The Microbiological Component of Six Major Water Standards

ASTM D1193 – 99

Standard specification for reagent water

	Type A	Type B	Type C
Maximum heterotropic bacterial count	10/1000 mL	10/100 mL	100/10 mL
Endotoxin, EU [,~~EU~~ Units (EU or IU/mL]	<0.03	[<]0.25	n/a

This specification is only a process specification – no measurement of product water limits is required [Section 1.2 – “The method of preparation of the various grades of reagent water determines the limits of impurities and shall be as follows:”].

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ASTM D5127 - 99

Standard guide for electronic grade water

	Type E-1	Type E-1.1	Type E-1.2
Maximum heterotropic bacterial count	10/1000 mL	10/1000 mL	1/1000 mL
Endotoxin, EU	≤0.03	≤0.03	≤0.03

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ASTM D5196 – 99

Standard guide for biomedical grade water

	Biomedical Grade
Heterotropic [sic – cross-eyed] bacterial counts	<10/1000 mL
Endotoxin unit (EU/mL)	≤0.03

This specification is only a process specification – no measurement of product water limits is required [Section 4.2 – “The method 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 meet the concentration limits in Table 1.”]. Furthermore, the limits in Table 1 appear to be arbitrary [Section 4.2 – “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.”].

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ISO 3696:1987

Water for analytical laboratory use

There is no microbiological limit for any of the three grades of water and ISO states that these grades of water are not intended for biological or medical purposes.

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NCCLS C3-A3

Preparation and testing of reagent water in the clinical laboratory

	Type I	Type II	Type III
Maximum microbial content, colony-forming units per mL (CFU/mL)	10	1000	NS

Section 9 – “The time intervals can be seasonally dependent for some contaminants; however, microbial content should be monitored at least weekly.”

Section 9.1.4.3 – “. . The sensitivity of a method is enhanced by sampling more than 1 mL of water . .”

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USP-24-NF 19

	Water for Injection
Resistivity (closed system)	0.769 megohms-cm (Ref. 25°)
TOC	500 ppb
Endotoxin (EU/mL)	≤0.25

USP does not specify microbiological limits for the 9 types of water described in USP-24-NF 19. The four types of *sterile* water are to have been treated by an effective sterilizing process."

These Pharmacopeial procedures [sterility tests] are not by themselves designed to ensure that a batch of product is sterile or has been sterilized. This is accomplished primarily by validation of the sterilization process or of the aseptic processing procedures."

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USP-24-NF 19 (Cont')

The sterilization processes can be tested for effectiveness; however USP does not expect the testing to be definitive.

"Consequently, it may not be necessary to detect all of the microorganisms present. The monitoring program and methodology should indicate adverse trends and detect microorganisms that are potentially harmful to the finished product or consumer."

"Several criteria should be considered when selecting a method to monitor the microbial content of a pharmaceutical water system. These include method sensitivity, range of organisms recovered, sample throughput, incubation period, cost, and technical complexity. An additional consideration is the use of the classical "culture" approaches vs. a sophisticated instrument approach."

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USP-24-NF 19 (Cont')

Instrument approaches

"Examples of instrument approaches include microscopic direct counting techniques (e.g., epifluorescence and immunofluorescence), radiometric, impedometric, and biochemically based methodologies. These methods all possess a variety of advantages and disadvantages.

"One advantage is their precision and accuracy, In general, instrument approaches often have a shorter lead time for obtaining results, which facilitates timely system control. This advantage; however, is often counterbalanced by limited sample processing throughput due to labor intensive sample processing or other instrument limitations. In addition, instrumental approaches are destructive in that further isolate manipulation for characterization purposes are precluded. Generally, some form of microbial isolate characterization may be a required element of water system monitoring. Consequently, culturing approaches have traditionally been preferred over instrumental approaches because they offer a balance of desirable test attributes and post-test capabilities."