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Water for haemodialysis and related therapies

Eau pour hémodialyse et thérapies apparentées

[Revision of first edition (ISO 13959:2002)]

ICS 11.040.40

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56 **Foreword**

57 ISO (the International Organization for Standardization) is a worldwide federation of national
58 standards bodies (ISO member bodies). The work of preparing International Standards is normally
59 carried out through ISO technical committees. Each member body interested in a subject for which a
60 technical committee has been established has the right to be represented on that committee.
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62 the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all
63 matters of electrotechnical standardization.

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

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

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

72 ISO 13959 was prepared by Technical Committee ISO/TC 150, Subcommittee SC 2, *Cardiovascular*
73 *implants and extracorporeal systems*.

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

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75 Introduction

76 Assurance of adequate water quality is one of the most important aspects of ensuring a safe and
77 effective delivery of haemodialysis, haemodiafiltration or haemofiltration.

78 This International Standard contains minimum requirements, chemical and microbiological, for the
79 water to be used for preparation of dialysis fluids, concentrates, and for the reuse of haemodialyzers
80 and the necessary steps to assure compliance with those requirements. Haemodialysis and
81 haemodiafiltration can expose the patient to more than 500 litres of water per week across the semi-
82 permeable membrane of the haemodialyser or haemodiafilter. Healthy individuals seldom have a
83 weekly oral intake above 12 litres. This near 40-fold increase in exposure requires control and
84 monitoring of water quality to avoid excesses of known or suspected harmful substances. Since
85 knowledge of potential injury from trace elements and contaminants of microbiological origin over long
86 periods is still growing and techniques for treating drinking water are continuously developed, this
87 International Standard will evolve and be refined accordingly. The physiological effects attributable to
88 the presence of organic contaminants in dialysis water are important areas for research. At the time
89 this International Standard was published it was premature to specify threshold values for organic
90 contaminants below those published by various regulatory authorities.

91 The final dialysis fluid is produced from concentrates or salts manufactured, packaged, and labelled
92 according to ISO 13958, *Concentrates for haemodialysis and related therapies*, mixed with water
93 meeting the requirements of this standard. Operation of water treatment equipment and
94 haemodialysis systems, including ongoing monitoring of the quality of water used to prepare dialysis
95 fluids, and handling of concentrates and salts are the responsibility of the haemodialysis facility or
96 addressed in other ISO standards. Haemodialysis professionals make choices about the various
97 applications (haemodialysis, haemodiafiltration, haemofiltration) and should understand the risks of
98 each and the requirements for safety for fluids used for each.

99 This International Standard is directed towards manufacturers and providers of water treatment
100 systems and also to haemodialysis facilities.

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101 Water for haemodialysis and related therapies

102 1 Scope

103 This International Standard specifies minimum requirements for water to be used in the preparation of
104 concentrates, dialysis fluids for haemodialysis, haemodiafiltration and haemofiltration and for the
105 reprocessing of haemodialysers.

106 This standard does not address the operation of water treatment equipment nor the final mixing of
107 treated water with concentrates to produce the dialysis fluids used in such therapies. That operation is
108 the sole responsibility of dialysis professionals.

109 This International Standard does not apply to dialysis fluid regenerating systems.

110 2 Terms and definitions

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

112 2.1

113 action level

114 concentration of a contaminant at which steps should be taken to interrupt the trend toward higher,
115 unacceptable levels

116 2.2

117 chlorine, total

118 sum of free and combined chlorine

119 NOTE chlorine can exist in water as dissolved molecular chlorine (free chlorine) or in chemically combined forms
120 (combined chlorine). Where chloramine is used to disinfect water supplies, chloramine is usually the principal
121 component of combined chlorine.

122 2.3

123 CFU

124 colony-forming unit

125 organism capable of replicating to form a distinct, visible colony on a culture plate

