

A Critique of ASTM Standard D 5196

Standard Guide for Biomedical Grade Water

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Foreword

ASTM D5196, Standard Guide for Biomedical Grade Water, is referenced only once in ASTM standards and does not appear to be supported by any laboratory or agency.^b It has been poorly edited and is overflowing with errors, internal contradictions, and vague, confusing, and misleading language. The D19 (Water) Committee of ASTM was aware of most, if not all, of its deficiencies when it was re-approved in 1999.^c This critique of D5196 has been evolving with input from many interested parties since January 1999 and its purpose is to serve as a banner around which the loyal opposition to D5196 can rally their forces in order to bring about a change.

D5196 is titled a guide; however, it tells the reader virtually nothing about how to prepare what it defines as biomedical grade water and it makes no attempt to justify the need for this water. D5196 lists limits for 29 substances that can be present in biomedical-grade water and declares these limits to be essentially arbitrary, because they are based

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^b D5196 is cited in ASTM E1924 (1997). At the ASTM D5196 Task Group Meeting held 06/13/99 in Louisville, KY, the author requested the chairperson of the D5196 Task Group to provide evidence that the D5196 was cited anywhere else. The challenge was repeated at the January 17, 2000 ASTM Meeting in Cocoa Beach, FL. No examples have been forthcoming.

^c Most of the information contained in this critique was presented to the D19.02 Subcommittee at the ASTM Meeting held on 06/13/99 in Louisville, KY.

primarily on the detection limits of available methods rather than on the requirements of biomedical applications.^d Yet, D5196 does not reference sufficiently sensitive and accurate methods to determine the limits for a significant number of the listed contaminants. And, without supporting evidence or discussion, D5196 declares the 29 limits should be met, if water is produced according to procedures described in a few short and confusing paragraphs in the appendix. D5196 has few, if any, redeeming features; it should be discontinued.

The editors and scientific experts, who have contributed to writing this Critique, accepted the challenge to be thorough and detailed for three reasons:

- 1) D5196 is essentially a legal document and an incorrectly used word, or what might seem like an insignificant editorial error, can create large loopholes and great confusion;
- 2) In order to avoid the possibility that D5196 will be reapproved with only minor changes, it is important to leave no doubt about the depth and breadth of its deficiencies; and
- 3) Laboratories and manufacturers, who are defending themselves in regulatory or contract disputes, want as much detail as possible.

^d “The limits in the guide[,] in most cases[,] are dictated not by the desired maximum concentration[s] of [for] the impurities, but by the methods of analysis.” (Section 4.2)

Critique

Important: The published text of D 5196 is shown in black. Comments and corrections are contained within square brackets, [], and shown in blue.

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Beginning of D 5196 . . .

ASTM Designation: D 5196 - 99

Standard Guide for Biomedical Grade Water¹ [In what way does this standard *guide* the reader to Biomedical Grade Water – It is an inadequate guide to the production of purified water and it is not a specification for purified water.]

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 reapproval. A superscript epsilon ([epsilon]) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This guide [“Guide” – should not the words, “Standard Guide” be used, because simply using “guide” leaves the reader wondering what happened to the title of the document.] is intended to describe the physical and chemical characteristics [What about physical chemical (e.g., resistivity) and biological (e.g., microorganisms, endotoxins, etc.) characteristics] of water to be used whenever critical [What is the meaning of “critical” in this context?] purity is essential to the use intended in [“to the use intended in” – would not the word, “for” be more clear?] clinical, pharmaceutical, biophysical, biomedical, chemical, physical [What about physical chemical, biochemical, physiological,

¹This 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.

biological applications? What is the purpose of providing a long, but incomplete, list of applications that can use biomedical-grade water?] research applications [Is the user to understand that biomedical-grade water can only be used for research applications?], or a combination of these. This guide is not intended for use in preparing water for injectables. [Poor choice of words – one certainly would not *use the guide* to prepare injectables, one would *reference* the guide to . . .] Generally, the appropriate use [Again, “Use” seems like a poor choice of words – it is not the guide that is *used*, it is the water produced as the result of following the guide that is *used*?] of this guide may include experiments involving tissue culture, chromatography, mass spectroscopy, or analysis where molecular quantities [“Quantities” – perhaps the word, “concentrations” would be a better choice.] of impurities may be important [“May be important” – what is meant by this phrase? The previous sentence listed typical applications for biomedical-grade water and this sentence provides a completely different list to which the Guide applies? No evidence is provided that the applications listed are sensitive to molecular concentrations of impurities. In any case, this Guide does not offer any real guidance for producing water of high purity.]

