Validation for Automated Washing Systems

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The 2011 US FDA guidance document divides process validation activities into three stages: process design, process qualification, and continued process verification ***(1).*** This lifecycle approach incorporates recommendations from ICH, particularly Q8, Q9, and Q10 ***(2–4),*** and standardizes manufacturing and cleaning processes.

In the lifecycle approach, there is more emphasis on the design and monitoring stages of the process, including understanding critical cleaning process parameters (CCPPs) and defining critical cleaning quality attributes (CCQAs) for the cleaning process. The increased emphasis on continuous process verification ensures the process operates in a state of control. Those monitoring may choose to use process analytical technology (PAT) to record and process data in a timely manner ***(5).***

Figure 1 depicts the lifecycle approach as it relates to traditional markers for sourcing an automated washer for cleaning parts using a validated cleaning process ***(6).***

Stage 1: Cleaning Process Design

A validation strategy and cleaning validation master plan are essential. Both should include details on cycle development, selection of cleaning agents, analytical and sampling methods, acceptance criteria calculations, handling and storage procedures for cleaned components, and cleaning equipment validation.

For new equipment installation—often the case with automated parts washer cleaning validation—the equipment user requirement specifications (URS), functional specifications (FS), and design specifications (DS) are important for successfully commissioning and validating the equipment.

As an example, **Table 1** captures vital information, including part description, item quantity, item dimensions, and specific washing requirements, such as soil and soil condition, and material of construction. The information also includes a drawing that helps in the description of the items.

Stage 2: Process Qualification

Stage 2 is a readiness check which includes qualification of the equipment and cleaning validation process. As a prerequisite to the performance qualification (PQ) or cleaning validation of the automated parts washer, the following items should be considered:

- Approved cleaning protocols and procedures
- Trained personnel
- Qualified utility supply systems

Table 1 Parts Information Table

Item #	Description	QTY	Height (mm)	Out. Dia. (mm)	Weight (kg)	Critical Information	Drawing Number or Picture Number	Notes/ Questions
1	Filling needle	8	110	15	NA	Process soil: Low concentration protein, material: 316LSS		photo 28
2	Filling pump	8	174.5 for pump 150 for plunger	pump out dia. 70.6 Plunger inner dia. 18	NA	Process soil: Low concentration protein, material: External is 316LSS, pump internal is procelaine, can seperate wash		photo 29
3	Glass bottle	1	300	180	NA	Process soil: Low concentration protein, material: glass		photo 30

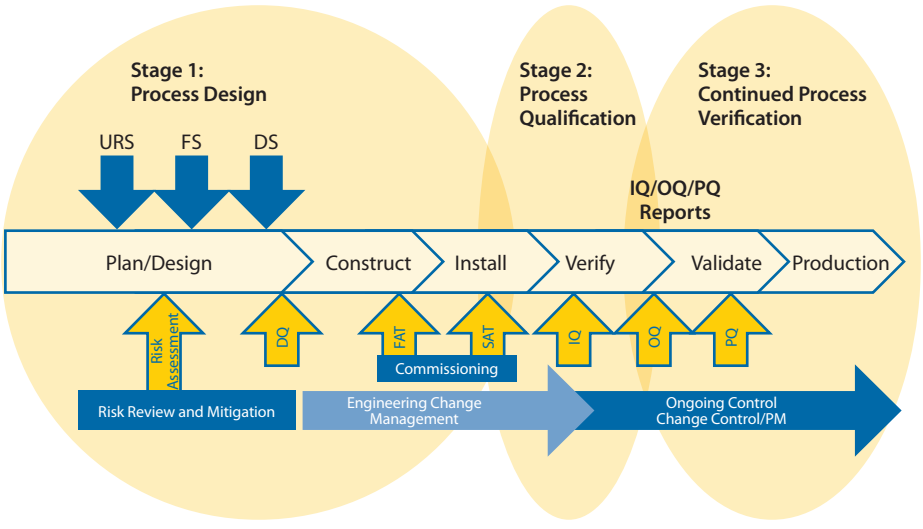

Figure 1 Lifecycle Approach Chart

- Validated analytical methods and sampling procedures
- Approved cleaning agent suppliers
- Fully functional automated washer equipment

Washer qualification consists of Installation Qualification (IQ) and Operation Qualification (OQ). This confirms that the equipment is installed as specified and utilities are sufficient to maintain operation as expected. The procedures include riboflavin coverage testing, successful runs of a complete cleaning wash cycle and verification that all alarms are functioning properly and that sensors/probes are calibrated and functioning as designed.

The cleaning validation, or PQ, of the washer includes sampling of the soiled parts to establish a baseline, as well as

evaluating the cleaned items (such as visual inspection, rinse or swab sampling) to demonstrate that the final rinse water acceptance criteria corresponds to the cleanliness of the parts washed.

The traditional cleaning validation approach of evaluating multiple runs may be optimized based on the testing performed during Stage 1, based on the design and risk assessment. The requirement to evaluate worst-case critical parameters may not be applicable if the critical parameters identified during the design stage are monitored and controlled during routine operation. The goal of the PQ is to demonstrate that the normal operating cleaning cycle using the automated parts washer successfully removes the residue(s) of interest to predetermined acceptable levels.

The cleaning validation process, including assessing deviation risks, changes, or out-of-specification (OOS) events, should be documented and approved.

Stage 3: Continued Process Verification

For an automated washing system, continued process verification relies on the analysis of the measured CCPPs and CCQAs, such as on-line conductivity and total organic carbon (TOC) of the final rinse water and items such as drying temperature/time and ramp rates which increase cycle times ***(7–8).*** A multiparameter analyzer/transmitter and TOC sensor could be integrated into the washer piping system to determine TOC concentrations in the final rinse water sample. The analyzer/transmitter is connected to the washer programmable logic controller (PLC) for trending the data. Trending data helps support corrective actions prior to development of OOS results, or deviations which can compromise the quality or release of products.

Change control that emphasizes understanding and continuous verification of the cleaning process allows for improvements, reducing production costs while maintaining high quality standards. **Table 2** lists changes to the cleaning process and possible impact as a result of the change ***(9).***

Conclusion

The *cleaning lifecycle approach* moves the emphasis from validation to design and monitoring of the cleaning process. An improved understanding of the design process (critical parameters and URS of the automated parts washer) and continued verification of the cleaning process promotes process improvement and scientific based resolution to OOS results, resulting in more efficient and effective change management. Industry tools such as Quality by Design and risk management provide the backbone to the *lifecycle approach* and how this approach can be incorporated into cleaning validation when using automated parts washers.

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Table 2 Impact of Modifying CQAs

Changes to	May Impact
Detergent	Cleanability of the soils
Cleaning Paramaters	Cleanability of the soils
Analytical Method	Detectibility and quantification of residues
Equipment Design	Surface coverage, equipment drainability, change over time
Personnel	Training and level of experience
Dirty Hold Time	Cleanability of the soils, levels of bioburden
Cleaning Hold Time	Extraneous matter, bioburden

References

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