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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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108 **Foreword**

109 ISO (the International Organization for Standardization) is a worldwide federation of national  
110 standards bodies (ISO member bodies). The work of preparing International Standards is normally  
111 carried out through ISO technical committees. Each member body interested in a subject for which a  
112 technical committee has been established has the right to be represented on that committee.  
113 International organizations, governmental and non-governmental, in liaison with ISO, also take part in  
114 the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all  
115 matters of electrotechnical standardization.

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

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

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

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

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

127

## 128 Introduction

129 This standard reflects the conscientious efforts of concerned physicians, clinical engineers, nurses,  
130 dialysis technicians, and dialysis patients, in consultation with device manufacturers and government  
131 representatives, to develop a standard for performance levels that could be reasonably achieved at  
132 the time of publication. The term “consensus” as applied to the development of voluntary medical  
133 device standards does not imply unanimity of opinion, but rather reflects the compromise necessary in  
134 some instances when a variety of interests must be merged.

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

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

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

# 147 Concentrates for haemodialysis and related therapies

## 148 1 Scope

### 149 1.1 General

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

### 160 1.2 Inclusions

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

### 166 1.3 Exclusions

167 Excluded from the scope of this standard are concentrates prepared from salts and water at a dialysis  
168 facility for immediate use. Although references to dialysis fluid appear herein, this standard does not  
169 address dialysis fluid as made by the end user. Also excluded from the scope of this standard are  
170 requirements for the monitoring frequency of water purity used for the making of dialysis fluid by the  
171 dialysis facility. Recommendations of this committee for monitoring water quality are contained in ISO  
172 23500, *Fluids for haemodialysis and related therapies*. Also, this standard does not address bags of  
173 sterile dialysis fluid or sorbent dialysis fluid regeneration systems that regenerate and recirculate small  
174 volumes of the dialysis fluid.

## 175 2 Normative references

176 The following referenced documents are indispensable for the application of this document. For  
177 dated references, only the edition cited applies. For undated references, the latest edition of the  
178 referenced document (including any amendments) applies.

179 ISO 13959, *Water for haemodialysis and related therapies*.

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

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

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

### 185 3 Terms and Definitions

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

#### 187 3.1

##### 188 acetate concentrate

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

#### 191 3.2

##### 192 acid concentrate

193 acidified concentrated mixture of salts that may contain glucose (sometimes referred to as “dextrose”),  
 194 which, when diluted with dialysis water and bicarbonate concentrate, yields dialysis fluid for use in  
 195 dialysis

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

#### 197 3.3

##### 198 acid concentrate—liquid

199 an acidified concentrated solution of salts that may contain glucose, which, when diluted with dialysis  
 200 water and bicarbonate concentrate, yields dialysis fluid for use in dialysis

201 NOTE The term “acid” refers to the small amount of acid (usually acetic acid) that is included in the concentrate  
 202 to establish the buffer system in the final dialysis fluid by reaction with a small amount of bicarbonate from the  
 203 bicarbonate concentrate.

#### 204 3.4

##### 205 acid concentrate—dry

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

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

#### 211 3.5

##### 212 additives

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

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

#### 216 3.6

##### 217 bacteriology

218 area of study within the field of microbiology that deals with the study of bacteria

#### 219 3.7

##### 220 batch system

221 apparatus in which the dialysis fluid is prepared in bulk before each dialysis session

#### 222 3.8

##### 223 bicarbonate concentrate

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

226 NOTE 1 Some bicarbonate concentrates also contain sodium chloride.



227 NOTE 2 Bicarbonate is also known as sodium hydrogen carbonate.

228 **3.9**

229 **bicarbonate concentrate—liquid**

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

232 NOTE Some bicarbonate concentrates also contain sodium chloride.

233 **3.10**

234 **bicarbonate concentrate—dry**

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

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

241 NOTE 2 Some bicarbonate concentrates also contain sodium chloride.

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

243 **3.11**

244 **bicarbonate dialysis fluid**

245 dialysis fluid containing physiological or higher concentrations of bicarbonate

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

248 **3.12**

249 **bulk delivery**

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

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

256 **3.13**

257 **bulk storage tank**

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

260 **3.14**

261 **central concentrate system**

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

264 **3.15**

265 **concentrate generator systems**

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

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

271 **3.16**  
 272 **concentrate mixer**  
 273 mixer for preparation of dialysis concentrate or dialysis fluid at a dialysis facility

