

Basics Of Labwasher Cleaning Validation

A Q&A With James Espiritu, Miele

Validation is vital to pharmaceutical processes because it assures quality, consistency, and keeps your operations compliant with GMPs. The FDA provides guidance for proper cleaning validation, however challenges occur because interpretation of those procedures vary between facilities.



To better understand the validation and qualification process, we turned to Miele's James Espiritu. In his 12 years with Miele, Espiritu's expertise has included glassware washer use in pharmaceutical, wastewater treatment, forensics, and research facilities. In this Q&A, he covers nine fundamentals to keep in mind for labwasher validation — including important validation guidelines to follow, issues that may occur, and the benefits you'll experience when you properly validate your labwashers.

What does labwasher cleaning validation entail?

Labwasher cleaning validation has two components: a) the validation of the cleaning process itself and b) the qualification of the labwasher equipment that carries out the process. Validation, as defined originally by the FDA in 1987, is "establishing documented evidence which provides a high degree of assurance that a specific process or analytical method will consistently produce a product meeting its pre-determined specifications and quality attributes." In the context of laboratory glassware washers, labwasher cleaning validation is the "documented evidence proving that a cleaning process will consistently result in laboratory glassware that are washed to an acceptable predetermined level of cleanliness." Qualification means "assuring, through inspection, testing and documentation that: a) the correct equipment has been installed, b) the equipment has been installed properly, and c) the equipment performs according to pre-established, written specifications."

Although the terms “validation” and “qualification” are often used interchangeably, it is generally agreed that we validate a process/method and qualify an instrument or equipment. Thus, a labwasher is “qualified” and the cleaning process is “validated.” For the purpose of validation, a labwasher is often viewed as a process (or part of a larger process called “cleaning”). Hence, I use the term “labwasher validation” for simplicity and to emphasize the labwasher’s pivotal role in the cleaning process.

How is a labwasher validated?

The guidelines for validation are set by the FDA, but the specifics of the validation are determined by the company based on the nature of its operations. Since guidelines are subject to different interpretations, there exists a multitude of versions of validation protocols. Generally speaking, labwasher validation is carried out in three steps: 1) define the cleaning process that the company requires, 2) describe your cleaning process (usually covered by written SOPs), and 3) qualify the labwasher and validate the cleaning process.

There are four ways to qualify a labwasher:

1. **Design qualification (DQ)** defines the specifications of the equipment and documents the vendor selection process to ensure the proper equipment is purchased to meet the user requirements.
2. **Installation qualification (IQ)** is often considered the first of the qualifications. It provides documentary evidence that the equipment has been installed correctly and that all supporting services are available and connected correctly.
3. **Operational qualification (OQ)** demonstrates that the equipment functions as expected and is capable of consistently operating within established limits and tolerances. This includes running of programs, testing of functions including error messages and controls. Essentially, OQ ensures that the equipment really does do everything that the user wants it to do. Completion of the OQ will allow the finalization of key items such as SOPs, user training and preventive maintenance tasks.
4. **Performance qualification (PQ)** Performance Qualification (PQ) is intended to prove the equipment operates as designed, in normal operation, and when there is a failure in the operating process. To do this each internal device must be manipulated to produce an actual failure so the appropriate fault will occur when this circumstance occurs. Prior to PQ, all SOP's must be finalized and

cleaning requirements addressed to assure the validation team considers all operating parameters used in the process.

The cleaning validation process is very specific to the lab. Issues that need to be addressed include setting acceptable limits, sampling protocol, what residues to test from daily work and from detergents, analytical methods and what to do if results are out of acceptable levels.

When is a validation necessary?

Validation of manufacturing processes is a requirement of the FDA's Current Good Manufacturing Practice (cGMP) regulations for finished pharmaceuticals. More and more, labs outside of the cGMP environment also validate their cleaning process. In fact, any lab that desires to achieve more process reliability when cleaning laboratory glassware should perform cleaning validation. The use of validated, residue-free glassware will boost productivity for: a) in-process-control labs that need to meet regulatory requirements, b) nonpharmaceutical labs that also produce products for clinical testing under cGMP conditions, c) contract labs that must avoid cross-contamination of different customer orders, d) quality control labs, and e) testing labs.

What must be validated?

cGMP guidelines (1978) state that any facilities or systems used in the manufacturing, processing, packing, or holding of a drug or device shall conform to cGMPs, to assure the product meets its predetermined quality characteristics. Some examples include these systems — sterilization, solution preparation, water for injection (WFI), environmental, labeling, and packaging. Utilities, sanitation/filtration processes, and aseptic filling operations are also required for validation.

What are the benefits of validating labwashers?

The most obvious benefit is conformance with regulatory requirements. Validation proves that a process produces a product that is consistent with predetermined requirements, or that an analytical method is robust and will perform as required using qualified equipment. Validation may significantly improve a company's profitability. By validating/qualifying their labwashers, pharmaceutical manufacturers experience reliable, reproducible, residue-free lab glassware, which translates into reduced downtime, improved quality, and reduced risk of product recalls, fatalities, lawsuits, etc.

