Optimization of Bioburden Samples Processing in the Microbiology Laboratory Using Six Sigma

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Abstract

This article presents the use of the Lean Six Sigma tool to identify factors affecting the processing of samples that require Bioburden testing in the Microbiology Laboratory. The objective of this article was to implement and design a system in which samples could be processed in the shortest time. The data was collected using LIMS System and behavior was evaluated by watching the analyst during test execution. Then, a statistics test helps to compared and determine if the new design fulfill the objectives of the research. Our findings suggest that the Bioburden tests of water samples and final products are more manageable than those of In-process samples. However, we conclude that the processing times of the samples were significantly reduced.

Introduction

The research is related to optimizing the processing of samples in the Bioburden test in the Microbiology Laboratory. The Bioburden test helps determine the number of bacteria or fungi associated with a particular product or sample before it is sterilized or continues with the manufacturing process [1]. The filtered samples also are related to the raw material, assembly processes, manufacturing environment, water, lubricants, and cleaning processes. It has vital importance due to the stability and quality of the product could be determined based on the results obtained in this test. For this reason, this research seeks to implement a system to process Bioburden samples in the shortest possible time. Lost time is considered waste according to the Six Sigma philosophy. Lean Six Sigma is a process improvement methodology used to increase product quality based on waste reduction [2].

Background

The pharmaceutical industry is identified as one of the most prominent and influential business sectors worldwide. Pharmacopeia is the official legal tool that guarantees product quality. Quality control is increasingly important in the manufacture of biopharmaceutical products. It can be defined as complying with customer requirements or federal and international regulations. Microbiology supports in the pharmaceutical industry is an essential resource because it plays a crucial role in the production and analysis processes that guarantee the quality of pharmaceutical products. Part of the tests performed in the Microbiology laboratory includes the Bioburden test. Bioburden refers to the microbial levels or content on a particular sample. This test can determine if any upstream/downstream steps or additives solutions are compromised. Bioburden testing uses membrane filtration or the pour plate method [1].

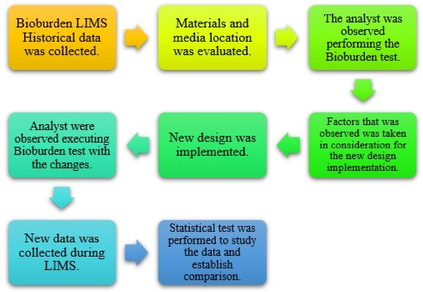
Lean Six Sigma establishes that to increase product quality, the waste associated with the process must be eliminated or reduced. One of these wastes is the loss of time and motion. [5]. Lean Six Sigma has five steps that must be performed to accomplish its implementation. These steps are called DMAIC (Define, Measure, Analyze, Improve, and Control) [6]. Several research results using the Six Sigma method proved that the success in the implementation is based on the consistency of DMAIC. They are providing positive results in problem-solving.

Problem

In this investigation it was demonstrated how a new reorganization of the materials could be implemented using the Lean Six Sigma tool to reduce the time it takes to perform the Bioburden test. The purpose of this project was to improve the efficiency of the test and to identify all those factors that could affect the analyst during the execution of the test. The research aims to implement and design a system by which the samples can be processed in a shorter period, avoiding the loss of time during Bioburden testing and manufacturing product processes.

Methodology

The project was initiated by performing a literature review of previous studies to evaluate how to implement the DMAIC methodology of Lean Six Sigma. This research helped to define the problem that needs to be solved. After this research, the employees were trained in this philosophy.



Results and Discussion

The results obtained in this project followed the improvement established by the DMAIC model.

Defining and Measuring

- Initial assessment was performed to evaluate Bioburden tests the time that took to process Water, Final products, and in-process products samples. Figure 1 shows the steps to follow when a sample is received in the laboratory until it is processed using the Bioburden test.

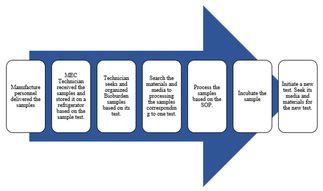


Figure 1. Process Map

- Also, infrastructure and materials/media location were evaluated to determine the changes and new organization. Figure 2 shows the initial location of the materials and media used in the bioburden test only.

Figure 2. Laboratory Facilities organization. Diagram legend: 1. Biosafety Cabinet 1, 2. Chemical Cabinet, 3. Biosafety Cabinet 2, 4. Buffers cabinet, 5. Funnels cabinet, 6. Computer, 7, Environmental media, 8. In-process samples & 9. Computer. It also includes the Incubators and Cold Room (where Bioburden material and media were stored).