274 **3.17**  
 275 **dialysis fluid**  
 276 aqueous fluid containing electrolytes, buffer, and, usually, glucose, which is intended to exchange  
 277 solutes with blood during haemodialysis

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

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

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

283 **3.18**  
 284 **dialysis water**  
 285 water that has been treated to meet the requirements of this standard and which is suitable for use in  
 286 haemodialysis applications, including the preparation of dialysis fluid, reprocessing of dialysers,  
 287 preparation of concentrates and preparation of substitution fluid for online convective therapies

288 **3.19**  
 289 **endotoxin**  
 290 major component of the outer cell wall of gram-negative bacteria

291 NOTE Endotoxins are lipopolysaccharides, which consist of a polysaccharide chain covalently bound to lipid A.  
 292 Endotoxins can acutely activate both humoral and cellular host defences, leading to a syndrome characterized by  
 293 fever, shaking, chills, hypotension, multiple organ failure, and even death if allowed to enter the circulation in a  
 294 sufficient dose (see also **pyrogen**).

295 **3.20**  
 296 **EU**  
 297 **endotoxin units**  
 298 units assayed by the *Limulus* amoebocyte lysate (LAL) method when testing for endotoxins

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

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

303 **3.21**  
 304 **haemodialysis**  
 305 form of renal replacement therapy in which waste solutes are removed primarily by diffusion from  
 306 blood flowing on one side of a membrane into dialysis fluid flowing on the other side

307 NOTE Fluid removal that is sufficient to obtain the desired weight loss is achieved by establishing a hydrostatic  
 308 pressure gradient across the membrane. This fluid removal provides some additional waste solute removal,  
 309 particularly for higher molecular weight solutes.

310 **3.22**  
 311 **LAL**  
 312 ***Limulus amoebocyte lysate* test**  
 313 assay used to detect endotoxin

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

- 316 **3.23**  
 317 **manufacturer**  
 318 entity that designs, manufactures, fabricates, assembles, formulates or processes a finished device
- 319 NOTE Manufacturers include, but are not limited to, those who perform the functions of contract sterilization,  
 320 installation, relabelling, remanufacturing, repacking, or specification development, and initial distributors of foreign  
 321 entities performing these functions.
- 322 **3.24**  
 323 **microbial**  
 324 referring to microscopic organisms, bacteria, fungi, and so forth
- 325 NOTE See also **bacteriology**.
- 326 **3.25**  
 327 **proportioning system**  
 328 apparatus that proportions dialysis water and haemodialysis concentrate to prepare dialysis fluid
- 329 **3.26**  
 330 **pyrogen**  
 331 fever-producing substance
- 332 NOTE Pyrogens are most often lipopolysaccharides of gram-negative bacterial origin. See also **endotoxin**.
- 333 **3.27**  
 334 **sterile**  
 335 free from viable microorganisms
- 336 NOTE For solutions used in haemodialysis and related therapies, "sterile" can be used to describe a packaged  
 337 solution that was prepared using a terminal sterilization process that has been demonstrated to achieve a  
 338 probability of  $10^{-6}$  that only one appropriate indicator microorganism can survive. Alternatively, "sterile" can be  
 339 used to describe a solution prepared for immediate use by a continuous filtration process that has been validated  
 340 to produce a solution free from viable microorganisms even if one filtration step fails.
- 341 **3.28**  
 342 **user**  
 343 physician or physician's representative responsible for the actual production and handling of dialysis  
 344 fluid
- 345 **4 Requirements**
- 346 **4.1 General**
- 347 **4.1.1 Requirements**
- 348 **4.1.2 Physical state**
- 349 The concentrate for haemodialysis may be supplied in dry or aqueous form. Packaging may be for  
 350 direct use with a single dialysis machine or for use in systems supplying multiple dialysis machines  
 351 (bulk use).
- 352 **4.1.3 Solute concentrations**
- 353 **4.1.3.1 Liquid solute concentrations**
- 354 All electrolytes identified on the label shall be present within  $\pm 5\%$  or  $\pm 0,1$  mEq/L (expressed as  
 355 dialysis fluid concentrations), whichever is greater, of the stated concentration, with the exception of