Setup Time Reduction in the Water for Injection Sampling Process on the Pharmaceutical Industry

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Abstract *– This work consists in the development of a new WFI sampling route that will bring several important benefits to the pharmaceutical industry. Reduction in the setup time will improve daily operations in terms of efficiency, budget, and cycle time reduction. A time study was done in this research that improve the WFI sampling time process for more than 50%, which was the current objective. Swimlane, SIPOC were used to illustrate the process. Furthermore, statistical analysis using mini tab were performed along with graphical illustrations. This research work concludes that the proposed setup time for WFI sampling process is more than 50% more efficient than the current one. Thus, improvement of daily operations is achieved in this work.*

Key Terms *— Setup Time, SIPOC, Swimlane, WFI Water for Injection.*

PROJECT STATEMENT

To improve and succeed in a highly regulated environment, manufacturing needs (pharmaceutical industries specially) requires attention to details. That is why the proposed topic will emphasize in the elimination of some of the wasting (waiting) processes that some industries are facing. Reducing the cycle time of the preparations of materials for Water for Injection (WFI) sampling in the manufacturing areas will save time and money to the company. That is why allocating a material storage area inside manufacturing area is proposed in this project. The main research will be to measure the improvement of the sampling setup and sampling time during the WFI water monitoring process. It is expected to accomplish the improvement proposed with the new measured results, in comparison with the old process.

Currently the process of water collection requires that the analyst prepare the sampling materials in the microbiology laboratory and then travel to the manufacturing areas, that are far from the lab (approximate 15 mins). Then, the materials need to be sanitized (10 mins more) to pick up inside the manufacturing area. The objective of this work is to establish a WFI material storage area to save time in transportation and sanitization and improve waiting sampling time.

Research Description

This research will compare and reduce the cycle time process of WFI sampling in a regulated industry. Using tools like 5S, Lean Six Sigma, and Kaizen techniques will help to illustrate and compare more precisely the improved WFI process versus the current WFI sampling process on the site. This study is important since it will benefit this manufacturing company in several areas, economically, manpower expenditure, and cycle time reduction.

Research Objectives

The expected objectives of this research will be:

- Compare and measure improvement for WFI sampling.
- Establish cycle time improvement of more than 50% of the original sampling setup time expenditure process.
- Demonstrate how 5S organization concepts improve operational needs.
- Validate the economic impact this improvement brings to the workplace.

Research Contributions

The research contributions of this work will improve the company performance over time as of:

- reducing several types of wastes from the WFI sampling process to improve daily operations.
- establishing economic impact in terms of time and money for the industry by reducing operational costs in the process.
- establishing a 5S organization for a flawless operational process.
- reducing the setup time involved in the WFI sampling process.

LITERATURE REVIEW

To comprehend this work, explanation is required to understand some of the lean concepts. First, establishing a lean culture in this task is highly important. Being able to implement and correctly execute lean concepts like 5S, Lean Six Sigma, and Kaizen techniques are of extremely significance. Now let define the concepts that will be used.

- 5S - Is also known as a visual improvement tool [1]. It stands for sort, shine, set in order, standardize, and sustain. This 5S system concentrate in removing, organizing, labeling material that are not needed, thus freeing up space in the area. Unneeded materials and tools that are obsolete or not in use are relocated or discarded depending on the item situation. 5S is also used to bring functional logical arrangement of items in the area and at the same time, bring cleanliness to the space where the items are assigned [2]. According to Vera [2] research of recycling bottle processes are the best way to improve cycle time and eliminate waste in some of the process utilizing visual aids like 5S, having a clear and labeled system will save time and thus the company will be more productive.
- Sort - in this step, the employee needs to separate items that can be used from the ones that cannot, based on your organization and utilization purposes. A red tag is usually used to identify inventory, equipment's or machines that will be needed to be removed from the area. The displacement of the equipment is basically for two main reasons: the equipment does not work, or the equipment is basically not functional in the area that is currently allocated and cannot be used. In the sorting process, freeing up the most space possible is a requirement.
- Shine - after reorganization of the equipment that will be used from the ones that are not, organization of those items is required. Retention and allocation of those items in a functional and productive area is needed. Commonly, the area is near where the process is taking place. Visual aids are highly needed in this step-in order to be easily understand by another person and save time seeking the needed item. Labeling is one of the most common used visual aid. For the set-in order step, basically it concentrates in the maintenance of the organization. After the equipment is organized and labeled, this step concentrates in maintaining the organization and cleanliness of the items during the day. Usually more than one person is assigned to this step; during the morning one person audits and secure the organization of the area and later, during the day or the end of the working shift, another person audits again and verify everything is in order. This step needs to be done when the equipment's are in used to identify some organization gaps, if any.
- Standardize - This step is basically concentrated in the standardization of the previous steps. Several people are accountable for this standardization steps because they are assigned to assure that the previous steps are still in order. Usually an employee assigned verifies the area during the morning to secure if the standardization process is flowing flawlessly and another one, 5 minutes previously the end of the working day, also checkup. If the plant operates 24/7, every shift

needs to verify this step when start and end their respective working shift.

