Unidirectional Flow Gasket

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Abstract *- To reduce the number of deviations that occur annually in the plant, through a design, it is expected to reduce this problem taking into consideration the cost factor, lead time and the quality of the products made. Using Lean Six Sigma, applying the DMADV methodology as a guide to define the problem, measure the parameters of the scope of work, analyze the current problem, design the part that will improve the process to be achieved, and finally validate that in effect it meets the objective of the research, to reduce the number of deviations. During the research, a reduction of 54% was observed, having a profit of $218,750, decreasing the original value of deviations occurred. It is worth mentioning that through this research, researcher saw improvements in the lead time process, cost, and even process quality.*

Key Terms *— Buffer Tank, DMADV, Improve Lead time, Lean Six Sigma.*

PROBLEM STATEMENT

Currently, as in any pharmaceutical organization that focuses on service and quality systems, a series of important factors are taken into consideration that are key to offer an excellent operational service in the market. It is for this reason that the focus throughout the manufacturing process is the quality of the different procedures that are executed on a daily basis, emphasizing on improving services to meet customer needs. To meet the focus, is important to draw a line of goals and approaches that allow to perform the work in an efficient way, in which always have as a priority to make improvements to a system to optimize it, exceeding the expectations to be achieved along the product that is being carried out to meet the needs of both the customer and the desired product.

Research Description

A company, which operates 24 hours a day, must use its resources constantly without stopping to meet several batches annually, for the various products that are made such as: Enbrel, Repatha, Epogen, Aranesp, among other products, that improve the quality of patients daily. During the process of making previous products, different problems arise daily, among them the deviations, which are known when the product that is being carried out is compromised in some way, either by an operational error or simply human error. Being deviations the biggest problem that can occur during the process, is the one that is sought to improve to obtain a quality, affecting the lead time, costs, quality, service, and product integrity. It is for this reason that the researcher looks to design a product that fulfills with characteristics that meet each of the tanks to prevent such problems continue to arise. Among them is to prevent products related to Personal Protection Equipment (PPE) fall into the same, plastics, that may affect the integrity of the product. As part of the process, try to make the operator feel comfortable working, since working 12-hour shifts compromises many factors that can affect the integrity of company products.

The focus is to minimize the number of deviations that occur on a weekly, monthly, and annual basis to reduce the amount of lost time, which represents cost and the quality of the product.

Research Objectives

This research seeks to reduce 54% of these deviations caused by errors made by the operator, who executes the different tasks or activities related to the pharmaceutical products carried out in the manufacturing that are being achieved by batch quantity, which seeks to maximize and increase the production of biomedical products without being interrupted by the various errors that may occur.

Research Contributions

As a biotechnological, pharmaceutical companies that currently operates in Juncos, Puerto Rico, that makes biomedical drugs, has as its focus to improve the quality of life of their patients. To carry out, there is an order that consists of a series of processes that at any time can affect the integrity, known as deviations, which generate losses, lack of integrity, lead time, and above all the integrity of the product as the main emphasis. The realization of this design contributes to all the factors that are considered important within the manufacturing process or better known as Good Manufacturing Process (GMP). Some of these characteristics are efficiency, integrity, cost, and above all, safety. One of the techniques to be used during the process of the selected methodology will be the application of Lean Six Sigma, because it is the one that seeks to minimize product losses. In addition, this research seeks to focus on customer needs and how the quality system can see improvements in the production and manufacturing system.

LITERATURE REVIEW

For years, manufacturers working with regulated drugs have used different organizational methods that have helped to structure a system that complies with the main approaches, using as main tool Six Sigma, a methodology that focuses on the needs of the customer or consumer of the product that is being carried out. On the other hand, the method of Lean Six Sigma is another resource that is used or applied much within the industry, due to the combination of focus on both customers and processes that are considered waste, which seek to reduce what is lead time, efficiency, cost, among other factors, that are considered within this quality to meet the goal to be achieved.

Throughout time, different manufacturing companies have sought to improve the different processes that are carried out the different quality processes, for this, the efficiency and effectiveness of the same; in this instance, focused on medical products, which directly help patients. William Shakespeare once said, "Our bodies are our gardens; our decisions, our gardeners." For this reason, it is important to be able to implement the correct methodology with an orientation to patients.

