SVENSK STANDARD
SS-EN ISO 23500-5:2019

Fastställd/Approved: 2019-03-28
Utgåva/Edition: 1
Språk/Language: engelska/English
ICS: 11.040.25; 11.040.40

SWEDISH STANDARDS INSTITUTE

Vägledning för tillredning och kvalitetsstyrning av vätskor för hemodialys och relaterade terapier – Del 5: Kvalitet på dialysvätska för hemodialys och relaterade terapier (ISO 23500-5:2019)

Preparation and quality management of fluids for haemodialysis and related therapies – Part 5: Quality of dialysis fluid for haemodialysis and related therapies (ISO 23500-5:2019)

Standarder får världen att fungera

SIS (Swedish Standards Institute) är en fristående ideell förening med medlemmar från både privat och offentlig sektor. Vi är en del av det europeiska och globala nätverk som utarbetar internationella standarder. Standarder är dokumenterad kunskap utvecklad av framstående aktörer inom industri, näringsliv och samhälle och befrämjar handel över gränser, bidrar till att processer och produkter blir säkrare samt effektiviserar din verksamhet.

Delta och påverka
Som medlem i SIS har du möjlighet att påverka framtida standarder inom ditt område på nationell, europeisk och global nivå. Du får samtidigt tillgång till tidig information om utvecklingen inom din bransch.

Ta del av det färdiga arbetet
Vi erbjuder våra kunder allt som rör standarder och deras tillämpning. Hos oss kan du köpa alla publikationer du behöver – allt från enskilda standarder, tekniska rapporter och standard-paket till handböcker och onlinetjänster. Genom vår webbtjänst e-nav får du tillgång till ett lättnavigerat bibliotek där alla standarder som är aktuella för ditt företag finns tillgängliga. Standarder och handböcker är källor till kunskap. Vi säljer dem.

Utveckla din kompetens och lyckas bättre i ditt arbete
Hos SIS kan du gå öppna eller företagsinterna utbildningar kring innehåll och tillämpning av standarder. Genom vår närhet till den internationella utvecklingen och ISO får du rätt kunskap i rätt tid, direkt från källan. Med vår kunskap om standarders möjligheter hjälper vi våra kunder att skapa verklig nytta och lönsamhet i sina verksamheter.

Vill du veta mer om SIS eller hur standarder kan effektivisera din verksamhet är du välkommen in på www.sis.se eller ta kontakt med oss på tel 08-555 523 00.

Standards make the world go round

SIS (Swedish Standards Institute) is an independent non-profit organisation with members from both the private and public sectors. We are part of the European and global network that draws up international standards. Standards consist of documented knowledge developed by prominent actors within the industry, business world and society. They promote cross-border trade, they help to make processes and products safer and they streamline your organisation.

Take part and have influence
As a member of SIS you will have the possibility to participate in standardization activities on national, European and global level. The membership in SIS will give you the opportunity to influence future standards and gain access to early stage information about developments within your field.

Get to know the finished work
We offer our customers everything in connection with standards and their application. You can purchase all the publications you need from us - everything from individual standards, technical reports and standard packages through to manuals and online services. Our web service e-nav gives you access to an easy-to-navigate library where all standards that are relevant to your company are available. Standards and manuals are sources of knowledge. We sell them.

Increase understanding and improve perception
With SIS you can undergo either shared or in-house training in the content and application of standards. Thanks to our proximity to international development and ISO you receive the right knowledge at the right time, direct from the source. With our knowledge about the potential of standards, we assist our customers in creating tangible benefit and profitability in their organisations.

If you want to know more about SIS, or how standards can streamline your organisation, please visit www.sis.se or contact us on phone +46 (0)8-555 523 00

Europastandarden EN ISO 23500-5:2019 gäller som svensk standard. Detta dokument innehåller den officiella engelska versionen av EN ISO 23500-5:2019.

Denna standard ersätter SS-EN ISO 11663:2015, utgåva 1

The European Standard EN ISO 23500-5:2019 has the status of a Swedish Standard. This document contains the official version of EN ISO 23500-5:2019.

This standard supersedes the SS-EN ISO 11663:2015, edition 1

Upplysningar om sakinnehållet i standarden lämnas av SIS, Swedish Standards Institute, telefon 08-555 520 00. Standarder kan beställas hos SIS som även lämnar allmänna upplysningar om svensk och utländsk standard.

Information about the content of the standard is available from the Swedish Standards Institute (SIS), telephone +46 8 555 520 00. Standards may be ordered from SIS, who can also provide general information about Swedish and foreign standards.

Denna standard är framtagen av kommittén för Förbrukningsmaterial inom sjukvården, SIS/TK 330.

Har du synpunkter på innehållet i den här standarden, vill du delta i ett kommande revideringsarbete eller vara med och ta fram andra standarder inom området? Gå in på www.sis.se - där hittar du mer information.