- After performing the initial assessment, it was found that one of the reasons for the long time spent processing the samples. It was found that although the technicians use the same procedure, the number of samples they filter will depend on who executes it. It could represent a delay if the number of samples received increases.
- In the graph, it was observed a significant dispersion of the values about the processing time in the different tests. After evaluating the data obtained, the personnel were trained.
- The training was related to the fundamentals of the Six Sigma methodology and its advantages. In addition, the changes that would be made in the laboratory were explained so that everyone knew the new location of the materials.

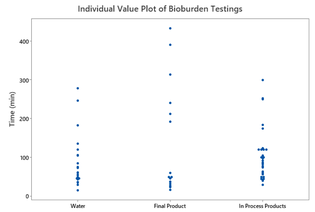


Figure 3. Individual value plot of initial assessment based on Bioburden tests.

Analyze

- In this phase, the results were analyzed on the new model implemented in the Microbiology Laboratory (see Figure 4).
- Also, a hypothesis test (T paired) was performed to compared the data (see figure 5). In all three tests based on the P value, the null hypothesis was rejected, so the alternate hypothesis was accepted. Therefore, it can be concluded that there is a significant difference between the means.

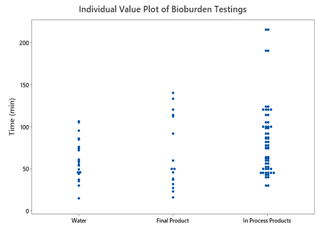


Figure 4. Individual value plot after new design implementation.

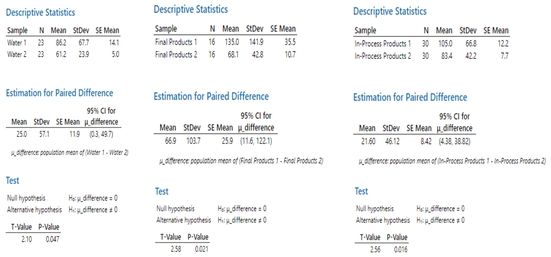


Figure 5. Descriptive statistics and Hypothesis test for water, Final products and In-process samples using Minitab Statistical Software (Significance level of 95%).

Improve

- After evaluating the results obtained in the hypothesis test, it was determined that as part of the training that will be provided to the employees, training should be included that reinforces the technician's confidence while handling the samples.
- The Fishbone Diagram was used to determine the root causes and the effects .
- The other equipment remained original; only the materials were reorganized so that they were more accessible to achieve the Bioburden testing (see Figure 9).

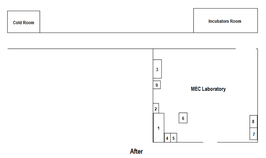


Figure 9. New Laboratory Facilities organization. Diagram legend: 1. Biosafety Cabinet 1, 2. Chemical Cabinet, 3. Biosafety Cabinet 2, 4. Buffers cabinet, 5. Funnels cabinet, 6. Computer, 7, Bioburden media, 8. In-process samples & 9. Computer. It also includes an Incubator room and Cold Room (where Environmental material and media were moved).

Control

- To sustain the changes made and suggested in this project, a periodic evaluation of the test will be executed.
- both Biosafety Cabinets enabled at times when the Bioburden test is saturated with tests pending to be processed.
- This flowchart can be incorporated as an annex to the procedures.
- if production increases, the changes should be re-evaluated to see if they continue to be effective.

Conclusions

- The main goal was to implement a new design to process the samples in a shorter period. It was completed and accomplished when the new rearrangements were implemented.
- These improvements have resulted not only in time reduction but also in cost reduction.
- Training the employees on the Six Sigma methodology was helpful for them to understand the reason for the changes.
- To prevent a recurrence of the problem, it is crucial to continue educating and training the employees.
- One of the main constraints of the project was the need for more staff training. Not all personnel master the Bioburden test, so this knowledge and skill should be reinforced so that sample processing is not affected.
- One of the most significant contributions of this project was to align laboratory personnel to a single modus operandi in the Bioburden test.

Future Work

- Bioburden test will continue to be evaluated to improve the sample processing until the training is not an obstacle.
- A future goal is to implement this philosophy and methodology in the different microbiological and analytical assays.
- Bioburden procedures will be modified to add flowcharts or pictograms to make them more understandable.

Acknowledgements

The results presented were done in collaboration with a peer at the laboratory. To be able to train the technicians on the Six Sigma methodology and to be able to get everyone to perform the test in the same way. In addition, my mentor was a great help during the planning and development of this project.

References

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