (RO) systems. They should not be used on ultra filters used in conjunction with deionization tanks for patient treatment.

Operating controls shall be positioned so as to minimize inadvertent resetting.

Electrical circuits shall be separate from hydraulic circuits and adequately protected from fluid leaks.

#### 4.2.1.2 Materials compatibility

Materials that are in contact with dialysis water (including materials used in piping, storage and distribution systems) shall not interact chemically or physically with that water so as to adversely affect its purity or quality. Water-contacting surfaces shall be fabricated from non-reactive materials (e.g. plastics) or appropriate stainless steel. The use of materials known to cause toxicity in haemodialysis, such as copper, brass, galvanized metal or aluminium, are specifically prohibited at any point beyond the water treatment device used to remove contaminating metal ions, most commonly a reverse osmosis system or a deionizer.

The materials of any water treatment devices (including piping, storage, and distribution systems) shall be compatible with the means used to disinfect those devices. Chemicals infused into the water in the pre-treatment section, such as chlorine, acid, flocculants and complexing agents, shall be adequately removed from dialysis water before they reach any point of use. Monitors or specific test procedures to verify removal of additives shall be provided.

#### 4.2.1.3 Regenerated or reconstituted devices

All devices that are regenerated or reconstituted at a site remote from the dialysis facility, such as deionizers, shall be disinfected at the time of regeneration or reconstitution so that contaminated water is not reintroduced into the system after regeneration or reconstitution. Separate processes shall be used to ensure no intermixing of devices or their component parts between devices returned from medical or other non-medical (e.g. domestic or industrial) water users.

#### 4.2.1.4 Disinfection protection

When the manufacturer recommends the use of chemical disinfectants, means shall be provided to restore the equipment and the system in which it is installed to a safe condition in respect of residual disinfectant presence prior to the dialysis water being used for dialysis applications. When recommending chemical disinfectants, the manufacturer shall also recommend methods for testing for residual levels of the disinfectants. When disinfection is accomplished automatically by chemical disinfectants, including ozone, or by high temperature procedures, the activation of the disinfection system shall result in the activation of a warning system and measures to prevent patient exposure to an unsafe condition.

If sodium hypochlorite (bleach) is used for cleaning or disinfecting the internal pathways of dialysis equipment, including but not limited to water treatment loops, concentrate containers, mixers and delivery

systems, the post rinse water residual level of free chlorine shall be as specified by the manufacturer's instructions.

### 4.2.2 Backflow prevention

A backflow prevention device e.g. pipe disconnector, system separator or free fall section to isolate the water treatment system from the water supply according to local plumbing codes should be fitted to all water treatment systems

NOTE The testing frequency of backflow prevention devices is specified by local plumbing codes or regulations.

### 4.2.3 Tempering valves

Tempering valves, if used, shall be sized to accommodate the anticipated range of flow rates of hot and cold water. They shall be fitted with a mechanism to prevent backflow of water into the hot and cold water lines and with a means to measure the outlet water temperature.

### 4.2.4 Sediment filters

Sediment filters should have an opaque housing or other means to inhibit proliferation of algae. Filters should be fitted with pressure gauges on the inlet and outlet water lines to measure the pressure drop, $\Delta P$, across the filter.

NOTE Sediment filters are also known as multimedia or sand filters.

### 4.2.5 Cartridge filters

Cartridge filters should have an opaque housing or other means to inhibit proliferation of algae. Filters should be fitted with pressure gauges on the inlet and outlet water lines to measure the pressure drop, $\Delta P$, across the filter during use.



### 4.2.6 Softeners

Water softeners should be fitted with a mechanism to prevent water containing the high concentrations of sodium chloride used during regeneration from entering the product water line during regeneration. Automatic regeneration can be performed on a volume schedule or on a time schedule. For softeners that are regenerated automatically on a time schedule, the face of the timers used to control the regeneration cycle should be visible to the user. Operating controls shall be positioned so as to minimize inadvertent resetting.

### 4.2.7 Anion exchange resin tank

Anion exchange resin, sometimes referred to as an organic scavenger, can remove organic matter and other contaminants from the source water and protect carbon media from fouling, which can shorten its effective life for chlorine/chloramine removal. If an organic scavenger is installed to protect the carbon media, the scavenger should be installed upstream of the carbon beds. Anion exchange resins can also be used to remove contaminants that can otherwise foul the reverse osmosis membrane.

