

Validating Laboratory Water Systems

Lab Water Purification Systems must be Operated under the same Regulatory Guidelines as Pharmaceutical Production Facilities, making System Validation and Quality Control

Absolute Musts | BY TRUDE WITHAM AND JANET WHITE

High-purity, point-of-use (POU) water systems are used in pharmaceutical quality control (QC) and research and development labs to provide water for product testing, basic research and ingredient water for products in various stages of development.

Many of these lab water purification systems must be operated within the same regulatory guidelines as pharmaceutical production facilities. Validation of the water system itself and the quality of the water produced by the system are necessary in many cases. To validate the equipment, there must be documented evidence that the equipment is operating consistently and according to system specifications. Even in applications, such as basic research, which do not require rigorous validation, proper commissioning of the equipment is needed to ensure that the process operates properly and the water produced meets quality requirements.

Let's say you are starting up a POU water system in a research lab, and are going to use the system to provide USP Purified Water and high-purity water for high-performance liquid chromatography (HPLC) testing. It is important to document the performance of the water system to prove that it does in fact meet purified water quality requirements.

The system should include a validation support manual (VSM) with qualification protocols for testing, maintaining, servicing, and calibrating the equipment, per manufacturer's instructions, to ensure that the system operates as specified. The manual allows a smooth progression through the validation process and should include installation qualification (IQ) and operation qualification (OQ), and recommendations for ongoing performance qualification (PQ). The IQ, OQ, and PQ documents are supported with a qualification plan, certificates of calibration, and certificates of conformity to support the validation process. The manual incorporates guidelines from the various regimes and protocols spelled out by the regulatory authorities and the industry bodies:

- USP, EP, JP: The water standards in the U.S. Pharmacopoeia;
- Current Good Manufacturing Practices (cGMPs);
- FDA Code of Federal Regulations 21 CFR 210 and 21 CFR 211;
- The rules governing medicinal products in the European Union Volume 4;
- ISPE Baseline Guide on water and steam;
- Current Good Laboratory Practices (cGLPs);
- ISO9001 Quality Management System approval by LRQA.

These standards are typically reviewed by the water treatment system manufacturing company when designing systems for the pharmaceutical industry. Water system manufacturers may also be regularly audited by leading pharmaceutical companies and consultants for compliance with ISO 9001 and cGLPs.

The system should also include certificates of conformity and certificates of calibration from the system manufacturer. Generated during the manufacturing and QC processes, these signed certificates provide documented evidence that the system was manufactured according to the specifications contained in the system master file, and that it has been shown to perform as originally intended. Certificates of compliance should also be included, as these show that the system passed the testing required to achieve certification such as CE certification and ETL certification, required in North America.

Before using your system for the first time, refer to the checklist in the validation support manual as you inspect the system to make sure everything you ordered is there. Laboratory personnel may choose to hire the water treatment equipment supplier to commission the water system and then train the on-site maintenance personnel in the ongoing operation and maintenance of the system to comply with the training requirements of cGLPs.

An Example of One Manufacturer's VSM

One lab water treatment system supplier provides a VSM that includes 11 sections, which are:

- Model identification and brochure, which verifies the identification of the product being validated and that the technician/engineer is fully trained in validation and knows what tools will be required to successfully complete a validation qualification;
- Qualification plan (QP), which explains

the validation approach, procedures and results;

- Installation qualification (IQ) that provides documented evidence to demonstrate that all key aspects of the lab water system adhere to the installation, design intentions and specifications;
- Commissioning procedure (CP), which manages the start-up approach and hand-over of the lab water system to the client, resulting in a safe and functional system that meets established design requirements;
- Operational qualification (OQ), which provides documented evidence to demonstrate that all key aspects of the lab water system adhere to the design intentions and specifications;
- Deviation control procedure, including forms and index, which defines the method to be used to document any deviations that occur during the execution of the lab water system validation;
- Drawing and schedules, which contain all the required drawings and schedules to support the validation of the lab water system;
- Operators' manual and a glossary of terms;
- Consumables and accessories; lists ac-

cessories and required consumables, and the maximum service and shelf life;

- Certification containing all required certificates to support the validation of the lab water system;
- Additional qualification documents, if required, are used for all additional information.

Installation Qualification

There are a number of steps a lab must go through during the installation qualification. Lab personnel can use the VSM as a guide. If the VSM contains the appropriate forms to fill out and sign, this will help ensure that all steps have been completed. The first step is to review protocol and then sign the pre-approval form before starting the work outlined in the IQ document. The test equipment/instrument calibration can now begin.

Test results should be recorded directly onto the test results sheet or on labeled printouts. All raw data, printouts, additional sheets, and so on that need to be added to the protocol should be numbered, cross-referenced to the appropriate test, retained with the protocol, initialed, and dated. The test documentation should be retained. All deviations should be recorded

and be traceable throughout correction and retest into final closure. Those performing the tests must complete the signature page. The executor will record the overall result of the test, which must be pass or fail. If a failure is recorded, a reference to a deviation must be recorded in the comments section.

