



DRAFT INTERNATIONAL STANDARD ISO/DIS 11663

ISO/TC 150/SC 2

Secretariat: ANSI

Voting begins on:
2008-02-01

Voting terminates on:
2008-07-01

INTERNATIONAL ORGANIZATION FOR STANDARDIZATION • МЕЖДУНАРОДНАЯ ОРГАНИЗАЦИЯ ПО СТАНДАРТИЗАЦИИ • ORGANISATION INTERNATIONALE DE NORMALISATION

Quality of dialysis fluid for haemodialysis and related therapies

Qualité des fluides de dialyse pour hémodialyse et thérapies annexes

ICS 11.040.40

In accordance with the provisions of Council Resolution 15/1993 this document is circulated in the English language only.

Conformément aux dispositions de la Résolution du Conseil 15/1993, ce document est distribué en version anglaise seulement.

To expedite distribution, this document is circulated as received from the committee secretariat. ISO Central Secretariat work of editing and text composition will be undertaken at publication stage.

Pour accélérer la distribution, le présent document est distribué tel qu'il est parvenu du secrétariat du comité. Le travail de rédaction et de composition de texte sera effectué au Secrétariat central de l'ISO au stade de publication.

THIS DOCUMENT IS A DRAFT CIRCULATED FOR COMMENT AND APPROVAL. IT IS THEREFORE SUBJECT TO CHANGE AND MAY NOT BE REFERRED TO AS AN INTERNATIONAL STANDARD UNTIL PUBLISHED AS SUCH.

IN ADDITION TO THEIR EVALUATION AS BEING ACCEPTABLE FOR INDUSTRIAL, TECHNOLOGICAL, COMMERCIAL AND USER PURPOSES, DRAFT INTERNATIONAL STANDARDS MAY ON OCCASION HAVE TO BE CONSIDERED IN THE LIGHT OF THEIR POTENTIAL TO BECOME STANDARDS TO WHICH REFERENCE MAY BE MADE IN NATIONAL REGULATIONS.

RECIPIENTS OF THIS DRAFT ARE INVITED TO SUBMIT, WITH THEIR COMMENTS, NOTIFICATION OF ANY RELEVANT PATENT RIGHTS OF WHICH THEY ARE AWARE AND TO PROVIDE SUPPORTING DOCUMENTATION.

PDF disclaimer

This PDF file may contain embedded typefaces. In accordance with Adobe's licensing policy, this file may be printed or viewed but shall not be edited unless the typefaces which are embedded are licensed to and installed on the computer performing the editing. In downloading this file, parties accept therein the responsibility of not infringing Adobe's licensing policy. The ISO Central Secretariat accepts no liability in this area.

Adobe is a trademark of Adobe Systems Incorporated.

Details of the software products used to create this PDF file can be found in the General Info relative to the file; the PDF-creation parameters were optimized for printing. Every care has been taken to ensure that the file is suitable for use by ISO member bodies. In the unlikely event that a problem relating to it is found, please inform the Central Secretariat at the address given below.

iTeh STANDARD PREVIEW
(standards.iteh.ai)
Full standard:
<https://standards.iteh.ai/catalog/standards/sist/014e73fe-655f-45ed-b9d8-6f67296e9b5e/iso-11663-2009>

Copyright notice

This ISO document is a Draft International Standard and is copyright-protected by ISO. Except as permitted under the applicable laws of the user's country, neither this ISO draft nor any extract from it may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, photocopying, recording or otherwise, without prior written permission being secured.

Requests for permission to reproduce should be addressed to either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

Reproduction may be subject to royalty payments or a licensing agreement.

Violators may be prosecuted.

8

33 **Contents**

	Page
34 Foreword	iv
35 Introduction	v
36 1 Scope	1
37 1.1 General	1
38 1.2 Exclusions	1
39 2 Normative references	1
40 3 Definitions	1
41 4 Requirements	5
42 4.1 Microbiological contaminants in dialysis fluid	5
43 4.2 Chemical contaminants in dialysis fluid	6
44 5 Tests for compliance with microbiological requirements	6
45 5.1 Microbiological contaminants in dialysis fluid	6
46 Annex A (informative) Rationale for the development and provisions of this standard	7
47 A.1 Microbiological contaminants in dialysis fluid	7
48 A.2 Chemical contaminants in dialysis fluid	8
49 A.3 Tests for compliance with microbiological requirements	8
50 Annex B (informative)	10
51 Table B.1 (reproduced from ISO 13959) — Maximum allowable levels of toxic chemicals	
52 and dialysis fluid electrolytes in dialysis water	10
53 Table B.2 (reproduced from ISO 13959) — Maximum allowable levels of trace elements in	
54 dialysis water	10
55 Table 3 (reproduced from ISO 13959) — Analytical tests for chemical contaminants	11

