Tech Sheet #S 605

Water Types and Systems for Pharmaceutical Use

Water is commonly used as a solvent and an ingredient in the generation of many pharmaceutical procedures. Purified water contains fewer solid impurities than ordinary potable water. There are four commonly used preparation methods used in the sanitary space: distillation, deionization, and reverse osmosis (RO) and filtration. Purified water is the source for pharmaceutical grade clean steam as well as Water for Injection (WFI).

This document addresses three common water types used in pharmaceutical processes as defined by the United States Pharmacopeia, USP 37 Monograph on Water for Pharmaceutical Purposes. These are the three most common types of water:

- Purified Water
- Pure Steam
- Water for Injection

PW – Purified Water – Purified Water (PW) is the starting point for most Pharmaceutical Waters. PW is made from drinking water meeting the requirements of the National Primary Drinking Water Regulations (NPDWR) as defined by 40 CFR 141 published by the US Environmental Protection Agency. The methods to produce PW include distillation, deionization, reverse osmosis, and filtration. These methods described below are most often used in combination.

Distillation is the process by which water is boiled, and the resulting vapor is condensed into a clean vessel. Double distillation (DDW) was the previous standard for producing water for bio labs and was created by slow boiling water created from an initial distillation process. This process leaves solid contaminates behind that must be removed after the process is complete, and this has caused many operators to migrate towards more economical methods.

Deionization is accomplished by using an electro chemical process using specifically formulated ion exchange resins to remove almost all mineral ions from the water such as sodium, calcium, chlorides, and sulfates. Since most particulate impurities in water are dissolved chemical salts, the water quality is like that produced by distillation with the exception that it does not remove "uncharged" organics like bacteria or viral material. The process involves three processes: electrolysis, exchange, and regeneration. Electrolysis involves application of DC current via electrodes that draw cations and anions from a diluting chamber into a concentrating chamber. The exchange process occurs in the diluting chamber by introducing specially formulated ion exchange resins causing cations and anions to bond to the resin. Regeneration is used to "refresh" the resin by splitting water into hydrogen and hydroxide ions. This process is now commonly used after reverse osmosis.

Reverse osmosis (RO) uses a semipermeable membrane that allows water to diffuse through as a function of applied pressure to overcome osmotic pressure. To better understand how RO works, it is necessary to understand how osmosis works in the "forward" direction. Using saltwater as an example, if a column of water with a high salt content is separated by a semipermeable membrane from a column of water with low salt content, water from the low salt side will pass through to the high salt side until the salt levels are equal on each side of the membrane. The force causing the water to diffuse through the membrane is called osmotic pressure. To reverse the direction of diffusion and cause water to flow from the high salt side to the low salt side, pressure that exceeds osmotic pressure must be applied, hence Reverse Osmosis. RO removes 99% of suspended solids. After the RO process is completed, a follow up treatment by deionization is used to remove the remaining solids. This practice is called "polishing".

Filtration –Filters work by physically blocking any solid above a certain size from passing through. A common filtration strategy used in the pharmaceutical industry is ultrafiltration. Filters typically have pores that are 0.01 micron in size. They can capture small particles from the flow in addition to removing some viruses or other microorganisms that may be present. Materials passing through the filter are called "permeates". Materials that are captured are called "retentates."

PS – Pure Steam – Pure Steam (PS) is made from Purified Water. The most common usage is for Steam-In-Place (SIP) to sterilize product contact surfaces in validated systems. It is also used for heating product and for humidification by direct injection into the process. PS is made from Purified Water using what is commonly referred to as a clean steam generator. The generators can be electrically heated for small amounts of steam or via a heat exchanger using plant steam as the heating source.

WFI – Water for Injection – Water for Injection (WFI) is used as a solution or thinner for the manufacture of parenteral and ophthalmic pharmaceuticals, cleaning of equipment, and packaging. WFI is created using RO followed by deionization, and finally UV sterilization and Double Distillation before packaging into vials. Vials are used for parenteral and ophthalmic pharmaceuticals or used for cleaning process equipment that pharmaceutical products will come into direct contact with.

The three most common water types for pharmaceutical use were discussed. These will meet 85-95% of the applicable applications, but if applications are outside of those discussed, one should refer to United States Pharmacopeia, USP 37 Monograph.

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