BS EN ISO 26722:2015

BSI Standards Publication

Water treatment equipment for haemodialysis applications and related therapies

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National foreword

This British Standard is the UK implementation of EN ISO 26722:2015. It is identical to ISO 26722:2014. It supersedes BS ISO 26722:2014 which is withdrawn.

The UK participation in its preparation was entrusted by Technical Committee CH/150, Implants for surgery, to Subcommittee CH/150/2, Cardiovascular implants.

A list of organizations represented on this subcommittee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

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Compliance with a British Standard cannot confer immunity from legal obligations.

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Date	Text affected
31 December 2015	This corrigendum renumbers BS ISO 26722:2014 as BS EN ISO 26722:2015. Annex ZA also added

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 26722

December 2015

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English Version

Water treatment equipment for haemodialysis applications and related therapies (ISO 26722:2014)

Équipement de traitement de l'eau pour des applications en hémodialyse et aux thérapies apparentées (ISO 26722:2014)

Ausstattung zur Wasseraufbereitung zur Verwendung in der Hämodialyse und in verwandten Therapien (ISO 26722:2014)

This European Standard was approved by CEN on 23 November 2015.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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European foreword

The text of ISO 26722:2014 has been prepared by Technical Committee ISO/TC 150 “Implants for surgery” of the International Organization for Standardization (ISO) and has been taken over as EN ISO 26722:2015 by Technical Committee CEN/TC 205 “Non-active medical devices” the secretariat of which is held by DIN.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by June 2016, and conflicting national standards shall be withdrawn at the latest by June 2016.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directive.

For relationship with EU Directive, see informative Annex ZA, which is an integral part of this document.

The following referenced documents are indispensable for the application of this document. For undated references, the latest edition of the referenced document (including any amendments) applies. For dated references, only the edition cited applies. However, for any use of this standard ‘within the meaning of Annex ZA’, the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this shall be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard, as listed below.

NOTE The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

Table 1 — Correlation between normative references and dated EN and ISO standards

Normative references as listed in Clause 2 of the ISO standard	Equivalent dated standard	
	EN	ISO or IEC
ISO 13959:2014	EN ISO 13959:2015 [1)]	ISO 13959:2014
ISO 14971:2007	EN ISO 14971:2012	ISO 14971:2007
IEC 60601-1-8	EN 60601-1-8:2007+Cor.:2010+A1:2013	IEC 60601-1-8:2006+A1:2012

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 26722:2014 has been approved by CEN as EN ISO 26722:2015 without any modification.

1) To be published.

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC on medical devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with Directive 93/42/EEC as amended by 2007/47/EC. This means that risks have to be reduced 'as far as possible', 'to a minimum', 'to the lowest possible level', 'minimized' or 'removed', according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with essential requirements 1, 2, 5, 6, 7, 8, 9, 11 and 12 of the Directive.

NOTE 3 This Annex ZA is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

Table ZA.1 — Correspondence between this European Standard and Directive 93/42/EEC on medical devices

Clause(s)/sub-clause(s) of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4.2.1.1	7.3	
4.2.1.1	7.5	
4.2.1.4	8	
1.2, 4.1.1	9.1	
4.1.1	13.3. (a)	
4.2.1.4	13.3. (i)	
1.2, 1.3	13.6. (c)	

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

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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 meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition cancels and replaces the first edition (ISO 26722:2009), which has been technically revised.

Introduction

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

The provisions of this International Standard apply to individual water treatment devices and to water treatment systems assembled from one or more of these devices. In the first instance, this International Standard 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 International Standard 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 International Standard is written principally to address water treatment systems for dialysis facilities treating multiple patients. However, many of its provisions equally apply 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.

The verbal forms used in this International Standard conform to usage described in Annex H of the ISO/IEC Directives, Part 2. For the purposes of this International Standard, the auxiliary verb

— "shall" means that compliance with a requirement or a test is mandatory for compliance with this International Standard,

— "should" means that compliance with a requirement or a test is recommended but is not mandatory for compliance with this International Standard, and

— "may" is used to describe a permissible way to achieve compliance with a requirement or test.

The requirements established by this International Standard should help protect haemodialysis patients from adverse effects arising from known chemical and microbial contaminants found in water supplies. However, proper 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 International Standard 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. Recommendations on the preparation and handling of water and dialysis fluid in a dialysis facility are provided in ISO 23500.

INTERNATIONAL STANDARD ISO 26722:2014(E)

Water treatment equipment for haemodialysis applications and related therapies

1 Scope

1.1 General

This International Standard is addressed to the manufacturer and/or supplier of water treatment systems and/or devices used for the express purpose of providing water for haemodialysis or related therapies.

1.2 Inclusions

This International Standard covers devices used to treat water intended for use in the delivery of haemodialysis and related therapies, including water used for: (1) the preparation of concentrates from powder or other highly concentrated media at a dialysis facility; (2) the preparation of dialysis fluid, including dialysis fluid that can be used for the preparation of substitution fluid; (3) the reprocessing of dialysers for multiple uses.

Included within the scope of this International Standard are all devices, piping and fittings between the point at which potable water is delivered to the water treatment system, and the point of use of the dialysis water. Examples of devices included within the scope of this International Standard are water purification devices, online water quality monitors (such as conductivity monitors), and piping systems for the distribution of dialysis water.

1.3 Exclusions

Excluded from the scope of this International Standard are 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 systems, haemofiltration systems, systems that process dialysers for multiple uses, and peritoneal dialysis systems. Some of these devices, such as dialysis fluid delivery systems and concentrates, are addressed in other International Standards. Also excluded from the scope of this International Standard are requirements for the ongoing monitoring of the purity of water used for dialysis fluid, concentrate preparation, or dialyser reprocessing.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 13959:2014, *Water for haemodialysis and related therapies*

ISO 14971:2007, *Medical devices — Application of risk management to medical devices*

IEC 60601-1-8, *Medical electrical equipment – Part 1-8: General requirements for basic safety and essential performance – Collateral standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems*

3 Terms and definitions

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

3.1
acid concentrate
A-concentrate
acidified concentrated mixture of salts that, when diluted with dialysis water and bicarbonate concentrate, yields dialysis fluid for use in dialysis

Note 1 to entry: The term "acid" refers to the small amount of acid (for example, acetic acid or citric acid) that is included in the concentrate.

Note 2 to entry: Acid concentrate can contain glucose.

Note 3 to entry: Acid concentrate can be in the form of a liquid, a dry powder, other highly concentrated media, or some combination of these forms.

3.2
action level
concentration of a contaminant at which steps should be taken to interrupt the trend toward higher, unacceptable levels

3.3
bicarbonate concentrate
B-concentrate
concentrated preparation of sodium bicarbonate that, when diluted with dialysis water and acid concentrate, makes dialysis fluid used for dialysis

Note 1 to entry: Sodium bicarbonate is also known as sodium hydrogen carbonate.

Note 2 to entry: Some bicarbonate concentrates also contain sodium chloride.

Note 3 to entry: Bicarbonate concentrate can be in the form of a liquid or a dry powder.

Note 4 to entry: Dry sodium bicarbonate, without added sodium chloride, is also used in concentrate generators to produce a concentrated solution of sodium bicarbonate used by the dialysis machine to make dialysis fluid.

3.4
biofilm
microbially derived sessile community characterized by cells that are irreversibly attached to a substratum or interface or to each other, are imbedded in a matrix of extracellular polymeric substances that they have produced, and exhibit an altered phenotype with respect to growth rate and gene transcription

Note 1 to entry: The matrix, a slimy material secreted by the cells, protects the bacteria from antibiotics and chemical disinfectants.

Note 2 to entry: A certain amount of biofilm formation is considered unavoidable in dialysis water systems. When the level of biofilm is such that the action levels for microorganisms and endotoxins in the dialysis water cannot be routinely achieved, the operation of the system is compromised from a medical and technical point of view. This level of biofilm formation is often referred to as biofouling.

3.5
chlorine, combined
chlorine that is chemically combined, such as in chloramine compounds

Note 1 to entry: There is no direct test for measuring combined chlorine, but it can be measured indirectly by measuring both total and free chlorine and calculating the difference.

3.6
chlorine, free
chlorine present in water as dissolved molecular chlorine (Cl), hypochlorous acid (HOCl), and hypoclorite ion (OCl^-)

Note 1 to entry: The three forms of free chlorine exist in equilibrium.

3.7
chlorine, total
sum of free and combined chlorine

Note 1 to entry: Chlorine can exist in water as dissolved molecular chlorine, hypochlorous acid, and/or hypochlorite ion (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.

3.8
concentrate generator
system where the concentrate is delivered to the user as a powder in a container, suitable for attachment to the dialysis machine with which it is intended to be used, and then the powder is converted into a concentrated solution by the dialysis machine

Note 1 to entry: The solution produced by the concentrate generator is used by the dialysis machine to make the final dialysis fluid delivered to the dialyser.

3.9
device
individual water purification unit, such as a softener, carbon bed, reverse osmosis unit, or deionizer

Note 1 to entry: This term is synonymous with the term “component” as used by the US. Food and Drug Administration.[26]

3.10
dialysis fluid
dialysate
dialysis solution
aqueous fluid containing electrolytes and, usually, buffer and glucose, which is intended to exchange solutes with blood during haemodialysis

Note 1 to entry: The term “dialysis fluid” is used throughout this International Standard to mean the fluid made from dialysis water and concentrates that is delivered to the dialyser by the dialysis fluid delivery system. Such phrases as “dialysate” or “dialysis solution” are used in place of dialysis fluid in some countries; however, that usage is discouraged to avoid confusion.

Note 2 to entry: The dialysis fluid entering the dialyser is referred to as “fresh dialysis fluid”, while the fluid leaving the dialyser is referred to as “spent dialysis fluid.”

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

3.11
dialysis fluid delivery system
device that prepares dialysis fluid online from dialysis water and concentrates or that stores and distributes premixed dialysis fluid, circulates the dialysis fluid through the dialyser, monitors the dialysis fluid for temperature, conductivity (or equivalent), pressure, flow, and blood leaks, and prevents dialysis during disinfection or cleaning modes

Note 1 to entry: The term includes reservoirs, conduits, proportioning devices for the dialysis fluid, and monitors and associated alarms and controls assembled as a system for the purposes listed above.

Note 2 to entry: The dialysis fluid supply system might be an integral part of the single-patient dialysis machine or a centralized preparation system which feeds multiple bedside monitoring systems.

Note 3 to entry: Dialysis fluid delivery systems are also known as proportioning systems and dialysis fluid supply systems.

3.12
dialysis water
water that has been treated to meet the requirements of ISO 13959 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

3.13
disinfection
destruction of pathogenic and other kinds of microorganisms by thermal or chemical means

Note 1 to entry: Disinfection is a less lethal process than sterilization because it destroys most recognized pathogenic microorganisms but does not necessarily destroy all microbial forms.