- Sustain - This step takes time because several external audits need to be taken place to arrive to the sustain step. The objective of this final step is to make the previously steps a habit, that everyone related to the area understand the functionality of this 5S process and use the newly organize area and at the same time, maintain its 5S characteristics keeping things clean, organize, and especially functional. Every operator needs to understand the 5S organizational importance to sustain and keep it effective.
- Lean Six Sigma - Six Sigma is a disciplined and data driven business improvement methodology that was developed to enhance the quality of process with the objective of establishing an almost zero-defect quality strategy, thereby increasing customer satisfaction as well as improving financial results [3]. The sigma symbol (σ) is used to represent the standard deviation of a process mean [3]. Lean process concentrates on eradicating waste from the process in study, while SS focuses on measuring and removing waste using statistical methods. Having this explained, Lean Six Sigma is a fusion of both terms. This term evolved since multiple researches founded that implementing Six Sigma alone was not as effective than integrating Lean concepts to the process. The implementation of Lean Six Sigma together has proved to obtain better financial results [4]. George illustrates in his book Lean Six Sigma for Service (Figure 1) that a graphical approach of how a lead time reduction of the lean tools, and a defect reduction from the Six Sigma tools, both achieve better results [5].

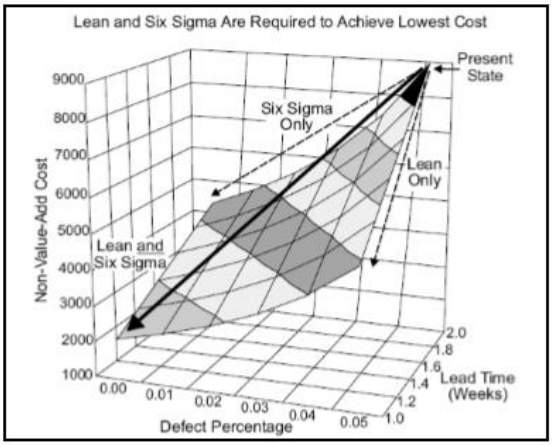


Figure 1

Lean + Six Sigma = Lower Costs [5]

One term that is necessary to be mentioned in the research is the Value Stream Map. Is a tool that identify activities that are value added and not value added in the manufacturing industry, making it easier to find the root problems in the process [6]. It utilizes certain symbols to describe process of waiting, storage, decision making queues, and inspection [6]. According to Santosa [6], the best way to measure improvement is to identify the specific waste in the research project and implement Value Stream Map and Kaizen techniques to illustrate findings and results.

- Kaizen - is a term in the Japanese language that that can interpreted as continuous improvement [6]. involving everyone, both the top management, managers, and employees and the principal strategy Kaizen used is to realize that management should strive to satisfy customers and meets their expectation and needs [7].

Waste will be explained to understand this research. Waste is anything other than the minimum amount of equipment, materials, parts, and labor (working time) which are essential to add value to the product [8]. There are 7 different kind of waste according to Hines [9]:

- Overproduction - is considered as the most serious waste as it discourages a smooth flow of goods or services. Producing more than can be managed is the root cause of this waste because it inhibits quality and productivity. As

a result, it tends to increase the storage times of the items.

- Defect - this waste is mainly caused by errors occurred in the working process stages as of by the machine or the operator; this affects product quality and bad delivery performance to the customers.
- Unnecessary Inventory - this waste is based on the excess of storage of goods, consuming space that can be use for other products. This waste also affects the delay of a product or material information.
- Inappropriate Processing - this waste in the production process is not appropriate for any of the procedures that can be the utilization of equipment or machinery that is not in accordance with the capacity or ability to work properly. It also can be a utilization of equipment that is not meant to produce certain step or product.
- Excessive Transportation - movement of people, information, and product material.
- Waiting - it occurs when time is not being used effectively. This can be for several factors including worker inactivity, seeking for information material or product spending long periods of time.
- Motion Unnecessary - movement of product, people or information that consumes time and really does not add any value to the product or process.