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

[A considerable number of methods must be added.]

2.1 ASTM Standards:

D 1125 Test Methods for Electrical Conductivity and Resistivity of Water²

D 1129 Terminology Relating to Water²

D 1426 Test Methods for Ammonia Nitrogen in Water²

D1428 Test Methods for Sodium and Potassium in Water and Water-Formed Deposits by Flame Photometry³

[D3867 Standard Test Methods for Nitrite-Nitrate in Water²]

D3919 Practice for Measuring Trace Elements in Water by Graphite Furnace Atomic Absorption Spectrophotometry²

D 3973 Test Method for Low Molecular Weight Halogenated Hydrocarbons in Water⁴

² Annual Book of ASTM Standards, Vol 11.01.

³ *Discontinued 1990* – See *1989 Annual Book of ASTM Standards*, Vol. 11.01. [Discontinued?]

⁴ Annual Book of ASTM Standards, Vol 11.02.

[D 4192 Test Method for Potassium in Water by Atomic Absorption Spectrophotometry²]

D 4453 Practice for Handling of Ultra-Pure Water Samples²

D 4517 Test Method for Low-Level Total Silica in High-Purity Water by Flameless Atomic Absorption Spectroscopy⁴

[D 4658 Standard Test Method for Sulfide Ion in Water²]

D 4779 Test Method for Total, Organic, and Inorganic Carbon in High Purity Water by Ultraviolet (UV) or Persulfate Oxidation, and Membrane Conductivity Detection⁴

[D 5391 Standard Test Method for Electrical Conductivity and Resistivity of a Flowing High

Purity Water Sample²]

[D 5542 Test Methods for Trace Anions in High Purity Water by Ion Chromatography²]

[D 5544 Test Method of On-line Measurement of Residue After Evaporation of High-Purity Water²]

[D 5673 Test Method for Elements in Water by Inductively Coupled Plasma/Mass Spectroscopy³]

[D 5996 Standard Test Method for Measuring Anionic Contaminants in High-Purity Water by On-Line Ion Chromatography²]

[D 5997 Test Method for On-Line Monitoring of Total Carbon, Inorganic Carbon in Water by Ultraviolet, Persulfate Oxidation and Membrane Conductivity Detection²

[D 6071 Test Method for Low Level Sodium in High Purity Water by Graphite Furnace Atomic Absorption Spectroscopy²]

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 Presterilized Plastic Bag Method⁵ [This method is likely understate the numbers of viable microorganisms by 100-1000 times. (McAlister MB, Kulakov LA, Larkin MJ, Ogden KL. *Microbials - Analysis of bacterial contamination in different sections of a high-purity water system*. *Ultrapure Water* 2001; 18(1):18-26.)]

3. Terminology

3.1 *Definitions* – For definitions of terms used in this guide, refer to Terminology D1129.

3.2 *Descriptions of Terms Specific to This Standard:*

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

3.2.2 *heterotropic [sic] bacterial counts/1000 mL* – total number of viable microorganisms present in the 1000-mL sample, excluding anaerobic and microaerophilic bacteria. [“Heterotropic”, was changed to “heterotropic”, meaning cross-eyed, with

⁵Annual Book of ASTM Standards, Vol 10.04.

the publication of this version. This occurred despite the fact that it took years to correct the same error in D1193, Standard Specification for Reagent Water.]

3.2.3 *total organic carbon* – carbon measured after inorganic carbon response [Response – to what?] has been eliminated by one of the prescribed ASTM methods.

3.2.3 *water* – water prepared in accordance with this guide. [Does this mean that “water” means “biomedical-grade water”? Since this Standard is a *guide* and does not actually define methods for preparing water, this definition is meaningless in any case.]

4. Significance and Use

4.1 The purity of water is only relative [Relative to what?] and is usually defined [If water purity is “relative”, how can it be “defined” in non-relative terms? Perhaps “characterized” would be a better word.] 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 [Actually, Appendix X1 provides a vague description of many possible approaches, which cannot really be called *methods*.] of preparation of moderate volumes of water [Section X1.1.2 describes a central building system – is that a moderate volume system?] with the highest purity practical using available equipment and techniques. [“Practical” – what does this word mean in the present context? “Available” – available where and to whom? Appendix X1 appears to be little more than a poorly worded series of sweeping generalities. Therefore, this sentence would lead users of this Guide to believe that it is impractical to produce biomedical-grade water with *available equipment and techniques*? However, Section 4.2 states, “The method of preparation of biomedical grade water described in Appendix X1 . . .” Is Appendix X1 supposed to be a description of how to produce *practical water* or *biomedical-grade water*?

