Process Time Reduction in Manufacturing Areas: Visual Valves Identification on Manufacturing Area specifically on Media Prep Area, Media Preparation tanks to Pursue Agility on the Visual inspections required before, during and after the Media Prep Solution are Prepared

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Abstract *— Time of production process and associate activities were evaluated for Media Prep manufacturing process on Juncos, P.R. The voice of the customer requested reduced time inspection process before, during and after batching preparative activities and process. DMAIC methodology was used to evaluate the production costs. Fishbone, Scatter, Grant Charts, and other tools were used to determine what was the possible cause of highest time associates take to find valves, and equipment in gray area, even though the valves are identified with its proper part number. Equipment and material identification were most probable causes. Improvements in procedures and identification tags were used to perform and established the new color code tags, based on the function and type of addition of the valves. Evaluated process and defined the color code for the valve and established a 5S in the gray area reduced time and cost, also process became more agile and effective.*

Key Term *— Agility, DMAIC, Grant Chart, Lean Manufacturing.*

INTRODUCTION

A continuous improvement project is an initiative that seeks the optimization of a product, a process, an area, or several of them within an organization. Extended execution time of visual inspections of valves and production tank lines during procedurally required beds to associates in the manufacturing area of building #6. The execution of this activity before, during, and after the manufacturing activities of a batch results in a delay to subsequent activities. The main cause of the time these visual inspections take is that the valves and lines of the tanks are not easy to identify visually. Each of these components has a unique identification number engraved on it, but at first glance they all look the same. To aggravate the situation, there are components that are not easily accessible, so it takes a little longer to get to them. This also gives way to human errors during the execution and documentation of the task since, due to the length of the process, many associates are exposed to the pressure of time to start other activities. This visual inspection came from a commitment established because high leaks observe in gray areas. During manufacturing media solutions with a particular product valve pressure increase and some leaks were observed during the validation phase, after adjusting pressure and flow rate, leaks were content, but as a prevention correction walkdown frequencies were implemented. These visual inspections are also performed by mechanics during the equipment maintenance process. The equipment identification will improve the activities during beginning, middle and end process, later the project is going to be leverage ton Preventive Maintenances for mechanics area.

Streamline the process of procedurally required beds for visual inspections of valves and production tank lines before, during, and after batch manufacturing activities. Reduce the incidence of human error during the task documentation process. Extend the improvement to maintenance activities. Reduce manpower cost rate per hour in the activity, with time reduction operational cost also reduce.

With the placement of a label or "tag" with a predetermined color code and the identification of each valve and line, it will be easier for the associate of the manufacturing area to identify them

visually during the walks. This will streamline the process of visual inspection of valves and production tank lines before, during, and after a batch's manufacturing activities. By reducing task time, you will reduce pressure on the associate and be able to document more calmly by reducing the incidence of human error. This improvement will also help in the visual inspections carried out as part of the maintenance. Refer to Figure 1. Also, an impact in labor cost could be identified as a contribution.

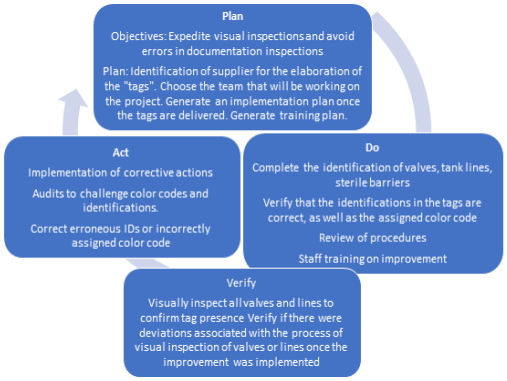

Figure 1
Project Process Chart using DMAIC strategy to improve process

Manufacturing pharmaceuticals are continuously looking to reduce waste to improve their processes and be more agile in their manufacturing process. Time and Cost are identified as top offenders in all pharmaceuticals. For that reason, continuous improvements and innovative ideas and projects are always identified and most of the projects are approved to improve process a met the goals expectations corporate goals and individual goals. For this project, the customer focused on reducing time for associates and process applying 5S system in gray areas and equipment identification color code.

Lean is a systematic methodology applied for continuous improvement that seeks to eliminate waste in a process to improve its productivity. Productivity is a measure of the efficiency of a person, machine, factory, or system in converting inputs into useful outputs. Lean Manufacturing principles were applied to this process to eliminate time looking for the valves providing a visual aid identification. Lean principles are to challenge the status quo, by continuous improvements project. Lean doesn't focus exclusively on reducing waste, these days, waste is defined as long wait times between steps in a process, context switching, rework, and unnecessary planning. Lean thinking also emphasizes holistic improvement. LEAN will be applied.