### 4.2.8 Carbon media

Carbon is used to remove small organic compounds, chlorine and chloramine. At least one carbon bed or filter should be installed even if the water supply is from a well and no chlorine is present. Carbon removes organic contaminants from ground water, including solvents, pesticides, industrial wastes and substances leaking from underground storage tanks.

To mitigate possible risks, due to depletion of available valences in activated carbon, regular replacement of activated carbon shall be undertaken, even when chlorine breakthrough hasn't occurred. Replacement frequency is typically based on manufacturer's instructions or activated carbon performance indicators (e.g. total organic compounds). Potential risks and dialysis treatment practices should be considered in choosing of replacement frequency.

When carbon is used for the removal of chloramine, it shall be adapted specifically to the maximum anticipated water flow rate of the system and the level of chloramine in the feed water.

If small cartridge filters are used, the data-sheet of the manufacturer regarding chlorine rejection capacity has to be observed."

Due to the risk of harm to a patient in the event of total chlorine breakthrough in cases where the water is known to be continuously chlorinated or chloraminated or subject to organic contamination, the system shall be designed to prevent patient exposure to unsafe product water in the event of a single point failure. Protective measures can be incorporated into the system design through several means including:

— the use of two carbon beds in series with off-line analysis or testing of product water from the first bed in each series (see off-line testing in ISO 23500-1:2024, 7.3.5). Each of the carbon beds shall have an empty-bed contact time (EBCT) of at least 5 min at the maximum product water flow rate (a total EBCT of at least 10 min);

— the use of redundant means of chloramines removal with off-line analysis or testing of product water after the primary device (see off-line testing in ISO 23500-1:2024, 7.3.5). Possible alternatives include a granular activated carbon bed followed by a dense carbon block or two carbon block filters in series;

— the use of carbon systems used to prepare water for portable dialysis systems are exempt from the requirement for the second carbon and a 10 min EBCT, provided there is a redundant means of chloramine removal with off-line sampling after the primary device (see off-line testing in ISO 23500-1:2024, 7.3.5);

— the use of batch systems used to prepare water for portable dialysis systems are exempt from the requirement for the second carbon and a 10 min EBCT, provided there is a redundant means of chloramine removal with off-line sampling after batch production (see chlorine test methods in ISO 23500-1:2024, 7.3.5);

— the use of carbon media with duration or process volume limitation in conjunction with online surveillance of the product water and diversion of the product water to drain or a blocking valve with system shutdown, should the total chlorine level in the product water exceed 0,1 mg/l (see online testing in ISO 23500-1:2024, 7.3.5). Periodic testing of the online monitor and the frequency of the testing is specified per the system manufacturer's instructions. If an online monitor failure occurs, manual testing can be implemented to observe for chlorine and chloramines for 72 h, similar to dual carbon designs in ISO 23500-1:2024, B.2.5.



To avoid overly large beds, carbon beds are sometimes arranged as parallel sets, each set consisting of two beds in series. The beds are equally sized and water flows in parallel through each set. In this situation, each bed shall have a minimum EBCT of 5 min at the maximum flow rate through the bed. When parallel sets of beds are used, the piping should be designed to minimize differences in the resistance to flow from inlet and outlet between each parallel set of beds in order to ensure that water flows equally through all beds. A means shall be provided to sample the product water from the first bed in each series-connected pair and a sample port should be installed following the carbon beds for use in the event of total chlorine breaking through the first bed in a series-connected pair.

In situations where chloramine is not used to disinfect the water and the ammonium ($NH_4^+$) [formed by the protonation of ammonia ($NH_3$)] level in the water is low, one carbon bed or a carbon cartridge filter with a shorter EBCT can be sufficient. Exhausted carbon media shall be discarded and replaced with new media according to a replacement schedule determined by regular surveillance. For example, with two beds, when testing between the beds shows that the first bed is exhausted, the second bed should be moved into the first position, the second bed replaced with a new bed and the exhausted bed discarded.

Granular activated carbon with an iodine number greater than 900 is considered optimal for chlorine/chloramine removal. However, some source waters, such as those with a high organic content can require alternate types of carbon that are more resistant to organic fouling. These types of carbon can have iodine numbers less than 900. When other forms of carbon or granular activated carbon with an iodine number of less than 900 are used, the manufacturer shall provide performance data to demonstrate that each adsorption bed has the capacity to reduce the total chlorine concentration in the feed water to less than 0,1 mg/l when operating at the maximum anticipated flow rate for the maximum time interval between scheduled testing of the product water for total chlorine. Regenerated carbon shall not be used. Automatically backwashed