



Standard Guide for Biomedical Grade Water ¹

This standard is issued under the fixed designation D 5196; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last approval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide is intended to describe the physical and chemical characteristics of water to be used whenever critical purity is essential to the use intended in clinical, pharmaceutical, biophysical, biomedical, chemical, physical research applications, or a combination of these. This guide is not intended for use in preparing water for injectables. Generally, the appropriate use of this guide may include experiments involving tissue culture, chromatography, mass spectroscopy, or analysis where molecular quantities of impurities may be important.

1.2 *This standard does not purport to address all of the safety problems, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

2. Referenced Documents

2.1 ASTM Standards:

- D 1125 Test Methods for Electrical Conductivity and Resistivity of Water ²
- D 1129 Terminology Relating to Water ²
- D 1426 Test Methods for Ammonia Nitrogen in Water ²
- D 1428 Test Methods for Sodium and Potassium in Water and Water-Formed Deposits by Flame Photometry ³
- D 3919 Practice for Measuring Trace Elements in Water by Graphite Furnace Atomic Absorption Spectrophotometry ²
- D 3973 Test Method for Low Molecular Weight Halogenated Hydrocarbons in Water ⁴
- D 4453 Practice for Handling of Ultra-Pure Water Samples ²
- D 4517 Test Method for Low-Level Total Silica in High Purity Water by Flameless Atomic Absorption Spectroscopy ⁴
- D 4779 Test Method for Total, Organic, and Inorganic Carbon in High Purity Water by Ultraviolet (UV), or Persulfate Oxidation, or Both, and Infrared Detection ⁴

F 1094 Test Methods for Microbiological Monitoring of Water Used for Processing Electron and Microelectronic Devices by Direct-Pressure Tap Sampling Valve and by the Pre-Sterilized Plastic Bag Method ⁵

3. Terminology

3.1 *Definitions*—For definitions of terms used in this guide, refer to Terminology D 1129.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *endotoxins*—substances or by-products usually produced by gram negative micro-organisms which give a positive test for endotoxin in accordance with 8.24.

3.2.2 *heterotropic bacterial counts/1000 mL*—total number of viable micro-organisms present in the 1000-mL sample, excluding anaerobic and microaerophilic bacteria.

3.2.3 *total organic carbon*—carbon measured after inorganic carbon response has been eliminated by one of the prescribed ASTM methods.

3.2.4 *water*—water prepared in accordance with this guide.

4. Significance and Use

4.1 The purity of water is only relative and is usually defined by the limits of impurities found in the water as well as by the methods used to prepare and handle the water. Appendix X1 describes a method of preparation of moderate volumes of water with the highest purity practical using available equipment and techniques.

4.2 The method of preparation of water described in Appendix X1 is designed to remove organic, inorganic, volatile, particulate, and biological impurities to provide water that should meet the concentration limits in Table 1. These are suggested limits, since the actual maxima of the individual impurities will depend upon the required end use of the water. The limits in the guide in most cases are dictated not by the desired maximum concentration of the impurities, but by the methods of analysis. More restrictive limits may be required by mutual consent of the parties concerned, provided a suitable test method is agreed upon.

4.3 The guide for the storage of high purity water is very important because impurities are added to the water in proportion to the solubility, area of contact, and time of contact between the water and the materials of containment. It is

¹ This guide is under the jurisdiction of ASTM Committee D-19 on Water and is the direct responsibility of Subcommittee D19.02 on General Specifications, Technical Resources, and Statistical Methods.

Current edition approved Oct. 15, 1991. Published February 1992.

² *Annual Book of ASTM Standards*, Vol 11.01.

³ *Discontinued 1990*—See 1989 *Annual Book of ASTM Standards*, Vol 11.01.

⁴ *Annual Book of ASTM Standards*, Vol 11.02.

⁵ *Annual Book of ASTM Standards*, Vol 10.04.

