ESTABLISHING CLEANING VALIDATION FOR A NEW INJECTABLE MANUFACTURING SITE

AT A GLANCE

A leading pharmaceutical manufacturer launched a new site in Durham, North Carolina, dedicated to producing injectable drug products. As part of this greenfield project, the client needed to validate their parts washers used to clean reusable components essential to sterile production.

Performance Validation (PV) provided hands-on execution support for the cleaning validation effort. Our engineer collaborated with the client's technical support and operations teams, contributing critical documentation, sample collection, and execution assistance.

CLEANING VALIDATION REQUIRED TO LAUNCH STERILE MANUFACTURING OPERATIONS

The client, a global pharmaceutical company, was constructing a new facility to manufacture injectable products in Durham, NC. To initiate full-scale production, they were required to validate cleaning processes for critically reusable components, including those used in aseptic filling lines. Without validated cleaning procedures, the facility could not meet FDA and ISPE regulatory standards or release product for commercial distribution.

Cleaning validation is particularly critical in sterile manufacturing due to the increased patient risk associated with contamination. The project centered on validating two industrial-scale, two-door Steris parts washers—widely used as industry-standard equipment for sterile environments—designed to maintain a strict dirty-to-clean equipment flow. PV was engaged to provide staff augmentation during the execution phase, delivering hands-on support to collect samples, execute test protocols, document discrepancies, and maintain compliance during a high-intensity and high-risk period for the client.

SERVICES PROVIDED

- Cleaning validation protocol execution and sampling
- Real-time cycle monitoring and inspection
- Discrepancy management and interim release documentation
- Dirty hold time validation support
- Root cause analysis and equipment troubleshooting
- Procedure updates to align with sterile manufacturing standards

HANDS-ON EXECUTION, CYCLE MONITORING, AND SAMPLING EXPERTISE

PV joined the project during protocol execution and supported the client across several critical validation activities. This included collecting swab and rinse samples, physically monitoring wash cycles in real time, and verifying post-wash inspection criteria. The parts washer pre-defined wash cycle consisted of many phases, including but not limited to pre-wash, wash, rinse, and drying, extending over 5 hours of cycle time.

PV directly supported 42 washer runs through on-site execution and documentation, ensuring each met protocol standards. Acceptance criteria required verification of:

- **Visually clean and dry parts** post-wash
- **Rinse water conductivity** readings
- **Surface sampling results** for Total Organic Carbon (TOC) and Bioburden
- **Blank samples** to verify that input water was free of contamination

Swabbing was performed at predefined locations determined by risk assessment, including equipment that directly contacts APIs (e.g., scoops and injection needles). TOC swabs measured for chemical residue, while Bioburden swabs checked for microbial levels. PV also identified and addressed an early protocol gap: personnel initially conducted swabbing without full gowning. After human flora was detected on a swab, procedures were updated to match production conditions.

DEEPER INSIGHT INTO CLEANING VALIDATION PHASES AND STRATEGY SHIFTS

PV supported three core validation phases:

1. **Document Execution**: Execution of pre-approved cleaning protocols in a GMP environment.
2. **Dirty Hold Time (DHT):** Validated the ability to clean items left soiled for extended periods (up to seven days), simulating worst-case residue.
3. **Deviation Documentation and Strategy Updates**: PV helped write and resolve 17 discrepancy reports (DRs), including a complex interim release report that allowed the client to proceed under limited conditions while final validation was pending.

EQUIPMENT FAILURES, SWABBING CONTAMINATION, AND STRATEGY REVALIDATION

Leaking Detergent Pump Triggers System Redesign
During execution, one washer failed rinse conductivity acceptance repeatedly. PV helped identify detergent leakage into the chamber during rinse cycles due to a defective valve. This prompted a manufacturer-led hardware redesign and eventual change control to requalify the washer.

Swab Contamination Leads to Gowning Protocol Revisions
A failed bioburden swab revealed the presence of human flora. PV helped determine that gowning practices during validation did not match those used in production. Full sterile personal protective equipment (PPE)—including goggles, masks, and other appropriate coverings—was immediately adopted to ensure validation aligned with intended operating conditions.

Recipe Failures and Automation Patches
A software issue prevented the proper wash recipe from downloading, invalidating an entire run. PV supported the automation patch and helped ensure cycle parameters were properly verified during reruns.

Inconsistent Drying Caused by Load Orientation
During post-cycle inspection, a scoop failed to dry over an extensive drying phase. PV worked with operations to modify the load orientation—flipping the scoop upside down to improve drainage and achieve compliance.

EQUIPMENT REDESIGN REQUIRED DECOUPLING AND REQUALIFICATION

The original validation strategy assumed both washers were equivalent. However, the detergent leak on one unit introduced uncertainty around functional equivalence. After internal debate, the impacted washer was removed from the initial scope and requalified independently following redesign.

PV supported this strategic pivot, helping the team document rationale, revise execution plans, and manage added test runs while adhering to global validation strategy.

PARTIAL VALIDATION ENABLED OPERATIONS, BUT TIMELINES REMAIN COMPRESSED

Despite extensive setbacks, the client achieved interim validation status, allowing limited production under defined conditions. PV contributed to drafting a comprehensive interim release report, which was critical in securing conditional approval to continue limited production. This report documented unresolved validation issues while demonstrating sufficient risk mitigation and control.

Unresolved clean hold time validations continue to limit batch staging flexibility, as cleaned equipment must currently be autoclaved immediately after washing.

PV's technical oversight, execution support, and real-time problem-solving enabled continued progress while preserving compliance. The team's flexibility and attention to detail helped sustain validation momentum and stakeholder confidence throughout the multi-month initiative.

LESSONS LEARNED FROM AN EVOLVING CLEANING VALIDATION INITIATIVE

- **Cycle performance must be verified beyond Factory Acceptance Testing (FAT)**: Post-installation issues—such as valve leaks—may go undetected during remote FATs or virtual commissioning. On-site validation requires close coordination across departments, including Operations, QA, and external sites. In this case, conflicting equipment needs required active scheduling support, and parts were temporarily sourced from other facilities to help tighten the validation timeline and maintain project momentum.

- **Swabbing and sampling are highly manual and technique-sensitive**: Protocols must account for full production-level gowning and risk-based site selection.

- **Acceptance criteria must be comprehensive and standardized**: Visually clean and dry, microbial, and chemical cleanliness are all critical measures of cleaning effectiveness. Each criterion must be clearly defined and consistently applied to ensure repeatability, compliance, and alignment with regulatory expectations.

- **Flexibility is key**: PV's ability to revise validation strategy, respond to mechanical failures, and address procedural gaps ensured steady progress despite ongoing challenges.

YOUR VALIDATION PARTNER FOR WHAT'S NEXT

Performance Validation is a trusted CQV partner for regulated manufacturers. Our experts provide strategic and execution-level support for complex projects, from startup facilities to routine process improvements. When quality and compliance matter, PV brings clarity, continuity, flexibility, and commitment to every project.