WATER FOR PHARMACEUTİCAL USES AND CONTROLS

Water which is used for pharmaceutical purposes is defined as purified water according to pharmacopoeias. Purified water can be named according to the properties they have or according to method used for purification of water. The classification according to the two pharmacopoeia is given in Table 4.1.

Table 4.1. According to the European Pharmacopoeia (EP 5) and the American Pharmacopeia (USP 27)

EP 5	USP 27
Purified Water	**Purified water**
a) Purified water in bulk	**Sterile purified water**
b) Purified water in containers)	**Water for injection**
Highly Purified Water	**Sterile water for injection**
Water for Injections	**Bacteriostatic water for injection**
a) Water for injections in bulk	**Sterile water for irrigation**
b) Sterilised water for injections	**Sterile water for inhalation**

According to USP 27 purified water: Used of drinking water as source for water, purified by deionization, distillation, ion exchange, reverse osmosis, filtration or other suitable methods.
Injection water: Must carry the same properties with purified water and also contains no endotoxin more than 0.25 USP Endotoxin Unit/ml.
Unlike purified water for injection water for pharmacopoeia, distillation or reverse osmosis methods should be applied for final purification. In Figure 4.1, a diagram is provided that classifies the water used for pharmaceutical purposes in USP 27 and the methods of obtaining these water.

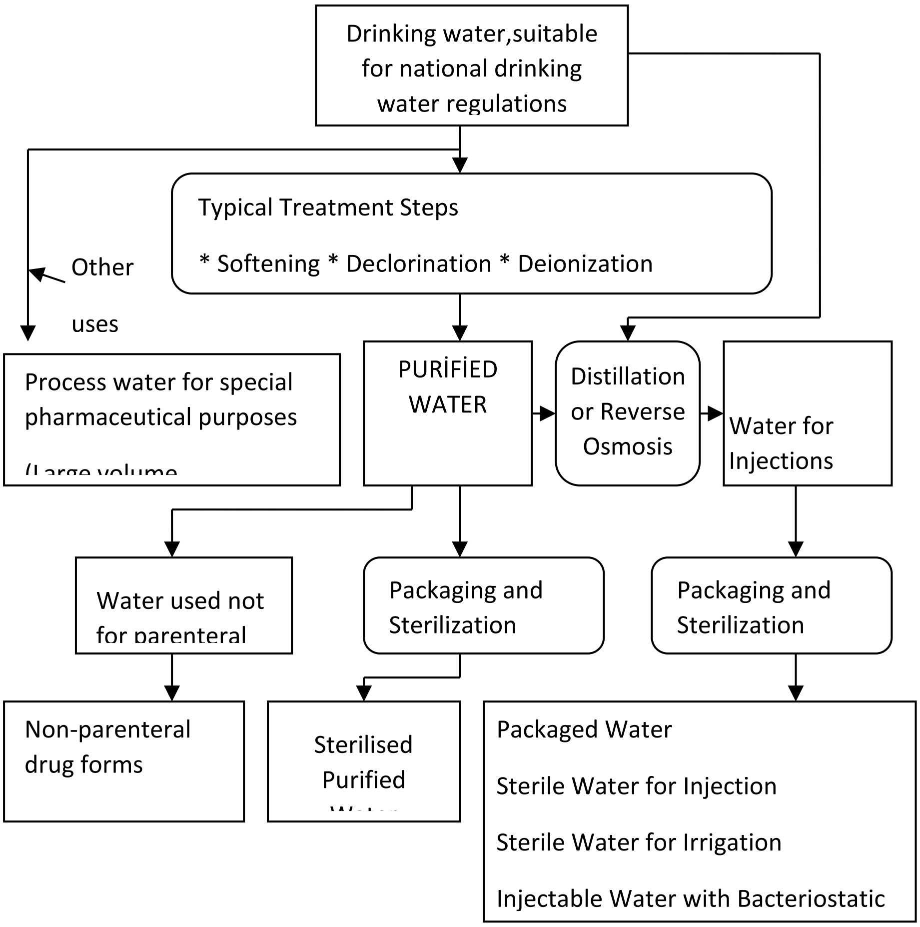

Figure 4.1. Water used for pharmaceutical purposes [USP 27]

Study 4.1.