3.14
empty bed contact time
EBCT
time taken by a fluid to pass through an empty volume equal to the volume of a particle bed

Note 1 to entry: EBCT (min) is calculated using the following equation:

$$\text{EBCT} = V/Q$$

where

V is the volume of the particle bed in cubic metres (m^3);

Q is the flow rate of water through the bed in cubic metres per minute (m^3/min).

Note 2 to entry: EBCT is used as an indirect measure of how much contact occurs between particles, such as activated carbon, and water as the water flows through a bed of particles.

3.15
endotoxin
major component of the outer cell wall of gram-negative bacteria

Note 1 to entry: 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* (3.26).]

3.16
endotoxin-retentive filter
ETRF
membrane filter used to remove endotoxins and microorganisms from dialysis water or dialysis fluid

Note 1 to entry: The performance of an endotoxin-retentive filter is usually expressed as the logarithmic reduction value (LRV), defined as $\log_{10}$(inlet concentration)/(outlet concentration).

Note 2 to entry: Endotoxin-retentive filters can be configured in a cross-flow or dead-end mode. Some endotoxin-retentive filters also remove endotoxins by adsorption.

3.17
feed water
water supplied to a water treatment system or an individual component of a water treatment system

3.18
germicide
agent that kills microorganisms

3.19
haemodiafiltration
form of renal replacement therapy in which waste solutes are removed from blood by a combination of diffusion and convection through a high-flux membrane

Note 1 to entry: Diffusive solute removal is achieved using a dialysis fluid stream as in haemodialysis. Convective solute removal is achieved by adding ultrafiltration in excess of that needed to obtain the desired weight loss; fluid balance is maintained by infusing replacement solution into the blood either before the dialyser (predilution haemodiafiltration), after the dialyser (postdilution haemodiafiltration), or a combination of the two (mixed dilution haemodiafiltration).

3.20
haemodialysis
form of renal replacement therapy in which waste solutes are removed primarily by diffusion from blood flowing on one side of a membrane into dialysis fluid flowing on the other side

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

3.21
haemofiltration
form of renal replacement therapy in which waste solutes are removed from blood by convection

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

Note 2 to entry: There is no dialysis fluid stream in haemofiltration.

3.22
manufacturer
entity that designs, manufactures, fabricates, assembles, or processes a finished device

Note 1 to entry: Manufacturers include, but are not limited to, those who perform the functions of contract sterilization, installation, relabelling, remanufacturing, repacking, or specification development and initial distributions of foreign entities performing these functions. The term does not cover preparation of concentrates from prepackaged dry chemicals at a dialysis facility or the handling of bulk concentrates at a dialysis facility after responsibility for the concentrate is transferred from the manufacturer to the user.

3.23
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.

3.24
product water
water produced by a water treatment system or by an individual device thereof

3.25
proportioning system
apparatus that proportions dialysis water and haemodialysis concentrate to prepare dialysis fluid

3.26
pyrogen
fever-producing substance

Note 1 to entry: Pyrogens are most often lipopolysaccharides of gram-negative bacterial origin [see also *endotoxin* (3.15)].

3.27
sodium hypochorite
chemical used for disinfection of hemodialysis systems

Note 1 to entry: Commercially available solutions of sodium hypochlorite are known in different countries by terms such as bleach and javel. These solutions are used for disinfection at concentrations recommended by equipment manufacturers.

3.28
source water
water entering a dialysis facility from an external supplier, i.e. water from a municipal water supply or equivalent

Note 1 to entry: Source water is sometimes referred to as feed water and is assumed to be potable water

3.29
storage tank
tank at the user's facility for storage of source water, dialysis water, or concentrate from bulk deliveries or for concentrate prepared in bulk at the user's facility from powder and dialysis water

3.30
substitution fluid
fluid used in haemofiltration and haemodiafiltration treatments which is infused directly into the patient's blood as a replacement for the fluid that is removed from the blood by filtration

Note 1 to entry: Substitution fluid is also referred to as substitution solution or replacement solution.

Note 2 to entry: Substitution fluid can also be used for bolus administration, for priming of an extracorporeal blood circuit, and for returning blood to the patient at the end of a treatment.

3.31
total dissolved solids
TDS
sum of all ions in a solution, often approximated by means of electrical conductivity or resistivity measurements

Note 1 to entry: TDS measurements are commonly used to assess the performance of reverse osmosis units. TDS values are often expressed in terms of $CaCO_3$, NaCl, KCl, or 442 equivalents in milligrams per litre (mg/l). [442 is a solution of sodium sulfate (40 %), sodium bicarbonate (40 %), and sodium chloride (20 %) that closely represents the conductivity to concentration relationship, on average, for naturally occurring fresh water.]

3.32
user
physician or physician's representative or healthcare professional with a responsibility for the prescription, production, and delivery of dialysis fluid

3.33
water treatment system
collection of water treatment devices and associated piping, pumps, valves, gauges, etc. that together produce water meeting the requirements of ISO 13959 for haemodialysis applications and deliver it to the point of use

4 Requirements

4.1 Dialysis water quality requirements

4.1.1 General

The requirements contained in this International Standard 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 for multiple uses. As such, these requirements apply to the water treatment system as a whole and not to each of the individual devices that make up the system. However, collectively, the individual devices shall produce dialysis water that, at a minimum, meets the requirements of the clause.

4.1.2 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 contain a total viable microbial count and endotoxin levels as specified in ISO 13959.

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 International Standard, including those related to action levels at the time of installation.

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 International Standard. 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 International Standard at the time of installation.

For disposable water treatment systems validated by the manufacturer to produce dialysis water meeting the quality requirements of this International Standard for a specified time, monitoring of the incoming feed water is required 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 monitoring 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 monitored as outlined for non-validated systems.

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

4.1.3 Maximum level of chemical contaminants

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 13959:2014, 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 this clause 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 International Standard at the time of installation.

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 International Standard. 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 International Standard 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 International Standard for a specified time, monitoring of the incoming potable water is required 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 monitoring 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 monitored as outlined for non-validated systems.

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

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 4.1.3. 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 4.1.3.

The water treatment and distribution system should include appropriate pressure gauges, flow meters, sample ports, and other ancillary equipment necessary to allow monitoring 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. 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.

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 contact 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 that are known to cause toxicity in haemodialysis, such as copper, brass, galvanized material, or aluminium, is 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 potable water users and devices returned from non-potable water users.

4.2.1.4 Disinfection protection

When the manufacturer recommends chemical disinfectants [see 6.3 item y)], means shall be provided to restore the equipment and the system in which it is installed, to a safe condition relative to residual disinfectant 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 disinfectant, including ozone, or by high temperature procedures, activation of the disinfection system shall result in activation of a warning system and measures to prevent patient exposure to an unsafe condition.

4.2.2 Backflow prevention device

All water treatment systems should be preceded by a backflow prevention device to isolate the system from the potable water supply according to local plumbing codes.

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 monitor 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 monitor the pressure drop, ΔP, 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 monitor the pressure drop, ΔP, across the filter.

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 might otherwise foul the reverse osmosis membrane.

4.2.8 Carbon media

Carbon is used to remove small organic compounds, chlorine, and chloramine. 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.

Where chloramine is used to disinfect the potable water supply at a level of 1 mg/l or more, two carbon beds shall be installed in series. Each of the carbon beds shall have an EBCT of at least 5 min at the maximum product water flow rate (a total EBCT of at least 10 min). 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.

NOTE 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 and that a total chlorine concentration of less than 0,1 mg/l is verified in a sample collected after the primary device before each treatment. Possible alternatives include a granular activated carbon bed followed by a dense carbon block and two carbon block filters in series.

In situations where chloramine is not used to disinfect the water, and the ammonium level in the water is low, one carbon bed or a carbon cartridge filter with a shorter EBCT might be sufficient.

Exhausted carbon media shall be discarded and replaced with new media according to a replacement schedule determined by regular monitoring. 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 could 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 flowrate for the maximum time interval between scheduled testing of the product water for total chlorine. Regenerated carbon shall not be used.

Automatically backwashed carbon beds should be fitted with a mechanism to prevent water containing chlorine or chloramine from entering the feed water line of downstream purification devices, such as reverse osmosis, while the carbon beds are being backwashed. For carbon beds that are backwashed automatically on a time schedule, the face of the timers used to control the backwash cycle should be visible to the user and the timer should be set so that backwashing occurs when dialysis is not being performed.

If carbon beds fitted with an online monitor for measuring total chlorine in the product water are used, there should be a means of preventing patient exposure to unsafe product water, such as the diversion of the product water to drain or a system shutdown, should the total chlorine level in the product water exceed 0,1 mg/l. Accompanying visual and/or audible alarms shall meet the relevant requirements of IEC 60601-1-8 for low-priority alarms if product water is diverted to drain or the system is shut down; otherwise, the alarms shall meet the relevant requirements of IEC 60601-1-8 for high-priority alarms.

In addition, the sound emitted by the audible alarm shall be at least 65 decibels (“A” scale) at 3 m and it shall not be possible to silence the alarm for more than 180 s. Alarms shall be situated so that they ensure a prompt response by personnel in the patient care area.

If the online monitor is placed between two carbon filters in series, a low-priority alarm can be accepted as long as manual monitoring is performed after the last filter or bed in the event of an alarm.

4.2.9 Chemical injection systems

Sodium bisulphite injected into the source water can be an effective means of reducing chlorine and chloramine concentrations. Ascorbic acid has also been used for this purpose. In addition, reducing the pH of alkaline feed water by the injection of mineral acids can enhance the efficiency of granular activated carbon. Chemical injection systems shall include a means of regulating the metering pump to control the addition of chemical. This control system shall be designed to tightly control the addition of chemical. The control system shall ensure that chemical is added only when water is flowing through the pre-treatment cascade and that it is added in fixed proportion to the water flow or based on some continuously monitored parameter, such as pH, using an automated control system. If an automated control system is used to inject the chemical, there shall be an independent monitor of the controlling parameter. Monitors shall be designed so that the monitor cannot be disabled while a patient is at risk, except for brief, necessary periods of manual control with the operator in constant attention.

4.2.10 Reverse osmosis

When used to prepare water for haemodialysis applications, either alone or as the last stage in a purification cascade, reverse osmosis systems shall be shown to be capable, at installation, of meeting the requirements of 4.1, when tested with the typical feed water of the user, in accordance with the methods described in 5.1.

Reverse osmosis devices shall be equipped with online monitors that allow determination of product water conductivity and should be equipped with monitors that determine rejection rate based on conductivity. Monitors that display resistivity or total dissolved solids (TDS) could be used in place of conductivity monitors. Resistivity, conductivity, or TDS monitors shall be temperature-compensated, generally to 25 °C. Monitors shall be designed so that the monitor cannot be disabled while a patient is at risk, except for brief, necessary periods of manual control with the operator in constant attention.