Furthermore, in the article of Rivera [10] he mentions that implementing the Lean Six Sigma techniques will lower operational cost and be more productive in the manufacturing process. These three articles are the basis of this research. This research will implement their techniques to wait for the expected results, which is improvement in the process of Water for Injection (WFI) sampling process in the manufacturing area of the pharmaceutical industry.

METHODOLOGY

The methodology this research use is quantitatively. The research will evaluate and compare the original setup time of WFI sampling versus the proposed setup time with the materials allocated in the manufacturing area, implementing Lean Six Sigma tools to compare the standard deviation of the original WFI setup time versus the proposed WFI setup time. Time will be the independent variable in both cases. Comparison between both setups' times with a confidence interval of 95% or an alpha of 0.05% will be studied. In addition, to establish conclusions with the obtained results normality tests, followed by P value test, are going to be performed.

The original setup time of WFI sampling process time data will be collected with a stopwatch when the analyst starts preparing the materials for the sampling process until the end. In the case of proposed WFI sampling setup time, the time will start when the analyst starts preparing sampling materials in the manufacturing area until the analyst finishes sampling. Value Stream Mapping will be used to demonstrate and identify more clearly the possible waste in the process. In addition, 5S organization will be implemented in the new area for WFI sampling materials inside the manufacturing area.

RESULTS AND DISCUSSION

Study and analysis of the collected data in the WFI monitoring process will take place. In addition, comparison of the differences between the current WFI monitoring process versus the proposed WFI monitoring process will be considered. Furthermore, measurement of the progress obtained by comparing and analyzing the standard deviation, normal distribution test and P value will be discussed. The comparison will be with a confidence interval of 0.05%.

In this research three analyst participated in the monitoring process. All of them were analysts of the microbiology laboratory since qualification is required to perform the task. The measurement of

the monitoring process was measured for two consecutive weeks. There were several meetings performed in the process. Gemba walks was the technique selected to gather feedback and process improvement ideas. Furthermore, Kaizen meetings were performed to evaluate the project for possible process certification of sustained improvement.

Table 1

Swimlane Illustration of Process

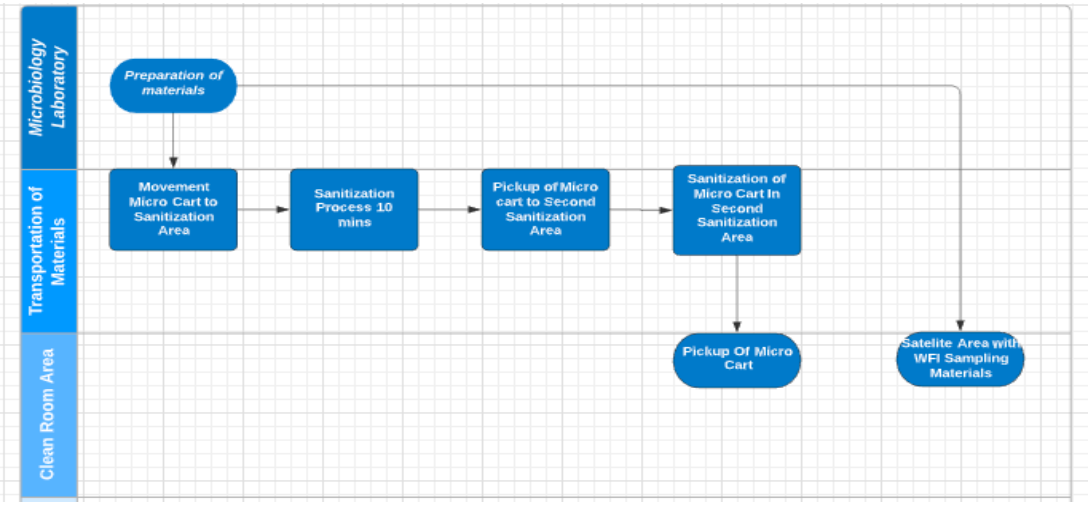


Table 2

SIPOC Table

Suppliers	Inputs	Processes	Outputs	Customers
Who supplies the process inputs?	**What inputs are required?**	**What are the major steps in the process?**	**What are the process outputs?**	**Who receives the outputs?**
New product development	Design and process CTQ's	Internal audit	Monthly quality report	Site management
Site quality steering team	External standards	Advanced quality planning	Corrective actions	Marketing leaders
Customer service	Quality control plans	Dock audit	Inspection and traceability records	External auditors
QC equipment suppliers	PFMEA risk factors	Control plan execution		
Warranty information system	Measurement equipment	Quality metrics reporting		
	Internal audit calendar	Continuous improvement		
	Customer complaints & warranty data			

On Table 1 it is shown the process map using the Swimlane technique. On the left side can be seen the current process step which is Microbiology Laboratory, Transportation of Materials, and Cleanroom area. The arrows show the order on which the task is followed until the end of the process. Note that the new process implemented have only two steps, which is much simple.

