Clean in Place Recipe Optimization

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Abstract *— This improvement project was based in reduce the fixed tanks and transfer lines Clean in Place (CIP) recipe execution by consolidating the Water for Injection (WFI) rinse and the WFI CIP recipes into one single recipe. This new recipe was used when system is employed for WFI collection and buffer preparation processes. DMAIC methodology was used as a tool to present the information required for the project. Is a series of steps used to measure the waste in an industry and improve the efficiency of it. These steps are Define, Measures, Analyze, Improve and Control. After implementation, a standard work was generated to be aligned with the time expected for each stage of the process. In general, the project obtained successful results reducing the new recipe 21% after the optimization performed in the process.*

Key Terms *— Recipe, CIP, Cycle time, and DMAIC methodology.*

PROBLEM STATEMENT

The goal of an improvement project is to reduce the fixed tanks and transfer lines Clean in Place (CIP) recipe execution by consolidating the WFI rinse and the WFI CIP recipes into one single recipe. This new recipe was used when system is employed for WFI collection and buffer preparation processes. The definition of WFI is water for injection, that describes that the cleaning is performed with water and some chemicals validated for the corresponding personnel to obtain a successfully cycle. Clean in Place can be defined as a process that is performed in the same place when the tanks are fixed.

As a Senior Associate Manufacturing, the researcher can identify this type of problem because is the day to day in the work area. The waste in process needs to be removed as soon as possible to obtain a more efficient and agile process, increasing the production in the area and satisfy client expectations. In some case this initiative could be avoided considering can cause additional cost and time for the company, but the industry needs to know that the associates can do a better job with the tools required. Barriers exists in all type of work, but the company need to challenge the process daily to be more competitive and if the employees encounter an opportunity area they need to work in the case.

Identified this gap of the current state of the recipe, the researcher saw that the organization have an area of opportunity that needs to be challenge with the consolidation of this two recipes in one. Improvement of the desired state of the process is focus on compensate time in other task and reduce the cleaning recipes cycle time.

Research Description

The research is about an improvement of an area of expertise in the industry. Optimization of these two recipes to one have significant benefits for the area. Is important to develop this study because can help organizations to reduce the cycle time. If an organization can reduce the cycle time of the process, then can eliminate waste in process and with the elimination of the waste at that time, can gain minutes to other tasks.

Research Objectives

The objective of this research is consolidating two cleaning recipes in one to be more agile and effective. The researcher expects to accomplish the benefits of reduce cycle time, obtain better labor utilization, increase the production, equipment availability, and meet with the schedule adherence.

The project seeks to reduce the process cycle time of ~4.10 to ~3.23, decreasing the waste time of the cleaning process in 21%. In other hand, with this objective on mind, the division can eliminate the repetitive task of create two recipes instead of one, reducing the recipe creation in 50%.

Research Contributions

The main contribution that the researcher will provide with the development of this project is an equipment availability in a short term. This contribution can benefit other areas because this division can formulate more products with this improvement and meet with the schedule adherence. The division will be able to reach this improvement project goal using the DMAIC tool.

The contributions of the project are more focus on time. The investigator specify time because the project implementation reduce process time to complete the cleaning required rapidly, avoiding additional steps of the recipe, as documentation. This improvement eliminates repetitive task and waste from the process. The project increase in man hours for technicians in the manufacturing since fewer exercises will be performed. In other hand, this assessment could be extended to other areas of the Annual Product Review, not evaluated as part of this project.

LITERATURE REVIEW

Clean In Place (CIP) is a method of cleaning that provide the elimination of the residues of a tank and transfer line with a recipe. The tank and transfer line are in stainless steel material and required some chemicals to be cleaned. These chemicals have some properties as detergents to culminate in an effective cleaning process. The process requires a creation of two recipes; the first recipe perform a rinse in the tank and transfer line before CIP process. When the rinse recipe ends, a creation of CIP recipe is required to execute a cleaning process with the properties validated to the process. CIP process pump a rinsing and cleaning through the same piping path as the product to eliminate product soil from all internal surfaces [2]. The advantages of the CIP system include the minimization of mistakes, keeps employees safe, production time, product quality, and utility savings.

