

## Water Purification, Storage and Distribution For Pharmaceutical Production

18. Water Samples at Points of Use should be collected in a manner consistent with manufacturing practices including, but not limited to, the following:
  - Where sanitization of outside surfaces of sample ports is performed prior to collecting a sample (e.g., wipe-down with a sterile alcohol wipe), a study should be performed to demonstrate that the sanitization process does not inhibit microbial recovery, unless the sampling procedure includes specific measures to neutralize or remove the sanitizer; and
  - If a hose is used to transfer the water for use in manufacturing, sampling should be performed through the same or an equivalent hose. If sampling through the hose is not possible on a routine basis, a study should be performed to demonstrate the equivalence of sampling with and without the hose.
19. Water Leaks should be reported and repaired.
20. Hoses should be disconnected, drained, and allowed to dry following use, and stored in a manner that provides for continuous drainage. If manufacturing requires prolonged use of hoses (e.g., > 24 hours), studies should be performed to demonstrate lack of microbial proliferation.
21. Bacterial Endotoxin Testings (BET) of Low Endotoxin Water, HPW, and WFI Storage and Distribution Systems should be performed according to the sampling frequency defined in Table 2 and selected samples representative of the water quality, including the worst case system location at a minimum, should be collected and tested after any repair or disturbance to the system. Samples for BET should be collected in pyrogen-free containers.

Bacterial endotoxin alert and action levels should initiate an immediate investigation, resample, and retest. When action levels are exceeded, further use of the water should be evaluated and approved by Site Quality Team. The investigation should extend to any batches or lots produced using the water that exceeded the action level.
22. Microbial Alert and Action Levels for water should be based on process capabilities and process requirements or the values in Table 1, whichever are lowest.
23. Chemical Alert and Action Levels for water should be based on process capabilities and process requirements, and the requirements in Table 1.