Save Time & Money on Cleaning Validation With These Easy Fixes: Manual Versus Mechanized Cleaning Processes

By Natalie Landrito

Introduction

Bio/pharmaceutical manufacturers need to validate their cleaning processes to comply with current Good Manufacturing Practices (cGMP) and federal regulations. The objective is for the manufacturer to prove that their documented cleaning processes effectively reduce the risk of cross-contamination to an acceptable level. This cross-contamination could consist of an active ingredient or unintended compound carrying over from one product to another via commonly used production equipment. The correct cleaning and maintenance of this equipment guarantees the safety and purity of the products being manufactured. Special thanks to Richard Yeaton, President of Atlantic Technical and Validation (NH), for his expert advice on best practices and overcoming the challenges related to upholding strict cleaning validation standards.

Key Considerations For Manual Cleaning

There's always been a cloud of doubt over manual cleaning processes. The contentious question is – with inevitable technician variability, can manual cleaning even be authentically validated? It's highly unlikely because of the difficulty involved in training a technician to execute each step in the procedure the exact same way, every single time (relative to disassembly, cleaning agent concentration, cleaning agent temperature, drying process, and record keeping). Actions such as applied cleaning pressure strength, scrubbing technique and length of scrubbing time are all variables. You may have to initiate your cleaning approach with a manual step, but it's best to aim to remove the technician or human element from the process altogether.

The challenges associated with manual cleaning are evident along every step of the way. Right from the start, the measure to remove soil out of the equipment is a complication in itself because the soil must be reduced to below a certain level of detection. You then have to reduce trace levels of cleaning agents, including in dead legs where stagnant water can accumulate and promote microbial growth.

If you're producing a product in your equipment that contains penicillin (or any kind of beta lactam antibiotic), you have to obey very strict regulations to prevent cross-contamination. The FDA requires that products produced on this equipment have their own dedicated washer. The washer must also be fully validatable, particularly for monitoring and tracking data. The FDA is also authoritatively watchful of potential cross-contamination of drug products involving hormones or steroids. Because of this, automated cleaning processes are more accommodating to validation because they are natively reproducible.

FDA investigators are in general skeptical of a manual cleaning process. Yeaton (ATV) says “you are expected to write procedures that are so thoroughly detailed it’s almost painstaking, just to accommodate inspectors”. This means your cleaning process needs to be robust to eliminate any chance of inconsistency applied by a different technician on any given day. The goal should be to remove anything that is technician-dependent.

Transitioning to an automated system will afford you the security of being able to repeatedly produce data that shows concrete evidence of consistently using the same temperature in your cleaning processes for i.e. Active Pharmaceuticals Ingredients (APIs) or resin parameters based on risk assessment, via records that are automatically printed out of the washing unit at the completion of a successful cleaning process. This is smart utilization of Critical Process Parameters (CPP), where the technician is able to suitably control: time, temperature, cleaning agent concentration, flow rate and pressure (by creating a number of validatable recipes in the machine which are ready to be run at the press of a button); and Cleaning Critical Quality Attributes (CQA) –surface and rinse water total organic carbon (TOC) and rinse water conductivity.

Ergonomics For Employees

Companies are becoming increasingly conscious of stress and strain incurred by their employees due to repetitive manual tasks. Not only does this cause an unwelcome workplace environment, but it greatly impacts productivity, especially given that some of the largest costs associated with running a manufacturing project is attributed to personnel. Mechanized cleaning systems extract the risk of workplace injuries by reducing water on the floor and physically handling heavy items. This also grants employees an opening to be able to apply themselves in other areas of production and optimized productivity equals a higher return on investment for manufacturing companies.

What’s So Messy About Dirty Hold Time?

It’s a regulatory requirement for cGMP manufacturing sites to have a fixed criteria for dirty hold time – the length of time dirty equipment can sit in the interval between the conclusion of production and the commencement of the cleaning process.

A growing number of cleaning technicians have argued in favor of extending the dirty hold time of their equipment, simply because of the labor-intensive tasks associated with manual cleaning applications. The problem with this becomes the production technician’s willingness to allow the cleaner to hold onto the equipment for a few days (consider more if over a holiday period), and still effectively clean it. The situation worsens once organic materials or proteins have dried on a stainless steel surface which makes it even tougher to clean. Additionally, when organics mix with water, bioburden is created. Repeated dirty hold times on equipment means repeated bioburden production. With manual cleaning, you’re also more likely to miss bioburden stuck in corrugated surfaces of your equipment.

