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Quality of dialysis fluid for haemodialysis and related therapies

Qualité des fluides de dialyse pour hémodialyse et thérapies annexes

ICS 11.040.40

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Foreword

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The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

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

ISO 11663 was prepared by Technical Committee ISO/TC 150, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems.*

Introduction

Haemodialysis patients are directly exposed to large volumes of dialysis fluid, with the haemodialyzer 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 13959, *Water for haemodialysis and related therapies*, and ISO 13958, *Concentrates for haemodialysis and related therapies*, 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 meeting the requirements of ISO 13959 and ISO 13958. Further, the dialysis fluid may 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 International Standard for dialysis fluid quality to complement the existing standards for water and concentrates, ISO 13959 and ISO 13958, respectively, was developed. Guidelines to aid the user in routinely meeting the requirements of this standard and ISO 13959 can be found in ISO 23500, *Guidance for the preparation and quality management of fluids for haemodialysis and related therapies*.

This International Standard reflects the conscientious efforts of health care professionals, patients, and medical device manufacturers to develop recommendations for the quality of dialysis fluid. This International Standard 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.

The requirements of this International Standard aim 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 requirements of all applicable quality standards.

The term "should" as used in this document reflects the committee's intent to define goals, not requirements. The term "shall" as used here denotes quality recommendations and procedures that are considered worthy of particular emphasis or that are required by regulating authorities. The term "must" is used only to describe unavoidable situations, including those mandated by government regulation.

The concepts incorporated in this International Standard should not be considered inflexible or static. The 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.

Quality of dialysis fluid for haemodialysis and related therapies

1 Scope

1.1 General

This International Standard specifies minimum requirements for dialysis fluids used for haemodialysis and haemodiafiltration, including substitution fluid for haemodiafiltration and haemofiltration. This standard does not address the requirements for the water and concentrates used to prepare dialysis fluid or the equipment used in its preparation. Those areas are covered by other ISO standards.

1.2 Exclusions

Excluded from the scope of this International Standard are sorbent-based dialysis fluid regeneration systems that regenerate and recirculate small volumes of dialysis fluid, systems for continuous renal replacement therapy that use prepackaged solutions, and systems and solutions for peritoneal dialysis.

2 Normative references

The following referenced documents are indispensable for the application of this document. The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

2.1 ISO 13958, Concentrates for haemodialysis and related therapies

2.2 ISO 13959, Water for haemodialysis and related therapies

2.3 ISO 26722, Water treatment equipment for haemodialysis and related therapies

3 Definitions

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

3.1
acid concentrate
acidified concentrated solution of salts that may contain glucose (sometimes referred to as "dextrose"), which, when diluted with dialysis water and bicarbonate concentrate, yields dialysis fluid for use in dialysis

NOTE The term "acid" refers to the small amount of acid (usually acetic acid) that is included in the concentrate.

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

3.3
bacteriology
area of study within the field of microbiology that deals with the study of bacteria

3.4
bicarbonate concentrate
concentrated preparation of sodium bicarbonate that, when diluted with dialysis water and acid concentrate, makes dialysis fluid used for dialysis

NOTE 1 Some bicarbonate concentrates also contain sodium chloride.

NOTE 2 Bicarbonate is also known as sodium hydrogen carbonate.

3.5
central dialysis fluid system
system that produces dialysis fluid from dialysis water and concentrate or powder at a central point and distributes the dialysis fluid from the central point to individual dialysis machines

3.6
chlorine, total
sum of free and combined chlorine

NOTE chlorine can exist in water as dissolved molecular chlorine (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.

3.7
CFU
colony-forming unit
organism capable of replicating to form a distinct, visible colony on a culture plate.

NOTE In practice, a colony may be formed by a group of organisms

3.8
dialysis fluid
aqueous fluid containing electrolytes, buffer and, usually, glucose, which is intended to exchange solutes with blood during haemodialysis

NOTE 1 The word “dialysis fluid” is used throughout this document to mean the fluid made from dialysis water and concentrates that is delivered to the dialyser by the dialysis fluid supply system. Such phrases as “dialysate” or “dialysis solution” can be used in place of dialysis fluid.