When a reverse osmosis system is the last chemical purification process in the water treatment system, it should include a means of preventing patient exposure to unsafe product water, such as diversion of the product water to drain or system shutdown, in the event that the product water conductivity exceeds a preset limit. Accompanying alarms shall meet the relevant requirements of IEC 60601-1-8 for low-priority alarms. If the reverse osmosis system does not have a means of preventing unsafe product water from entering the dialysis machines, the product water conductivity monitor shall activate audible and/or visual alarms when the product water conductivity exceeds the preset limit. Those alarms shall meet the relevant requirements of IEC 60601-1-8 for medium priority alarms. In addition, for medium priority alarms, the sound emitted by the audible alarm shall be at least 65 decibels (“A” scale) at 3 m and it shall not be possible to silence the alarm for more than 180 s. Alarms shall be situated so that they ensure a prompt response by personnel in the patient care area.

4.2.11 Deionization

Deionization systems, when used to prepare water for haemodialysis applications, shall be monitored continuously with monitors generally temperature-compensated to 25 °C, to produce water of 1 MΩ·cm or greater specific resistivity (or conductivity of 1 µS/cm (0,1 mS/m) or less). Monitors shall be designed so that the monitor cannot be disabled while a patient is at risk, except for brief, necessary periods of manual control with the operator in constant attention. An audible and visual alarm shall be activated when the product water resistivity falls below 1 MΩ·cm and the product water stream shall be prevented from reaching any point of use, by being diverted to a drain. Such alarms shall meet the relevant requirements of IEC 60601-1-8 for low-priority alarms if the product water is diverted to drain, or if the system is shutdown; otherwise, the alarms shall meet the relevant requirements of IEC 60601-1-8 for high-priority alarms. In addition, the sound emitted by the audible alarm shall be at least 65 decibels (“A” scale) at 3 m and shall be audible in the patient care area. It shall not be possible to silence these alarms for more than 180 s. Feed water for deionization systems shall be pretreated with activated carbon, or a comparable alternative, to prevent nitrosamine formation. If a deionization system is the

last process in a water treatment system, it shall be followed by an endotoxin-retentive filter or other bacteria- and endotoxin-reducing device.

NOTE The requirements given above for deionization might not apply to electrodeionization (EDI) technology, which can be used as an alternative to deionization following reverse osmosis in haemodialysis applications.

4.2.12 Endotoxin-retentive filters

When an endotoxin-retentive filter is used in a water treatment system for haemodialysis applications, the manufacturer of the filter shall disclose the performance of the filter and the conditions under which that performance can be obtained. It is recommended that filters be configured in a cross-flow mode. However, dead-end filters that have validated endotoxin and bacterial removal characteristics can also be used.

Endotoxin-retentive filters should have an opaque housing or other means to inhibit proliferation of algae. Endotoxin-retentive filters should be fitted with a means of assessing filter integrity and fouling. One suitable means is to monitor the pressure drop, ΔP, across the filter using pressure gauges on the inlet and outlet water lines.

4.2.13 Storage and distribution of dialysis water

4.2.13.1 Piping systems

The dialysis water distribution system shall not contribute chemicals (such as aluminium, copper, lead and zinc) or bacterial contamination to the product water. Dialysis water distribution systems should be designed to minimize bacterial proliferation and biofilm formation, such as by using a continuous recirculation loop with flow in the return line. Areas of stagnant flow (dead zones) in the loop system shall be avoided. Direct feed systems shall include a means of verifiably preventing retrograde flow of water into the distribution loop from the feed side of the reverse osmosis unit.

4.2.13.2 Storage tanks

When used, storage tanks should have a conical or bowl-shaped base and should drain from the lowest point of the base. Bladder tanks and pressurized surge tanks should not be used in the dialysis water distribution system. Storage tanks should have a tight-fitting lid and be vented through a hydrophobic 0,45 µm air filter. Sight tubes should be avoided due to the possible growth of algae and fungi. If an overflow pipe is used, it shall be fitted with a means of preventing contamination. Means shall be provided to effectively disinfect any storage tank installed in a dialysis water distribution system. An endotoxin-retentive filter, or some other form of microbial control device, should be installed distal to the storage tank.

4.2.13.3 Ultraviolet irradiators

When used to control bacterial proliferation in dialysis water storage and distribution systems, UV irradiation devices shall emit light at a wavelength of 254 nm and provide a dose of radiant energy of 30 mW sec/cm^2. If the irradiator includes a calibrated ultraviolet intensity meter, the minimum dose of radiant energy should be at least 16 mW sec/cm^2. The device shall be sized for the maximum anticipated flow rate according to the manufacturer's instructions. UV irradiators should be followed by an endotoxin-retentive filter.

Ultraviolet irradiation can also be used to control bacteria in the pretreatment section of a water treatment system, such as following carbon beds to reduce the bacterial burden presented to a reverse osmosis unit.

To prevent the use of sublethal doses of radiation that could lead to the development of resistant strains of bacteria, UV irradiators shall be equipped with a calibrated ultraviolet intensity meter, as described above, or with an online monitor of radiant energy output that activates a visible alarm, which indicates that the irradiation source should be replaced. Alternatively, the irradiation source should be replaced on

a predetermined schedule according to the manufacturer's instructions to maintain the recommended radiant energy output.

When ultraviolet irradiators are dipped in a storage tank, to control bacteria, they should be designed to keep the required energy at the farthest position in the tank considering the flow situation during operation. The required energy depends on whether sterilization or bacteriostasis is aimed for.

NOTE The recommendations provided in this clause concern UV irradiators used specifically for bacterial control. UV irradiators also can be used for other applications in a water treatment and distribution system. If an ultraviolet irradiator is utilized for reduction of chlorine or chloramine as an adjunct to carbon media, the manufacturer should verify the performance of the device and supply instructions regarding minimum radiant energy and wavelength for continuing performance.

4.2.13.4 Hot water disinfection systems

When used to control bacterial proliferation in water treatment, storage, and distribution systems, the water heater of a hot water disinfection system shall be capable of delivering hot water at the temperature and for the exposure time specified by the manufacturer. Hot water disinfection systems should be equipped with a monitoring system that indicates if the temperature at the point farthest from the water heater drops below the manufacturer's recommended minimum temperature during the disinfection cycle. When disinfection is accomplished automatically by high temperature procedures, activation of the disinfection system shall result in activation of a system indicating that disinfection is in process. Operating controls should be positioned so as to minimize inadvertent resetting.

NOTE For dialysis water distribution loops, the point farthest from the water heater is where the water re-enters the storage tank (indirect feed systems) or where the water returns to the reverse osmosis system (direct feed systems).

4.2.13.5 Ozone disinfection systems

When used to control bacterial proliferation in dialysis water storage and distribution systems, an ozone disinfection system shall be capable of delivering ozone at the concentration and for the exposure time specified by the manufacturer. An ozone concentration of 0,2 mg/l to 0,5 mg/l, combined with a contact time of 10 min, measured at the end of the distribution loop, is capable of killing bacteria, bacterial spores, and viruses in water. Following sanitation, the residual ozone level should be reduced to less than 0,1 mg/l.

When ozone disinfection systems are used, monitoring of the ambient air ozone levels in the area of the ozone generator shall be performed to ensure compliance with exposure limits established by the appropriate health and safety organization.

Activation of an ozone disinfection system shall result in activation of a system to indicate that disinfection is in process and activation of measures to prevent patient exposure to an unsafe condition. Operating controls shall be positioned so as to minimize inadvertent resetting.

5 Tests

5.1 Compliance with dialysis water quality requirements

5.1.1 General

This clause defines test methods by which compliance with the requirements of Clause 4 can be verified.

NOTE The test methods listed do not represent the only acceptable test methods available but are intended to provide examples of acceptable methods. Methods other than those stated can be used provided that they have been appropriately validated and compared to established test methods.

The requirements of ISO 13959 apply to the dialysis water as it enters the equipment used to prepare concentrates from powder 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 and not to each of the individual devices that make up the system. However, collectively, the individual devices shall produce water that meets the requirements of ISO 13959 when provided with potable water as received at the facility or dialysis clinic. Tests for compliance with water quality requirements should be performed when the system is operating under stable conditions representing normal operation.

5.1.2 Microbiology of dialysis water

Samples shall be collected immediately prior to where the water re-enters the storage tank in an indirect feed system or immediately prior to where the water returns to the reverse osmosis system in a direct feed system. Additional samples shall be collected at, or immediately prior to, the point where water enters the equipment used to prepare concentrates or reprocess dialysers if the line supplying that equipment with water is separate from the distribution loop supplying the dialysis machines.

Microbial analysis of water should be conducted as soon as possible after sample collection to avoid unpredictable changes in the microbial population. If samples cannot be analysed within 4 h of collection, follow the laboratory's instructions for sample storage and shipping. Samples intended for colony counts should not be frozen.

Total viable counts (standard plate counts) shall be obtained using the membrane filter technique, spread plates, or pour plates. The calibrated loop technique shall not be used. Culture media shall be tryptone glucose extract agar (TGEA), Reasoner's 2A (R2A) or equivalent. Blood agar and chocolate agar shall not be used. Incubation is at 17 °C to 23 °C and colonies shall be counted after 168 h (7 d) of incubation. Alternative incubation conditions and colony counting times can be used if validated and proven to be equivalent or better than the stated conditions. Endotoxin concentrations shall be determined by the LAL assay or kinetic method validated to yield results that are equivalent to LAL.

5.1.3 Maximum level of chemical contaminants

Chemical analyses of the water contaminants listed in ISO 13959:2014, Table 1 (reproduced as Table B.1) can be obtained by using methods referenced by the American Public Health Association,[3] methods referenced by the US. Environmental Protection Agency,[24] methods referenced in applicable pharmacopoeia, or other equivalent validated analytical methods.

Compliance with the requirements listed in ISO 13959:2014, Table 2 (reproduced as Table B.2) can be shown in one of three ways.

— Where such testing is available, the individual contaminants in ISO 13959:2014, Table 2 can be determined using chemical analysis methods referenced by the American Public Health Association,[3] methods referenced by the US. Environmental Protection Agency,[24] methods referenced in applicable pharmacopoeia, or other equivalent validated analytical methods.

— Where testing for the individual trace elements listed in ISO 13959:2014, Table 2 is not available and the source water can be demonstrated to meet the standards for potable water as defined by the WHO[28] or local regulations, an analysis for total heavy metals can be used with a maximum allowable level of 0,1 mg/l.

— If neither of these options is available, compliance with the requirements of ISO 13959:2014, Table 2 can be met by using water that can be demonstrated to meet the potable water requirements of the WHO[28] or local regulations and a reverse osmosis system with a rejection of >90 % based on conductivity, resistivity or TDS.

Samples shall be collected at the end of the water treatment cascade or at the most distal point in each water distribution loop.