The objective of the test equipment/instrument calibration during the IQ is to ensure that test equipment or instrumentation used for IQ execution has a current calibration certificate that can be traced to a national standard. The steps are: identify all instruments that will be used during the IQ; complete the table in the VSM for each instrument; and attach a copy of the calibration certificate to the certificate section of the VSM.

Acceptance criteria are as follows:

- Instrument should have a calibration certificate that is traceable to a national standard;
- The instrument should be calibrated across the range used for testing; the certificate should be in date;
- A copy of the calibration certificate should be attached to the certification section of the VSM.

Once the test equipment/instrument calibration qualification is complete, the documentation verification must be executed to verify that all system documentation is available and referenced. Document issues and locations should be recorded in a table, which is then signed and dated.

Next, the water purification system must be identified by the system description and serial number, and recorded on a form that is signed and dated.

Visual inspection of the system is carried out and verified to ensure that the unit is free from visible damage, transportation packing, and construction debris, and that all required parts and consumable items listed in the installation kit in the operators' manual are correct and have been supplied. This is also entered on a form, which is signed and dated.



Lab Water Purification System Control Panel

Feed water (potable tap water) would enter the system inlet and would be pumped to the cartridges in series, where the water would be purified in each stage of the unit. Sensors located after the cartridges would monitor the outlet water quality and the temperature. A recirculation loop would intermittently re-circulate the water, ensuring high purity. The water might pass through an optional POU final filter before exiting the system for use in lab applications.

A typical POU lab water purification system might include pretreatment components, such as a pre-filter, followed by the primary purification components, such as a reverse osmosis (RO) cartridge, followed by an ultraviolet (UV) lamp and polishing filtration, such as deionization and ultrafiltration (UF). Feed water (potable tap water) would enter the system inlet and would be pumped to the cartridges in series, where the water would be purified in each stage of the unit. Sensors located after the cartridges would monitor the outlet water quality and the temperature. A recirculation loop would intermittently recirculate the water, ensuring high purity. The water might pass through an optional POU final filter before exiting the system for use in lab applications.

The system may also include a sanitization feature to minimize bacterial growth. A system control panel displays the results of the system water quality monitoring feature.

Once the system is inspected to make sure all components are there and that they are free from damage, a utility verification is performed. This verifies that the feed water to the system is suitable. A feed water analysis should be conducted if it was not done before the system was purchased. The feed water quality should be recorded (total hardness, total chlorine, and fouling index), and the power supply to the system should be verified with a voltmeter. The feed water temperature, flow, and pressure must be within specification. This should also be verified and recorded. Drains must be available and able to handle the maximum drain flow.

Installation verification should be done next to verify that the system layout is correct, per the general assembly system drawing, and that there is adequate access for operation and maintenance. If the

water purification system will be maintained by the vendor via a service contract, this must be documented as well.

Operation Qualification

The operational qualification should provide evidence that the equipment operates as designed in all operational modes, including sanitization. This can be tested and documented by lab personnel or a qualified maintenance person.

Performance Qualification

The performance qualification documents that the product water quality continues to meet the required specification. Tests must be performed during system start-up and on a regular basis thereafter, to ensure consistent water quality.

Importance of Maintenance

To make sure the water purification system continues to operate as specified and produces the required water quality, it is important to follow a maintenance schedule. Maintenance includes changing of consumables such as filters, regular sanitization, and recalibrating the system water quality sensors according to national reference standards.

Water System Design for Ease of Validation

Lab water purification systems generally have features built in that make them easy to validate and that comply with good laboratory practice (GLP). These features may include a data tag on the purification pack, automatic calibration of electronics, printout of system operating parameters, real time clock, and a PIN access code (password).

An encrypted data tag on the purification pack contains information about the pack manufacturing, traceability of the

media and media usage history. When the pack is installed in the lab water system, the electronic circuitry recognizes the pack and generates an error message on the system control panel if the pack is not the correct one for the application or if it is incorrectly installed, out of date, or used previously.

The water purification system aids in automatic calibration of electronics with a microprocessor management system that scans the water quality monitoring circuitry and compares it with two traceable resistor standards at each end of the monitoring range. It then indicates whether the electronics are out of calibration.

To help in validation and system operation and maintenance, a printout of system operating parameters, including the date and time, is available if an accessory printer is installed. A real time clock with battery backup allows the date and time to be printed out with other data as part of the system validation protocol. A password, when selected, enables only authorized personnel to change the allowed parameters and alarm set points. This helps ensure that the unit is operated in accordance with the user requirement specification.

Conclusion

Many lab water purification systems must be operated within the same regulatory guidelines as pharmaceutical production facilities. Validation of the water system itself and the quality of the water produced is necessary in many cases. To validate the equipment, there must be documented evidence that the equipment is operating consistently and according to system specifications. Various qualification protocols outline the procedures for testing, maintaining, servicing and calibrating the equipment, as set forth by the manufacturer, to ensure that the system continues to operate as specified. Systems may include a validation support manual and/or design features that make validation that much easier for the user. ■

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