In dealing with the human aspect of this process, you also can’t forcibly make production technicians remain at work just to allow the cleaning technician to run a manual cleaning cycle. The even greater obstacle lies with repeatability. If you’re targeted by the FDA, you’ll need to demonstrate to the inspector that your cleaning process is validatable. The inspector won’t care for a dirty hold time (especially not for one that endures for a few days), they’ll just want to know and see that you can validate your process at a thorough and methodical level and meet their cleaning requirements.

You'll also need to have data showing your dirty hold time is reliable (in duration and process), which is why the more you can automate your cleaning validation procedures with mechanized equipment, the better. A mechanized washer allows you to simply press "Go" to initiate your cleaning cycle and upon completion, will print out your fail-safe data. An automated washer facilitates your "Set & Forget" convenience.

Putting the "Good" in Good Manufacturing Practices

When dealing with current Good Manufacturing Practices (cGMPs) in a heavily regulated environment, a cleaning technician has no choice but to get it right when showing the inspector that they understand and comply with federal regulations and criteria.

It's essential to implement strategies and methodologies in regulatory guidelines such as ICH Q9 (Quality Risk Management), the 2011 PV Guidance, ASTM E2500 and Process Analytical Technology (PAT) into your cleaning and cleaning validation procedures. Concerning documentation, it's not about creating a dense, overwhelming binder filled with a legion of pages outlining every detail of your procedures as it's unnecessary and FDA inspectors don't have a lot of time. Instead, assemble the pivotal documentation and add an executive summary to relay the key elements.

The New Best Thing in Cleaning Automation

IWT, a division of Tecniplast, have been a pioneer in the design, development, and industrialization of industry-benchmark mechanized washing systems for over 26 years. Their European engineering embraces advanced techniques encompassing: fully validated processes inclusive of critical parameters for monitoring and tracking (including contact time, temperature and duration, cleaning agent concentration and water pressure); control of cross contamination; improved safety for technicians; and high throughput resulting in minimal production downtime.

IWT solutions include:

- Fully cGMP compliant product contact parts washers
- High- pressure impingement (up to 70 bar (1015 PSI)/40 LPM (10GPM)) washing systems for bulk containers involved in Clean-In-Place or Clean-Out-Of-Place applications
- Cabinet washers for bulk parts, containers and Clean-Out-Of-Place

IWT's washing systems offer TOC and conductivity monitoring and separate wash and rinse circuits to not only prevent the movement of particles and media from one product to the next, but to also monitor the quality of final rinse water being used. This is crucial for performance when considering CQA as these washing systems have the capability to control chemical properties (including conductivity and pH). HEPA filtered drying minimizes the buildup of potential bioburden when residual moisture gets left behind. Single pass high-pressure impingement washing systems (pressure up to 70 bar/1015 PSI) with 360° hydrokinetic head provides full coverage for all surfaces that must be cleaned, and also gives you the ability to minimize or eliminate the use of chemicals and heated water usage in your cleaning processes, for substantial cost savings and increased production.

In an age where pharmaceutical companies have described cell and gene therapy as a robust area for growth (2017 saw more therapies starting to gain approval), you may be in the operation of working to replicate cells. Considering that cells age over time, these cells must reside within bioreactors for extended periods to allow for their growth and reproduction to achieve optimal density of their

proteins. It can be taxing to then clean these bioreactors which can sit for weeks and easily develop bacteria. It's here that the impact of a mechanical impingement action from an IWT high-pressure washing system can vastly assist in removing dirty, stubborn proteins. The impact of the impingement and its ability to naturally cut through dirt also exceeds the need to use any detergent or silica or alumina particles in the water stream.

Bio/pharmaceutical manufacturers cannot afford variable results when it comes to patient safety. As manual cleaning can't reliably recover endotoxins off of stainless steel1 (which can potentially kill a patient), it's critical to invest in mechanized cleaning systems with automated data reporting, coupled with developed acceptance criteria incorporating the deactivation of biological properties and their breakdown products. Records used for electronic submissions to the FDA, or those replacing paper records must also be 21 CFR Part 11 compliant. Rich Yeaton (Atlantic Technical and Validation Services) says that in over 20 years of dealing with FDA inspections, he and partner Kelly Thompson have learnt that "patient safety is their number one concern" which means you need to be prepared to present them with good rationales and "lots of data" because all claims must be backed up with data, and the purpose of an inspection is "the collection of data".

