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Concentrates for haemodialysis and related therapies

Concentrés pour hémodialyse et thérapies apparentées

[Revision of first edition (ISO 13958:2002)]

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

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 13958 was prepared by Technical Committee ISO/TC 150, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

This second edition cancels and replaces the first edition, which has been technically revised.

Introduction

This 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 a 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 standards does not imply unanimity of opinion, but rather reflects the compromise necessary in some instances when a variety of interests must be merged.

Throughout the standard, recommendations are made to use ISO-quality water. Therefore, it is recommended to review ISO 13959, *Water for haemodialysis and related therapies,* along with this standard.

This International Standard*, Concentrates for haemodialysis and related therapies,* does not cover the dialysis fluid that is used to clinically dialyse patients. Dialysis fluid is covered ISO 11663, *Fluids for haemodialysis and related therapies*. The making of dialysis fluid involves the proportioning of concentrate and water at the bedside or in a central dialysis fluid delivery system. Although the label requirements for dialysis fluid are placed onto the labelling of the concentrate, it is the user's responsibility to ensure proper use.

In addition, this standard does not cover haemodialysis equipment, which is addressed in the new edition of IEC 60601-2-16, *Medical electrical equipment, Part 2-16: Particular requirements for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment.*

Concentrates for haemodialysis and related therapies

1 Scope

1.1 General

This International Standard specifies minimum requirements for concentrates used for haemodialysis and related therapies. For the purpose of this standard, “concentrates” are a mixture of chemicals and water, or a mixture of chemicals in the form of dry powder or other highly concentrated media, that are delivered to the end user to make dialysis fluid used to perform haemodialysis and related therapies. This standard is addressed to the manufacturer of such concentrates. In several instances in this standard, it became necessary to address the dialysis fluid, which is made by the end user, to help clarify the requirements for manufacturing concentrates. Because the manufacturer of the concentrate does not have control over the final dialysis fluid, any reference to dialysis fluid is for clarification and is not a requirement on the manufacturer. The requirements and goals established by this standard will help ensure the effective, safe performance of haemodialysis concentrates and related materials.

1.2 Inclusions

This standard includes bicarbonate and acid concentrates in both liquid and powder forms. Also included are additives also called spikes, chemicals which may be added to the concentrate to increase the concentration of one or more of the existing ions in the concentrate and thus in the final dialysis fluid. This standard also gives requirements for equipment used to mix acid and bicarbonate powders into concentrate at the user’s facility.

1.3 Exclusions

Excluded from the scope of this standard are concentrates prepared from salts and water at a dialysis facility for immediate use. Although references to dialysis fluid appear herein, this standard does not address dialysis fluid as made by the end user. Also excluded from the scope of this standard are requirements for the monitoring frequency of water purity used for the making of dialysis fluid by the dialysis facility. Recommendations of this committee for monitoring water quality are contained in ISO 23500, *Fluids for haemodialysis and related therapies*. Also, this standard does not address bags of sterile dialysis fluid or sorbent dialysis fluid regeneration systems that regenerate and recirculate small volumes of the dialysis fluid.

2 Normative references

The following referenced documents are indispensable for the application 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 13959, *Water for haemodialysis and related therapies*.

ISO 11663, *Fluids for haemodialysis and related therapies.*

UNDERWRITERS LABORATORIES. *Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use - Part 1: General Requirements*. UL-61010-1, Northbrook (IL): UL, 2004.

IEC 60601-1-1:2004, *Medical electrical equipment — Part 1-1: General requirements for safety — Collateral standard: Safety requirements for medical electrical systems*

3 Terms and Definitions

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

3.1
acetate concentrate
concentrated solution of salts that may contain glucose (sometimes referred to as “dextrose”), which, when diluted with dialysis water, yields dialysis fluid for use in dialysis

3.2
acid concentrate
acidified concentrated mixture 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.

3.3
acid concentrate—liquid
an acidified concentrated solution of salts that may contain glucose, 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 to establish the buffer system in the final dialysis fluid by reaction with a small amount of bicarbonate from the bicarbonate concentrate.

3.4
acid concentrate—dry
dry salts that may contain glucose that are provided to a user in the appropriate proportions, that when mixed with a specific quantity of dialysis water will create a liquid concentrate that can be used in conjunction with bicarbonate concentrate and dialysis water to make dialysis fluid in a dialysis machine

NOTE An acid concentrate may consist of a dry part, e.g. sodium chloride, and a liquid part.