4.2 The method [“Methods” – see comment in Section 4.1.] of preparation of biomedical grade water described in Appendix X1 is designed to remove organic, inorganic, volatile, particulate, and biological impurities to provide water that should [“Should” – does this mean that the *methods* described in the Appendix “may” not produce water that meets the limits described in Table 1? And since the methods in the Appendix are described as producing “water with the highest purity practical” (Section 4.1), does the use of the word, “should”, imply that the limits in Table 1 may not be *practical*?] meet the concentration limits in Table 1. These are suggested limits, since the actual maxima [“Maxima” – plural of maximum. There can be only one maximum limit for an individual impurity.] of [For?] the individual impurities will depend upon [“Upon” – the correct word would be “on”.] the required end use [“Required end use” – these words seems inappropriate. Exactly who or what would *require* which *end use*?] of the biomedical grade water. The limits in the guide [Punctuation?] in most cases [But not in all cases – how are users of this Guide supposed to know when a limit is limited by the methodology and when it is not.] are dictated not by the desired maximum concentration

[Plural – concentrations] of the impurities, but by the methods of analysis [This sentence is saying, in essence, that the limits for the parameters in Table 1, which define biomedical-grade water, are based on the limits of the analytical methods used to measurement of the parameters, not the requirements of the applications for which biomedical-grade water would likely be used.]. More restrictive limits may be required [“Required” – this standard is a Guide, not a specification.] by mutual [Two persons or groups?] consent [Written, verbal, or unspoken consent?] of the parties concerned [Any person with an interest in this Standard Guide is potentially a “concerned party”. This paragraph can be interpreted to mean that nobody knows what this Standard Guide may be at any given moment in time.], provided a suitable test method [What is a “suitable test method”?] is agreed upon.

4.3 The guide for the storage of biomedical grade water [Where is this “Guide” to be found? Presumably, ASTM meant to refer to Appendix X2] is very important because impurities are added [“Added” – who or what is *adding* the impurities? Perhaps it would be better to say, “will dissolve into the water”.] to the water in proportion to the [Their?] solubility [In?], area of contact [With?], and time of contact between [“Between – the word, “with” would be better.] the water and the materials of containment [“Materials of containment”? – this sentence should be rewritten for clarity]. It is important to minimize the contact time of storage [Exactly how would one go about “minimizing the contact time of storage”? It would appear that ASTM is recommending the storage of very large volumes of water and the use of spherical containers in order to maximize the ratio of volume to surface; however, it is really not clear what ASTM means to say.] and to realize that the containment materials [“Containment materials“?] will determine the type of contaminants [Singular and plural are tangled – Type of contamination, types of contaminants, or contaminants. This sentence could be rewritten for clearly. However, it seems unnecessary to say that it is important to realize that water will be contaminated by the container materials that come in contact with the water.]. Particular emphasis must be placed upon [“Upon” – “on” is the correct word. Perhaps ASTM meant to say, “Particular attention should be paid to. . .”] possible contamination from [and by?] the atmosphere [Perhaps ASTM meant to say, “ambient air”.] which may add [“May add” – the atmosphere does not exercise discretion.] biological as well as gaseous and particulate impurities [The terms “biological”, “gaseous”, and “particulate impurities” have overlapping meaning, and they represent an incomplete list of the potential contaminants.].

4.4 The distribution systems [Which distribution systems?] present a large [Perhaps ASTM meant to say, *represent a potentially large area . . .?*] area of contact between the water [Which water?] and the pipe or tubing and, therefore, must be of a very pure insoluble substance. [“Must be of very pure insoluble substance” – poor sentence construction (unclear meaning). Many piping materials are made of mixtures of components (e.g., polymerized plastics, so the use of the word, *pure*, would appear to be a poor choice in this context.) Organic impurities, such as plasticizers, micro-organisms and their by-products, etc., are often more important considerations than inorganic impurities [Exactly, but what does the “purity” or “insolubility” of the piping materials have to do with microbiological contamination? Biofilms have been shown to thrive on virtually

every type of piping material.]. Because plastic materials may vary from batch to batch, it is desirable to include limits of specific impurities [Which “impurities”, those in the water or those in the piping material?] as part of any installation specification.