IWT's experience in cleaning, combined with proven scientific skills and know-how, in collaboration with STEQ America's local service and support team, are here to help you define the most suitable and cost- efficient solution to meet your needs. Transitioning to a more systematic machine to automate laborious tasks will not only enhance productivity and eliminate technician errors, but more importantly ensure the purity and safety of your products.

Contact STEQ America for a personal consultation on GMP washing solutions to meet your needs. For more expert advice on managing FDA inspections, contact Rich Yeaton at ATV (yeaton@atlanticvalidation.com) or (603) 421-2748.

For more information call us at **(267) 245-7010** or email **info@steqamerica.com**.

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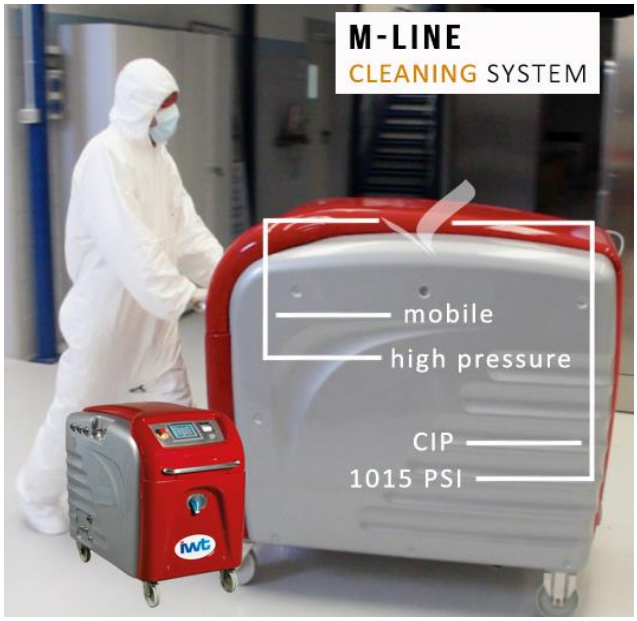

About STEQ America

STEQ America is to helping biotechnology and pharmaceutical companies find the right solutions to be leaders in their industry. A division of the STEQ group, which has been in operation for more than 17 years, STEQ America have garnered much success offering technology-led solutions to the pharmaceutical, biotech & life science industries. We are also much more than the solution providers for European and local manufacturers to be represented in the Americas. We are a team of great people, inspired by our ability to make a positive impact on the sectors we serve, by helping the companies within them discover healthcare solutions so that people may live happy and fulfilling lives. For the STEQ America organization, the customer relationship does not end at the delivery of the equipment. STEQ America Services cares to offer a unique and differentiated after-sales service, focused on customer needs related to the entire state of quality of the process and finished product. We provide you with customized training and services for our partner lines of equipment.

We offer German engineered and manufactured solutions for dissolution, disintegration, hardness, friability, blister density, granulate and powder flow testing for the pharmaceutical, veterinary, chemical, food and biotechnology industries, with a focus on laboratory needs and research and development. We also offer European solutions for the storage of hazardous and flammable materials, HPLC waste collection systems, cGMP washing systems, ultra-low temperature freezers, and autonomous, mobile, and turnkey cleanroom containment PODs.

About Atlantic Technical and Validation Services (ATV)

ATV is a GMP Validation and Compliance consulting company dedicated to providing high quality, cost effective services to the Biotechnology, Pharmaceutical, and Medical Device industries across the country and around the world. They have no significant debt or outside investors, so they can respond quickly to changing situations without having to get permission from unseen Boards. ATL have specific expertise in the areas of validation, regulatory compliance and GMP training.

About IWT

For more than 20 years IWT have specialized in the design, manufacture and installation of energy efficient, cost-effective and environmentally friendly washing systems. Innovative IWT high performance washing solutions have been installed in life science and pharmaceutical companies worldwide.

Find out more at www.iwtpharma.com.

References

- FDA Guidance Validation of Cleaning Processes (7/93), last updated 11/25/2014, link to inspection guide: https://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm074922.htm
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