D R A F T

PREPARED BY: N. K. P. P. K. E. V. I. V. V.
 (www.amsar.inch.ii)
 Full standard: <https://standards.itec.ai/catalog/standards/iso/11663-2009>
 655f45ed-9dd-6572968b5/iso/11663-2009

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.
61 International organizations, governmental and non-governmental, in liaison with ISO, also take part in
62 the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all
63 matters of electrotechnical standardization.

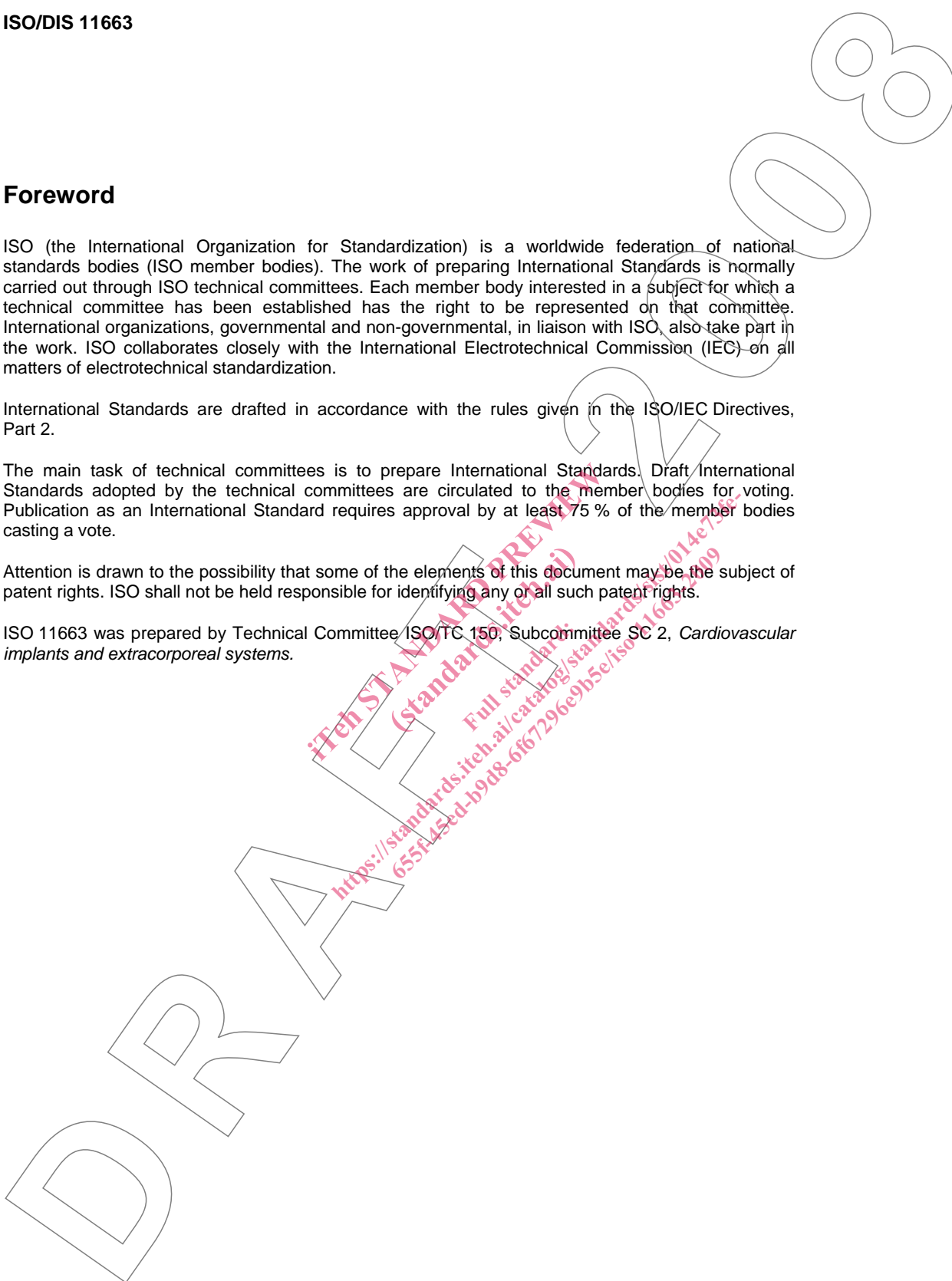
64 International Standards are drafted in accordance with the rules given in the ISO/IEC Directives,
65 Part 2.