3.5
additives
a small amount of a single chemical that when added to the concentrate will increase the concentration of a single existing chemical by a value labelled on the additive packaging

NOTE The added chemical is also called a “spike.”

3.6
bacteriology
area of study within the field of microbiology that deals with the study of bacteria

3.7
batch system
apparatus in which the dialysis fluid is prepared in bulk before each dialysis session

3.8
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.

3.9
bicarbonate concentrate—liquid
a concentrated preparation of sodium bicarbonate that, when diluted with dialysis water and acid concentrate, makes dialysis fluid used for dialysis

NOTE Some bicarbonate concentrates also contain sodium chloride.

3.10
bicarbonate concentrate—dry
dry bicarbonate that may contain sodium chloride that is provided to a user in the appropriate proportions, that when mixed with a specific quantity of dialysis water will create a liquid concentrate that can be used in conjunction with acid concentrate and dialysis water to make dialysis fluid in a dialysis machine

NOTE 1 Dry bicarbonate is also used in concentrate generators to produce a saturated solution of sodium bicarbonate used by the dialysis machine to make dialysis fluid.

NOTE 2 Some bicarbonate concentrates also contain sodium chloride.

NOTE 3 In some machines dry powder is used to produce a batch of final dialysis fluid.

3.11
bicarbonate dialysis fluid
dialysis fluid containing physiological or higher concentrations of bicarbonate

NOTE Bicarbonate dialysis fluid is generally produced from two concentrates: one containing bicarbonate and the other containing acid and other electrolytes (see **acid concentrate** and **bicarbonate concentrate**).

3.12
bulk delivery
delivery of large volumes of concentrate in which the product is transferred (pumped) from the delivery container to a user's storage tank

NOTE Bulk delivery includes containers such as drums, which may be pumped into a storage tank maintained at the user's facility. Alternatively the drums can be left at the facility and used to fill transfer containers to transfer the concentrate to the dialysis machines. Bulk delivery may also include large containers for direct connection to a central dialysis fluid supply system.

3.13
bulk storage tank
large tank at the user's facility for storage of dialysis water or concentrate from bulk deliveries, or for concentrate prepared in bulk at the user's facility from powder and dialysis water

3.14
central concentrate system
system that prepares and/or stores concentrate at a central point for subsequent distribution to its points of use

3.15
concentrate generator systems
system in which the concentrate is delivered to the consumer either as a powder in a container, or as a combination of powder in a container and a highly concentrated liquid, and then converted online into a saturated solution by a dialysis delivery machine

NOTE This solution is used by an individual proportioning system to make the final dialysis fluid delivered to the dialyzer.

3.16
concentrate mixer
mixer for preparation of dialysis concentrate or dialysis fluid at a dialysis facility

3.17
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” may be used in place of dialysis fluid.

NOTE 2 In some cases glucose is also known as dextrose.

NOTE 3 Dialysis fluid does not include prepackaged parental fluids used in haemodialfiltration.

3.18
dialysis water
water that has been treated to meet the requirements of this standard 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

3.19
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 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**).

3.20
EU
endotoxin units
units assayed by the *Limulus* amoebocyte lysate (LAL) method when testing for endotoxins

NOTE 1 Because 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.

3.21
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.

3.22
LAL
***Limulus amebocyte lysate* test**
assay used to detect endotoxin

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

3.23
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.

3.24
microbial
referring to microscopic organisms, bacteria, fungi, and so forth

NOTE See also **bacteriology**.

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

3.26
pyrogen
fever-producing substance

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

3.27
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.

3.28
user
physician or physician’s representative responsible for the actual production and handling of dialysis fluid

4 Requirements

4.1 General

4.1.1 Requirements

4.1.2 Physical state

The concentrate for haemodialysis may be supplied in dry or aqueous form. Packaging may be for direct use with a single dialysis machine or for use in systems supplying multiple dialysis machines (bulk use).

4.1.3 Solute concentrations

4.1.3.1 Liquid solute concentrations

All electrolytes identified on the label shall be present within ± 5 % or ± 0,1 mEq/L (expressed as dialysis fluid concentrations), whichever is greater, of the stated concentration, with the exception of