5.2 Compliance with water treatment equipment requirements

5.2.1 General

5.2.1.1 Water treatment system

The need for tests to determine the quality of water used to feed water treatment equipment is dependent upon specific features of the devices. Suppliers of water treatment devices should select and perform such tests (e.g. iron, pH, silica, total dissolved solids, alkalinity, and total hardness) as are necessary to ensure the reliable performance of their devices.

5.2.1.2 Materials compatibility

Biocompatibility testing should begin with a risk analysis. Using the results of that risk analysis, a testing rationale should be developed using, for example, methods described in applicable pharmacopoeia or other appropriate documents.

5.2.1.3 Regenerated or reconstituted devices

The adequacy of disinfection procedures can be demonstrated by culturing a sample of the device's product water following the disinfection procedure. Where regenerated or reconstituted devices are provided by a vendor as medical devices, the disinfection and intermixing requirements of 4.2.1.3 can be demonstrated by certification that the device has been disinfected using validated procedures during regeneration or reconstitution and that validated procedures have been used to ensure that the devices and their component parts have been kept separate from devices and component parts used in non-potable water applications.

5.2.1.4 Disinfection protection

Compliance with the requirements of 4.2.1.4 for chemical disinfection procedures can be determined by testing for the disinfectant in the product water at the end of the disinfection procedure. If a commercially available chemical disinfectant, such as peracetic acid, is used, an established test for residual disinfectant shall be used according to the test manufacturer's instructions, and the residual level shall be less than that recommended by the manufacturer of the specific disinfectant.

When formaldehyde is used, residual levels can be determined by the Hantzsch reaction, Schiff's reagent, or by an equivalent test. Residual levels shall not exceed 3 mg/l or that stated in local requirements.

When sodium hypochlorite is used, the residual level shall be less than 0,1 mg/l.

Compliance with the requirements of 4.2.1.4 for high-temperature disinfection can be shown by demonstrating that the product water has returned to a safe temperature.

Compliance with the requirements of 4.2.1.4 for ozone disinfection can be shown by demonstrating that the ozone concentration in the product water has returned to a safe level (less than 0,1 mg/l).

Compliance with the patient protection requirements of 4.2.1.4 can be demonstrated by inspection.

5.2.2 Backflow prevention devices

Compliance with the requirements of 4.2.2 can be determined by visual inspection.

5.2.3 Tempering valves

Compliance with the requirements of 4.2.3 can be determined by visual inspection and review of manufacturer's specifications.

5.2.4 Sediment filters

Compliance with the requirements of 4.2.4 can be determined by visual inspection.

5.2.5 Cartridge filters

Compliance with the requirements of 4.2.5 can be determined by visual inspection.

5.2.6 Softeners

Compliance with the requirements of 4.2.6 can be determined by inspection.

5.2.7 Anion exchange resin tanks

The performance of anion exchange resin tanks can be checked by periodically testing the feed and product water for total organic carbon (TOC) or tannins. Proper regeneration of the resin tank can be determined by monitoring salt usage and regeneration timer settings.

5.2.8 Carbon media

Total chlorine removal can be used as an indication of carbon capacity. A DPD test kit selected for this purpose or a similar method shall be used to detect breakthrough of total chlorine, carbon exhaustion, or both. DPD materials shall be those designed for total chlorine detection and shall be used according to manufacturers' instructions. Alternatively, online monitors or "dip and read" test strips based on Michler's thioketone (MTK) can be used to measure the concentration of total chlorine. Tests for both free and total chlorine can also be performed to determine if chloramine is present. The difference between total chlorine and free chlorine is combined chlorine, which shall be considered chloramine. The utility of any test is dependent upon the sensitivity and detection limits of the analytical method used. Tests for total chlorine in product water shall have a sensitivity of at least 0,1 mg/l. Alternative tests (e.g. titrometry) should be used to follow up questionable results. Tests are not required for organic or radioactive materials.

Compliance with the configuration requirements of 4.2.8 can be determined by inspection.

5.2.9 Chemical injection systems

Compliance with the requirements of 4.2.9 can be determined by inspection.

5.2.10 Reverse osmosis

Compliance with the performance requirement of 4.2.10 can be determined by the tests of 5.1.2 and 5.1.3.

Compliance with the alarm requirements of 4.2.10 can be determined by the tests of IEC 60601-1-8.

Conductivity, resistivity, or TDS measurements of product water of reverse osmosis devices can be accomplished by using conventional monitors that incorporate temperature compensation features. Compliance with this requirement and the other configuration requirements of 4.2.10 can be determined by inspection.

5.2.11 Deionization

Resistivity measurements for product water of deionizers can be accomplished using conventional resistivity cells that incorporate temperature compensation features. The presence of required safety systems can be verified by inspection.

Compliance with the alarm requirements of 4.2.11 can be determined by the tests of IEC 60601-1-8.

5.2.12 Endotoxin-retentive filters

Compliance with the requirements of 4.2.12 can be shown using the test methodologies for determining bacteria and endotoxin given in 5.1.2.

5.2.13 Storage and distribution of dialysis water

5.2.13.1 Piping systems

The absence of copper, lead, and zinc and the configuration of a water treatment device or system can be determined by visual inspection. Non-contribution of bacteria and specific chemical contaminants to the water by the distribution system can be verified by using the tests described in 5.1.2 and 5.1.3.

5.2.13.2 Storage tanks

Compliance with the requirements of 4.2.13.2 can be determined by visual inspection.

5.2.13.3 Ultraviolet irradiators

Compliance with the requirements of 4.2.13.3 can be determined by visual inspection.

5.2.13.4 Hot water disinfection systems

Compliance with the requirements of 4.2.13.4 can be determined by measuring water temperatures in the fluid pathway being disinfected at the most distal point for the disinfection time specified by the manufacturer.

Compliance with the configuration requirements of 4.2.13.4 can be determined by inspection.

5.2.13.5 Ozone disinfection systems

Compliance with the requirements of 4.2.13.5 can be determined by using an online monitor for dissolved ozone or by analysis of water samples using test kits based on indigo trisulfonate or DPD chemistry.

Compliance with the configuration requirements of 4.2.13.5 can be determined by inspection.

6 Labelling

6.1 General

The term “labelling,” as used in this International Standard, includes any written material accompanying any water treatment device or system, such as instructions for use and operator’s manuals, or any instructions or control feature markings attached to the device or system.

6.2 Device markings

The following information shall accompany each water treatment device or system. Items a) to c) shall be directly affixed to the device or system or, in the case of disposable elements, to the immediate packaging, whereas items d) to f) can be provided in accompanying product literature.

a) Name and address of manufacturer;

b) Trade name and type of device;

c) Model and serial number;

d) A warning that product literature should be read before use (if appropriate);

e) Prominent warnings about substances (e.g. germicides) needing to be removed from the device before using the product water for dialysis;

f) Identification of fitting type or specification when necessary to prevent improper connections.

6.3 Product literature

The manufacturer shall provide literature to each user which contains, but is not necessarily limited to, the following information.

a) Warnings that selection of water treatment equipment for dialysis is the responsibility of the user and that product water should be tested periodically.

b) A description of the device or system, including a list of monitors, alarms, and ancillary devices provided as standard equipment.

c) A schematic diagram of the device or system showing the location of any valves, online monitors, or sampling ports.

d) Operating specifications, such as maximum and minimum input water temperature, pressure and flow rate, limits on input water quality, pressure of product water at various flow rates, and maximum output of product water.

e) Detailed instructions for use, including initial start-up, testing, and calibration, operation and meaning of alarms, operational adjustments to monitors, alarms and controls, and connections to other equipment.

f) For systems, the minimum quality of feed water required for the system to produce dialysis water meeting the chemical requirements of this International Standard.

g) For systems, a warning that although a water treatment system produces water of sufficient quality to meet the requirements of this International Standard, distribution of that water could degrade its quality to the point where it no longer meets the requirements of the International Standard if the distribution system is not maintained appropriately.

h) Safety features and warnings concerning the consequences if these features are circumvented.

i) Information pertaining to online monitors of water quality, including operational factors that could affect monitor performance (e.g. temperature).

j) In the case of systems whose product water is proportionally related to feed water quality, warnings that feed water quality shall be monitored. Since changes in product water could exceed acceptable limits if feed water deteriorates significantly, the user is responsible for monitoring.

k) In the case of activated carbon beds, a warning that exhausted or contaminated carbon should be discarded and replaced with new beds.

l) For devices regenerated or reconstituted offsite, instructions on how to safely reconnect the device to the water treatment system and how to remove any contaminant or disinfectant in the device before use.

m) A statement on regenerated or reconstituted devices, such as deionizers, certifying that there was no intermixing of regenerated or reconstituted devices returned from medical or potable water users and devices returned from process or non-potable water users. A statement that a description of the methods used to ensure that no intermixing occurred is available on request.

n) For automatically regenerated water treatment devices, identification of the mechanism (for example, lock-out valves) that prevents excessive levels of contaminants entering the product water during regeneration.

o) In the case of deionizers, a warning that deionizers should be preceded by an activated carbon bed and a recommendation that they be followed by an endotoxin-retentive filter or other bacteria- and endotoxin-reducing device.

p) In the case of ultraviolet (UV) irradiators, a requirement that the manufacturer disclose the effectiveness of the device in killing specific bacteria under specified operating conditions and a recommendation that UV irradiators be followed by an endotoxin-retentive filter or other bacteria- and endotoxin-reducing device.

q) In the case of hot water disinfection systems, a requirement that the manufacturer disclose the effectiveness of the system in killing specific bacteria under specified operating conditions.

r) In the case of ozone disinfection systems, a requirement that the manufacturer disclose the effectiveness of the system in killing specific bacteria under specified operating conditions and that he provide a warning that product water shall not be used until the minimum time required for ozone to dissipate has elapsed.

s) In the case of hot water disinfection systems, a warning that appropriate heat-resistant materials be used for the fluid pathways to be disinfected with hot water.

t) In the case of ozone disinfection systems, a warning that appropriate ozone-resistant materials be used for the fluid pathways to be disinfected with ozone.

u) Construction materials, identified generically, that contact water.

v) Typical life expectancy, capacity, or indication of the end of life of devices that are non-durable or require periodic regeneration or reconstitution and a statement that additional information on device life expectancy or capacity relative to the user's typical feed water is available upon request. The two principal mechanisms by which carbon removes contaminants from water is by adsorption and catalytic reduction. Organic compounds are removed by adsorption, while residual disinfectants are removed by catalytic reduction. In the case of carbon beds, manufacturers or suppliers should provide a warning that unexpected exhaustion could occur because of variable feed water characteristics. The only safeguard against such unforeseeable eventuality is diligent monitoring of carbon filter effluent by the user.

w) Specified water supply or operating conditions that could cause the device to fail.

x) Information about germicides and cleaning agents known to be compatible with materials used in the device, as well as information about chemicals with which materials used in the device are incompatible.

y) If applicable, a method of cleaning and disinfecting the equipment, and of removing residual germicide, so that the system of which the equipment is part is capable of meeting the requirements for microbial and endotoxin contamination given in 4.1.2.

z) Other maintenance and service instructions, including recommended preventive maintenance procedures and schedules, recommended monitoring schedules, troubleshooting guidelines intended for the user, service information, a recommended spare parts list, and a warning of the consequences if maintenance instructions are not followed.

aa) A warning that if, after installation and subsequent use, any device in the water treatment system is changed or replaced, the user should conduct appropriate tests to ensure that the revised system meets the initial design criteria.

bb) Information on storage, if allowed, of devices while not in use, including appropriate packing chemicals, storage conditions, and duration.