The Lean Philosophy was the main methodology for this project, for this reason it was observed the current process which has waste, time, and resources.

In this case, the associates spend a long time looking for the part number of the valve, that is in a chrome metal tag, as required on the 21 CFR 211.105 "Equipment Identification". The CFR regulations on 211.105-part A and B Equipment identification requires "All compounding and storage containers, processing lines, and major equipment used during the production of a batch of a drug product shall be properly always identified to indicate their contents and, when necessary, the phase of processing of the batch. Major equipment shall be identified by a distinctive identification number or code that shall be recorded in the batch production record to show the specific equipment used in the manufacture of each batch of a drug product. In cases where only one piece of equipment exists in a manufacturing facility, the name of the equipment may be used in lieu of a distinctive identification number or code" [1]

DMAIC methodology will be developed to effort in the customer needs and to improve the process. Define, measure, analyze, improve, and control is a data driven quality strategy used to improve process. Refer to Figure 2 [2].

The current process is performed by manufacturing personnel. Process will remain as usual, only a color code system for addition valves will be created. For example, acid addition valve tags are red, base addition valve blue, waste valve green. Preventive Maintenance is required for confirm the presence of "tag", make visual inspection to rule out or confirm the presence of

corrosion in the chains, confirm that the color of the tag is in accordance with the established code and that its identification is the same as that of the valve or line**.**

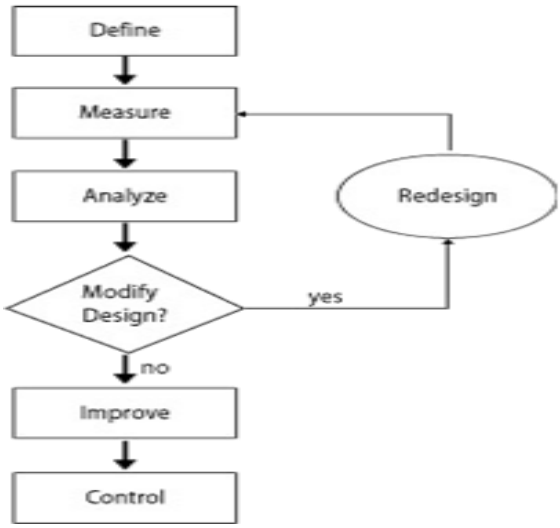

Figure 2
DMAIC Methodology Phases

METHODOLOGY

This project will apply the DMAIC (Define, Measure, Analyze, Improve, Control) methodology to improve the time, equipment identification and eliminate the non-value time in before, during and after inspections. The five phases that structure the process in which this project is based are:

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- Step 1- Define: consisted in describe the problem, select a project team and stakeholders, and develop goals based on the voice of customer. The team defines the problem, identifies customers and their requirements, and selects the project team, including members who are directly affected by those issues related to the problem.
- Step 2- Measure: is to measure the process to determine its current performance and quantify the problem. Baseline performance is established with trustworthy data. Data and information about the current process is collected to understand the problem.
- Step 3 - Analyze: the cause of the problem is identified. The critical inputs are identified. These critical inputs are the drivers of performance.
- Step 4 - Improvement: consists in improving the actual process by designing solutions to fix and prevent problems. Potential solutions are identified and evaluated, and the process is optimized. Process capability and project finances are estimated.
- Step 5 - Control: this phase is controlling the improvements to keep the process on the new path. This phase promotes continuous improvement for a process. This is the stage that establishes mistake proof, long term measurement and reaction plans[2][3]. The team develops standard operating procedures, establishes process capability. Project are updated, verified, and reported. Control is transitioned to the process owner, and lessons and opportunities are documented[4].

RESULTS AND CONCLUSIONS

This project came from the need to improve the processes. A focus on a culture of continuous improvement in pharmaceutical environment.

Excessive costs in the waste of time, associates task and manufacturing process areas were identified as a potential problem to be reduced using Lean Methodology and DMAIC approach.

A multidisciplinary team was selected to work with this project. The team consisted of one (1) Project Manager, three (2) Mechanics Department representatives, one (1) Operational Excellence representative, one (1) Capital Support representative, one (1) Quality Assurance Specialist, two (2) Associates Manufacturing. The team developed a project charter that presented the process problem, the process performing today, baseline, and performance after executing the process improvement. Activities for the team during the DMAIC measure phase included: evaluate data of the current process, focusing on time of each step, having meetings to discuss, and

executing brainstorming activities for viable solutions.