EUROPEAN STANDARD

NORME EUROPÉENNE

EUROPÄISCHE NORM

EN ISO 23500-5

March 2019

ICS 11.040.40

Supersedes EN ISO 11663:2015

English Version

Preparation and quality management of fluids for haemodialysis and related therapies - Part 5: Quality of dialysis fluid for haemodialysis and related therapies (ISO 23500-5:2019)

Préparation et management de la qualité des liquides d'hémodialyse et de thérapies annexes - Partie 5: Qualité des liquides de dialyse pour hémodialyse et thérapies apparentées (ISO 23500-5:2019)

Vorbereitung und Qualitätsmanagement von Konzentraten für die Hämodialyse und verwandte Therapien - Teil 5: Qualität von Flüssigkeiten für die Hämodialyse und verwandte Therapien (ISO 23500-5:2019)

This European Standard was approved by CEN on 14 January 2019.

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.

CEN members are the national standards bodies of 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, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and United Kingdom.

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

CEN-CENELEC Management Centre: Avenue Marnix 17, B-1000 Brussels

Ref. No. EN ISO 23500-5:2019: E

Contents

Page

European foreword

This document (EN ISO 23500-5:2019) has been prepared by Technical Committee ISO/TC 150 "Implants for surgery" in collaboration with 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 September 2019, and conflicting national standards shall be withdrawn at the latest by September 2019.

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

This document supersedes EN ISO 11663:2015.

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, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 23500-5:2019 has been approved by CEN as EN ISO 23500-5:2019 without any modification.

Introduction

Haemodialysis patients are directly exposed to large volumes of dialysis fluid, with the dialyser membrane being the only barrier against transfer of hazardous contaminants from the dialysis fluid to the patient. It has long been known that there could be hazardous contaminants in the water and concentrates used to prepare the dialysis fluid. To minimize this hazard, ISO 23500-3 and ISO 23500-4 set forth quality requirements for the water and concentrates used to prepare dialysis fluid. However, if the dialysis fluid is not prepared carefully, it could contain unacceptable levels of contaminants even though it is prepared from water and concentrates, conforming to the requirements of ISO 23500-3 and ISO 23500-4. Further, the dialysis fluid might be used as the starting material for the online preparation of fluids intended for infusion into the patient, for example, in therapies such as online haemodiafiltration. For these reasons, this document for dialysis fluid quality was developed to complement the existing International Standards for water and concentrates, ISO 23500-3 and ISO 23500-4, respectively. Guidelines to aid the user in routinely meeting the requirements of this document and ISO 23500-3 can be found in ISO 23500-1.

Within these International Standards, measurement techniques current at the time of preparation have been cited. Other standard methods can be used, provided that such methods have been appropriately validated and are comparable to the cited methods. The rationale for the development of this document is given in Annex A.

This document reflects the conscientious efforts of healthcare professionals, patients, and medical device manufacturers to develop recommendations for the quality of dialysis fluid. This document is directed at the healthcare professionals involved in the management of dialysis facilities and the routine care of patients treated in dialysis facilities, since they are responsible for the final preparation of dialysis fluid. The recommendations contained in this document are not intended for regulatory application.

This document aims to help protect haemodialysis patients from adverse effects arising from known chemical and microbiological contaminants that can be found in improperly prepared dialysis fluid. However, the physician in charge of dialysis has the ultimate responsibility for ensuring that the dialysis fluid is correctly formulated and meets the applicable quality standards.

The concepts incorporated in this document should not be considered inflexible or static. The requirements and recommendations presented here should be reviewed periodically in order to assimilate increased understanding of the role of dialysis fluid purity in patient outcomes and technological developments.

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

Part 5: Quality of dialysis fluid for haemodialysis and related therapies

1 Scope

This document specifies minimum quality requirements for dialysis fluids used in haemodialysis and related therapies.

This document includes dialysis fluids used for haemodialysis and haemodiafiltration, including substitution fluid for haemodiafiltration and haemofiltration.

This document excludes the water and concentrates used to prepare dialysis fluid or the equipment used in its preparation. Those areas are covered by other International Standards.

Sorbent-based dialysis fluid regeneration systems that regenerate and recirculate small volumes of dialysis fluid, systems for continuous renal replacement therapy that use pre-packaged solutions, and systems and solutions for peritoneal dialysis are excluded from this document.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

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

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

ISO 23500-4, *Preparation and quality management of fluids for haemodialysis and related therapies — Part 4: Concentrates for haemodialysis and related therapies*

3 Terms and definitions

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

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

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

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

4 Requirements

4.1 Microbiological contaminants in dialysis fluid

4.1.1 General

The requirements contained in this clause apply to a sample of the dialysis fluid collected at the inlet to the dialyser or the reinfusion point.

4.1.2 Microbiological requirements for standard dialysis fluid

Standard dialysis fluid shall contain a total viable microbial count of less than 100 CFU/ml (when tested in accordance with Clause 5) and an endotoxin concentration of less than 0,5 EU/ml (when tested in accordance with Clause 5).

Action levels for the total viable microbial count and endotoxin concentration in dialysis fluid should also be set based on knowledge of the microbial dynamics of the system. Typically, the action levels are set at 50 % of the maximum allowable levels for total viable microbial count and endotoxin; other levels can be set.