Annex A
(informative)

Rationale for the development and provisions of this International Standard

A.1 Scope

The items included within the scope of this International Standard are equipment used to treat water for the preparation of concentrates and dialysis fluid, or for the reprocessing of dialysers for multiple uses, and the devices used to store and distribute this water.

This International Standard seeks to prevent the use of options that are hazardous to patients treated with haemodialysis and related therapies. For example, this International Standard is needed to prevent poisoning caused by formulation of dialysis fluid with water that contains high levels of certain contaminants.

Water treatment and distribution systems incorporate a variety of devices. These devices can be provided and installed by different vendors, making it difficult to assign responsibility for compliance with this International Standard to any one individual or company. To address this concern, primary responsibility for compliance with this International Standard was placed on the individual or company that specifies the water treatment and distribution system installed in a given situation. Responsibility could also lie with the vendor who assembles and installs the system and with the manufacturer of any individual device of the water treatment and distribution system if that manufacturer specifies that their device is intended for haemodialysis applications.

A.2 Requirements

A.2.1 Dialysis water quality requirements

A.2.1.1 General

Individual water treatment devices might not provide water that meets the requirements of this International Standard in its entirety. ISO 13959 for dialysis water gives the requirement that a water system be maintained in a condition to continually meet ISO 13959 defined water quality without giving a method of accomplishing the requirements. This International Standard is directed at the manufacturer of the dialysis water treatment systems and defines the requirements that the manufacturer should meet prior to the user assuming responsibility for the water system. However, manufacturers of individual water treatment devices should be aware of the requirements for the final dialysis water and that they should be prepared to recommend other water treatment devices that might need to be used in conjunction with their device to produce water which meets the requirements of this International Standard.

A.2.1.2 Microbiology of dialysis water

The supplier of water treatment equipment is responsible for recommending a method of cleaning the equipment so that dialysis water meeting the microbial requirements of ISO 13959 can routinely be produced when typical feed water is presented. Beyond this qualification, it becomes the responsibility of the user of the system to monitor the system for ongoing compliance with ISO 11663. The rationale for these microbiological contaminant requirements is set forth in Annex A of ISO 13959:2014.

A.2.1.3 Maximum level of chemical contaminants

The rationale for the chemical contaminant requirements is set forth in Annex A of ISO 13959:2014

Tables B.1 and B.2 should not be taken as a definitive list of harmful substances, but as a partial listing of those that might reasonably be expected to be present and have clinical implications. At the time this International Standard was prepared, it was not possible to specify threshold values for organic contaminants permitted in water used for the preparation of dialysis fluids, concentrates, and reprocessing of haemodialysers. The issue of organic contaminants will be reassessed during the next revision of this International Standard.

Iron is not included because it does not enter the patient's blood in sufficient quantities to cause toxicity. Iron can, however, cause fouling of water treatment devices (see 4.2.1.1) or dialysis fluid supply systems. While a specific limit was not set, water treatment equipment suppliers are encouraged to consider the iron content of the feed water when recommending suitable equipment. A concern was raised regarding the injection of formulated phosphates (known as polyphosphates) primarily to bind iron and manganese to avoid the staining of fixtures and clothing. The concern was raised that this practice could cause significant problems in water treatment. Some municipal water suppliers were considering the use of chlorine dioxide as a disinfectant for potable water supplies. Chlorine dioxide breaks down in water to yield chlorite, chlorate, and chloride ions. Little information about the potential for chlorine dioxide and its daughter products to be toxic to haemodialysis patients could be found. A limited study of 17 patients unknowingly treated with water prepared by carbon and reverse osmosis from water disinfected with chlorine dioxide showed no evidence of adverse effects.[2] In that study, the water used to prepare dialysis fluid contained 0,02 mg/l to 0,08 mg/l of chlorite ions and no detectable chlorate ions. However, the patient population was small and potentially important haematological parameters were not measured. Further, there were only sparse data included on the removal of chlorine dioxide, chlorite ions, and chlorate ions by carbon and reverse osmosis, and it was not clear that sufficiently sensitive methods were available for their analysis in a dialysis facility. Therefore, there was no basis for setting maximum allowable levels of chlorine dioxide, chlorite ions, or chlorate ions in water to be used for dialysis applications or for making recommendations on methods for their removal at that time. However, in specifying water treatment systems, manufacturers of such systems should be aware of the possibility that municipal water suppliers can add chlorine dioxide to the water.

A.2.2 Water treatment equipment requirements

A.2.2.1 General

A.2.2.1.1 Water treatment system

The supplier of the complete water treatment system is responsible for assuring that the water produced by the system can routinely meet the maximum allowable chemical contaminant levels specified in Tables B.1 and B.2, or the prescription of the physician, at installation. Beyond this qualification, it becomes the responsibility of the physician in charge of dialysis to monitor the system to ensure that the treatment device or devices maintain an acceptable level of purity of the water. Variations in water quality or the presence of as-yet-unidentified toxic substances will obviously compromise the system's safety.[13] Such variations typically do occur, and while the supplier cannot be held accountable for the performance of the water treatment system during such variations, selection of water purification equipment should include careful consideration of methods to cope with such changes, many of which can be anticipated through consultation with state and local water authorities.

The medical director has the ultimate responsibility for the selection and use of water treatment devices on the basis of the supplier's recommendations. If a supplier is convinced that the local water quality is such that the selection of a minimum system does not provide an adequate margin of safety, then the supplier should recommend additions to the system or alternative systems with corresponding rationale. Continued monitoring of the water supply is necessary to maintain treatment methods consistent with safety.

A.2.2.1.2 Materials compatibility

Non-toxicity of construction materials for haemodialysis water treatment equipment is of major importance. Some well-recognized non-toxic materials include certain stainless steel formulations, silicon rubber, borosilicate glass, polypropylene, polyvinylchloride (PVC), chlorinated PVC (CPVC), polyvinylidene fluoride (PVDF), polyethylene, cross-linked polyethylene (PEX), and polytetrafluorethylene (PTFE). Data are now available that demonstrate that materials once regarded as inert can in fact be toxic in this application (e.g. copper leaches from copper conduits, especially in the presence of low pH, which can result when a deionizer is exhausted).[13] Other materials have been documented as being hazardous to the patient (e.g. brass, zinc, iron, and aluminium), and these materials should also be avoided. The hidden hazard with respect to construction materials derives from long-term cumulative toxicity. Hemodialysis is a long-term chronic treatment modality, and this fact should be acknowledged when selecting construction materials. A risk analysis according to ISO 14971 should be used to assess the suitability of materials based on existing data. If that analysis suggests the need for additional testing, that testing should be based on the approaches outlined in the ISO 10993 series of standards. Users of this document should be aware of the requirements of those standards.

Repeated exposure to ozone or hot water might have a deleterious effect on some plastic or metal materials. Therefore, manufacturers are required to include warnings that only ozone- or heat-compatible materials be used in piping systems intended for use with ozone or hot water disinfection devices, respectively (see 6.3).

A.2.2.1.3 Regenerated or reconstituted devices

Regenerated or reconstituted devices are subject to bacterial contamination that can cause excessive bacterial counts in product water (see 4.1.2). Disinfection procedures are required to minimize this risk. When devices are regenerated at a central facility, there is a risk of cross-contamination and improper disinfection and rinsing.[13] Some exchange-type deionizers are used for both dialysis and industrial recovery of plating metals, such as chromium and silver, from effluent process water. In some regeneration facilities, resins from both processes or non-potable users and from medical or potable users are regenerated together as a batch. Traces of these toxic metals will remain bound to the resins and could be eluted into water during subsequent use. For that reason, such mixed use is prohibited in this International Standard.

A.2.2.1.4 Disinfection protection

Disinfection procedures can render product water unsafe because of toxic chemicals or excessive temperatures. Therefore, provision was made for restoring the water treatment system to a safe condition after disinfection. Although the user is responsible for carrying out manual disinfection procedures, the manufacturer should demonstrate that recommended disinfection procedures meet the requirements of 4.2.1.4.

A.2.2.2 Backflow prevention device

A backflow prevention device isolates the water treatment system from the potable water supply, thereby protecting the potable water system from possible contamination in the event of a sudden reduction in pressure in the potable water supply.

A.2.2.3 Tempering valves

The performance of many water treatment devices is temperature sensitive. In less temperate climates, seasonal fluctuations in cold water temperature could impact the performance of these devices. A tempering valve can be used to blend hot and cold water to provide a constant feed water temperature independent of any seasonal changes in feed water temperature. Excessive water temperatures resulting from malfunction of a tempering valve can damage downstream devices, including reverse osmosis membranes and plastic pipes and pipe fittings. For that reason, consideration was given to requiring that tempering valves be fitted with a water temperature monitor that activates an audible alarm in the

event that a high temperature is sensed. While recognizing the potential for equipment to be damaged by hot water, no consensus could be reached on the need for such a requirement.

A.2.2.4 Sediment filters

Accumulation of organics, bacteria, and algae in filters can lead to proliferation of bacteria to the point of overloading downstream devices or producing dangerous endotoxin levels. Use of opaque housings to reduce the light that promotes algae growth and differential pressure monitoring can reduce this risk.

A.2.2.5 Cartridge filters

Accumulation of organics, bacteria, and algae in filters can lead to proliferation of bacteria to the point of overloading downstream elements or producing dangerous endotoxin levels. Use of opaque housings to reduce the light that promotes algae growth and differential pressure monitoring can reduce this risk. In the pretreatment cascade, transparent filter housings can be useful because they allow any carbon or resin leakage to be seen without the need to break the integrity of the system. The housing can be cleaned to remove any growth when the filter cartridges are changed. For this reason, use of opaque housings for cartridge filters is recommended, but not required. If transparent housings are used, they should not be exposed to natural light, in order to minimize proliferation of algae.

A.2.2.6 Softeners

The process by which "hard" water (containing high levels of calcium and magnesium) is made "soft", involves the exchange of sodium ions for the calcium and magnesium in the water supply. The resin should be regenerated with brine to sustain capacity for exchange. Regeneration can be either manual or automatic with a timer to regenerate outside operating hours. During regeneration, excess sodium can enter the product water stream if there is a temporary interruption of power, a malfunction in regeneration control, or inadequate water pressure. There are no monitors on a softener to detect excess sodium in the product water stream, and the physiological effects of excess sodium in the patient are severe.[18],[21] Therefore, protection against such excessive levels of sodium, as can occur during regeneration of a water softener, is required. An automatic bypass valve most easily provides this protection during the regeneration cycle.