The idea of consolidating these two recipes in one can provide some benefits to the manufacturing area as of reduction in the cycle time, better labor utilization, and meet with schedule adherence. As a result, the division gain more time for other activities, reducing waste in time. Consolidating the recipes, short the cycle time because the division can adjust the recipe with the parameters required to be effective and agile without any interference with the validation parameters.

As part of the improvement process, manufacturing area need to be aware of the risk in the process; risk that can avoid the success of the project. The project needs to be evaluated with the impacted areas to capture any gap in the process, system, documentation, or any area related to the recipe optimization. After the initiatives of the project, the researcher evaluated all these requirements with the team required to obtain effective results during the project and after the implementation. Initially, the more impacted area needs to generate a Change Control to document all the changes made during the improvement project. The principal area impacted is the automation area because they need to create a new recipe and challenge the recipe offline to prove the parameter and requirements validated. Other areas impacted are documentation, that needs to modify the step in the SOP. Supervisors need to evaluate all the impacted area before starting the project to understand more the process and the work that can be causing. In addition, this is not a barrier to start a project but help engineers to find other option to improve the process or area.

To reach the expectation, DMAIC methodology as a tool of 6σ projects are formalized and highly structured, making use of scientific approaches in the selection and management of projects. Six Sigma (6σ) projects use a Define-Measure-Analyze-Improve-Control (DMAIC)

structure, considered by many practitioners to be the primary reason for 6σ's success. [1].

METHODOLOGY

The method use for this project was DMAIC to introduce all the step required to obtain successfully results and Gantt Chart to estimate the time that required to complete each activity. The research was develop defining the problem statement, measuring the cycle time of the recipe, analyzing the current process, the improvement of the project and the controls required to culminate the project. Using these methods mentioned, engineers can obtain a better idea of the improvement project of the consolidation of the two recipes to one contemplating all the risk or areas impacted.

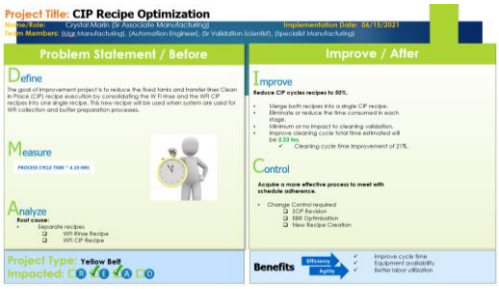


Figure 1
DMAIC

As define, the problem statement and goal expected were described to work with both in the process. For measure, analyze, and improve tables were used to identify the waste in process and the calculation were perform as the status. Control in other hands, was presented in a manner that the required areas sustained the improvement perform as a Change Control to includes all the controls required during and after the implementation. The figure presented can help the readers to understand in a short way the project and expectations. Figures and tables presented are visual aid that can be imagine easily to people that did not has the knowledge of the process but can have a better idea with the problem statement and improvement presented. Figure 1 explains the acronyms of DMAIC methodology in each stage.

In addition, the Gantt Chart could bring to the team members and relevant stakeholders the time expected for any activities and tasks in the process. In the chart, each activity and task are plotted on a linear calendar. The process of building the chart requires to consider all interdependencies between tasks [3].

Gantt Chart can present activities and due dates for the improvement project, that help the owner to coordinates meetings to comply with the time expected. Furthermore, the team members can organize and prioritized activities according to the time expected. If this type of tool was used, engineers can be more focus in activities of interest by week, month, years or as required. The table can be modified in any step, but it is much better trying to comply with the requirements in the time contemplated to include additional task that maybe are not contemplated at the beginning. Some additional tasks appear during the process because were not considered in the plan expected, so engineers need to be aware for changes in the process that can impact the initial project.