If microbial counts exceeding the action levels are observed in the dialysis fluid, corrective measures, such as disinfection and retesting, should be taken promptly to reduce the levels.

Associated with the presence of bacteria and endotoxin in dialysis fluid is the likely presence of fungi (yeasts and filamentous fungi). After extensive discussion, the working group has not recommended maximum limits, for such contaminants.

Tests for bacterial growth and endotoxins are not required if the dialysis machine fluid pathway is fitted with an appropriate capacity bacteria-retentive and endotoxin-retentive filter validated by the manufacturer and operated and surveilled according to the manufacturer's instructions, unless the manufacturer requires such tests in the instructions for use.

4.1.3 Microbiological requirements for ultrapure dialysis fluid

Ultrapure dialysis fluid shall contain a total viable microbial count of less than 0,1 CFU/ml (when tested in accordance with Clause 5) and an endotoxin concentration less than 0,03 EU/ml (when tested in accordance with Clause 5). If those limits are exceeded in ultrapure dialysis fluid, corrective measures should be taken to reduce the levels to an acceptable level. The user is responsible for surveilling the dialysis fluid bacteriology of the system following installation. It is incumbent on the user to establish a regular surveillance routine.

Tests for bacterial growth and endotoxins are not required if the dialysis machine fluid pathway is fitted with an appropriate capacity bacteria-retentive and endotoxin-retentive filter validated by the manufacturer and operated and surveilled according to the manufacturer's instructions, unless the manufacturer requires such tests in the instructions for use.

4.1.4 Microbiological requirements for online prepared substitution fluid

The requirements contained in this clause apply to online prepared fluid intended to be infused into the patient as it enters the patient's blood.

This fluid shall be sterile and nonpyrogenic.

Substitution fluid for convective therapies, such as haemodiafiltration and haemofiltration, can be produced online by a process of ultrafiltration with bacteria-retentive and endotoxin-retentive filters. This online process shall be validated to produce fluid that is sterile and nonpyrogenic.

Conformity of online produced fluid with the requirements of this document cannot be demonstrated with traditional test procedures. For this reason, conformity with this document shall be ensured by

proper operation of a validated system, verified according to the manufacturer's instructions at the time of installation, and confirmed by the user with a regular surveillance and maintenance schedule. The user shall follow the manufacturer's instructions for use of the validated system, and the user's surveillance and maintenance schedule shall be designed to confirm that the water and concentrates used to prepare the substitution fluid continue to meet the specifications of ISO 23500-3 and ISO 23500-4.

4.2 Chemical contaminants in dialysis fluid

Dialysis fluid shall be prepared from water meeting the requirements of ISO 23500-3 and acid and bicarbonate concentrates meeting the requirements of ISO 23500-4. The water and concentrates shall be combined using individual dialysis fluid delivery systems or a central dialysis fluid delivery system constructed from materials that do not contribute chemical contaminants to the final dialysis fluid.

The maximum levels of chemical contaminants permitted in water used to prepare dialysis fluid and concentrates are given in ISO 23500-3 and are also shown in informative Annex B of this document (Tables B.1 and B.2) together with methods of determination (Table B.3). Other equivalent analytical methods can be used. Where testing for the individual trace elements listed in Table B.2 is not available, an analysis for total heavy metals can be used with a maximum allowable level of at 0,1 mg/l.

5 Tests for conformity with microbiological requirements

5.1 Sampling

In some newer dialysis machines, dialysis fluid flow stops when the effluent line is disconnected from the dialyser. In these instances, the machines are equipped with dialysis fluid sampling ports that can be accessed using a syringe. Sample ports can be disinfected with alcohol and allowed to air-dry. A sterile syringe should be used to aspirate at least 10 ml of dialysis fluid out of the sampling port. The filled syringe is discarded and a fresh sample of dialysis fluid collected using a new sterile syringe. For sample ports consisting of a simple septum penetrated with a needle, the use of a second syringe is not necessary. Alternatively, if the dialysis machine permits, samples can be collected immediately before the dialyser by disconnecting the inlet connector and aseptically collecting a "free/clean" catch sample after allowing dialysis fluid to run for at least 60 s unless manufacturers' instructions state otherwise.

Microbial analysis of any fluid sample should be conducted as soon as possible after collection to avoid unpredictable changes in the microbial population. If samples cannot be analysed within 4 h of collection, they should be stored at <10 °C without freezing and during transit to the laboratory. Sample storage for more than 24 h should be avoided, and sample shipping should be in accordance with the laboratory's instructions.

5.2 Culture methods

Accurate microbiological surveillance is important in the indication of the microbial content of dialysis water and dialysis fluid. Culture results obtained using the methods outlined in this document and summarized in Table 1 are only a relative indicator of the bioburden and do not provide an absolute measure of the absolute bacterial burden.

Total viable microbial counts (standard plate counts) shall be obtained using conventional microbiological assay procedures (pour plate, spread plate, membrane filter techniques). The calibrated loop technique shall not be used.

Preferred methods and sample volumes:

Standard dialysis fluid:

— spread plate, 0,1 ml to 0,3 ml;

— pour plate, typically 1 ml.