4.5 The distribution outlets or faucets [Which distribution outlets and faucets? What is the distinction between an *outlet* and a *faucet*?] must be of non-contaminating design and materials [The words, “design and materials”, are superfluous and confusing.]. Particular care [“Care” – does ASTM mean *attention*?] must be given to the [The word, “the”, should be removed.] valve seat and joint [What “joint” – is ASTM mixing pipe joints into a discussion of outlets and faucets or they referring to valve *seals*?] construction. [Why must special attention be paid to . . .] The outlets must be protected [“Protected” – does ASTM mean *designed to prevent contamination or kept from being contaminated*?] from biological contamination [Punctuation?] particularly when the [Their?] use is only occasional [Perhaps the words, *they are used only occasionally*, would be more appropriate? If microbiological contaminants can backflow into a system through a valve, so can every other type of contamination. Moreover, it has not been established that reasonably designed valves, equipped with anti-backflow features, necessarily represent a major source of microbiological contamination in typical water distribution systems.]. Ultraviolet (UV), chemical, or heat sterilization should be considered. [Does ASTM mean that the valves should be internally treated with UV, chemicals, or heat on a regular basis, or is ASTM referring to external treatment?]

TABLE 1 Suggested Maximum Analyte Concentrations [The use of the word “analyte” suggests that the presence of the contaminant is known and it is being measured. Perhaps it would be better to use the word, “contaminant” or “impurity”, especially since resistivity, endotoxins, and plate counts are included in the table? Note that in section 4.2 ASTM states, “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.”]

Contaminant	Maximum Concentration, µg/L
Arsenic	0.1 [Methods cited cannot go below 0.9]
Cadmium	0.1
Chromium	1.0
Cobalt	1.0
Copper	1.0
Fluoride	1.0
Iron	1.0
Lead	1.0
Nickel	0.1 [Methods cited cannot go below 0.2]
Potassium	2.0
Silica (total)	5.0 [Methods cited cannot go below 25.]
Sodium	0.5 [Methods cited cannot go below 3.]
Titanium	1.0
Zinc	0.5
Acetate	3.0
Ammonia	1.0 [Methods cited cannot go below 300.]

Chloride	1.0
Chloroform	5.0
Formate	2.0
Nitrate	1.0
Phosphate	1.0
Phthalates	0.1
Sulfide	1.0 [No method is given, but the limit of the most sensitive ASTM test is 40.]
Sulfate	1.0
TOC	20.0
Volatile chlorinated hydrocarbon	5.0
Endotoxins (Endotoxin Unit)	0.03 EU/mL [The limit of the assay is 0.001 and a level of 0.03 amounts to 300-3000 gram negative bacteria, or the cell wall equivalent, per ml. Such a level would not be acceptable for biomedical grade water in most laboratories.]
Heterotropic [sic – cross-eyed] bacterial counts	<10/1000 mL [The method, F1094, understates the number of viable microorganism by 100-1000 times.]
Electrical Resistivity ^A , min, MΩ-cm at 25°C	
– measured at the production point not in contact with air	10.0 [Note that the limit suggested for Type II water, distilled water, is set at only 1.0 in Table 1 of D1193 – Why such a disparity?]
– measured from storage or distribution system in contact with air	1.0 [The resistivity of pure water in equilibrium with air is certain to be lower than 1 MΩ-cm.]

^A Electrical resistivity [“Resistivity” – ASTM means *conductivity*.] can be [Is there any reason why it would not always be expressed in μS/cm at 25°C?] expressed in microsiemens per centimeter conductivity at 25°C. The [“The” – this word should be removed.] conductivity is reciprocal of the resistivity, 1/R.

5. Reagents

5.1 *Purity of Reagents* – Reagent grade chemicals shall be used in all tests. [No ASTM reagent water (D1193) is sufficiently pure!]. 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 [ACS water

would not be pure enough for most of the test limits in Table 1.].⁶ Other grades may be used, provided it is first ascertained that the [A?] reagent is of sufficiently high purity to permit its use without lessening the accuracy of the determination [“Determination” – ASTM definitions require the word, “measurement”. The first sentence states that reagent-grade chemicals *shall be used* and the last sentence states that other grades *may be used*.].

5.2 *Purity of Water* – Unless indicated otherwise, references to water shall be understood to mean water as defined in this guide. [It is not clear that this Standard Guide has, in fact, defined the purity of any type of water. Also, following this *requirement* will result in nonsense (see Section 1 where the term “water” is used generically several times).].