NOTE 2 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.”

3.9
dialysis fluid supply system
devices that: (1) prepare dialysis fluid online from dialysis water and concentrates or that store and distribute premixed dialysis fluid; (2) circulate the dialysis fluid through the dialyzer; (3) monitor the dialysis fluid for temperature, conductivity (or equivalent), pressure, flow, and blood leaks; and (4) prevent dialysis during disinfection or cleaning modes

NOTE 1 The term includes reservoirs, conduits, proportioning devices for the dialysis fluid, and monitors and associated alarms and controls assembled as a system for the characteristics listed above.

NOTE 2 The dialysis fluid supply system may be an integral part of the single patient dialysis machine or a centralized preparation system which feeds multiple bedside monitoring systems.

NOTE 3 Dialysis fluid supply systems are also known as proportioning systems and dialysis fluid delivery systems.

3.10
disinfection
destruction of pathogenic and other kinds of microorganisms by thermal or chemical means

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

NOTE 2 This definition of “disinfection” is equivalent to low-level disinfection in the Spalding classification.

3.11
endotoxin
major component of the outer cell wall of gram-negative bacteria

NOTE Endotoxins are lipopolysaccharides, which consist of a polysaccharide chain covalently bound to lipid A. Endotoxins can acutely activate both humoral and cellular host defenses, 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**)

3.12
EU
endotoxin units
units assayed by the *Limulus amoebocyte lysate* (LAL) method when testing for endotoxins

NOTE 1 Because the activity of endotoxins depends on the bacteria from which they are derived, their activity is referred to a standard endotoxin.

NOTE 2 In some countries, endotoxin concentrations are expressed in international units (IU). Since the 1983 harmonization of endotoxin assays, EU and IU are equivalent.

3.13
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 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 a replacement solution into the blood either before the dialyser (pre-dilution haemodiafiltration) or after the dialyser (post-dilution haemodiafiltration).

3.14
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 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 higher molecular weight solutes.

3.15
haemofiltration
form of renal replacement therapy in which waste solutes are removed from blood by convection

NOTE 1 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 (pre-dilution haemofiltration) or after the haemofilter (post-dilution haemofiltration).

NOTE 2 There is no dialysis fluid stream in haemofiltration.

3.16
LAL
***Limulus amoebocyte lysate* test**
assay used to detect endotoxin

NOTE The detection method uses the chemical specific response of the horseshoe crab (*Limulus polyphemus*) to endotoxin.

3.17
manufacturer
entity that designs, manufactures, fabricates, assembles, formulates or processes a finished device

NOTE Manufacturers include, but are not limited to, those who perform the functions of contract sterilization, installation, relabelling, remanufacturing, repacking, or specification development, and initial distributors of foreign entities performing these functions.

3.18
microbial
referring to microscopic organisms, bacteria, fungi, and so forth

NOTE see also **bacteriology**.

3.19
microbiological contamination
contamination with any form of microorganism (e.g., bacteria, yeast, fungi, and algae) or with the by-products of living or dead organisms such as endotoxins, exotoxins, and microcystin (derived from blue-green algae)

3.20
non-pyrogenic
Less than 0,03 EU/mL by the LAL assay.

3.21
pyrogen
fever-producing substance

NOTE Pyrogens are most often lipopolysaccharides of gram-negative bacterial origin (see also **endotoxin**).

3.22
sterile
free from viable microorganisms

NOTE For solutions used in haemodialysis and related therapies, “sterile” can be used to describe a packaged solution that was prepared using a terminal sterilization process that has been demonstrated to achieve a probability of 10^{-6} that only one appropriate indicator microorganism can survive. Alternatively, “sterile” can be used to describe a solution prepared for immediate use by a continuous filtration process that has been validated to produce a solution free from viable microorganisms even if one filtration step fails.

3.23
substitution fluid
fluid used in haemofiltration and haemodiafiltration treatments that is infused directly into the patient’s blood as a replacement for the fluid that is removed from the blood by filtration

NOTE 1 Substitution fluid may also be referred to as substitution solution or replacement solution.

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