A.2.2.7 Anion exchange resin tank

High levels of organic matter in the source water can foul carbon media. Organic molecules (usually very large) are attracted to carbon and become attached at the pore sites, effectively blocking the pore and sealing off the surface area within that pore. As organic molecules accumulate on the surface of the carbon, there is less surface area available for removal of chlorine. Organic scavengers operate similar to a water softener, exchanging anions and organic matter for chloride ions. Source water testing for organics (TOC or tannins) can indicate if an organic scavenger will help protect carbon media.

A.2.2.8 Carbon media

Carbon beds are particularly prone to bacterial growth because of their porosity and affinity for organics. More stringent requirements for the installation of carbon beds and their monitoring are included because of continued reports of clusters of haemolysis related to insufficient removal of chloramine from municipal water supplies.[8],[23],[27] In the United States, changes to the *Safe Drinking Water Act*, designed to eliminate lead and copper from tap water,[20] have reinforced the need for careful monitoring of carbon beds because the increase in water pH that can accompany the institution of these changes can decrease the capacity of carbon for chloramine.

Activated carbon can be regenerated by a number of techniques, including oxidation at high temperatures and stripping with low-pressure steam or solvents. Regeneration of activated carbon, also known as reactivation, is used in industrial applications where activated carbon can be used to remove organic and inorganic substances such as pollutants from process streams. No evidence that regenerated carbon was being used for haemodialysis applications could be found. However, it was deemed prudent

to prohibit the use of regenerated carbon in haemodialysis applications to avoid any potential hazard resulting from residual toxins that could remain in the carbon following regeneration.

Depending on the source material used for its manufacture, and the manufacturing process, granular activated carbon can contain carbon fines and other contaminants, such as aluminium. If present, these substances will leach out of a carbon bed during the initial stages of operation. Carbon fines can contribute to fouling of reverse osmosis membranes downstream of the carbon beds and any metal ions can add to the burden of contaminants, which should be removed from the water. Acid washing of carbon minimizes the amount of fines and other contaminants, and a requirement for the use of acid-washed carbon was considered. No consensus could be reached on this issue because rinsing of carbon beds before they are placed online in a water treatment cascade will also effectively remove fines and other contaminants.

The requirement for two beds in series and a 10 min empty-bed-contact-time was waived for portable dialysis systems provided there is a redundant means of chloramine removal because of the impracticality of providing these features while retaining the portability of the system. Possible alternatives include a granular activated carbon bed followed by a dense carbon block and two carbon block filters in series. However, when a single carbon bed is used, it is important to ensure that the bed has adequate capacity to remove chloramine for the duration of an entire treatment given the typical feed water concentration of chloramine in the setting where the bed is being used.

Although treatment of water by carbon is the usual method of meeting the requirement of 4.1.3 when the feed water contains chloramine, in certain situations, such as acute or home dialysis with portable water treatment systems, it might not be practical to use the volume of carbon required for this purpose. In such circumstances, combining limited carbon with the addition of ascorbic acid to the acid concentrate has been used to eliminate chloramine from the final dialysis fluid.[27] It should be noted that some minimum contact time is required for ascorbic acid to neutralize chloramine in water. If ascorbic acid is being used to neutralize chloramine, and unexplained red blood cell destruction or anaemia occurs, the effectiveness of the ascorbic acid neutralization of chloramine should be investigated.

In most circumstances, conventional carbon systems provide months of effective chlorine/chloramine removal. Occasionally, conventional carbon systems experience premature breakthrough necessitating carbon bed replacement/exchange within days rather than months. These occasions could be episodic or persistent in nature. Episodic carbon filter breakthrough is often associated with periodic municipal water treatment practices, such as short-term substitution of free chlorine for chloramine. Persistent difficulties with premature breakthrough of carbon systems could be related to the source water itself (pH, TOC level, etc.) or a routine municipal water treatment practice, such as the addition of corrosion inhibitors. The occurrence of these problems seemed to be increasing. Therefore, clauses on optional water purification system devices that might help address recurrent premature exhaustion of carbon media or enhance the efficiency of the carbon media were added. Two approaches were included: anion exchange resins that scavenge large organic molecules that can coat the carbon surface, and systems that inject sodium bisulfite, which reduces chloramine to chlorine, or acid to adjust the pH to the optimal range for removal of chloramine by carbon. Including the use of redox alloy media (RAM), also referred to as kinetic degradation fluxion (KDF), was also considered. This material can be an effective pretreatment for conventional carbon filters experiencing premature breakthrough due to municipal short-term substitution of free chlorine for chloramine or for supply waters having high organic loading. A disadvantage of KDF media is that both copper and zinc are eluted from the medium, albeit at very low levels. Concerns about how the eluted copper and zinc might affect downstream devices, together with questions about the effectiveness of KDF media, lead to the omission of this alternative.

A.2.2.9 Chemical injection systems

There were reservations about the addition of chemicals to the water. However, it was recognized that the addition of chemicals could be necessary in some circumstances if a facility is to meet the maximum contaminant levels set forth in 4.1.3. For example, if the municipal water contains high levels of *N*-chloramines or chloramine in the presence of orthophosphate or polyphosphate, injection of sodium bisulfite could be one of the few options available for chloramine removal. If chemical injection is used in the pretreatment cascade, users should ensure that the addition of the chemical does not interfere with the operation of subsequent purification processes, including the primary purification process. For

example, the performance of thin-film composite reverse osmosis membranes can be affected by the pH of the feed water. At pH levels below 7, the rejection of fluoride can be substantially reduced, compared to its rejection at a pH of 8.

A.2.2.10 Reverse osmosis

A reverse osmosis system should demonstrate delivery of water meeting the requirements of 4.1.2 and 4.1.3; otherwise, additional treatment devices should be recommended to the user. Monitoring requirements for reverse osmosis systems are recommended on the basis of totally different degradation characteristics of these systems as compared with deionizer systems. On initial setup, the reverse osmosis device should have a rejection rate that ensures that the product water of the water treatment system meets the requirements of 4.1.3. Because this rejection rate varies with different installations, an absolute level is not required. Monitoring is defined in terms of the salt passage rate or percent rejection and a threshold level of product water resistivity or conductivity. Compliance with both monitored parameters is required because an increase in feed water contaminants could result in product water unsuitable for haemodialysis applications even though the percent rejection of the membrane modules remains high.

Consensus could not be reached on how to establish the alarm limits for rejection and product water resistivity or conductivity. As noted above, changes in feed water quality will result in changes in product water quality even though rejection remains constant. Also, a significant change in the feed water concentration of one trace inorganic contaminant might not appreciably alter the product water resistivity even though the product water concentration of that contaminant exceeds the allowable limit. For that reason, some felt that routine analysis of feed water quality should be emphasized. Others felt that the rejection alarm limit could be set based on the reduction ratio for each contaminant that can be achieved by reverse osmosis[15] and the assumption that the feed water would meet the requirements of the *Safe Drinking Water Act* or other applicable standards. Either approach could be effective when incorporated into an overall monitoring programme designed to protect the patient against exposure to contaminant levels in excess of those listed in Tables B.1 and B.2.

Consensus could not be reached regarding the inclusion of a requirement that reverse osmosis systems incorporate as a means of diverting the product water to drain in the event of a product water conductivity or rejection rate alarm. Some felt that a divert-to-drain should be required because reverse osmosis is frequently the primary means of water purification. However, others felt that including a divert-to-drain should be optional. They pointed out that, because reverse osmosis membranes tend to fail gradually, the risk is different from exhaustion of a deionizer where very high levels of contaminants, such as fluoride, can occur abruptly in the product water because of competitive binding at the ion exchange sites of the deionizer resin. Furthermore, with direct feed water distribution systems, a divert-to-drain would cause an immediate alarm condition with all dialysis machines as a result of interrupting their water supply. Under such circumstances, the ability to discontinue dialysis effectively could pose the lowest risk to the patients. Therefore, a divert-to-drain was included as a recommendation and not as a requirement.

Requirements for alarm systems in medical electrical equipment are addressed in IEC 60601-1-8. During the 2012 revision of this International Standard, consideration was given to substituting reference to IEC 60601-1-8 for the alarm system requirements included in the 2009 version of the International Standard. Because reverse osmosis systems are often remote from the treatment area, an audible alarm in the treatment area was considered necessary if the reverse osmosis system did not have a means of preventing water from reaching the dialysis machine as its primary safety system should the product water conductivity exceed a preset value. There was concern that IEC 60601-1-8 did not necessarily require an audible alarm. Therefore, it was decided to retain the requirements for an audible alarm, in addition to the requirements of IEC 60601-1-8. IEC 60601-1-8 classifies alarms as low-priority, medium-priority, and high-priority based on potential harm to patients should a system failure occur. For reverse osmosis systems with a means of preventing water from entering the dialysis machine, if product water conductivity exceeded a preset value, a low-priority alarm was considered sufficient; whereas, for a reverse osmosis system without a means of preventing water from entering the dialysis machine if product water conductivity exceeded a preset value, i.e. one in which the alarm is the primary safety system, a medium priority alarm was required. A medium-priority, rather than a high-priority, alarm was chosen because the risk of immediate death or injury as the result of reverse osmosis system failure

was considered to be very low. The question of whether or not audible alarms should be capable of being silenced provoked some discussion. On one hand, some felt that audible alarms should not be capable of being silenced because the alarm condition could be overlooked, allowing a dangerous situation to ensue. On the other hand, an audible alarm capable of being temporarily silenced was suggested so that the operator would have a relatively unharried period of time to correct the fault condition. It was concluded that the ability to silence an audible alarm for up to 180 s was a reasonable requirement.

A.2.2.11 Deionization

Deionizer systems, during exhaustion, have the capability of releasing into the water potentially harmful contaminants at levels much higher than are present in the untreated feed water.[12],[6] The monitor level of 1 MΩ·cm specific resistivity was selected as the point at which most of the useful capacity of the deionizers used in dialysis water treatment has been consumed and below which rapid degradation of ion removal efficiency takes place; 1 MΩ·cm specific resistivity is not the minimum safe value for dialysis water, but deionizer systems producing water dropping below this value are in danger, during the following dialysis treatment, of producing water high in toxic contaminants as the final deterioration of resin accelerates. A requirement that the product water be diverted to drain was included because of the acute danger that an exhausted deionizer can pose to patients.[4] The requirement for activated carbon in advance of the deionizer prevents generation of possibly carcinogenic nitrosamines.[22] Deionizers are subject to bacterial contamination because of the porous structure of the resins. Although the level of bacterial contamination in product water from deionizers varies widely, it is generally highest after the deionizer has been idle for some time and lowest after continuous use. Because deionizers are usually placed last in a purification cascade, they should be followed by an endotoxin-retentive filter or another bacteria and endotoxin removing device to prevent bacterial contamination of the water storage and distribution system.