Over the past 30 years, biomedical manufacturing has been focusing on the productivity of the medical products that are worked daily. During these, a series of deviations occur, a term known as a malpractice, either by the plant operator or a system failure, affecting the desired quality. Many of these problems represent losses in time, cost, quality, safety, being a problem that stops and affects the quality of the product being made. As many organizations have different protocols to work with them and to solve the problem that affected the achievement, therefore there is a Standard Operation Process (SOP) guide, which indicates the operational steps to follow when this type of incident occurs.

It is for this reason that this research proposes to make or create the implementation of a piece using the material 316, which will be placed in the upper part of the hatch of the tank to be worked to decrease the number of deviations that occur annually, with the purpose of reducing losses in cost, time, quality, and safety.

Some of the main causes that cause this type of error in the system creating the deviations are plastics, glass, Personal Protection Equipment (PPE) tools, among others. With this new implementation is expected to reduce this number of deviations to 55%, increasing using as a tool the methodologies of Lean Six Sigma and DMADV to meet research objective or goal.

DMADV is one of the most applied methodologies within the pharmaceutical since it describes through a series of five steps a series of phases which are composed of: define, measure, analyze, design, validate. (a) **Define** the obstacle that is being posed and how it will be solved (b) **Measure** the parameters that will be used to solve the problem that is posed (c) **Analyze** to think what tools will be used to meet the objective or goal (d) Implement a **design** that demonstrates how the problem will be solved (e) Analyze to think what tools will be used to meet the objective or goal a design that

demonstrates how the solution of the problem is going to be carried out and finally (f) **Validate** to verify that in effect the problem or investigation proves by means of calculations that it was a success and fulfilled the goal of improving a quality system using the correct and applied methodology. It is for this reason to be applied has or offers many opportunities for continuous improvement to the quality that seeks to be improved.

METHODOLOGY

To carry out the following research researcher will use the methodology of DMADV (Define, Measure, Analyze, Design and Validate), due to its focus in analysis and validations, two factors of great importance on the other hand, the implementation of lean six sigma will be vital to identify losses with a focus on customer needs, to optimize a quality process.

Define Phase

- Conduct meetings and interviews with the employees who work on this issue daily to see what solutions they have or want to be worked on to improve the process.
- Raise the problem to the client able to work on it, until finding a solution that meets the established goal of continuous improvement.

Measure Phase

- Measure the monetary losses caused by this process.
- Perform a Value Stream Map to see the result of the manufacturing line.
- Perform a Voice of Customer (VOC) to see the customer's needs and see how to satisfy them.
- Processes that are related to the interaction of the product to be improved.

Analyze Phase

- Perform a Fishbone diagram to identify the problem to be solved through this research.
- Identify the problems or causal variables that affect the product and its different components during the manufacturing process.

Design Phase

- Conduct a brainstorming individually collecting ideas to improve a system being studied and one together with the operators to see what other ideas they can share to the next research.
- Make a possible design using the SolidWorks platform to give the reader a clearer idea of what is to be done to reduce the number of deviations that occur during the different processes that are carried out.
- Define the different implementations that can be carried out to be able to design the product.

Validate Phase

- Validate that the applied parameters and conditions meet the customer's needs.
- Validate that in effect organization’s system was a success which meets the company's reduction goals.
- Execute a training that shows the correct use of the part to be implemented to give the proper use of it.
- Identify what improvements can be implemented to our part to increase the percentage of deviation reduction.

RESULTS AND DISCUSSIONS

1. Define

Currently, the leader of manufacturing companies in Puerto Rico has been affected by a series of deviations, a term used to identify processes that have been affected or compromised when talking about the quality of a product, this throughout history has represented monetary losses. This process is a very distinctive within the organization, since it is the process where a process is conditioned to be able to cultivate a cellular process used to develop medicines for the home, to improve the quality of life of patients. Now this process has been identified as a process of

continuous improvement to expand a quality system by increasing many factors that are affected within the manufacturing process, which want to be improved to avoid losses and reduction of quality of the products that are made to patients. As a result, a project charter was developed to demonstrate the origin of the problem and how it will be worked throughout this research to minimize the losses that are seen daily in the workplace, which can be seen in Figure 2.