6. Sampling

6.1 The test methods specified in Section 8 assume that great care and skill [“Great care and skill” – these are very subjective terms!] will be employed in obtaining the water samples to be tested. It is assumed [“Assumed” – why not say, “operators must . . .”] that the operators will prevent container and airborne contamination to the best of their ability [And what if *they* have little ability and *their* interpretation of “great care and skill” is at odds with what ASTM had in mind?], making note of possible sources of contamination due to the sampling procedure [Depending on the level of training of the operators, they might not even be aware of many sources of possible contamination.]. It is recommended that the samples be handled in accordance with Practice D 4453.

6.2 Extreme care [“Extreme care” – does this imply clean-room conditions?] must be exercised in handling samples when making analyses. Experimental [“Experimental” – why is this adjective necessary; it is confusing.] laboratory-ware should be made of PFA- or TFE-fluorocarbon [Volatile contaminants will penetrate PFA and TFE very rapidly.], and less desirably from quartz or borosilicate glass, to minimize the contamination of the water. Borosilicate glassware may [Can?] leach ions at picogram-per-litre [“Litre” – is this the approved ASTM spelling?] levels. [Quartz may be more soluble than borosilicate glass, depending on the conditions. In any case, the contamination is on the order of a femto-gram per ml, 1 part in 10¹⁵, which is completely insignificant when compared with the limits specified in Table 1, so any concern about the use of borosilicate glass would seem to be entirely misplaced.] The major contaminants from borosilicate glass are sodium (Na), potassium (K), boron (B), and silica (SiO₂). No detectable ions [Is the reader to understand that undetectable ions might leach?] leach out of PFA- or TFE-fluorocarbon that has been

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.”

properly cleaned. [Glass can be cleaned of organics more effectively than plastics by heating the glass to high temperatures under oxygen rich conditions - see below. On the other hand, it can be difficult to remove organic materials from plastic surfaces and many volatile substances can pass through the walls of plastic containers - see below.]

[What is the point of making an outline format of the following list of short steps?]

6.2.1 Containers should be cleaned with HNO_3 (1+4) or HCl (1+4) [“1+4” – does ASTM mean 1:4?], or both, by filling the container and allowing it to stand for a minimum of 1 h.

6.2.2 The containers [Which containers?] should be rinsed with three container volumes [“Container volume” – this volume has not been defined, because the sentence is discussing *containers* (plural).] of a sampled water and then allowed to stand for 24 h with the same [Which same sampled water, the rinse water?] sampled water.

6.2.3 The containers should be rinsed again twice with the sampled [Sample?] water before filling.

6.2.4 The containers should be filled by flushing [Rinsing?] at least five volumes of the sampled [Sample?] water into the vessel [“Vessel” – what vessel?] before sealing [“Sealing” – there has been no mention that the containers have seals.]. The seal must be of a non-contaminating material. [How can one obtain a sample, if the sample container must be filled with the sample water and stored for 24 hours, before the sample water can be collected? This assumes that the source of the water has not changed in 24 hours.]

6.2.5 Storage of the sample may be required for the detection of metals [Why would storage be “required” for the detection of metals?], in which case 1 mL of redistilled HNO_3 (1+99) or HCl (1+99) [“1+99” – does ASTM mean 1:99? Molar, weight, or volume?] should be added per litre [“Litre” – is this the approved spelling?] to reduce the pH and to preserve solubility of the metals within the sample [Would metals become insoluble at the trace levels specified in Table 1?].

6.2.6 The water sample should remain in storage a minimal length [Period?] of time [How long is this - minutes, hours, days?] since [Because?] some impurities have a tendency to adhere to the container surface. Endotoxins may become irreversibly stuck to glass walls, as will certain insoluble colloids. [If a colloid is a “colloid”, how would it be soluble? Other organics may also become stuck to plastic ware.]

7. Recommendations for Purity

7.1 Recommendations for [Missing word(s)?] purity of water [Biomedical-grade water?] should conform [“Recommendation” and “conform” – how does one conform to a general recommendation?.] to the properties and chemical limits given in Table 1 [Why should this

be true, since this Standard provides no supporting evidence and claims that the limits in Table 1 are in large part a function of the detection limits of the analytical methods?]; however the suggested maximum limits and the actual impurities considered [“Actual impurities considered” – does ASTM mean to say, “impurities actually measured”?, or both, may be modified by the user based upon [“Upon” – the correct word would be “on”.] the intended [“Intended” – the use of this adjective is unnecessary.] use of the water. [Biomedical-grade water? This Standard is not a specification. Is ASTM explaining that if someone were to create a specification, based on this Standard Guide, it would be acceptable to make modifications? And would this user-redefined water be considered biomedical-grade water?]