RESULTS AND DISCUSSION

The results of the project were successful because the method used was the correct one. The method use was the integration of two cleaning recipe to one of the fixed tanks and transfer lines. The initial recipes took a time of 4.10 hours overall. This optimization reduces the time of the cycle, time of documentation, time of the associate, and cost of the water use. Initially, the process has two cleaning recipes validated and after the research and meetings with the areas associated, the researcher suggested an improvement project to optimize the recipes. Talked with personnel areas required as cleaning validation, automation, process owner, quality, project manager, system, and manager to determine the best option to start with the project. After feedback was received, then start the project with the tools required, and areas of impact help in the process to be aligned and obtain better results.

Measure

This phase is interpreted regularly in table and graphic to evaluate the status of the process. As shown in Table 1 the status of both recipes (Rinse and CIP) needs to be consolidated to obtain a more efficient and agile process.

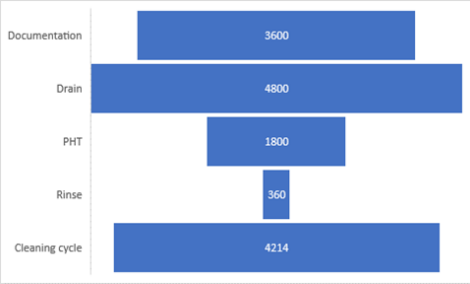
Table 1

Recipe of Rinse and CIP

Recipe 1	Time (sec)	Recipe 2	Time (sec)
Documentation	1200	Documentation	600
Drain	1500	PHT	600
PHT	1200	Cleaning cycle	4214
Rinse	360	Drain	1500
Drain	1800	Documentation	900
Documentation	900		

Figure 2

Recipe time (sec) before improvement



The data included in the figure above have the consumption time of each stage. If the chart was studied, many stages are repetitive. The total time of each stage were evaluated and consolidated in the project to reduce the cycle time of the cleaning recipe. Each stage was consulted with the validation personnel to determine the critical step of the recipe and they confirmed that no step can be eliminated, but can be consolidated.

Moreover, if a determined person as an owner of the project eliminate any stage, the corresponding personnel needs to re-validate the process that can cause major difficulties in the approbation of the project by the Project Management. The Project Management can approve the project but depend of the benefits of them; this type of project needs to be evaluated at this point because an improvement can be made to avoid additional cost, time, and risk. As mentioned, this is not a barrier to acknowledge the project, but it is better if personnel have all the tools required to perform the improvement.

Statistical analysis is the action of collect the data required to summarize the data. In this case, the data was summarized in a bar chart representing the current status of the process and the time that the division needs to improve at the end. This chart represents the repeated stages and presented the waste time in the process with the time accumulated for stages. The drain step is the longest process (in time) considering the accumulated time; this information facilitates to attack the root cause of the wasting time process.

Analyze

To analyze the waste in the process, engineers need to know all the process. These recipes are performed in stainless steel tanks and transfer line after WFI Collection or buffer preparation, due to after these processes, the tanks and transfer line still have residues. The material of the tanks and transfer line that are executed by this recipe are important in the manufacturing process because all the details are related to the process, the chemical substances used for the cleaning of this materials are evaluated and validated to obtain the equipment usable and available in the required time. The tanks and transfer line are represented in Figure 3. The equipment mentioned before needs to be available in a short term to continue with the process; for that, is important to improve the cycle time recipes.

The cycle time were validated to complete the cleaning process successfully to avoid contamination with different solution preparations. One of the root causes is that the four tanks are match with formulation rooms: 2 tanks for suite; 1 and 2 tanks for suite 2; for this reason, then is needed to re-process the tanks rapidly. After the root cause was identified, that is the separate recipes, then determine what improvement is needed, that is to consolidate the two recipes in one to have available equipment and better labor utilization. In Figure 3, we can observe the tanks and transfer line that are used and cleaned in the process.