This brainstorming process, as can be seen in Figure 3, is carried out using as a tool the different employees who work operationally in the manufacturing area of the plant working directly with the different products that are made daily to see what ideas arise to improve the problem that is being brought related to the deviations that arise during the buffer processes. The following suggestions have been taken into consideration to solve the research problem that we are trying to solve to see improvements in terms of cost and quality processes.

During the measurement phase, an analysis was completed using the corresponding data to be able to carry out this process and to be able to understand the actual product cost problem when a deviation occurs during the processes that are carried out.

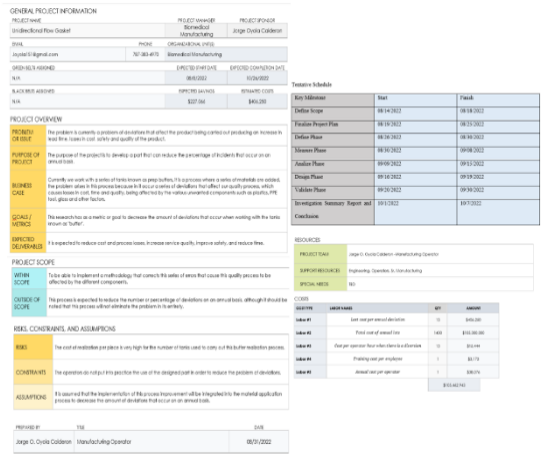

Figure 1
Project Charter of Buffer Prep

Brainstorming

Idea	Pros	Constrains	Contributors	Ranking (1-7)
Divide the group with more members	Increased safety when applying solutions	Increased amount of work	Sr. Manfacturing Operator	7
Integrating a fixed part to the tank	Decrease in deviations	Higher cost inflation	Process Engineer / My person	1
Use PPE equipment when required	Unnecessary equipment	Increased security in the area	Operators	4
Apply the solutions in a manner homogeneous	The weight of the product has a great influence on the application of the product.	Weight may not be the most appropriate	Operators / Sr. Manager	5
Always have a supervisor in the area	Reduction of errors during processes	It is not possible to participate in all activities	Operators	6
To have the necessary equipment	Reduction of lead time	The work would not be reviewed	Operators	2
Use funnel to apply solutions	Avoid loss of product or solution	Increase in application lead time	Operators	3

Figure 2
Brainstorming for Ideas Related to Define de the Investigation

This buffer process is composed of 4 phases that define the SIP/XOL process that is performed to create the required connections or line so that the tank can make the required water consumption to be able to apply the different solutions. The second step is the consumption of the materials to be used as containers such as filters, materials such as salts or chemicals to be able to use them. The third step is to apply the different solutions needed to successfully perform the buffer tank and to develop the required or necessary product, a recipe is made based on the product using the OIT (computer used to exercise the different functions related to the manufacturing process of the plant) process that can take about 5-8 hours of work to complete. The fourth phase consists of transferring the material to either a supply tank or the bags, to collect the sample and read the sample to see if the results of product batch match the results as stipulated by the SOP after having standardized the reading equipment. These four phases define the entire process to perform a buffer prep process and measure the scope of work that is required to understand the objective of our research.

Now, when talking about buffering, the process can take about 10 hours approximately, because in addition to considering the lead time of product creation, a series of cleanings must be performed to the tanks which consists of 4 phases, Clean in Place (CIP), Pressure Test (PT), Steam in Place (SIP), and Water Point (WFI Point).

For the first phase, a cleaning process will be carried out in which a series of connections will be made to execute the same and carry out this cleaning process. The second phase or process consists of the removal of the connections that are made to carry out the cleaning of the tanks that are working. It should be emphasized that the volume of the tanks varies, where the lead time of each one works independently. The third phase consists of the sanitation of the lines to be used for the product to be carried out. This being one of the shortest processes in terms of time variation and finally have the last phase. This being a very simple one, since only a recipe must be made using the OIT of the manufacturing area in which the process is being carried out. In this way, the operators can measure the different processes to determine the different costs, deviations and everything that must do or is related to quality.

2. Measure

Figure 4 shows a value stream map, which represents the process that needs to be carried out to make the different products that are made daily for patients. Shows how it is carried from the batch order process, where about 70 batches are produced annually, which represents an amount of 1,500 tanks per year. That figure illustrates the amount of lead time of each of the processes using as a reference the connotation of minutes to have a homogeneous pattern in the process to obtain company results as the total amount of lead time with a value of 11,185 minutes of process and change over with a total of 1,710 minutes. These two results show the amount of duration of the processes from its origin to be delivered to the consumer or customer.