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

74



75 Introduction

76 Haemodialysis patients are directly exposed to large volumes of dialysis fluid, with the haemodialyzer
77 membrane being the only barrier against transfer of hazardous contaminants from the dialysis fluid to
78 the patient. It has long been known that there could be hazardous contaminants in the water and
79 concentrates used to prepare the dialysis fluid. To minimize this hazard, ISO 13959, *Water for*
80 *haemodialysis and related therapies*, and ISO 13958, *Concentrates for haemodialysis and related*
81 *therapies*, set forth quality requirements for the water and concentrates used to prepare dialysis fluid.
82 However, if the dialysis fluid is not prepared carefully, it could contain unacceptable levels of
83 contaminants even though it is prepared from water and concentrates meeting the requirements of
84 ISO 13959 and ISO 13958. Further, the dialysis fluid may be used as the starting material for the
85 online preparation of fluids intended for infusion into the patient, for example, in therapies such as
86 online haemodiafiltration. For these reasons, this International Standard for dialysis fluid quality to
87 complement the existing standards for water and concentrates, ISO 13959 and ISO 13958,
88 respectively, was developed. Guidelines to aid the user in routinely meeting the requirements of this
89 standard and ISO 13959 can be found in ISO 23500, *Guidance for the preparation and quality*
90 *management of fluids for haemodialysis and related therapies*.

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

97 The requirements of this International Standard aim to help protect haemodialysis patients from
98 adverse effects arising from known chemical and microbiological contaminants that can be found in
99 improperly prepared dialysis fluid. However, the physician in charge of dialysis has the ultimate
100 responsibility for ensuring that the dialysis fluid is correctly formulated and meets the requirements of
101 all applicable quality standards.

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

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

111

iTeh STANDARD PREVIEW
(standards.iteh.ai)

Full standard:
<https://standards.iteh.ai/catalog/standards/sist/014e73fe-655f-45ed-b9d8-6f67296e9b5e/iso-11663-2009>

Quality of dialysis fluid for haemodialysis and related therapies

114 1 Scope

115 1.1 General

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

120 1.2 Exclusions

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

125 2 Normative references

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

131 2.1 ISO 13958, Concentrates for haemodialysis and related therapies

132 2.2 ISO 13959, Water for haemodialysis and related therapies

133 2.3 ISO 26722, Water treatment equipment for haemodialysis and related therapies

