

The rationale should conclude that no quality or regulatory risk is identified for the API and for the drug product in which it is used.

3. For Highly Purified Water (HPW) and Water for Injection (WFI) Systems recirculating distribution loops should be maintained at $> 70^{\circ}\text{C}$. Such heated distribution loops are considered self-sanitizing.
For HPW and WFI systems with distribution loops and/or storage tanks that are maintained at $< 70^{\circ}\text{C}$, written system sanitization procedures should be followed that are based upon accepted sanitization methods (e.g., thermal treatment), and should be validated.

4. Distribution Systems for Purified Water (PW), HPW, and WFI should include:
 - Water circulation with continuous flow velocity sufficient to achieve turbulent flow during normal operating conditions and sufficient return flow to ensure positive pressure in the distribution system during periods of peak draw (i.e., maximum water use);
 - Provisions for maintaining sanitary conditions through periodic sanitization and/or flushing should be established in cases where the preferred length of a dead-leg is not designed to meet the maximum 3 hydraulic diameter guideline;
 - Sloped pipes to drain pitched 1/16 inch per foot (5 mm/m) minimum;
 - Diaphragm or compression valves that allow complete drainage;
 - Sample ports at defined locations;
 - Air breaks in drain piping; and
 - Piping from water distributions systems to manifolds and process vessels should provide draining following use or should be blown down 5.

Passivation Procedures should be performed upon system installation and upon observation of widely distributed rouge on inspection of piping and gaskets. After system modification, the need and degree of passivation should be determined based upon impact assessment. After passivation, the water system should be flushed, sampled, and tested to ensure that passivating chemicals have been removed.

6. Quality Monitoring of (Potable) Water used as Feed Water for Water Purification Systems should be performed by obtaining and reviewing test data from the supplier or tested on Site or by a contract lab at least semi-annually, and through monthly sampling for coliforms and total viable organism (TVO) counts. Potable water used in manufacturing should be sampled and tested as indicated in Table 2.
7. Reverse Osmosis (RO) Systems, used for water treatment, should be monitored on-line by measuring the conductivity of the output water. RO systems should be cleaned and sanitized based on validated intervals.