The problem statement is the extended execution time of visual inspections of valves and production tank lines during procedurally required beds to associates in the manufacturing area of building #6. The execution of this activity before, during, and after the manufacturing activities of a batch results in a delay to subsequent activities. The main cause of the time these visual inspections take is that the valves and lines of the tanks are not easy to identify visually. Each of these components has a unique identification number engraved on it, but at first glance they all look the same. To aggravate the situation, there are components that are not easily accessible, so it takes a little longer to get to them. This also gives way to human errors during the execution and documentation of the task since, due to the length of the process, many associates are exposed to the pressure of time to start other activities. These visual inspections are also performed by mechanics during the equipment maintenance process.

In this stage, project plan, cost and a workload distribution plan were established. The project budget of $25,000.00, was established for the 12 weeks duration. Audit Visual and recurring inspections was carried out to verify that the tags are in compliance.

The annual budget allocated for the replacement of "tags" and implementation of corrective actions was audited.

The main goal of this project is to obtain a time cost reduction of between 15 to 20% focused on the voice of the client. Streamline the process for the required beds for visual inspections of valves and production tank lines before, during, and after batch manufacturing activities. Reduce the incidence of human error during the task documentation process. And extend the improvement to maintenance activities and other main and support areas. Based on our company agility goal.

In this stage, the data gathering was obtained from MES system. First, we define the media solutions to observe, according to base, acid, or neutral solution. The query was focused on batch process from the beginning to end based on the start and end hour recorded on EBR system. Then, the inputs and output were identified. The data was classified.

The statistical analysis was performed for 10 months and 12 months from January and December 2020 and 2021(around 100 samples, Refer to Graphs 1, Different Stages Data Evaluation). The mean for the time for the process is around 60-80 minutes in each walkthrough. (3 minimum walkthroughs per batch). A similar behavior was shown in the Cell Culture Area, Purification Area, and Buffer Area, also in mechanical PM process the estimated time increase to 75-90 min. Refer to Figure 3.

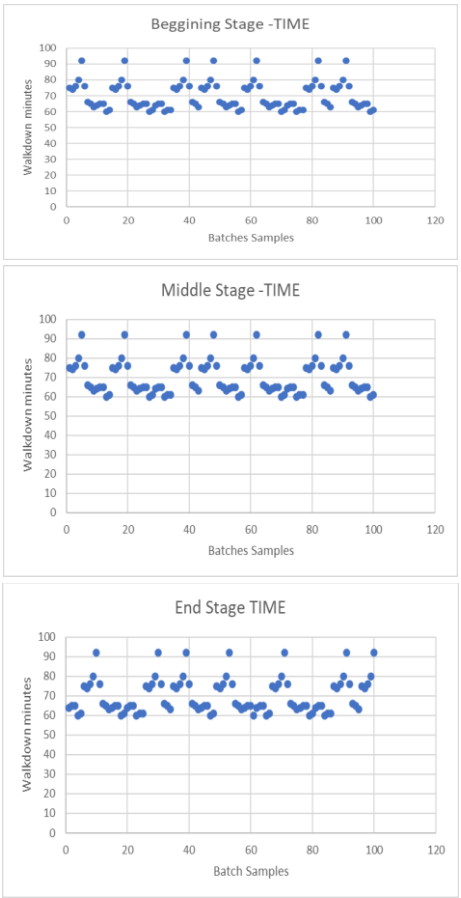

Figure 3
Different Stages Data Evaluation

As part of the evaluation process associates and salaries were analyzed to see if there is any improvement in cost. The average salary for a

manufacturing associate is $ 18.00 per hour. If we used two (2) manufacturing associates, in every process beginning, middle and end with an average between 60- 75 minutes, the salary rate of $54.00 per one and half hour.

The previous analysis and information were necessary to review the tasks in the frequencies, and the reason/purpose of the work assignment. This was performed through Gemba walks and interviewing the associates, media prep area but extended to mechanics, cell culture, buffer, and purification area.

In this phase the cause (s) of the problem are identified. Inputs that have a strong relationship with the outputs and root-causes were determined. During this exercise were evaluated material, method, valves, SOP, and management. The top offender of the current process that are identified as visual equipment identification, based on distinction, not the required identification by CFR regulations[1].

For equipment, the design of the equipment was evaluated, and decided that with the placement of a label or "tag" with a predetermined color code and the identification of each valve and line, it will be easier for the associate of the manufacturing area to identify them visually during the walks. This streamlines the process of visual inspection of valves and production tank lines before, during, and after a batch's manufacturing activities. By reducing task time, you will reduce pressure on the associate and be able to document more calmly by reducing the incidence of human error. This improvement will also help in the visual inspections carried out as part of the maintenance.

After evaluating the causes of the findings during the it was determined actions to be taken to correct or prevent these failures. Some of these actions are:

- Finding #1: Identification require for all valves all was the same
  - To create an agility measure, valve must be identified in color code and in a 5S diagram per area. Visual aids are often common opportunities to facilitate and provide time adequacy for task.
- Finding #2: No clearly instructions
  - During the evaluation of the procedure, it was found that valve number was the only information provide to perform the walkthrough, the intent used of the valve was not clearly state on the procedures. For example, acid, base, neutral or waste valve. The gray area design is not included in the SOP for references.