Validation may shorten the time required for a product to reach the mass market. Before going into the mass market, a pharmaceutical manufacturer is expected to have

accumulated enough data and knowledge about the commercial production process. Equipment and system qualification is one of the elements of this process.

How important is the role of the labwasher in cleaning validation?

The level of sophistication of a laboratory's cleaning validation depends largely upon the capabilities of the labwasher being used. The quantity and quality of relevant wash data that a labwasher can monitor, plus the number of wash parameters that it can control, have a direct bearing on the quality of the cleaning validation. The role of a well-validated cleaning protocol in a pharmaceutical company's operations may be profound and far-reaching. In addition to regulatory issues, the high costs of over- or under-validation could be staggering, yet undetected.

For over-validation, each error made during the validation will be repeated every single day that the labwasher is in operation. For example, there are cases of companies validating washing protocols that are 2 hours long, when 1 hour would have been enough by rearranging the factors that affect the cleaning process. Most likely, this error will perpetuate undetected. Wash length is just one source of error. Other possibilities include using excess quantities of cleaning chemicals and water (tap and especially DI), having too many wash steps, and overly high wash and dry temperatures. The waste may be in the range of tens of thousands of dollars per year per washer!

For under-validation, the implications may be even more staggering. If a laboratory truly requires a tightly controlled validation, it may be a good idea to employ more advanced, so-called "intelligent labwashers" available on the market today. The daily cost savings that result from an optimized cleaning protocol could more than justify the higher acquisition cost of the labwasher.

What is required of a labwasher for a successful cleaning validation?

For new installations, the labwasher must be qualified first before the cleaning validation can be performed. For existing labs, the labwasher must be maintained and serviced in accordance with the manual. Then, an operational check plus a performance qualification of the labwasher should be done before proceeding with the cleaning validation.

How can the equipment/detergent manufacturer help in the validation/qualification of a labwasher?

The best sources of help for your validation/qualification requirements are your labwasher and detergent suppliers. They are the experts on your cleaning system, and working with them could save you a lot of time and money. Phone support is usually

offered by these companies for customers who prefer to do their own validation. They also can supply the validation documents and validation service for a modest fee. Detergent suppliers may be able to provide ample assistance in cleaning validations. Support from labwasher manufacturers may be limited to installation and operational qualification (IQ/OQ). Labwasher validation service (IQ/OQ only) usually takes two days to perform — assuming the unit is installed correctly. Before purchasing a washer that will need to be qualified / validated, you should verify that the equipment manufacturer can support you in this process with documentation and technical service assistance.

Are there other types of companies performing validation work?

Yes. There are independent labs and consultants who offer various levels of validation service. While there are many companies that are very good with validation services, they cannot possibly know the specifics of all the equipment on the market. For this reason, it is good to know that most reputable equipment manufacturers can support you in the process, even if using a third-party validation company.

What factors must be considered regarding labwasher validation?

There are several:

- **Choice of residue.** Make sure that the residue(s) for which you analyze is the most relevant in terms of the risks involved, the effects on the production process and the quality of the final product, and the effect on the profitability of the company. Choosing residue that represents the worst-case scenario is also a good approach.
- **Over-validation.** Resist the urge to overdo your validation process, or you may get stuck with a cleaning protocol that will cost your company unnecessary time and money. Most common over validation mistakes include: excessively long washes and drying times, high detergent usage, high temperatures, and excessive number of wash cycles.
- **One size does not fit all.** If warranted, do not treat all processes the same. For example, wash protocol for inorganics is totally different from organics.
- **Know your chemistry.** The chemistry of aqueous cleaning is both a science and an art. Understand the interplay of time, wash water circulation rate, and temperature, detergents, and drying system in creating your desired wash results. Ask your prospective supplier of labwashers and detergents to explain how their products are designed to optimize these factors. It may also be a good idea to request them to perform test washes in order to generate actual wash

data before making any purchase decisions. This will make your actual cleaning validation less daunting.

- **Changing brands; changing validated wash protocols.** One labwasher brand's wash cycle is not the same as another's. Keep an open mind and welcome the possibility of completely changing your current wash protocol. If you can achieve the same or better results faster or for less money, then a brand change could be considered. Sometimes, once a piece of equipment is validated, even if the protocol makes no sense. Companies are hesitant to change because it is validated.
- **Be creative.** Science and the law need not be boring. Think outside the box. Understand your washer's full capabilities. The FDA provides the guidelines; you decide (based on guidelines) what's best for your particular operation. Even the FDA constantly changes its guidelines to encourage innovation, permit introduction of new technology, enable the FDA to operate on the same technological level as industry, and allow some slack by using "enforcement discretion." The latest development involves the use science-based risk assessment to ensure better public health protection.