TABLE 1 Suggested Maximum Analyte Concentrations

Analyte	Maximum Concentration, $\mu\text{g/L}$
Arsenic	0.1
Cadmium	0.1
Chromium	1.0
Cobalt	1.0
Copper	1.0
Fluoride	1.0
Iron	1.0
Lead	1.0
Nickel	0.1
Potassium	2.0
Silica (total)	5.0
Sodium	0.5
Titanium	1.0
Zinc	0.5
Acetate	3.0
Ammonia	1.0
Chloride	1.0
Chloroform	5.0
Formate	2.0
Nitrate	1.0
Phosphate	1.0
Phthalates	0.1
Sulfide	1.0
Sulfate	1.0
Total organic carbon (TOC)	20.0
Volatile chlorinated hydrocarbon	5.0
Endotoxins (Endotoxin Unit)	<0.03 EU/mL
Heterotropic bacterial counts	<10/1000 mL
Electrical resistivity, ^A min, $\text{M}\Omega\text{-cm}$ at 25°C:	
–measured at the production point not in contact with air	10.0
–measured from storage or distribution system in contact with air	1.0

^AElectrical resistivity can be expressed in microsiemens per centimetre conductivity at 25°C. The conductivity is reciprocal of the resistivity, $1/\rho$.

important to minimize the contact time of storage and to realize that the containment materials will determine the type of contaminants. Particular emphasis must be placed upon possible contamination from the atmosphere above the water which may add biological as well as gaseous and particulate impurities.

4.4 The distribution systems present a large area of contact between the water and the pipe or tubing and, therefore, must be of a very pure insoluble substance. Organic impurities, such as plasticizers, micro-organisms and their by-products, etc., are often more important considerations than inorganic impurities. Because plastic materials may vary from batch to batch, it is desirable to include limits of specific impurities as part of any installation specification.

4.5 The distribution outlets or faucets must be of non-contaminating design and materials. Particular care must be given to the valve seat and joint construction. The outlet must be protected from biological contamination particularly when the use is only occasional. Ultraviolet (UV), chemical, or heat sterilization should be considered.

5. Reagents

5.1 *Purity of Reagents*—Reagent grade chemicals shall be used in all tests. Unless otherwise indicated, it is intended that all reagents shall conform to the specifications of the Committee on Analytical Reagents of the American Chemical Society,

where such specifications are available.⁶ Other grades may be used, provided it is first ascertained that the reagent is of sufficiently high purity to permit its use without lessening the accuracy of the determination.

5.2 *Purity of Water*— Unless indicated otherwise, references to water shall be understood to mean water as defined in this guide.

6. Sampling

6.1 The test methods specified in Section 8 assume that great care and skill will be employed in obtaining the water samples to be tested. It is assumed that the operators will prevent container and airborne contamination to the best of their ability, making note of possible sources of contamination due to the sampling procedure. It is recommended that the samples be handled in accordance with Practice D 4453.

6.2 Extreme care must be exercised in handling samples when making analyses. Experimental laboratory-ware should be made of PFA- or TFE-fluorocarbon, and less desirably from quartz or borosilicate glass, to minimize the contamination of the water. Borosilicate glassware may leach ions at picogram-per-litre levels. The major contaminants from borosilicate glass are sodium (Na), potassium (K), boron (B), and silica (SiO_2). No detectable ions leach out of PFA- or TFE-fluorocarbon that has been properly cleaned.

6.2.1 Containers should be cleaned with HNO_3 (1 + 4) or HCl (1 + 4), or both, by filling the container and allowing it to stand for a minimum of 1 h.

6.2.2 The containers should be rinsed with three container volumes of a sampled water and then allowed to stand for 24 h with the same sampled water.

6.2.3 The containers should be rinsed again twice with the sampled water before filling.

6.2.4 The containers should be filled by flushing at least five volumes of the sampled water into the vessel before sealing. The seal must be of a non-contaminating material.

6.2.5 Storage of the sample may be required for the detection of metals, in which case 1 mL of redistilled HNO_3 (1 + 99) or HCl (1 + 99) should be added per litre to reduce the pH and to preserve solubility of the metals within the sample.

6.2.6 The water sample should remain in storage a minimal length of time since some impurities have a tendency to adhere to the container surface. Endotoxins may become irreversibly stuck to glass walls, as will certain insoluble colloids.

7. Recommendations for Purity

7.1 Recommendations for purity of water should conform to the properties and chemical limits given in Table 1; however the suggested maximum limits and the actual impurities considered, or both, may be modified by the user based upon the intended use of the water.

⁶ "Reagent Chemicals, American Chemical Society Specifications," Am. Chemical Soc., Washington, DC. For suggestions on the testing of reagents not listed by the American Chemical Society, see "Analar Standards for Laboratory Chemicals," BDH Ltd., Poole, Dorset, U.K., and the "United States Pharmacopeia."