One of the tools more commonly used for process improvement tasks is SIPOC, that stands for Suppliers, Inputs, Processes, Outputs and Customers. It summarizes the inputs and outputs of

one or more processes using a table format as of Table 2. In this table it is showed the specific departments or areas that may be affected.

Table 3

Value Stream Map Between Current Process and Proposed Process

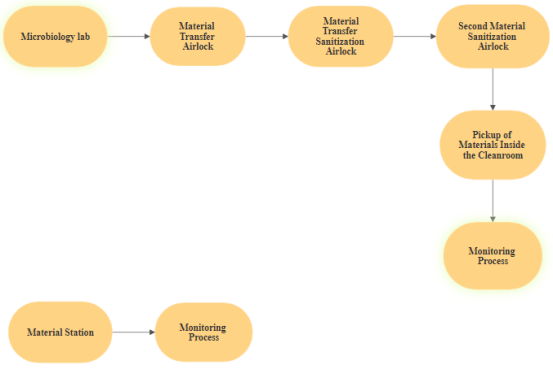


Table 3 establishes the contrast between the two processes. The first one is the current process that involved several steps. The original setup gathers the WFI materials in the microbiology laboratory and then transport them to the material transfer airlock. Then the items are headed to the first material transfer sanitization airlock, on this step the sanitization time is 10 minutes for each material transfer sanitization airlock. After that, an analyst acquires the materials and transfer them to the second material sanitization airlock. Then assigned personnel picks up the materials inside the cleanroom and in the last step, the monitoring process starts. On the other hand, in the proposed WFI collection process, will be establish a satellite area with materials previously located and transported inside the manufacturing area to simplify the previously mentioned process. As illustrated, the proposed setup time of materials only have two steps, which is gathering the WFI sampling materials from the material station and the monitoring process.

Figure 2

Satellite Material Location Inside Manufacturing Area

Figure 3

First Sanitization Room

Figure 4

Second Sanitization Room

Table 4

Data Time Collection of Two Weeks

Week 1 Day's	Time setup 1 (minutes)	Setup Time 2 (minutes)
Monday	70.11	6.02
Tuesday	72.30	5.40
Wednesday	69.03	4.55
Thursday	75.07	5.10
Friday	68.26	6.20
Saturday	74.15	5.18
Sunday	77.09	4.99

Week 2 Day's	Time setup 1 (minutes)	Setup Time 2 (minutes)
Monday	71.32	5.55
Tuesday	72.11	5.36
Wednesday	70.35	6.08
Thursday	73.23	5.20
Friday	70.54	6.11
Saturday	75.49	5.10
Sunday	76.32	5.02

Table 4 shows the time in minutes of two consecutive weeks. Setup 1 is stated as the original process and Setup 2 is the data collected from the new proposed process. Further explanation will take place on the next sections.

Table 5

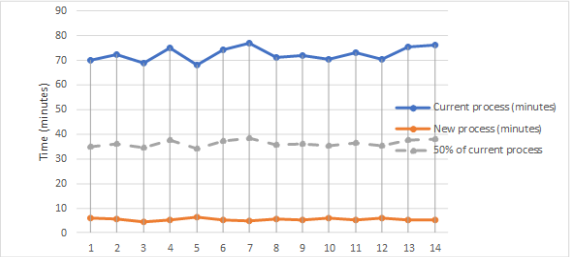
Data Obtained from Two Weeks

Current process (minutes)	New process (minutes)	50% of current process
70.11	6.02	35.055
72.3	5.4	36.15
69.03	4.55	34.515
75.07	5.1	37.535
68.26	6.2	34.13
74.15	5.18	37.075
77.09	4.99	38.545
71.32	5.55	35.66
72.11	5.36	36.055
70.35	6.08	35.175
73.23	5.2	36.615
70.54	6.11	35.27
75.49	5.1	37.745
76.32	5.02	38.16

The results presented on Table 5 shows the data collected of two consecutive weeks of Water For Injection monitoring process. In the data presented it is clearly visible process improvement having a satellite inside the manufacturing area. Evaluation and contrast of the graphical illustration is simple, since the differences between the results are huge. Figure 3 also denotates the established 50% decrease of time of the new process, also accomplished, much lower than the 50% previously established.