126 NOTE In practice, a colony can be formed by a group of organisms.

127 2.4

128 dialysis fluid

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

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

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

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

- 136 **2.5**
 137 **dialysis water**
 138 water that has been treated to meet the requirements of this standard and which is suitable for use in
 139 haemodialysis applications, including the preparation of dialysis fluid, reprocessing of dialysers,
 140 preparation of concentrates and preparation of substitution fluid for online convective therapies
- 141 **2.6**
 142 **endotoxin**
 143 major component of the outer cell wall of gram-negative bacteria
- 144 NOTE Endotoxins are lipopolysaccharides, which consist of a polysaccharide chain covalently bound to lipid A.
 145 Endotoxins can acutely activate both humoral and cellular host defences, leading to a syndrome characterized by
 146 fever, shaking, chills, hypotension, multiple organ failure, and even death if allowed to enter the circulation in a
 147 sufficient dose (see also **pyrogen**).
- 148 **2.7**
 149 **EU**
 150 **endotoxin units**
 151 units assayed by the *Limulus amoebocyte lysate* (LAL) method when testing for endotoxins
- 152 NOTE 1 Because the activity of endotoxins depends on the bacteria from which they are derived, their activity is
 153 referred to a standard endotoxin.
- 154 NOTE 2 In some countries, endotoxin concentrations are expressed in international units (IU). Since the 1983
 155 harmonization of endotoxin assays, EU and IU are equivalent.
- 156 **2.8**
 157 **feed water**
 158 water supplied to a water treatment system or an individual component of the system
- 159 **2.9**
 160 **LAL**
 161 ***Limulus amoebocyte lysate* test**
 162 assay used to detect endotoxin
- 163 NOTE The detection method uses the chemical specific response of the horseshoe crab (*Limulus polyphemus*)
 164 to endotoxin.
- 165 **2.10**
 166 **microbial**
 167 referring to microscopic organisms, bacteria, fungi, and so forth
- 168 **2.11**
 169 **microbial contamination**
 170 contamination with any form of microorganism (e.g. bacteria, yeast, fungi, and algae) or with the by-
 171 products of living or dead organisms such as endotoxins, exotoxins, and microcystin (derived from
 172 blue-green algae)
- 173 **2.12**
 174 **pyrogen**
 175 fever-producing substance.
- 176 NOTE Pyrogens are most often lipopolysaccharides of gram-negative bacterial origin (see also **endotoxin**).

177 3 Dialysis water requirements

178 3.1 Dialysis water verification and monitoring

179 The quality of the dialysis water, as specified below, shall be verified upon installation of a water
180 treatment system. Monitoring of the dialysis water quality shall be carried out thereafter.

181 3.2 Microbiological requirements

182 Total viable microbial counts in dialysis water shall be less than 100 CFU/ml, or as required by national
183 legislation or similar. An action level shall be set based on knowledge of the microbial dynamics of the
184 system. Typically, the action level will be 50 % of the maximum allowable level.

185 Endotoxin content in dialysis water shall be less than 0,25 EU/mL, or as required by national legislation or
186 similar.

187 NOTE See A.1 for a history of these requirements.

188 3.3 Chemical contaminants

189 Dialysis water shall not contain chemicals at concentrations in excess of those in Tables 1 and 2, or
190 as required by national legislation or similar.

191 NOTE See A.2 for explanation of values supplied.

192 Where the dialysis water is used for the reprocessing of haemodialysers, (cleaning, testing and mixing
193 of disinfectants) the user is cautioned that the dialysis water shall meet this standard. The dialysis
194 water should be measured at the input to the dialyser reprocessing equipment.

195 **Table 1 — Maximum allowable levels of toxic chemicals and dialysis fluid electrolytes in**
196 **dialysis water**

	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
	Sulphate	100
	Zinc	0,1
Electrolytes normally included in dialysis fluid		
	Calcium	2 (0,05 mmol/L)
	Magnesium	4 (0,15mmol/L)
	Potassium	8 (0,2 mmol/L)
	Sodium	70 (3,0 mmol/L)
^{a)} The physician has the ultimate responsibility for ensuring the quality of water used for dialysis.		
^{b)} Unless otherwise noted.		

197

198

Table 2 — Maximum allowable levels of 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

199

200 4 Tests for compliance with chemical and microbiological requirements

201 4.1 Microbiology of dialysis water

202 Samples shall be collected where a dialysis machine connects to the water distribution loop, from a
203 sample point in the distal segment of the loop, or where water enters into a mixing tank.

204 Samples shall be assayed within 4 h of collection, or be immediately refrigerated and assayed within
205 24 h of collection on a regular schedule. Total viable counts (standard plate counts) shall be obtained
206 using conventional microbiological assay procedures (pour plate, spread plate, membrane filter
207 techniques). Membrane filtration is the preferred method for this test. The calibrated loop technique is
208 not accepted.

209 Culture media should be tryptone glucose extract agar (TGEA), Reasoners 2A (R2A), or other media
210 that can be demonstrated to provide equivalent results. Blood agar and chocolate agar shall not be
211 used. Incubation temperatures of 17° C – 23° C and incubation time of 168 h (7 days) are
212 recommended. Other incubation times and temperatures may be used if it can be demonstrated that
213 they provide equivalent results. No method will give a total microbial count.

214 The presence of pyrogens shall be determined by the *Limulus* amoebocyte lysate (LAL) assay for
215 endotoxins. Other test methods may be used if it can be demonstrated that they provide equivalent
216 results.

217 4.2 Chemical contaminants test methods

218 Compliance with the requirements listed in Table 1 can be shown by using chemical analysis methods
219 referenced in the American Public Health Association's *Standard methods for the examination of*
220 *water and wastewater*, methods referenced in the U.S. Environmental Protection Agency's *Methods*
221 *for the Determination of metals in environmental samples*, and/or other equivalent analytical methods.

222 Compliance with the requirements listed in Table 2 can be shown in one of three ways:

223 — Where such testing is available, the individual contaminants in Table 2 can be determined using
224 chemical analysis methods referenced in the American Public Health Association's *Standard*
225 *methods for the examination of water and wastewater*, methods referenced in the U.S.
226 Environmental Protection Agency's *Methods for the Determination of metals in environmental*
227 *samples*, and/or other equivalent analytical methods.