7.2 The precision of detection [“The precision of detection” – does ASTM mean, “The accuracy of the measurements to determine the purity of the reagent-grade water . . .”? Is ASTM referring to the analysis of biomedical-grade water or the experiment in which the water is to be used?] will depend on the purity of the reagents used, equipment employed, experience of the lab personnel, the sampling technique, and cleanliness of the working area.

7.3 A suggested guide of [For?] producing, storing, and distributing water for critical purity applications is described in the Appendix. [Is the Appendix a guide within this Guide? What is a “critical purity” application; would this be a biomedical application? Is the Appendix intended to serve as a guide to the production, storage, and distribution of biomedical-grade water?] Other procedures may be employed provided the product water meets the limits in Table 1 as modified by the specific requirements of the use [Application?]. [This last sentence appears to be in sharp contrast with the language of the Appendix, where the word, “shall” appears frequently. Furthermore, after all that has been said about the user’s options for varying the limits and choice of components listed in Table 1, it is a nested non sequitur to authorize the user to alter the *nonmandatory* process summaries in the Appendix, provided he “meets the limits of Table 1.”]

8. Test Methods

8.1 *Arsenic* – Graphite Furnace, ⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D 5673, with a limit of 0.9 µg/L, should be referenced.]

8.2 *Cadmium* – Graphite Furnace, ⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673, with a limit of 0.1 µg/L, should be referenced.]

8.3 *Chromium* – Graphite Furnace, ⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673, with a limit of 0.07 µg/L, should be referenced.]

⁷ See *The Guide to Techniques and Applications of Atomic Spectroscopy*, Perkin-Elmer Corporation, Norwalk, CT.

8.4 *Cobalt* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673, with a limit of 0.03 µg/L, should be referenced.]

8.5 *Copper* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673, with a limit of 0.03 µg/L, should be referenced.]

8.6 *Fluoride*⁸ [– Test Methods D5542, with a limit of 0.5 µg/L, and D5996, which does not provide limits, but has a typical range down to 0.02 µg/L, should be referenced.]

8.7 *Iron* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method ????? with a limit of 0.03 µg/L should be referenced]

8.8 *Lead* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673 with a limit of 0.08 µg/L should be referenced.]

8.9 *Nickel* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673 with a limit of 0.2 µg/L should be referenced.]

8.10 *Potassium* – Flame Photometry.⁹ [Test Method D4192, with a limit of 0.1 µg/L, should be referenced.]

8.11 *Silica* – Test Method D 4517 [D 4517 has not been tested below 35, where the bias was -20%, and the footnote referenced method has an SD of 6% at 25 and the limit of detection is 2.5, which suggests that it will not be useful for determining a level of 3 or lower.]

8.12 *Sodium* – Flame Photometry.⁹ [Test Method D6071, with a limit of 1 µg/L, should be referenced.]

8.13 *Titanium* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – There is no ASTM method for Titanium.]

8.14 *Zinc* – Graphite Furnace,⁷ Practice D3919 [D3919 does not provide any limits of detection – Test Method D5673 with a limit of 0.2 µg/L should be referenced]

8.15 *Acetate*⁸ [– Test Methods D5542, with a limit of 80 µg/L, and D5996, which does not provide limits, but has a typical range down to 0.02 µg/L, should be referenced.]

⁸ A draft test method for trace anions and cations in high-purity water by ion-chromatography procedure is currently under development by Subcommittee D19.11.02.02. [How is it possible to reference a method that this not yet available? – ASTM regulations do not permit such a reference.]

⁹ An acceptable flame photometry method is given in the 1982 version of Test Methods D1428. [This method has been discontinued. – ASTM regulations do not permit such a reference.]

8.16 *Ammonia Nitrogen* - Test Method D 1426 (Test method C) [This test is not sufficiently accurate – there is no Test Method C in the method!]

8.17 *Chloride*⁸ [– Test Methods D5542, with a limit of 0.7 µg/L, and D5996, which does not provide limits, but has a typical range down to 0.02 µg/L, should be referenced.]

8.18 *Chloroform* - Test Method D 3973

8.19 *Electrical Resistivity* – Test Method D 1125 [and D5391]

8.20 *Formate*⁸ [– Test Methods D5542, with a limit of 70 µg/L, and D5996, which does not provide limits, but has a typical range down to 0.02 µg/L, should be referenced.]