Purified water and controls

Use purified water (deionized and distilled water), perform the following controls and write the results in a table.

1. Organoleptic Control

Check clarity, color, smell and taste of the purified water.

2. Acidity and alkalinity

2.1. Identification by indicator (EP 5)

When adding 0.05 ml of methyl red R solution to 10 ml of freshly boiled and cooled purified water in a vessel made of borosilicate glass, there should be no red color and no blue color should be formed when 0.1 ml bromothymol blue R1 is added to 10 ml of the water with same property.

2.2. PH measurement (USP 27)

Add 0.3 ml of saturated potassium chloride solution to 100 ml of purified water to measure the potentiometric pH of the prepared solution.

3. Chloride (EP 5)

Add 1 ml of diluted nitric acid R and 0.2 ml of silver nitrate solution R2 to 10 ml of water. The solution should remain clear and colorless for at least 15 minutes.

4. Calcium (USP 27)

Add 2 ml of ammonium oxalate TS to 100 ml of purified water. It should ocur no turbidity.

5. Nitrate (EP 5)

Take 5 ml of the water in a test tube and put it in an ice bucket. And add 0.4 ml of potassium chloride solution R at a concentration of 100 g/l and 0.1 ml of the diphenylamine solution R. Add dropwise 5 ml of nitrogen-free sulfuric acid R while stirring the tube. Take the tube on a water bath with temperature of 50 ° C. After 15 minutes, the solution should not have a different blue color from the mixture containing 4.5 ml of non-nitric water R and 0.5 ml of standard nitrate solution R (2 ppm NO3) in the same conditions and at the same time.

6. Sulfate (USP 27)

Add 1 ml of barium chloride TS to 100 ml of water. The liquid should remain clear and colorless.

7. Carbon dioxide (USP 27)

Add 25 ml of calcium hydroxide TS to 25 ml of water. The mixture should remain clear.

8. Substances which may be oxidized (EP 5)

Add 10 ml of diluted sulfuric acid R and 0.1 ml of 0.02 M potassium permanganate to 100 ml of the water and boiled for 5 minutes. The pink color should not completely disappear.

9. Nonvolatile residue (EP 5)

Evaporate 100 ml of water on a water bath and dried at 100-105 ºC. The nonvolatile residual weight should not be more than 1 mg (0.001%).

Study 4.2.

Determination of the capacities of ion exchangers used in the preparation of deionized water

Weigh 1 g of anion exchanger or 1 g of cation exchanger in a 200 ml flask with glass cap. Add 100 ml of 0.1 N NaOH for the cation exchanger and 100 ml of 0.1 N HCl for the anion exchanger. Shake it occasionally for 24 hours. Determine the alkalinity or acidity of the supernatant by titration using 0.1 N HCl or 0.1 N NaOH and a methyl orange as indicator. Calculate the anion or cation held by the 1 g ion exchanger from the spent acid or alkali amounts in terms of equilibrium / g.

$ROH + HCl \longrightarrow RCl + H_2O$ (Anion exchanger)
$RSO_3H + NaOH \longrightarrow RSO_3Na + H_2O$ (Cation exchanger)

Questions:

1. Write a comparative table for the results of controls for deionised water and distilled water
   Are these samples appropriate to pharmacopoeias?
2. Define different sterile waters in the USP. Comparatively review required controls for these waters. Is there any difference? If there is any difference, why?
3. According to USP, write the difference of water for injection and sterile purified water
4. Write pH intervals for different types of purified waters classified according to USP
5. Why total organic Carbon test is done for pharmaceutical waters? What is the total organic carbon limit given in the European Pharmacopoeia
6. How to determine ammonia in purified waters according to USP and EP
7. Heavy metal extraction is done for which type of purified water?
8. What is the purpose of the aluminum quantity determination for the water to be used according to EP and how is this test applied?