Figure 3 [4]
Tank and transfer line

Hypothesis testing to reduce the cycle time was interpreted with the data collected as part of the measures. The hypothesis was validated because the process was challenged after the implementation and the results represented a high % of improvement. Data collected of the process were from 2019 until 2021 and differences indicated a major improvement for the client's areas that depend on the equipment used for the process. Although, if compared with the initial two recipes and the new recipe optimization in the tables, engineers can assume that the differences in the cycle time have changed in most stages in the process. This open to the manufacturing department a door to continue improvements in the areas of opportunity within the manufacturing process.

Table 2
Hypothesis Test (Summary Report)

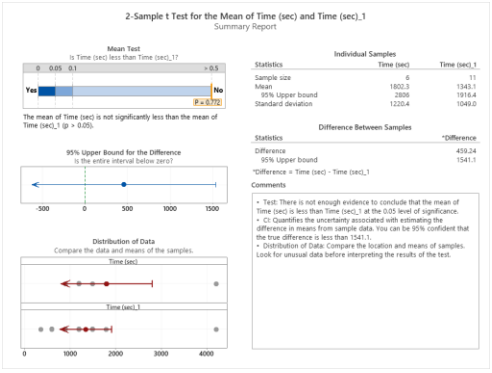
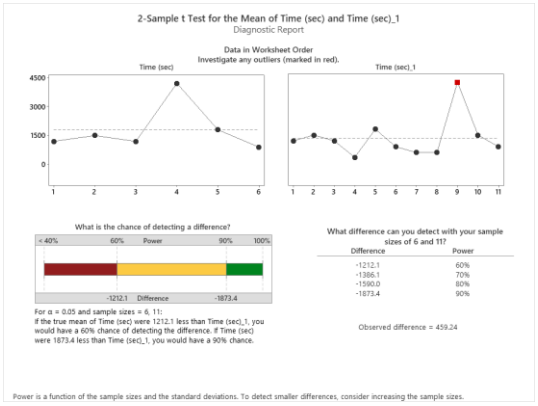


Table 3
Hypothesis Test (Diagnostic Report)



2-Sample *t* Test for the mean of Recipe Optimization/Time (sec) and Old Recipe/Time (sec) were identified to represent the null hypothesis and alternative hypothesis with the results. *P* value is a measure of the evidence force in the data against *H0*. For any *p*-value> α, *H0* cannot be rejected, and for any *p*-value α, *H0* is rejected. The interpretation of *P* value indicates that α is .05 and the *p* value is 0.77. *H0* cannot be rejected. There is not enough evidence to conclude that the mean of Recipe Optimization/Time (sec) is less than Old Recipe/Time (sec) at the 0.05 level of significance. This may result from having samples sizes that are too small; therefore, for the future a higher sample size is recommended.

Improvement

A new recipe was created and tested to evaluate the impact in the process, documentation, and system. After different types of test, the recipe culminated with a good improvement considering the recipe time reduced in 21 %. Finally, the observed recipe cycle time was 3.23 hours, a reduction in time consumed in each stage. Validation was not required after new recipe creation adjustment. Also, was observed that, with this improvement, eliminate steps, reducing the cycle time in the recipe optimization. The steps eliminated consumed additional time in the process as of additional documentation, PHT, and Drain. The consolidation of these two recipes in one

reduce the cycle time significantly and eliminates the multiple steps that did not impact the cleaning validation because any steps eliminated have risk parameters approved by validation personnel.

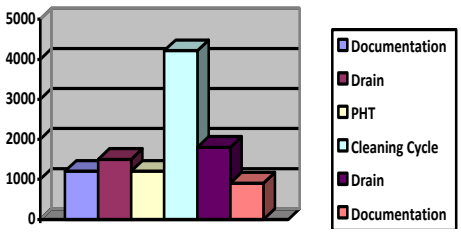
Table 4

Consolidation of the two recipes in one.