Table 6

Graphical Comparison Between the Current Process and the New Process with the 50% Reduction Graphical Line



On Table 6 graphical illustration of the collected data of two weeks is presented. In the middle, the 50% reduction of the objective established is shown. As illustrated, the new process is more than 50% efficient than the objective established since the values are very low and not even one single set of the values reach the 30 minutes line. On the other hand, the original process line is way up in the upper side of the graphical illustration.

Table 7

Results from Statistical Analysis

Assuming a Normal Distribution of Times in Both Processes

Current process (minutes)		*New process (minutes)*	
Mean	72.52643	Mean	5.418571
Standard Error	0.742102	Standard Error	0.134931
Median	72.205	Median	5.28
Mode	#N/A	Mode	5.1
Standard Deviation	2.776693	Standard Deviation	0.504866
Sample Variance	7.710025	Sample Variance	0.25489
Kurtosis	-1.11921	Kurtosis	-0.86815
Skewness	0.177103	Skewness	0.300374
Range	8.83	Range	1.65
Minimum	68.26	Minimum	4.55
Maximum	77.09	Maximum	6.2
Sum	1015.37	Sum	75.86
Count	14	Count	14

Hypothesis

$H_0: \sigma_1 = \sigma_2$

$H_a: \sigma_1 \neq \sigma_2$

Significance level is $\alpha = 0.05$

Test Statistic

$$F = \frac{s_1^2}{s_2^2} = \frac{7.710025}{0.25489} \approx 30.248445$$

P value for the test statistic,

$$ValorP = 1.46 \times 10^{-7}$$

Therefore, there is enough evidence to establish a difference between the standard deviation of both procedures. Obviously, the deviation from the new process is significantly less than the current one.

Table 8

Normality Test Data for the Current Process

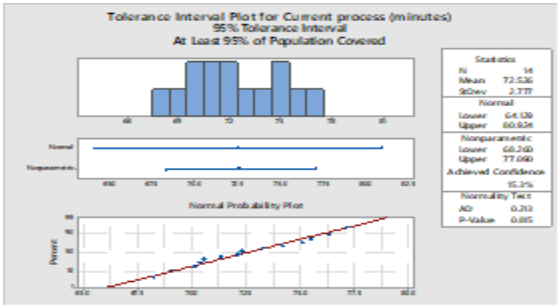
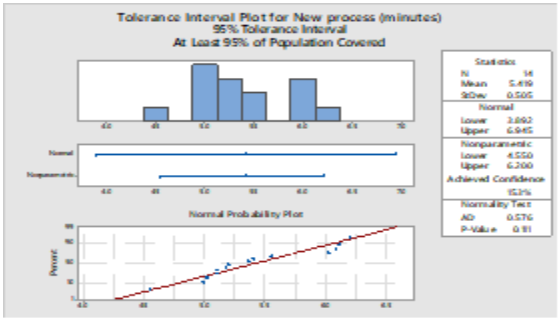


Table 8 shows the normal distribution and all the values were aligned quite close to the line. The P value found is 0.815, which determined that there is not enough evidence that the distribution is not normal.

Table 9

Normality Data Test for the New Process



On Table 9, for the new procedure, the data is less aligned, but still appeared to be close to the line. The P value found is 0.111, so it is less than the current process. There is not enough evidence either to say that the data do not follow a normal distribution.

CONCLUSION

During this research and according to the results obtained, development and successful demonstration of improvement has been showed. Innovation and efficiency in the WFI sampling process had been stated. The most important finding during this research is the unexpected results of a progress of more than 50% of efficiency in the task. Establishing the 5S structure in the sampling process really helped the results. The problem stated in the problem statement has been solved thanks to the statistical analysis made in section results and discussion. The contributions that the research brings are reduced the downtime in the WFI sampling process, increased productivity by eliminating waste and established positive economic impact to the pharmaceutical industry by reducing the process length.

Future research works recommendation will be to establish satellite area in all three manufacturing areas. This work will bring a lot of benefit to the company by increasing their productivity by reducing the cycle times in the WFI monitoring process.

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