Particularly, creating innovate solutions using technology and discipline. For this stage, Project Management Fundamentals & Kaizen DMAIC tools were used to develop and deploy an implementation plan [2][3]. The following actions and their benefits were part of the implementation plan.

These actions and benefits included:

- Complete the identification of valves, tank lines, sterile barriers. Refer to Figure 4 Tag Photo.
- Verify that the identifications in the tags are correct, as well as the assigned color code
- Review of procedures and add all the relevant instructions and new initiatives
- Training staff on improvement.

Figure 4
Tag Photo

The main purpose of this phase is to control the improvements identified, keep the desired path. This phase promotes continuous improvement for a process. This phase requires the development, documentation, and implementation of the established plan. Finally, institutionalize the improvements through the installation of the visual

color code tags, and established the training sections and explain to associates its benefits. Some tasks periodically monitored area:

Preventive maintenance will be created with bi-annual frequency for which the work plan will require:

- confirm the presence of "tag", make visual inspection to rule out or confirm the presence of corrosion in the chains
- confirm that the color of the tag is in accordance with the established code and that its identification is the same as that of the valve or line.

Using DMAIC approach it was possible to reduce waste of time and improve associates' activities during media preparation. After collecting and classifying the data, Lean Manufacturing tools were used to determine the possible cause of the highest waste of time in batching process, solutions were started much later than expected because the finding of the valves for inspections. Same, at the end of the batch, the completion of documentation was not contemporaneous because of the time wasted looking for the valve, to the documentation errors were highest by this moment. During process inspection were not included because data cannot be collected since the process is continuous and equipment is not stop for this inspection. Even though the valves color codes tags, they help to improve the time during this inspection. Inspection is required by a regulatory commitment because of the highest leak identified in the past, so improvement to this walkthrough is important and considered because this task was added as a preventive action. Improvements in the procedure, established a bi-annually preventive maintenance and confirming with associates the improvements is part of the scope in the control phase.

A reduction from 60 -75 min to 30-45 min, includes the walk to gray area reduce the time to start or end the process and improve the good documentation practices. In the case of preventive maintenance, the time reduction forms 75-90 min to 45-60 min, this will increase the time to perform the PM and to document contemporaneous, clear and with calm, other areas and support areas are part of other project extending this one to those areas. This represents a reduction of hours released annually for the associates to perform other tasks. Refer to Figure 5.

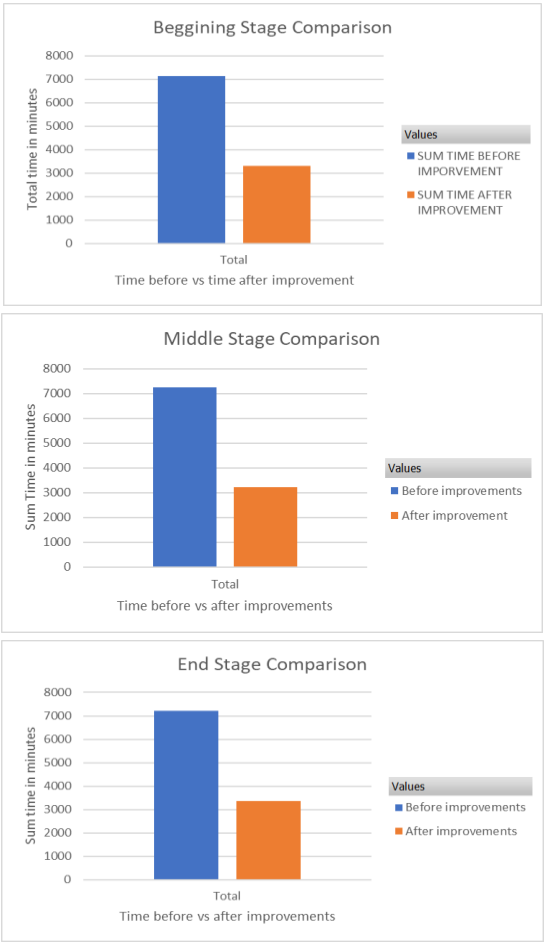

Figure 5
Comparison and Improvement Data

Even though the improvements were successful, and the expectations and goals fulfilled. The lessons learned, and opportunities to improve the batch process are:

- Extending program improvements Other Operations Areas (Cell Culture, Purification, Buffer, and Mechanics).
- Evaluate visual aids, or visualization tools for other process, for example color code folders per products for artifacts and related documents.

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