For the reasons outline in A.2.2.10 for reverse osmosis, it was decided to retain the requirements for an audible alarm in addition to requiring that the alarms comply with IEC 60601-1-8. High-priority alarms were selected for deionizers because of the risk of immediate death or injury should the product water specific resistivity drop below 1 MΩ·cm and the divert to drain fail.[4] The question of whether or not audible alarms should be capable of being silenced provoked some discussion. On one hand, some felt that audible alarms should not be capable of being silenced because the alarm condition could be overlooked, allowing a dangerous situation to ensue. On the other hand, an audible alarm capable of being temporarily silenced was suggested so that the operator would have a relatively unharried period of time to correct the fault condition. It was concluded that the ability to silence an audible alarm for up to 180 s was a reasonable requirement.

A.2.2.12 Endotoxin-retentive filters

Endotoxin-retentive filters are increasingly being used to provide water of high microbiologic quality for dialysis applications. Endotoxin-retentive filters include ultrafilters that remove endotoxin primarily by size exclusion, although some can also remove some endotoxin by adsorption to the membrane material, and microfilters that remove endotoxin primarily by adsorption to the membrane material. Because of the two different mechanisms of endotoxin removal, and because the role of endotoxin-retentive filters is to remove bacteria and endotoxins, they have been defined in these terms. This choice also provides a basis for monitoring the performance of endotoxin-retentive filters after they have been installed in a water treatment purification system. Consensus could not be reached regarding minimum performance criteria for the removal of bacteria and endotoxins by an endotoxin-retentive filter. One factor contributing to this impasse is the dependence of filter performance on the test conditions. Therefore, it was decided to require that manufacturers disclose the minimum performance of their device and that the device be required to perform to at least this level under stated operating conditions. Some considered that an endotoxin-retentive filter should be able to reduce the concentration of bacteria in the feed water to the filter by a factor of at least 10^7 and that of endotoxin by a factor of at least 10^3. Methods for determining bacteria and endotoxin rejection by ultrafilters have been published by the Japanese Standards Institute[10],[11] and ASTM.[5]

The recommendation to use endotoxin-retentive filters in a cross-flow configuration is aimed at preventing excessive replacement of membrane modules, which could result from rapid fouling if the

filter is operated in the dead-end mode. However, a dead-end configuration might perform satisfactorily in situations where the water quality is generally good (for example, as final filtration of water immediately before its use in dialyser reprocessing equipment). Differential pressure measurements can be used to monitor fouling of both cross-flow and dead-end filters.

A.2.2.13 Storage and distribution

A.2.2.13.1 Piping systems

The distribution system has been implicated in several bacterial contamination episodes involving dialysis patients.[19] Specific design criteria, such as minimum flow velocities, to minimize bacterial proliferation and biofilm formation[9] were considered. Desirable design criteria include use of a distribution loop, an absence of multiple branching and dead-ended pipes, the use of simple wall outlets with the shortest possible fluid path, a minimum of pipe fittings, and the use of valves with minimal dead space. Also, joints between sections of piping and between piping and fittings should be formed in a manner that minimizes the formation of crevices and other voids that could serve as sites for bacterial colonization. Agreement could not be reached concerning a minimum flow velocity. Some were of the opinion that the low shear stresses existing at the internal surface of a pipe operating at flow rates that are feasible in distribution systems for dialysis water are insufficient to prevent bacterial adhesion and biofilm formation. On the other hand, data from the semiconductor industry were presented showing that a Reynolds number of 3 000 in a piping system was sufficient to prevent bacterial contamination in water.[14] A Reynolds number of approximately *Re* 3 000 is obtained with a flow velocity of about 0,15 m/s in a 2 cm diameter pipe (0,5 ft/s in a 3/4" diameter pipe). However, even in systems operating with *Re* 3 000, biofilm was found on the internal surface of the pipes.[14] Further, in many dialysis facilities, there is no flow through the distribution system when the dialysis facility is not in operation, such as at night and on Sundays. Even if it were possible to specify a minimum flow velocity that was effective in reducing biofilm formation and bacterial contamination, use of such a minimum flow velocity would not provide a substitute for regular disinfection of the distribution system.

Direct feed systems commonly return water from the dialysis water distribution loop to the feed side of the reverse osmosis unit, before the pressurizing pump. With this configuration, it is possible for water from the feed side of the reverse osmosis unit to flow retrograde into the dialysis water distribution loop if the pressure in the distribution loop suddenly decreases as the result of a sudden increase in demand for dialysis water. Because retrograde flow allows contaminated water to enter the dialysis water distribution system, it was considered necessary to recommend some means of preventing retrograde flow. A common method is to include dual check valves at the end of the distribution loop. Some were concerned that there is no means of monitoring the integrity of these valves. A second approach is to return the dialysis water into a break tank at the inlet to the pressurizing pump of the reverse osmosis unit.

A.2.2.13.2 Storage tanks

When storage tanks form part of the water treatment infrastructure, the volume and low water velocities in such tanks predispose them to bacterial contamination. As a consequence, tanks should be designed with features that facilitate disinfection procedures and prevent the entry of bacteria.

A.2.2.13.3 Ultraviolet irradiators

The effectiveness of UV irradiation depends on the dose of radiant energy. Several studies have demonstrated that a dose of 30 mW sec/cm^2 will kill greater than 99,99 % of a variety of bacteria, including *Pseudomonas* species, in a flow-through device.[16],[17] However, certain gram-negative water bacteria appear to be more resistant to UV irradiation than others, and use of sub-lethal doses of UV radiation, or an insufficient contact time, could lead to proliferation of these resistant bacteria in the water system (Carson and Petersen[7]).

The radiant energy emitted by the mercury vapour lamps used in UV irradiators decreases with time. If the lamp is not replaced before its radiant energy decreases below the effective threshold, resistant bacteria could also develop. Therefore, the requirement for an online monitor of the radiant

energy emitted by the lamp is included in this International Standard. Because the effectiveness of UV irradiation depends on the geometry of the device and the exposure time of water to the radiation, the manufacturer of a UV irradiation device is required to provide information on the killing of specific bacteria under specified operating conditions. Because UV irradiators do not eliminate endotoxin and could even increase endotoxin concentrations by killing bacteria, a recommendation was included that they be followed by an endotoxin-retentive filter. Use of an endotoxin-retentive filter was not made a requirement however, because reliance on an endotoxin-retentive filter to remove endotoxin should not be considered an alternative to identifying and eliminating the source of bacterial contamination.

Ultraviolet irradiation has also been used to eliminate chloramine as an alternative or adjunct to activated carbon. Ultraviolet irradiation at a wavelength of 254 nm converts chloramine (NH_2Cl) to chloride and ammonium ions, which are easily rejected by reverse osmosis. Hard water, high total dissolved solids (TDS), or high levels of fluoride, iodine, iron, or manganese could interfere with penetration of ultraviolet irradiation through the water and inhibit the effectiveness of ultraviolet irradiation in eliminating chlorine/chloramine.

A.2.2.13.4 Hot water disinfection systems

Hot water disinfection of dialysis water storage and distribution systems is one means of controlling bacterial proliferation. The manufacturer of a hot water disinfection system should validate the recommended operating conditions to demonstrate that they provide adequate reduction in bacterial levels and also disclose these operating specifications of the system. Repeated exposure to hot water might have a deleterious effect on some plastic piping. Therefore, a requirement that manufacturers of hot water disinfection systems include a warning in their product labelling about the need to use heat-resistant materials in piping systems to be disinfected with hot water was added to this International Standard.

A.2.2.13.5 Ozone disinfection systems

Ozonation is being introduced as a new means of controlling bacterial proliferation in dialysis water storage and distribution systems. This technology might have widespread applicability in dialysis facilities in light of the increased concern about endotoxin contamination of dialysis fluid. Insufficient data are available to set performance standards for such systems, such as ozone concentration and exposure time. Therefore, a requirement that the manufacturer of an ozone disinfection system disclose the operating specifications of the system until such time as performance criteria could be established was included. The manufacturer of an ozone disinfection system should validate the recommended operating conditions to demonstrate that they provide adequate reduction in bacterial and, if applicable, endotoxin levels. The presence of ozone in dialysis water could be harmful to patients, however robust data demonstrating clinical effects is currently absent. It is, however, known that low levels of ozone have the potential to supress immune system response.[30] Therefore, a requirement for manufacturers to include a warning that product water should not be used until ozone produced in the disinfection process has dissipated [see 6.3 item r)] was included. The manufacturer should validate that residual ozone in the product water falls to acceptable levels at the end of the recommended minimum elapsed time between disinfection and use of the product water. Alternatively, the manufacturer of an ozone disinfection system can provide the user with a means of verifying that the residual ozone is within acceptable limits before product water is used. Repeated exposure to ozone could have a deleterious effect on some plastic piping. Therefore, a requirement that manufacturers of ozonation systems include a warning in their product labelling about the need to use ozone-resistant materials in piping systems to be disinfected with ozone was added to this International Standard.

A.3 Tests

A.3.1 Compliance with dialysis water quality requirements — Microbiology of dialysis water

The rationale for the culturing methods required in this International Standard is set forth in Annex A of ISO 13959:2014.

A.3.2 Compliance with water treatment equipment requirements — Materials compatibility

It has been argued that the biocompatibility tests outlined in the appropriate *pharmacopeia* were not useful for water treatment equipment because they were not sensitive enough to detect the presence of small amounts of toxin in large volumes of water. It was proposed that the appropriate *pharmacopeia* biocompatibility tests be replaced by leach testing and measurement of total organic carbon in the leachate. After discussion, this proposal was rejected because there was no clinical outcomes data suggesting a change was necessary and because no standardized methodology for such leach testing was available.

A.4 Labelling

Some existing regulations contain requirements for the labelling of medical devices, including such information as name and address of manufacturer and lot number. Redundancy of these requirements was deemed preferable to omission however, and a requirement that some of the same information already mandated by other regulations was included. The provisions of the other requirements of 6.2 and 6.3 are intended to ensure that certain information specifically necessary for the safe and effective use of haemodialysis systems will be included in the device labelling. For most of this information, the underlying reasoning for the requirement is self-evident. Additional rationale for certain of these requirements is provided below.

Display of basic information about precautions before use is provided to ensure the safe and effective use of the device.

The quality of water used during dialysis is critical. Thus, certain information should be provided to the user so that appropriate precautions can be taken before the use of water for dialysis applications. The specialized information of 6.3 reflects an attempt to provide the user with sufficient information to minimize the risks of using improper water during dialysis.

