Improving Product Changeover in Pharmaceutical Manufacturing Through Lean Six Sigma

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Abstract

Pharmaceutical bulk manufacturing is essential for producing important lifesaving drugs, but often faces delays during changeovers that can lead to increased costs for the company. This study focuses on applying Lean Six Sigma methodologies to streamline complex changeover processes within a pharmaceutical manufacturing facility. With tools such as fishbone diagrams and Pareto analysis, root causes were identified, and solutions were implemented to reduce changeover delays. An Andon board was employed which helped mitigate delays caused by equipment failure. Standardized flowcharts provided consistency for the process among all employees. The 5S initiative reduced wasted time and unnecessary movement during changeovers. The successful application of these methodologies in this study highlights the potential for Lean Six Sigma to drive significant operational improvements in highly regulated environments like pharmaceutical manufacturing

Introduction

Multiproduct Pharmaceutical Manufacturing Facilities must implement a changeover between each product campaign to ensure cross contamination does not occur. A changeover in pharmaceutical bulk manufacturing facility can involve tasks such as mayor equipment cleaning, swabbing, filter replacements, among other tasks that can consume a large amount of time. The activities often vary depending on which products are going to be manufactured and how similar their raw materials are. When you add the complexities of larger equipment cleaning such as hygienic vessels, this seemingly simple task becomes a production nightmare. Overall, these activities consume resources, extend production times, and ultimately lead to higher costs without directly contributing to the quality of the final product.

Background

Biopharmaceutical manufacturers face increased competition and pressure to maintain efficient operations, leading to the rise of multiproduct facilities that offer economic advantages by maximizing resource utilization. These facilities spread fixed costs across multiple drugs and allow flexible production shifts without building new plants [1]. However, they face challenges like downtime during product changeovers, where cleaning and preparation are necessary to prevent cross-contamination. Efficient changeovers are essential for maintaining regulatory compliance, ensuring drug purity, and minimizing downtime, which impacts productivity. In Lean Six Sigma, things that don't meet customers' needs are either defects or waste [2]. Lean Six Sigma methodologies, which combines Lean's waste reduction with Six Sigma's focus on reducing variation, can significantly reduce changeover times [3]. Furthermore, Lean Six Sigma tools help eliminate common types of waste, such as defects, overproduction, waiting, and unnecessary movement, thus enhancing efficiency.

Pharmaceutical regulations, such as Good Manufacturing Practices (GMP), add complexity to the process by imposing strict protocols, requiring meticulous documentation, and extensive validation [3]. While these measures ensure drug safety and quality, they can slow production. Balancing regulatory demands with process efficiency is crucial for manufacturers. Strategies like automation and digital record-keeping can help streamline compliance while improving production speed and reducing waste that doesn't affect GMP standards. Implementing Lean Six Sigma helps manufacturers meet regulatory requirements, minimize errors, and improve overall production efficiency

Problem

Multiproduct pharmaceutical facilities aim at supplying reliable medicine that adapts to current product demand. Consequently, these multiproduct facilities have many reasons to improve their changeover procedures. Fast, cost-effective changeovers allow higher output of products, increasing revenue and helping the companies fulfill their mission of delivering life-saving medicine to patients around the world. Lean Six Sigma provides a comprehensive framework for identifying and eliminating inefficiencies, improving quality, and delivering exceptional value to customers. Applying Lean Six Sigma to implement improvements will consequently help streamline processes and reduce waste within the manufacturing floor while staying cost effective..

Methodology

The DMAIC cycle, which defines the five core phases of LSS projects – Define, Measure, Analyze, Improve, and Control – provided the framework for this improvement initiative [4]. By focusing on waste reduction and process improvement, this approach aims to minimize changeover times, leading to increased production capacity and customer satisfaction.

Define Phase

The Define phase of the DMAIC methodology centers around defining the project scope, expectations and goals. A SIPOC diagram was developed to highlight information that is critical to the project success. With this SIPOC diagram, we identify key inputs, outputs, activities and boundaries.

