Changeover Reduction Time by Adjusting the Cleaning Critical Parameters in Automated CIP Systems

Author: Lynnette Garay
Advisor: Dr. Carlos J. Gonzalez Miranda
Manufacturing Competitiveness

Abstract

Clean In Place (CIP) is an automated cleaning method that involve minimum to no equipment disassembling thereby reducing labor and time expense. The objective of this project was to reduce the changeover time by determining where are the wastes in the cleaning process and campaign changeovers of the manufacturing equipment. In field-testing were performed under combination of critical parameters to clean the manufacturing vessels to acceptable limits. Different combinations were tested and samples once the cleaning process where completed. The goal was to not rework the equipment with the optimal CIP condition, which will lead to the changeover reduction time and compliance satisfaction.

Introduction

This project is about the cleaning process of automated processes in the biotechnology field. The investigation allows the industry to understand how to develop the cleaning processes to reduce the changeover time. This is achieved by determining where are the wastes in the cleaning process that are reflected as effective design of the automated CIP systems.

Background

Optimization of a changeover procedures is needed to stay competitive and to minimize the slowdowns in manufacturing waiting for availability of equipment [1]. This changeover cleaning optimization is the process of determining the most efficient and effective cleaning process design to achieve lesser time and cost to change from Product A to product B without adversely affect the quality of the products manufactured and the safety of the patients. Appropriate cleaning design involve the distribution of the TACT (Temperature, Action, Concentration of chemical, Time) parameters to fit an effective cleaning process.

Figure 1. TACT Key Parameters Representation

Available cleaning methodologies are Clean-In-Place (CIP), Clean-Out-of-Place (COP), and Manual cleaning. These methodologies can be implemented by automated the cleaning systems or by extensive and detailed procedure instructions.

Problem

Pharmaceutical processes faces some challenges in the cleaning processes when changing between products campaign. These challenges can lead to extensive cleanings and sampling that result in downtime of the equipment for more than 12 hours. Appropriate waste assessment ensures that the cleaning activities performed will reduce the changeover time between manufacturing campaigns while maintaining the critical parameters of the process and complying with the acceptance criteria defined.

Methodology

The study was conducted applying different variables to the automated recirculated cleaning cycles. The tested variables were adjusted accordingly to the cleaning critical parameters of temperature, mechanical action, cleaning agent concentration, and contact time. Equal percentage contribution of each parameter as a baseline was the starting point as presented in Figure 2.

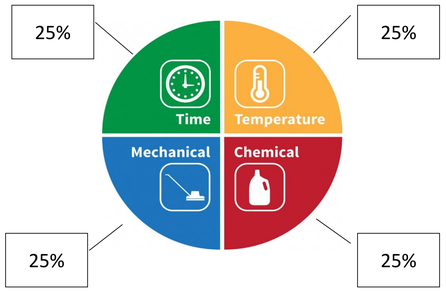

Figure 2. TACT Parameters Adjustment

The experimental runs consisted of soiling the manufacturing vessels ranged from 60,000 L to 15,000 L with the normal production material. Then, a cleaning run is applied according to Table 1: “Cleaning Parameters Adjustment Matrix”. First, the surfaces were inspected for cleanliness and surface sampling were collected. Locations evaluated were wall, bottom, dome, inlet product, and agitator. Evaluation of the cleanliness of the surfaces required the applicability of the acceptance criteria of NMT 100 ppm for change over.

Sample results were considered in the statistical analysis even if the acceptance criteria was exceeded, which means that the equipment needed to be re-clean in order to be release for manufacturing purposed.

Table 1: Cleaning Parameters Adjustment Matrix.

Run Number	Temperature	Cleaning Agent	Mechanical Action	Contact Time
1	No adjustment	No adjustment	No adjustment	No adjustment
2	No adjustment	No adjustment	Manually clean the locations	No adjustment
3	Increase from 65°C to 75°C	Increase 3X molarity	No adjustment	Extend 3X recirculation time
4	Increase from 65°C to 75°C	Increase 3X molarity	Change to rotation head jet	Extend 3X recirculation time

Results and Discussion

Experimental data shows significant results when adjusting the cleaning critical parameters. The set of data points were average for the population of vessels assessed during each experimental run. This means, that if five (5) different vessels that are similar were tested, then the data was an average of all the results obtained. Figure 3 summarized the results obtained by run.

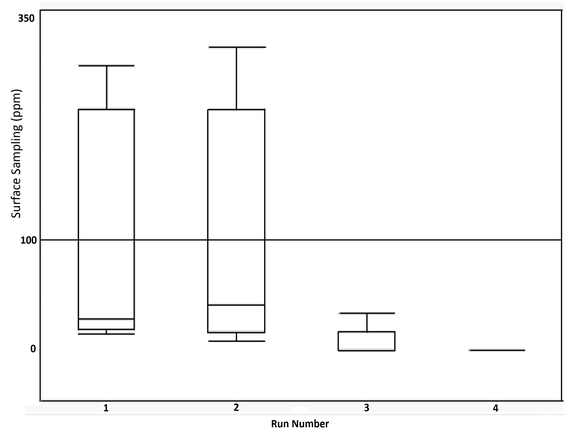

Figure 3. Surface Contact Protein Sampling by Experimental Group.

Run 1 shows most of the results above the acceptance criteria of 100 ppm. This run represent the experimental control with no adjustment perform to the TACT parameters. Run 2 adjusted the mechanical action as a testing mechanism. This run applies the technique of manual cleaning to the inlet product. It was observed inconsistency between operators when applying the mechanical force pattern. Run 3 adjusted the cleaning agent concentration, increase the temperature and extended the contact time of the higher parameters demonstrate significant results for vessels range 15,000 L to 30,000 L. Vessels larger than 30,000 L did showed failures in the upper side of the walls. This confirms that the mechanical force applied by a static sprayball can be optimized for larger vessels. Run 4 demonstrate satisfactory results with larger vessels. Rotation spray head provide an increase of the system pressure to 10X psi. Even that this showed a better cleaning process, it is not recommended to routinely applied this pressure to the surfaces of the equipment. Constant high pressure could lead to a surfaces reliability issue in the lifetime of the vessel.

Cleaning a larger vessel can take up to three (3) working days operating 24/7. More than one (1) operator is required to intervene the equipment along with mechanics if disassembling is required. Designing the CIP systems with the capacity to adapt the parameters and avoid manual interventions resulted in an optimization of the TACT parameters during changeover. These times are reduced by adjusting these parameters satisfactory cleaned the equipment without rework meaning that the change over time is reduced. In addition, rework avoid cleaning until clean which is a phrase recognized to be avoided by the industry. Therefore, having the equipment cleaned the first time guarantee to maintain the equipment within compliance [2].

Conclusions

The results of the investigation confirms the feasibility of optimizing the CIP critical parameters by automated changing the CIP recipe. The investigation was based on vessel equipment connected to pipping and to a CIP Skid that is automated controlled. It was possible to test different combination of TACT to reach the final proposal of clean the equipment to acceptable limits without rework.

Based on the results of the study, adjusting concentration of the cleaning agent, temperature, and contact time provides a viable approach to reduce the rework of equipment and to optimize the cleaning process. Not only helps the change over time but also the waste of materials such as water, energy, cleaning agents used during the rework

Future Work

Miscellaneous equipment or loose part must be cleaned within a Cabinet washer to also apply the concepts proven within this investigation. Equipment that is cleaned manually should be evaluated to be included into the automated systems and provides the flexibility to adjust to future projects.

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