

## Water Quality Testing and Treatment Systems for Pharmaceuticals

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[Nearly half of all Americans take one or more prescription drugs](#), with the percentage soaring to 85 percent for persons aged 60 and above (myself included). Water is the most widely used substance in the production, formulation, and packing of myriad pharmaceuticals, which are compounds manufactured for use as medicinal drugs. Given the public health importance and global footprint of pharmaceuticals, including [antibiotics](#), there are extensive testing and safety requirements to control the quality of water used throughout the manufacturing processes. This article explains how water impacts the medicines you take, and what lengths are taken to keep them safe.

In spite of it all, a steady stream of news articles document [prescription medication recalls](#), often linked to chemical or [microbial contamination](#). The latter can be devastating to persons with weakened immune systems. The U.S. Food and Drug Administration (FDA) maintains a [series of lists](#) related to recalls “that may potentially present a significant or serious risk to the consumer or user of the product,” including [MedWatch](#) for drugs.

Pharmaceuticals should be safe to consume, inject, inhale, or apply, *when used as directed*. The Water Quality & Health Council has written about [antibiotic resistant bacteria and genes](#) in wastewater and drinking water and reducing [pharmaceuticals in the water supply](#) (they should be [disposed of properly!](#)) but never about water quality in the manufacture of pharmaceuticals, which can get complicated quickly.

### *Water for Pharmaceutical Use*

Because water is able to dissolve, soak up, collect, or suspend many different compounds and gasses, it can include physical (particles), chemical, and microbiological contaminants that can be health hazards. Although water treatment, testing, and safety—particularly for microbiological quality—are priorities in pharmaceutical manufacturing, per the [FDA](#), **there are no absolute microbial standards for water used in pharmaceuticals** other than for water packaged as sterile such as injectable drug products. Rather, [Current Good Manufacturing Practice regulations](#) require that appropriate specifications be established, monitored, and be in accordance with the intended use of the water.

There are [at least eight types of water](#) used in the manufacture of drug products and substances, including, potable (drinkable) water, non-potable water, and six classes of “USP” water (sterile, nonpyrogenic,<sup>1</sup> distilled water) for use as



Top: Water treatment system at a pharmaceutical plant

<sup>1</sup> A pyrogen is any substance that can cause a fever. [Bacterial pyrogens include endotoxins](#) found in the outer membrane of gram-negative bacteria like *E. coli*, which are released after cell death along with other cellular debris. Several USP waters used in pharmaceutical manufacturing include numeric bacterial endotoxin limits.

either “ingredient materials” in the manufacture of drug products or that are packaged and labeled as finished products for direct use in injection, inhalation, or irrigation. The USP designation refers to its inclusion in the current [US Pharmacopeia](#), which provides guidance ranging from chemical and microbiological purity to validation of water treatment systems.

Many other water types, standards, and specifications exist for water used in pharmaceuticals in the United States and internationally. For example, there are four types of “reagent grade” water, each with their own specifications and treatment requirements. Type I is the highest quality and must be prepared and used immediately for critical applications like reagent preparation while Type IV is used for general laboratory activities like glassware washing and can be stored. Reagent grade water quality is often further classified based on the presence of substances that can cause fever (pyrogen/endotoxin content; see footnote 1). Notably, [conventionally treated and disinfected potable water](#) **may not be used directly to prepare dosed drug products.**

### *Water Treatment Systems and Water Quality Testing*

Like any other storage and distribution system, microbial contamination of water used for pharmaceutical manufacturing is possible, especially contamination associated with [biofilms](#) such as *Pseudomonas* and [Mycobacterium avium complex](#). A long-standing concern for water used in pharmaceutical manufacturing, particularly packaged waters, is eliminating or minimizing bacterial endotoxins. Microbial contamination recalls of oral liquid and topical drug products are usually linked to the use of contaminated water and the presence of endotoxins.

To eliminate or minimize microbial contamination, the USP notes that water systems for pharmaceutical manufacturing should have ready access to built-in sanitization systems, including super-heated water at all locations, ozone or UV (ultraviolet) radiation, or ensure an adequate chlorine residual ([FDA inspection and compliance enforcement guidance](#) states that chlorination of potable water is an effective treatment if minimum levels of 0.2 mg/L of free chlorine are maintained.) A variety of online [reviews and best practices](#) are available to help design, operate, and maintain an effective pharmaceutical water treatment system and microbiological testing program to *prevent* microbial contamination in the first place. They also include the establishment of alert and action levels as part of standard operating procedures (SOPs) for testing, validating and troubleshooting, as well as routine, periodic sanitization procedures for all pharmaceutical water systems.

### *Final Thoughts*

Whenever we use a pharmaceutical as directed, it is reasonable to believe that it is contaminant-free and will help, not harm. Given the central importance and diverse role of water in the manufacture and packaging of pharmaceuticals, it is comforting to know that these uses are subject to extensive guidance, monitoring standards, and specifications for their treatment, storage, and most of all—quality. We can be proud of the work the FDA does in protecting the U.S. pharmaceutical-consuming public.

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