Recipe Optimization	Time (sec)
Documentation	1200
Drain	1500
PHT	1200
Cleaning Cycle	4214
Drain	1800
Documentation	900

Figure 4

Recipe Optimization



After the recipe optimization was evaluated, can determined that the improvement was significantly. Each stage was consolidated reducing the cycle time of the recipe, providing equipment availability and better labor utilization. The longest process is the cleaning process, considering the time of execution is 4214 sec. The steps eliminated in the new recipe were Rinse, Drain, Documentation of the first recipe and documentation and PHT of the second. These steps were evaluated with the cleaning validation before the implementation of the new recipe to analyze if any of the stage eliminated impacted the new recipe or if any have critical parameters. Cleaning validation process was not impacted; considering this, then proceeded with the projected plan, obtaining results much better than expected. New recipe generation obtained successful results in the testing perform by automation personnel and after validation reducing more time than was expected. In some cases, the new recipe process time ended in ~3.55 hours instead ~4.10 hours because the associates faced benefits in the documentation too.

Control

A new recipe was created to acquire a more effective process to meet with schedule adherence. This recipe was designed after change control creation to identify all the requirements as SOP Revision, creation of the new recipe, System optimization, and training to the associates. The recipe created contemplated all the risk assessment and critics parameter to include the information validated without impact in the validation process. After the implementation, a standard work was created to evaluate the improvement and that the operator keeps doing the process per standard work. This control is important because the associates need to sustain that the project improvement is effective after implementation and the company need to monitor the same.

Table 5

Standard work of ClP

Activity	Tasks	Time (sec)
Documentation	Enter to system	600
	Document tank and transfer line	300
	Create recipe and start	300
Drain	Disassembly	600
	Assembly	600
	System	300
PHT	Adjust equipment	100
	Execute recipe	1100
Cleaning Cycle	System	4214
Drain	System	1800
Documentation	Visual Inspection of equipment	200
	Close documentation	700

Standardized work is a very common tool used in the manufacturing areas due to the associated measure, the time for each stage after mean calculated for the execution of the co-workers, and evaluation of any task. The industries are interested in reducing budget and compressed project schedules. It allows a process to be analyzed for its steps, key points, and their corresponding reasons [5]. To introduce this tool in manufacturing process, the project owner must classify all the steps required per process according to task variety and task analyzability. Standardized work is not to make all tasks highly repetitive; the intention is to

define the best methods and to reduce variation in the work process.

However, to obtain desired results, the assigned personnel need to identify key points and reasons that were required to be a standardized work procedure. This tool can help associates segregate the tasks with other employees, maintaining a good communication with the corresponding tool. If a project must be performed with specific time, this is the perfect tool for that. In addition, this tool can help senior managers evaluate the productivity of the area according to the time expected for each stage. Although managers can obtain better results at the end of the process, employees must perform a standard work with the average of the process because is important to be focus on the initial plan and managers do not want that any associate compete in the environment work.

CONCLUSION

As the research has demonstrated, the project required the support of areas impacted for the improvement. The areas impacted were documentation, system, and automation. Test results were successful, and the project improvement has benefits for the area as of equipment availability, better labor utilization, and improve cycle time. The benefits are related to efficiency and agility for the process and area. Results can be defined as 21% of reduction in the recipe after the consolidation of two recipes in one, and the final time of the recipe optimize was 3.23 hours instead 4.10 hours.

However, the methodology used to describe the project can be to identify the problem using this type of tools and obtain better results. All projects can have a better idea, but they can fall at the end if they were unattended in any required phase. As a conclusion, successful results were obtained following all steps of DMAIC methodology. Finally, if all steps were evaluated and identified in the process, better results can be obtained. Associates perform some execution in a fast mode than others, but standard work can be performed to be aligned with all the teams. Standard work is a Lean methodology concept that can be define as a practice of setting, communication, direction, and improve standard. An improvement in the standard work can be made later; this is the plan of these tools as part of a continuous improvement cycle. If you have control of the initial plan, then something better is possible and could be different from others, considering other areas of interest, including clients. Other benefits can include takt time, work sequence, inventory, better labor utilization, and reduction of waste.

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