8.21 *Nitrate*⁸ [– Test Method D3867 should be referenced.]

8.22 *Phosphate*⁸ [– Test Methods D5542, with a limit of 1 µg/L, and D5996, which does not provide limits, but has a typical range down to 0.02 µg/L, should be referenced.]

8.23 *Phthalates* – Gas chromatography, electron capture detector¹⁰

8.24 *Endotoxins* – Limulus Amebocyte Lysate Test¹¹

8.25 *Sulfide* – No specific method is recommended [D 4658, which has a lower limit of 40 µg/L, should be referenced.]

8.26 *Sulfate*⁸ [– Test Methods D5542, with a limit of 2 µg/L, and D5996, which does not provide limits, but has a typical range down to 0.02 µg/L, should be referenced.]

8.27 *Heterotropic [sic – cross-eyed] Bacterial Count* – Test Method F 1094 [This method grossly understates the number of viable microorganisms in purified water.]

8.28 *Total Organic Carbon (TOC)* – Test Methods D 4779 & D 5997

8.29 *Volatile Chlorinated Hydrocarbons* – Test Method D 3973.

¹⁰ See “USP Current Edition Phthalate Gas Chromatography-Electron Capture Detector,” EPA Method 606, Federal Register, Vol 44, No. 233, Dec. 3, 1979.

¹¹ U. S. Pharmacopeia, Current Edition, The United States Pharmacopeia Convention, Inc.

9. Keywords

9.1 biomedical; clinical; pharmaceutical; research

APPENDIXES

(Nonmandatory Information)

[In section 4.1 and X1.1, ASTM states that the process by which biomedical-grade water is produced is every bit as important as the product limits described in Table 1. If the process is that important, why is it “nonmandatory”? In any case, this Standard is a guide; it is supposed to be instructive, so nothing is mandatory.]

X1. SUMMARY OF METHODS OF PREPARATION

[Suggested Methods for Preparation? Why does the numbering system change?]

X1.1 The method of preparation of the biomedical grade water affects the limits [The limits specified in Table 1 or some other limits?] of impurities. It is recommended that it [Biomedical-grade water?] be prepared, distributed, and stored by two distinct [They would seem to be identical in most respects.] systems, as follows:

X1.1.1 *Laboratory System* - In the laboratory system, the purification of tap water shall [“Shall” – No deviations from the following vague description? Is it not the case that this Standard is a guide that is supposed to provide information and instruction, not requirements.] be accomplished by either double-distillation [Distilling twice does not necessarily guarantee a better product water. In fact, double distilling may concentrate many volatile water impurities.] or by deionization, adsorption [Is *absorption* not permissible? Would it not be better to use the word, “sorption”?], reverse osmosis, continuous electrodeionization [“Continuous electrodeionization” (CEDI) is a term apparently coined by, and used almost exclusively by, the Vivendi/USFilter Company, which is active on the D19 committee. Electrodeionization is simply a form of deionization in which the resins are regenerated in place; perhaps it should not be listed separately in this list. Note that “electrodeionization” is not included in a similar list in paragraph X1.1.1.2.], ultrafiltration, or membrane filtration [What is the distinction between *membrane filtration* and *ultrafiltration* or *reverse osmosis*?], or a combination thereof, followed by distillation and suitable [Suitable for what?] storage. [This sentence is poorly structured and can be read to have many different meanings. Does the *preparation* of Biomedical Grade water require storage?]

X1.1.1.1 The double-distillation method [Process?] of purifying water utilizes the distillation apparatus [Which distillation apparatus?], which produces water of [With a?] minimum resistivity of 1.0 MΩ-cm at 25°C, followed by a properly [“Properly” – a very subjective term.] designed distillation apparatus manufactured from a non-contaminating material [Singular – followed by a list of materials?] such as fluorocarbons [Plural?], quartz, pure tin, titanium or, in many situations, borosilicate glass [This list is incomplete and arbitrary.], which will upgrade the water to meet the requirements [What requirements? There are no requirements; this Standard is a guide.]

X1.1.1.2 The adsorption [Is “absorption” not permissible? Would it not be better to use the word, *sorption*?], reverse osmosis, deionization, filtration apparatus step [“Step” – “stages” or “pretreatment stages” would seem more appropriate? This sentence is poorly constructed]., followed by use of [The use of a?] distillation apparatus, which must be manufactured from a non-contaminating material [Singular?], will upgrade the water to meet the requirements [What “requirements”? There are no *requirements*; this Standard is a guide.].

