CLEANING PROCESS DESIGN STAGE

In July 1993, the United States Food and Drug Administration (FDA) issued the Guide to Inspections of Validation of Cleaning Processes to assist the industry in compliance with current Good Manufacturing Practices (cGMP) requirements[1]. Following the release of the FDA 1993 guide, other countries issued similar guides to provide insight to the industry on how to comply with the regulations[2,3]. These guidance documents are focused on validation ensuring manufacturing control of the cleaning process. The pre- and post-validation phases may be factored into the process, but are neither emphasized in the regulatory guides nor in the industry practices.

In 2011 the FDA issued a revision to the process validation guide focusing on the life cycle of product manufacturing[4]. The process life cycle approach is a way to harmonize a company's approach to ensuring a robust and consistent manufacturing process.

Although the FDA process validation guide formally applies to manufacturing processes, many of the principles in that document apply to cleaning processes as well. The process life cycle consists of three stages (FDA, 2008): (1) process design, (2) process qualification, and (3) continued process verification.

Along with the process life cycle approach, other guides have been issued by the FDA and International Conference for Harmonization (ICH) which include the concepts of Quality by Design (QbD), Risk Management and Process Analytical Technology (PAT) [5,6]. The purpose of these guidance documents is to promote enhanced understanding of product and process, to build quality into manufacturing and to provide the basis for continuous improvement of products and processes. The primary goal is to ensure that all sources of variability affecting critical quality attributes are identified, explained and managed by appropriate measures.

Implementing a process life cycle approach to cleaning validation may be difficult especially for legacy processes. In their process validation guidance, the FDA has indicated that implementing a life cycle approach for legacy products is likely to begin with the continued process verification stage. Nonetheless, the better a company is at understanding and implementing the design phase, the better it will be at assessing issues later on during the continued process verification phase, such as risk with deviations, change controls and non-conforming results.

The following occurs in Stage 1 of the cleaning process design:

- Variables should be identified and their criticality to the cleaning process assessed.
- The cleaning agent and cleaning parameters should be defined.
- Residue from the process and cleaning agent, if applicable, should be identified.
- Analytical methods and sampling techniques used to demonstrate the surfaces are clean should be qualified.
- Utilities and equipment required to clean the production equipment should be defined.

Stage 1 should include input from product development, quality control, quality assurance, operations and validation.

Laboratory, pilot and field testing are essential in the design of the cleaning process and should be used to help identify conditions that would lead to consistent cleaning performance. Laboratory testing should provide a cleaning recommendation at normal operating range or area of control and an understanding of the design space or area of success (where adjustments can be made to the different cleaning parameters) without adversely affecting the quality of the cleaning process. Whether performing a laboratory study, pilot study or field trial, everyone should understand the manufacturing process, dirty hold time, materials of construction and utility restrictions.

The services provided in the Process and Cleaner Evaluation (PACE® Evaluation) are designed to be the first step in the development of a cleaning process for STERIS Customers. The primary focus of PACE Evaluation is to determine which STERIS detergent(s) and corresponding cleaning parameters best suit the needs of STERIS Customers[7]. For example, PACE Evaluation may include coating of the soil onto a stainless coupon and conditioning it in an oven for a specified time and temperature. After the coupon is conditioned, it can be cleaned by a number of different cleaning methods. An agitated immersion system consists of the cleaning agent solution mixed in a beaker and equilibrated to temperature and concentration. The pre-conditioned coupon, with the process soil, is placed into the cleaning agent solution. After select intervals, the coupon can be visually inspected and either returned to the cleaning agent for additional time or evaluated for cleanliness using more sensitive methods.

PACE Evaluation is performed by a fully staffed technical service laboratory that works together with the local STERIS Account Manager to evaluate the goals of the STERIS Customer in cleaning and cleaning validation. This service can be used to support the activities characteristic of the cleaning design stage as part of the process life cycle approach. For more information on how STERIS can help please contact your local STERIS Account Manager or email PACE@steris.com.

References

1. United States Food and Drug Administration. Guide to Inspections Validation of Cleaning Processes. July 1993.
2. Health Canada, Guide-0028 Cleaning Validation Guidelines. January 2008.
3. Pharmaceutical Inspection Convection/Pharmaceutical Inspection Co-Operation Scheme (PIC/S). PI-006-3 Validation Master Plan Installation And Operational Qualification Non-Sterile Process Validation Cleaning Validation. Sept 2009.
4. United States Food and Drug Administration. Process Validation: General Principles and Practices. January 2011.
5. United States Food and Drug Administration. Guide for Industry. PAT – A Framework for innovative pharmaceutical development, manufacturing, and quality assurance. September 2004.
6. International Conference Harmonization. Harmonized Tripartite Guideline- Q9 Quality Risk Management. November 2005.
7. STERIS technical tip #410-200-3087 “What is the PACE Evaluation?”.

For further information, please contact:

STERIS Life Sciences

STERIS Corporation
5960 Heisley Road
Mentor, OH 44060-1834 • USA
440-354-2600 • 800-444-9009

www.STERISLifeSciences.com