Annex B
(informative)

Reference tables from ISO 13959

NOTE The maximum allowable levels of contaminants listed in Tables B.1 and B.2 are identical to the reference tables in ISO 13959:2014. The values shown include the anticipated uncertainty associated with the analytical methodologies listed in Table B.3.

Table B.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	0,1
Copper	0,1
Fluoride	0,2
Lead	0,005
Nitrate (as N)	2
Sulfate	100
Zinc	0,1
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)

NOTE This table is reproduced from ISO 13959.

[a] A dialysis facility's Medical Director has the ultimate responsibility for ensuring the quality of water used for dialysis.

[b] Unless otherwise noted.

Table B.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	0,0004
Cadmium	0,001
Chromium	0,014
Mercury	0,0002
Selenium	0,09
Silver	0,005
Thallium	0,002
NOTE This table is reproduced from ISO 13959.	

Table B.3 — Analytical test methods for chemical contaminants

Contaminant	Analytical technique	Reference, method number
Aluminium	Inductively-coupled plasma mass spectrometry or Atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3113
Antimony	Inductively-coupled plasma mass spectrometry or Atomic absorption (platform)	ISO 17294-2:2003 US EPA, #200.9
Arsenic	Inductively-coupled plasma mass spectrometry or Atomic absorption (gaseous hydride)	ISO 17294-2:2003 American Public Health Assn, #3114
Barium	Inductively-coupled plasma mass spectrometry or Atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3113
Beryllium	Inductively-coupled plasma mass spectrometry or Atomic absorption (platform)	ISO 17294-2:2003 US EPA, #200.9
Cadmium	Inductively-coupled plasma mass spectrometry or Atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3113
Calcium	Inductively-coupled plasma mass spectrometry or EDTA titrimetric method or atomic absorption (direct aspiration) or ion specific electrode	ISO 17294-2:2003 American Public Health Assn, #3500-Ca D American Public Health Assn, #3111B
Total chlorine	DPD ferrous titrimetric method or DPD colourimetric method TMK/MTK colourimetric method	American Public Health Assn, #4500-Cl F American Public Health Assn, #4500-Cl G
Chromium	Inductively-coupled plasma mass spectrometry or Atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3113
Copper	Inductively-coupled plasma mass spectrometry or Atomic absorption (direct aspiration), or neocuproine method	ISO 17294-2:2003 American Public Health Assn, #3111 American Public Health Assn, #3500-Cu D

Table B.3 *(continued)*

Contaminant	Analytical technique	Reference, method number
Fluoride	Ion chromatography or Ion selective electrode method or sodium 2-(parasulfophenylazo)-1,8-dihydroxy-3,6-naphthalenedisulfonate (SPADNS) method	ISO 10304-1:2007 ISO 10359-1:1992 American Public Health Assn, #4500-F^- C American Public Health Assn, #4500-F^- D
Lead	Inductively-coupled plasma mass spectrometry or Atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3113
Magnesium	Inductively-coupled plasma mass spectrometry or Atomic absorption (direct aspiration) Ion chromatography	ISO 17294-2:2003 American Public Health Assn, #3111 EPA300.7;1986
Mercury	Flameless cold vapour technique (atomic absorption)	American Public Health Assn, #3112
Nitrate	Ion chromatography or Spectrophotometric method suing sulfosalicylic acid or Cadmium reduction method	ISO 10304-1:2007 ISO 7890-3:1988 American Public Health Assn, #4500-NO_3 E
Potassium	Inductively-coupled plasma mass spectrometry or Atomic absorption (direct aspiration) or flame photometric method or ion specific electrode	ISO 17294-2:2003 American Public Health Assn, #3111 American Public Health Assn, #3500-K D American Public Health Assn, #3500-K E
Selenium	Inductively-coupled plasma mass spectrometry or Atomic absorption (gaseous hydride), or atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3114 American Public Health Assn, #3113
Silver	Inductively-coupled plasma mass spectrometry or Atomic absorption (electrothermal)	ISO 17294-2:2003 American Public Health Assn, #3113
Sodium	Inductively-coupled plasma mass spectrometry or Atomic absorption (direct aspiration) or flame photometric method or ion specific electrode	ISO 17294-2:2003 American Public Health Assn, #3111 American Public Health Assn, #3500-Na D
Sulfate	Ion chromatography or Turbidimetric method	ISO 10304-1:2007 American Public Health Assn, #4500-SO_4^{2-} E
Thallium	Inductively-coupled plasma mass spectrometry or Atomic absorption (platform)	ISO 17294-2:2003 US EPA, #200.9
Total heavy metals	Colourimetric	European Pharmacopoeia, 2.4.8 US Pharmacopoeia, < 231 >
Zinc	Inductively-coupled plasma mass spectrometry or Atomic absorption (direct aspiration), or dithizone method	ISO 17294-2:2003 American Public Health Assn, #3111 American Public Health Assn, #3500-Zn D

Bibliography

[1] ISO 23500, *Guidance for the preparation and quality management of fluids for haemodialysis and related therapies*

[2] Ames R.G., & Stratton J.W. Effect of chlorine dioxide water disinfection on haematologic and serum parameters of renal dialysis patients. *Arch. Environ. Health*. 1987, **42** pp. 280–285

[3] American Public Health Association. *Standard Methods for the Examination of Water and Wastewater*. Washington, DC, Twenty first Edition, 2005

[4] Arnow P.M., Bland L.A., Garcia-Houchins S. et al. An outbreak of fatal fluoride intoxication in a long-term haemodialysis unit. *Ann. Intern. Med.* 1994, **121** pp. 339–344

[5] ASTM F0838-05, *International. Standard test method for determining bacterial retention of membrane filters utilized for liquid filtration, Book of Standards, volume 11.02, 2006*

[6] Bland L.A., Arnow P.M., Arduino M.J. et al. Potential hazards of deionization systems used for water purification in haemodialysis. *Artif. Organs*. 1996, **20** pp. 2–7

[7] Carson L.A., & Petersen N.J. Photoreactivation of *Pseudomonas cepacia* after ultraviolet exposure: A potential source of contamination in ultraviolet-treated waters. *J. Clin. Microbiol.* 1975, **1** pp. 462–464

[8] Caterson R.J., Savdie E., Raik E. et al. Heinz-body haemolysis in haemodialysed patients caused by chloramines in Sydney tap water. *Med. J. Aust.* 1982, **2** pp. 367–368

[9] Chapman K.G., Alegnani W.C., Heinze G.E. et al. Protection of water treatment systems, part IIa: Potential solutions. *Pharm. Technol.* 1983, **7** pp. 86–91

[10] JIS K 3823:1990, *Testing methods for determining bacterial rejection of ultrafiltration modules*

[11] JIS K 3824:1990, *Testing methods for endotoxin rejection of ultrafiltration modules*

[12] Johnson W.J., & Taves D.R. Exposure to excessive fluoride during haemodialysis. *Kidney Int.* 1974, **5** pp. 451–454

[13] Keshaviah P., Luehmann D., Shapiro F. et al. *Investigation of the Risks and Hazards Associated with Haemodialysis Systems*. (Technical report, Contract #223-78-5046) Silver Spring, MD: U.S. Dept. of Health and Human Services, Public Health Service/Food and Drug Administration/Bureau of Medical Devices, June 1980

[14] Libman V. Use of Reynolds number as a criterion for design of high-purity water systems. *Ultrapure Water*. 2006, **23** (7) pp. 26–34

[15] Luehmann D.A., Keshaviah P.R., Ward R.A., Klein E. *A Manual on Water Treatment for Haemodialysis*. (HHS Publication FDA 89-4234) Rockville, MD: U.S. Dept. of Health and Human Services, Public Health Service/Food and Drug Administration/Center for Devices and Radiological Health, July 1989

[16] Martiny H., Wlodavezyz K., Harms G., Rueden H. The use of UV-irradiation for the disinfection of water. I. Communication: Microbiological investigations in drinking water. *Zbl. Bakt. Hyg. B*. 1988, **185** pp. 350–367

[17] Martiny H., Brust H., Rueden H. The use of UV radiation for the disinfection of water. IV. Microbiological studies of the UV sensitivity of different aged cells of E. faecium, E. coli and P. aeruginosa. *Zbl. Hyg. Umweltmed.* 1990, **190** pp. 39–50

[18] Nickey W.A., Chinitz V.L., Kim K.E. et al. Hypernatremia from water softener and malfunction during home dialysis. *JAMA*. 1970, **214** pp. 915–916

[19] Petersen N.J., Boyer K.M., Carson L.A., Favero M.S. Pyrogenic reactions from inadequate disinfection of a dialysis fluid distribution system. *Dial. Transplant.* 1978, **7** pp. 52–55

[20] Petersen M.D., & Thomas S.B. The new EPA lead and copper rule, *Contemp. Dial. Nephrol.*, Sept., 1991, pp. 26-29

[21] Robson M. Dialysate sodium concentration, hypertension, and pulmonary edema in haemodialysis patients. *Dial. Transplant.* 1978, **7** pp. 678–679

[22] Simenhoff M.L., Dunn S., Fiddler W., Pensabene J.W., Smiley J. Generation of dimethylnitrosamine in water purification systems. Detection in human blood samples during haemodialysis. *JAMA*. 1983, **250** pp. 2020–2024

[23] Tipple M.A., Shusterman N., Bland L.A. et al. Illness in haemodialysis patients after exposure to chloramines in contaminated dialysate. *ASAIO Trans.* 1991, **37** pp. 588–591

[24] U.S. Environmental Protection Agency. *Methods for the Determination of Metals in Environmental Samples, Supplement 1 (EPA-600-R-94-111)*. Environmental Monitoring Systems Laboratory, Cincinnati, Ohio, 1994

[25] U.S. Environmental Protection Agency. *Safe Drinking Water Act,* 1996 (Public law 104-182). Washington, DC, 1996. [See *National Primary and Secondary Drinking Water Regulations*. U.S. Environmental Protection Agency, Office of Ground Water and Drinking Water

[26] U.S. Food And Drug Administration. *Guidance for the Content of Premarket Notifications for Water Purification Components and Systems for Haemodialysis*. U.S. Food and Drug Administration, Rockville, MD, 1997

[27] WARD D.M.. Chloramine removal from water used in haemodialysis. *Adv. Ren. Replace. Ther.* 1996, **3** pp. 337–347

[28] World Health Organization. *Guidelines for drinking-water quality,fourth edition* [electronic resource]: 2011, Geneva http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/

[29] ISO 11663, *Quality of dialysis fluid for haemodialysis and related therapies*

[30] BECKER. S.,JORDAN, R.L., ORLANDO.G.S., and KOREN H.,S., In vitro ozone exposure inhibits mitogen-induced lymphocyte proliferation and IL-2 production. *J. Toxicol. Environ. Health*. 1989, **26** pp. 469–483

[31] *European Pharmacopoeia*. European Pharmacopoeia Commission, Strasbourg, Eighth Edition, 2014

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