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Standard Guide for Bio-Applications Grade Water[1]

This standard is issued under the fixed designation D5196; 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 reapproval. 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 chemical and biological characteristics of water to be used whenever critical purity is essential to the use intended in laboratory bio-applications, for example, clinical, pharmaceutical, and biomedical. The importance of such a reagent is often underestimated despite the impact that it can have.

1.2 This guide is not intended to be used as a reference in preparing water for injectables. Generally, the appropriate use of this guide may include experiments involving tissue culture, chromatography, mass spectrometry, polymerase chain reaction (PCR), deoxyribonucleic acid (DNA) sequencing, DNA hybridization, electrophoresis, molecular biology or analyses where molecular concentrations of impurities may be important.

1.3 For all the other applications linked to an ASTM method and not bio-sensitive that require purified water, it is recommended that Specification D1193 or Guide D5127 be consulted.

1.4 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

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

1.6 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D1125 Test Methods for Electrical Conductivity and Resistivity of Water

D1129 Terminology Relating to Water

D1193 Specification for Reagent Water

D4453 Practice for Handling of High Purity Water Samples

D5127 Guide for Ultra-Pure Water Used in the Electronics and Semiconductor Industries

D5173 Guide for On-Line Monitoring of Total Organic Carbon in Water by Oxidation and Detection of Resulting Carbon Dioxide

D5245 Practice for Cleaning Laboratory Glassware, Plasticware, and Equipment Used in Microbiological Analyses

D5391 Test Method for Electrical Conductivity and Resistivity of a Flowing High Purity Water Sample

D5542 Test Methods for Trace Anions in High Purity Water by Ion Chromatography

D5673 Test Method for Elements in Water by Inductively Coupled Plasma—Mass Spectrometry

D5996 Test Method for Measuring Anionic Contaminants in High-Purity Water by On-Line Ion Chromatography

F1094 Test Methods for Microbiological Monitoring of Water Used for Processing Electron and Microelectronic Devices by Direct Pressure Tap Sampling Valve and by the Presterilized Plastic Bag Method

3. Terminology

3.1 *Definitions:*

3.1.1 For definitions of terms used in this standard, refer to Terminology D1129.

3.2 *Definitions of Terms Specific to This Standard:*

3.2.1 *endotoxins, n*—substances or by-products usually produced by gram negative micro-organisms that give a positive test for endotoxin in accordance with 13.2.

3.2.2 *heterotrophic bacterial counts/100 mL, n*—total number of viable micro-organisms present in the 100-mL sample, excluding anaerobic and microaerophilic bacteria.

[1] This guide is under the jurisdiction of ASTM Committee D19 on Water and is the direct responsibility of Subcommittee D19.02 on Quality Systems, Specification, and Statistics.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

3.2.3 *total organic carbon, n*—carbon in the form of organic compounds.

3.2.4 *water, n*—water complying with compositions given in Table 1.

4. Significance and Use

4.1 The purity of water is relative and is usually characterized by the limits of impurities found in the water as well as by the methods used to prepare and handle the water. Section 7 mentions the suitable methods for water preparation.

5. Composition

5.1 Water for bio-applications should be prepared (using water purification technologies) starting from water complying with the U.S. Environmental Protection Agency (EPA) National Primary Drinking Water Regulations, or from comparable regulations from the European Union or Japan. The use of such a minimum standard quality for feed water is important to decrease the risk of producing and using final purified water that would be compliant with the compositions given in Table 1 but could contain certain specific contaminants in concentrations that could affect the applications.

5.2 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.

5.3 Although these water types and associated grades have been defined specifically for use with ASTM standards, they may be appropriate for other applications. It is the responsibility of the users of this standard to ensure that the selected water types or grades are suitable for their intended use.

6. Reagents

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

7. Summary of Preparation Methods

7.1 The method of preparation used for the water must be designed to remove organic, inorganic, volatile, biological impurities and particulates to provide water that meets the concentration limits in Table 1. These are suggested limits, since the actual maximum levels for the individual impurities will depend on the end use for which the water is required. More restrictive limits than those suggested in Table 1 may be required by mutual consent of the parties concerned, provided a suitable test method is agreed upon.

7.2 The bio-applications grade water needs to be prepared from tap water complying with U.S. EPA National Primary Drinking Water Regulations or comparable regulations of the European Union or Japan.

7.3 The purification of tap water shall be accomplished by a single technology or a combination of suitable purification technologies such as distillation, deionization, electrodeionization, carbon adsorption, reverse osmosis, ultrafiltration, nanofiltration, ultraviolet (UV) photo-oxidation, or screen membrane filtration, or combination thereof, to meet the compositions given in Table 1.

7.4 The water purification systems containing these technologies should be constructed from materials shown to contribute to low contamination to the final product water.

7.5 Because quality assurance is key to ensure safety, efficiency and reliability, validation of the water purification installation is highly recommended (see Section 14).

TABLE 1

Analytes	Maximum Concentration
Total Inorganic Analytes	1 µg/L or resistivity of 18.2 Mohm.cm at 25°C. See Note 1
Total Organic Carbon (TOC – on-line measurement)	20 ppb
Heterotrophic bacterial counts	100 cfu/100 mL
Endotoxins (Endotoxin Unit)[A]	0.01 EU/mL
Nucleases[B]	See Note 2
Proteases[C]	See Note 2

[A] If application sensitive to endotoxins. Commercial kits and methods are available for such purpose.
[B] If applications are linked to DNA or ribonucleic acid (RNA) work, or both.
[C] If applications involved proteins.

8. Monitoring and Trends

8.1 The monitoring of different parameters should be performed at a frequency defined by the user to ensure with a high degree of confidence that the water quality used is always compliant with the specifications and the purpose.

8.2 Regular calibration and maintenance of the measuring instruments is the best way to ensure, with a high level of confidence, the validity of the values obtained to determine the compliance with the specifications of the water used. Trending parameters is the main reliable source of information to define maintenance schedule and to anticipate failures.

8.3 *Inorganic Analytes*—Resistivity is the most widely used parameter to monitor the overall ionic purity. According to their mobility, each ionic species will have a different effect on the resistivity. The limit of Table 1 apply to the water sampled at the point of use or, when for practical reasons or to avoid contamination (for example connection of an equipment after a 0.2-µm filter), or both, as close as possible to the point of use and with a regular verification of a low impact of the purification steps or equipment placed downstream of the monitoring sampling point, or both. If in-line measurements are not possible then analyses of the water produced should be conducted to determine that the total ionic concentration of all the analytes described in Table 2 does not exceed the compositions given in Table 1 (≤1 µg/L total). Table 2 lists common cations and anions that have an impact on the resistivity value and may have an impact on some bio-applications. The user should add any other ionic contaminants (not already indicated) to this list if the application being performed may be sensitive to those ions.

8.4 *Heterotrophic Bacterial Count*—The maximum concentrations proposed in Table 1 is given for determination by a plate-count method. If this method is selected, Test Methods F1094 can be used as a reference. Such determination can be