Measure Phase

The measure phase involves gathering and measuring the current state of the process to establish a baseline for our project improvements. To properly understand changeover processes, observations and group discussions were conducted. This provides an opportunity for manufacturing personnel to express any areas for improvement they have come across. Stratification factors were identified to help guide the discussions in a way that generated a deeper understanding of the problem.

Analyze Phase

This step focuses on identifying root causes and key inputs important for the process. The information gathered throughout the data collection will be analyzed with a pareto chart to identify the major causes for changeover delays. A root cause analysis for the major changeover delays will be conducted using the fishbone diagram method. Additionally, a t-test will be performed to determine statistical significance of any measurable improvements during de project. Other statistical analysis will be conducted depending on the data collected in the previous step.

Improve Phase

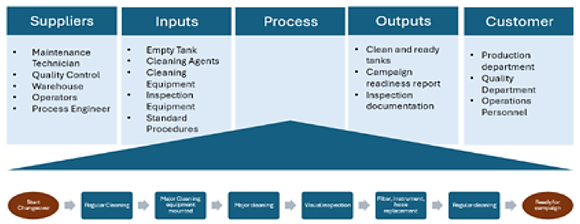
In this phase is where improvements are made, and tools are implemented. It is important that before any tool is implemented, a proper risk assessment has been conducted and operator feedback has been considered. Some tools that will be implemented Include 5S and Andon Boards, among others.

Control Phase

The control phase is one of the most important steps in this methodology as it ensures that the gains are sustained, and the process doesn't fall back to its previous state. Metrics for changeover efficiency can be implemented and measured periodically to ensure goals are met and kept. Procedure improvements will be implemented to ensure standardization of the new flow implemented in the project.

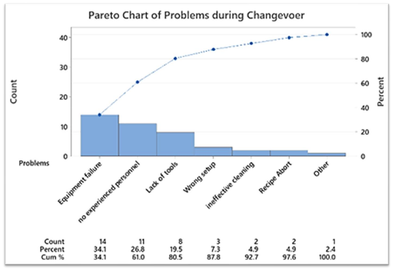
Results and Discussion

The project began with a SIPOC diagram (Suppliers, Inputs, Process, Outputs, Customers), which mapped out the entire changeover process to provide clarity on its scope and identify the departments involved. From this, potential bottlenecks were identified, notably in the manual operations of major cleaning and the replacement of instruments and filters, which caused delays in the automated cleaning processes. To better understand the root causes of changeover delays, the team used data from interviews and brainstorming sessions to create a fishbone diagram.



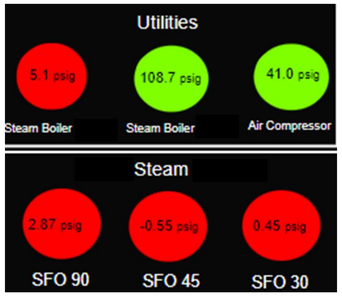
A deeper analysis of defects and schedule delays from changeovers in 2024 was conducted, which included 41 reported problems. Using a Pareto chart, the team identified the key few causes that lead to the most delays. These main issues were prioritized for resolution, focusing on the highest-impact problems to maximize improvement.

The top three issues were:

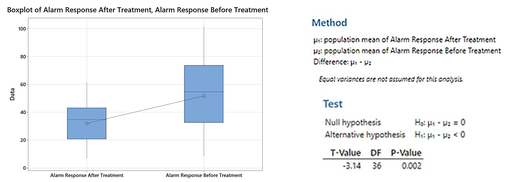


Pareto Diagram

- **Equipment failures:** Operators noted that equipment issues were often identified late, which caused critical delays. To address this, the team developed an Andon board, a visual tool that displays the status of equipment in real-time. The board shows different equipment areas, with color-coded indicators—green for normal operation, yellow as a warning, and red for critical issues. This enabled production staff to quickly identify and resolve problems before they escalated. The information for the board is automatically fed from the existing automation and control systems, requiring minimal manual intervention. After implementing the Andon board, the response time to alarms improved significantly, decreasing from an average of 51.8 minutes to 32.1 minutes, a 39% reduction. A t-Test confirmed the statistical significance of this improvement, and a boxplot illustrated the reduced variability in response times post-implementation, demonstrating more consistent performance.