134 3 Definitions

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

136 3.1

137 acid concentrate

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

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

- 142 **3.2**
143 **action level**
144 concentration of a contaminant at which steps should be taken to interrupt the trend toward higher,
145 unacceptable levels
- 146 **3.3**
147 **bacteriology**
148 area of study within the field of microbiology that deals with the study of bacteria
- 149 **3.4**
150 **bicarbonate concentrate**
151 concentrated preparation of sodium bicarbonate that, when diluted with dialysis water and acid
152 concentrate, makes dialysis fluid used for dialysis
- 153 NOTE 1 Some bicarbonate concentrates also contain sodium chloride.
- 154 NOTE 2 Bicarbonate is also known as sodium hydrogen carbonate.
- 155 **3.5**
156 **central dialysis fluid system**
157 system that produces dialysis fluid from dialysis water and concentrate or powder at a central point
158 and distributes the dialysis fluid from the central point to individual dialysis machines
- 159 **3.6**
160 **chlorine, total**
161 sum of free and combined chlorine
- 162 NOTE chlorine can exist in water as dissolved molecular chlorine (free chlorine) or in chemically combined forms
163 (combined chlorine). Where chloramine is used to disinfect water supplies, chloramine is usually the principal
164 component of combined chlorine.
- 165 **3.7**
166 **CFU**
167 **colony-forming unit**
168 organism capable of replicating to form a distinct, visible colony on a culture plate.
- 169 NOTE In practice, a colony may be formed by a group of organisms
- 170 **3.8**
171 **dialysis fluid**
172 aqueous fluid containing electrolytes, buffer and, usually, glucose, which is intended to exchange
173 solutes with blood during haemodialysis
- 174 NOTE 1 The word "dialysis fluid" is used throughout this document to mean the fluid made from dialysis water
175 and concentrates that is delivered to the dialyser by the dialysis fluid supply system. Such phrases as "dialysate"
176 or "dialysis solution" can be used in place of dialysis fluid.
- 177 NOTE 2 The dialysis fluid entering the dialyser is referred to as "fresh dialysis fluid," while the fluid leaving the
178 dialyser is referred to as "spent dialysis fluid."
- 179 **3.9**
180 **dialysis fluid supply system**
181 devices that: (1) prepare dialysis fluid online from dialysis water and concentrates or that store and
182 distribute premixed dialysis fluid; (2) circulate the dialysis fluid through the dialyzer; (3) monitor the
183 dialysis fluid for temperature, conductivity (or equivalent), pressure, flow, and blood leaks; and (4)
184 prevent dialysis during disinfection or cleaning modes
- 185 NOTE 1 The term includes reservoirs, conduits, proportioning devices for the dialysis fluid, and monitors and
186 associated alarms and controls assembled as a system for the characteristics listed above.

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

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

191 **3.10**
192 **disinfection**
193 destruction of pathogenic and other kinds of microorganisms by thermal or chemical means

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

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

197 **3.11**
198 **endotoxin**
199 major component of the outer cell wall of gram-negative bacteria

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

204 **3.12**
205 **EU**
206 **endotoxin units**
207 units assayed by the *Limulus amoebocyte lysate* (LAL) method when testing for endotoxins

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

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

212 **3.13**
213 **haemodiafiltration**
214 form of renal replacement therapy in which waste solutes are removed from blood by a combination of
215 diffusion and convection through a high-flux membrane

216 NOTE Diffusive solute removal is achieved using a dialysis fluid stream as in haemodialysis. Convective solute
217 removal is achieved by adding ultrafiltration in excess of that needed to obtain the desired weight loss; fluid
218 balance is maintained by infusing a replacement solution into the blood either before the dialyser (pre-dilution
219 haemodiafiltration) or after the dialyser (post-dilution haemodiafiltration).

220 **3.14**
221 **haemodialysis**
222 form of renal replacement therapy in which waste solutes are removed primarily by diffusion from
223 blood flowing on one side of a membrane into dialysis fluid flowing on the other side

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

227 **3.15**
228 **haemofiltration**
229 form of renal replacement therapy in which waste solutes are removed from blood by convection

230 NOTE 1 Convective transport is achieved by ultrafiltration through a high-flux membrane. Fluid balance is
231 maintained by infusing a replacement solution into the blood either before the haemofilter (pre-dilution
232 haemofiltration) or after the haemofilter (post-dilution haemofiltration).

233 NOTE 2 There is no dialysis fluid stream in haemofiltration.

234 **3.16**
235 **LAL**
236 ***Limulus amoebocyte lysate test***
237 assay used to detect endotoxin

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

240 **3.17**
241 **manufacturer**
242 entity that designs, manufactures, fabricates, assembles, formulates or processes a finished device

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

246 **3.18**
247 **microbial**
248 referring to microscopic organisms, bacteria, fungi, and so forth

249 NOTE see also **bacteriology**.

250 **3.19**
251 **microbiological contamination**
252 contamination with any form of microorganism (e.g., bacteria, yeast, fungi, and algae) or with the by-
253 products of living or dead organisms such as endotoxins, exotoxins, and microcystin (derived from
254 blue-green algae)

255 **3.20**
256 **non-pyrogenic**
257 Less than 0,03 EU/mL by the LAL assay.

258 **3.21**
259 **pyrogen**
260 fever-producing substance

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

262 **3.22**
263 **sterile**
264 free from viable microorganisms

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

270 **3.23**
271 **substitution fluid**
272 fluid used in haemofiltration and haemodiafiltration treatments that is infused directly into the patient's
273 blood as a replacement for the fluid that is removed from the blood by filtration

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

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