Status: Currently Official on 12-Feb-2025
Official Date: Official Prior to 2013
Document Type: General Chapter
DocId: GUID-03C831A5-CB53-4A4A-A907-ECD3BCAB6CAB_1_en-US
DOI: https://doi.org/10.31003/USPNF_M301_01_01
DOI Ref: 28aqx

⟨1230⟩ WATER FOR HEMODIALYSIS APPLICATIONS

GENERAL PURIFICATION CONSIDERATIONS

Chemical and microbial components that can be found in drinking water meeting U.S. Environmental Protection Agency National Primary Drinking Water Regulations (or equivalent) may have the potential to produce significant negative effects in patients undergoing hemodialysis. It is, therefore, necessary to subject the water to further treatment to reduce these components to acceptable levels. The *Water for Hemodialysis* monograph provides bacterial and chemical tests that are required to ensure patient safety. Additional testing is recommended as follows:

1. Excess levels of aluminum, fluorides, and chlorine may be found seasonally in drinking water as a result of chemicals used in water treatment. These components should be monitored in Water for Hemodialysis being produced in accordance with established standard operating procedures. The maximum acceptable levels of these and other elements and compounds, as proposed by AAMI (Association for the Advancement of Medical Instrumentation) are listed in *Table 1.* These attributes should be periodically monitored to ensure they are being controlled by the routine testing performed in accordance with the *Water for Hemodialysis* monograph.
2. A comprehensive validation testing of the system producing Water for Hemodialysis should be performed initially and periodically thereafter to ensure that the water treatment equipment and system sanitization processes are functioning properly.

Table 1. Maximum Allowable Chemical Levels in Water for Hemodialysis (water used to prepare dialysate and concentrates from powder at a dialysis facility and to reprocess dialyzers for multiple use)*

Element or Compound	Maximum Concentration (mg/L)
Contaminants with documented toxicity in hemodialysis	
Aluminum	0.01
Chloramines	0.1
Free chlorine	0.5
Copper	0.1
Fluoride	0.2
Lead	0.005
Nitrate (as N)	2
Sulfate	100
Zinc	0.1
Contaminants normally included in dialysate	
Calcium	2 (0.1 mEq/L)
Magnesium	4 (0.3 mEq/L)
Potassium	8 (0.2 mEq/L)
Sodium	70 (3.0 mEq/L)

Element or Compound	Maximum Concentration (mg/L)
Other contaminants	
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

* Reprinted with permission from ANSI/AAMI RD62: 2006, "Water treatment equipment for hemodialysis applications", ©Association for the Advancement of Medical Instrumentation, Arlington, VA.

The chemical limits included in *Table 1* have been recognized by federal government agencies as standards for Water for Hemodialysis. Written standard operating procedures for water testing should be established by the physician in charge or the designated facility manager. The test frequency decision should be based upon historical data analysis, the quality of the source water as reported by the municipal water treatment facility or public health agency in the area, etc. Records should be maintained to document levels and any necessary remedial action taken promptly.

Chemical analysis of water components listed should be performed using methods referenced in the American Public Health Association's *Standard Methods for the Examination of Water and Wastewater,* 21st Edition,[1] those referenced in the U.S. Environmental Protection Agency's *Methods for the Determination of Metals in Environmental Samples,*[2] or equivalent methods as referenced in ANSI/AAMI RD 62:2006.

MICROBIAL CONSIDERATIONS

The *Water for Hemodialysis* monograph includes total aerobic microbial count (TAMC) limits of 100 cfu/mL and endotoxin limits of 1 USP Endotoxin Unit/mL. In addition, the absence of *Pseudomonas aeruginosa* should be routinely determined because this is an opportunistic pathogen hazardous to acutely ill hemodialysis patients. Both the high microbial counts and the presence of *Pseudomonas aeruginosa* can be associated with inadequate water system maintenance and sanitization. Sampling the water should be done at all use points where the water enters the dialysis equipment. Samples should be assayed within 30 minutes of collection or immediately refrigerated and then assayed within 24 hours of collection. The microbial enumeration and absence tests are performed using procedures found in the USP general test chapters *Microbial Enumeration Tests ⟨61⟩* and *Tests for Specified Microorganisms ⟨62⟩*. Quantification of bacterial endotoxins is performed using procedures found in the USP general test chapter *Bacterial Endotoxins Test ⟨85⟩*.

Because of the incubation time required to obtain definitive microbiological results, water systems should be microbiologically monitored to confirm that they continue to produce water of acceptable quality. "Alert" and "Action Levels" are therefore necessary for the monitoring and control of the system. An Alert Level constitutes a warning and does not require a corrective action. An Action Level indicates a drift from normal operating conditions and requires that corrective action be taken to bring the process back into the normal operating range. Exceeding an Alert or Action Level does not imply that water quality has been compromised. The maximum recommended Action Level for a total viable microbial count in the product water should be no greater than 25 cfu/mL, and the maximum recommended Action Level for bacterial endotoxins should be no greater than 0.25 USP Endotoxin Unit/mL. As with all process control values, Action and Alert Levels should be established from normal system monitoring trends and process capabilities in a fashion that allows remedial actions to occur in response to process control level excursions well before specifications are exceeded (also see *Microbial Considerations* under *Water for Pharmaceutical Purposes ⟨1231⟩*).

[1] American Public Health Association, Washington, DC 20005.

2 U.S. Environmental Protection Agency Publication EPA-600-R-94-111, Cincinnati, OH.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
<1230> WATER FOR HEMODIALYSIS APPLICATIONS	Antonio Hernandez-Cardoso Senior Scientific Liaison	GCCA2020 General Chapters - Chemical Analysis 2020

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 35(6)

Current DocID: GUID-03C831A5-CB53-4A4A-A907-ECD3BCAB6CAB_1_en-US
DOI: https://doi.org/10.31003/USPNF_M301_01_01
DOI ref: 28aqx