X1.1.2 Central Building System – In the [A?] central building system, where large volumes of biomedical grade water are produced daily, the system shall be of a special design [“Shall be of special design”? – many facilities would be grateful for some hints as to how to build and install such a *special design* still, which ASTM seems to be *requiring* as part of this *Guide*.] to produce, store, and distribute high purity water [Storage and distribution are being discussed in a section apparently intended for production; storage and distribution are discussed in the next two appendices.]. The system shall include the components described in this appendix used to prepare laboratory quantities of biomedical grade water except that the capacity of the system will be larger, which in most cases will mandate [Require?] the use of metal stills rather than those fabricated of quartz or glass. [Section X1.1.1.1 listed many materials from which a still could be constructed; why are only quarts or glass listed here? This sentence is poorly constructed; “used to prepare” is not properly tied in and it needs punctuation. Also, the end of the sentence could be changed to read, “. . . metal stills, rather than glass stills.” Is ASTM aware of any commercial, large-scale, metal stills that produces water with a resistivity of $\geq 10 \text{ M}\Omega\text{-cm}$?].

X1.2 The systems mentioned above shall be fabricated from materials that shall not contaminate water [What water?] with undesirable [The word “undesirable” is very subjective.] substances. Undesirable [The word “undesirable” is very subjective.] materials [In the last sentence ASTM was speaking of undesirable *substances* and in this sentence ASTM is speaking of undesirable *materials* – which is it, *materials* or *substances*.] include copper improperly coated with tin [Is it possible to coat copper with tin and not have some pin holes?], tin containing lead, stainless steels of all types, aluminum, monel [Monel Metal (a brand)?], soft glass, PVC, polypropylene, and many other plastic and metallic materials [“Many other plastic and metallic materials” could be construed to mean nearly every material that one might use to construct a still.]. Suitable materials include pure tin, titanium, TFE-fluorocarbon, PFA-fluorocarbon, platinum, tantalum, quartz, and if traces of silica are not a problem, borosilicate glass [Quartz will contribute as much, or more, silica to water as borosilicate glass. There are many materials that can be used in the construction of high-quality stills, but tin, platinum, and tantalum are among the least likely to be used.]

X2. SUMMARY OF METHOD OF STORAGE

[Suggested Methods for Storage?]

X2.1 The storage tanks of ["Of" – use "for."] the [The?] ultrapure grade water grade systems ["Ultrapure grade water grade systems" – does ASTM mean, "biomedical-grade water systems"?] shall ["Shall" – this Standard is a guide, not a specification.] be constructed from [Of?] materials that do not add ["Add" is not the appropriate word to use.] impurities to high purity water. The maintenance of purity and sterility [Is ASTM suggesting that using air filtration, inert gas blanketing, and UV is guaranteed to result in sterile water, especially in view of the fact that biomedical-grade water is not expected to be sterile.] of the storage system shall be accomplished by one or a combination of these procedures: air filtration, inert gas blanketing, or UV sterilization technique. It must be recognized that the mere fact that the water is stored will reduce its purity despite attempts to prevent contamination [In the previous two sentences ASTM advised the user how to maintain the purity of stored water and in this sentence ASTM is saying that it is not possible to store water without contamination.]; therefore, storage should be avoided or kept at a minimum.

X3. SUMMARY OF METHOD OF DISTRIBUTION

[Suggested Methods for Distribution?]

X3.1 The distribution systems used to transfer the [Omit “the”] biomedical grade water to the individual laboratories shall [“Shall” – this Standard is a guide, not a specification.] be of special design [“Shall be of special design”? – many facilities would be grateful for some hints as to how to build and install such a *special design* distribution system, which ASTM seems to be *requiring* as part of this *Guide*.] to minimize contamination. Gravity feed is the preferred method, since pumps generally add contaminants to the water [This sentence implies that the purity of water in a large distribution system can be maintained without re-circulation, which is simply not true.]. If circulating systems are employed, the pumps must be of non-contaminating design [Is there a pump made, which will not cause some contamination?]. The piping materials, fittings, faucets, and joints must be of non-contaminating materials and design [This is a sweeping generality that suggests the existence of simple off-the-shelf solutions and dodges the complexity of the issue altogether. Volumes have been written on this subject and there are no easy solutions; even the best distribution systems require intensive maintenance and supervision]. Outlets should be protected by UV or other means to prevent “back contamination” by airborne biological impurities [Should not the outlets also be designed to prevent back contamination caused by impurities other than “airborne biological impurities”?].

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... End of D 1193