above microbial action limit, it is important to monitor WFI systems for both endotoxins and microorganisms.

None of the limits for water are pass/fail limits. All limits are action limits. When action limits are exceeded the firm must investigate the cause of the problem, take action to correct the problem and assess the impact of the microbial contamination on products manufactured with the water, and document the results of their investigation.

WFI and SWFI may not contain added substances. Bacteriostatic Water for Injection (BWFI) may contain one or more suitable antimicrobial agents in containers of 30 mL or less. This restriction is designed to prevent the administration of a large quantity of a bacteriostatic agent that probably would be toxic in the accumulated amount of a large volume of solution, even though the concentration was low.

The USP also provides monographs giving the specifications for Sterile Water for Inhalation and Sterile Water for Irrigation. The USP should be consulted for the minor differences between these specifications and those for SWFI.

With regard to sample size, 100–300 mL is preferred when sampling WFI systems. Sample volumes less than 100 mL are unacceptable.

Organisms exist in a water system either as free floating in the water or attached to the walls of the pipes and tanks. When they are attached to the walls they are known as biofilm, which continuously slough off organisms. Thus, contamination is not uniformly distributed in a system and the sample may not be representative of the type and level of contamination. A count of 10 CFU/mL in one sample and 100 or even 1000 CFU/mL in a subsequent sample would not be unrealistic.

Water System Validation

Validation basically relies on periodic testing for microbiological quality and on the installation of monitoring equipment at specific checkpoints to ensure that the total system is operating properly and continuously, fulfilling its intended function.

Documentation should include a description of the system along with a print. The drawing needs to show all equipment in the system from the water feed to points of use. It should also show all sampling points and their designations. The print should be compared to the actual system annually to ensure its accuracy, detect unreported changes, and confirm reported changes to the system.

After all the equipment and piping have been verified as installed correctly and working as specified, the initial phase of the water system validation can begin. During this phase, the operational parameters and the cleaning/sanitization procedures and frequencies will be developed. Sampling should be done daily after each step in the purification process and at each point of use for 2–4 weeks. The sampling procedure for point-of-use sampling should reflect how the water is to be drawn; for example, if a hose is usually attached, the sample should be taken at the end of the hose. If the SOP calls for the line to be flushed before use of the water from that point, then the sample is taken after the flush. At the end of the 2–4-week time period, SOPs should be finalized for operation of the water system.

The second phase of the system validation is to demonstrate that the system will consistently produce the desired water quality when operated in conformance with the SOPs. The sampling is performed as in the initial phase and for the same time period. At the end of this phase, the data should demonstrate that the system will consistently produce the desired quality of water.

The third phase of validation is designed to demonstrate that when the water system is operated in accordance with the SOPs over a long period of time, it will consistently produce water of the desired quality. Any variations in the quality of the feed water that could affect the operation, and ultimately the water quality, will be picked up during this phase of the validation. Sampling is performed according to routine procedures and frequencies. For WFI systems the samples should be taken daily from a minimum of one point of use, with all points of use tested weekly. The validation of the water system is completed after at least 1 year of data have been accumulated.

While the above validation scheme is not the only way a system can be validated, it contains the necessary elements for validation of a water system. There must be data to support