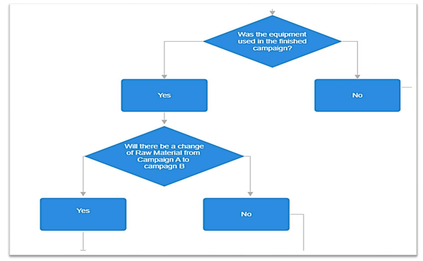


Andon Board



Boxplot and t-test of alarm response rate before and after treatment

- **No experienced personnel on shift:** The second major problem was a shortage of experienced staff during changeovers. Less-experienced employees often struggled due to insufficiently detailed procedures and were unsure of how to manage certain tasks. Experienced staff typically knew by memory how to handle specific tasks and equipment, but their absence led to delays. To mitigate this issue, the team developed flowcharts for each piece of equipment. These flowcharts provided clear, step-by-step guides that standardized the changeover process and reduced human error.. This kind of specificity helps clarify procedures and ensured that employees knew exactly what to do at each stage of the process.



Excerpt from flow charts designed for changeover

- **Tool unavailability:** The third most frequent problem was the lack of tool organization. Changeover equipment was often scattered across different areas, forcing operators to waste time searching for tools. The team created a spaghetti diagram of the current flow of materials and compared it to a proposed new layout. The diagram revealed extensive wasted movement across production floors. A 5S initiative was introduced to organize and streamline the workspace with unnecessary items removed and remaining tools arranged neatly. The improved flow reduced wasted time and allowed operators to focus on more critical tasks.

As part of the Control phase, measures were put in place to ensure the sustainability of these improvements. The Andon board was assigned to a technical specialist for ongoing maintenance and updates. The equipment flowcharts were incorporated into the standard operating procedures (SOPs), ensuring that all personnel follow the standardized process.

Conclusions

The tools developed in this project serve as aids to improve changeover by reducing defects, waste, and time. The Andon board developed to help gain better visibility for equipment status is an important addition for the production personnel. There was a notable reduction in alarm response time by 39%. The flowcharts developed are a simple yet effective way to ensure standardization across all shifts and personnel regardless of their experience. A designated changeover equipment area was set up as part of a 5S which helped reduce time for the operator looking the right tools as well as unnecessary movement and transportation across various production floors. The involvement of production personnel is paramount to ensure these initiatives are sustained.

Future Work

Future projects can be focused on measuring the impact of these tools and further improving other campaign procedures. There should also be future projects focused on expanding the DMAIC methodology onto other areas of production.

Acknowledgements

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References

1. Z. E. Gungor and S. Evans, "Understanding the hidden cost and identifying the root causes of changeover impacts," Journal of Cleaner Production, vol. 167, pp. 1138–1147, Nov. 2017. doi:10.1016/j.jclepro.2017.08.055
2. X. Li, X. Liang and Z. Li, "The Strategy of Strengthening Efficiency and Environmental Performance of Product Changeover in the Multiproduct Production System," Sage Open, vol. 13, (3), 2023. DOI: https://doi.org/10.1177/21582440231193390.
3. Authorship and I. R. SCIMAGO, "Analysis of Lean Six Sigma Use in Pharmaceutical Production," Brazilian Journal of Pharmaceutical Sciences, vol. 59, 2023. DOI: https://doi.org/10.1590/s2175-97902023e22949.
4. M. L. George and D. L. Rowlands, The Lean Six Sigma Pocket Toolbook: A Quick Reference Guide to Nearly 100 Tools for Improving Process Quality, Speed, and Complexity. Ipswich, New York: McGraw-Hill Professional Publishing Ebsco Publishing distributor, 2004.