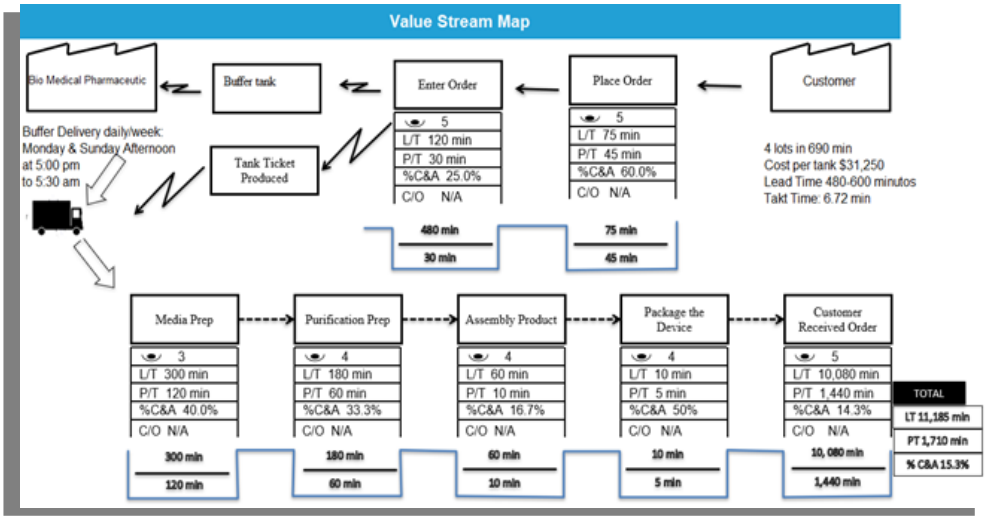

Figure 4
Value Stream Map

Figure 5 presents a series of calculations that will help both the reader and the researcher to measure costs. The following calculations demonstrate and measure the amount of losses that are generated on an annual basis when a deviation occurs during a buffering process, where it can be seen from the operator costs, training per employee, cost per operator hour when there is a deviation, total cost of batches on an annual basis, and finally the costs lost due to deviations on an annual basis. Using the following reference of Bement and Mitra [1] helps company to improve its quality process and necessary tools to understand the processes of continuous improvement.

The purpose of this research is to reduce the value in costs for deviations of $406,250 dollars

annually and obtain a reduction of $187,500 dollars to achieve only an annual loss of $218,750 dollars.

$$Cost\ of\ annual\ deviation\ loss$$
$$13\frac{desviation}{annual}\left(\frac{31{,}250\ dollars}{1\ desviation}\right) = \$406{,}250\frac{dollars}{annual}$$

$$Total\ cost\ of\ annual\ lots$$
$$= 1{,}400\ tanks\left(\frac{75{,}000}{1\ tank}\right) = \$105{,}000{,}000\ dollars$$

$$Cost\ per\ operator\ hour\ when\ there\ is\ a\ diversion$$
$$= 12\ operator\left(\frac{\$19.80\ dollars/hour}{1\ operator}\right)\left(\frac{5\ hour}{1\ desviation}\right)$$
$$= \$1{,}188\ \frac{dollars}{desviation}$$

$$Cost\ of\ training\ per\ employee$$
$$= \left(\frac{\$238\ dollars}{12\ hours}\right)\left(\frac{1440\ hours}{9\ month}\right) = \$3{,}173\ \frac{dollars}{month}$$

$$Annual\ cost\ per\ operator$$
$$= \$3{,}173\left(\frac{dollars}{month}\right)(12\ month) = \$38{,}076\ dollars$$

Figure 5
Data Entry of Calculus

To develop a better understanding to demonstrate a complete process and how it is impacted, a system was developed via a diagram known as Supply, Input, Processes, Outputs and Customers (SIPOC), represented in Figure 6. A series of five steps define the importance of it, where in the first step is the supply part, responsible for supplying such as customers, contractors and other factors that provide some entity; then the inputs that are orders, products, money.

SIPOC diagram

Suppliers	Inputs	Processes	Outputs	Customers
Client or customer	Orders of clients	Buffer Prep	Orders are entered	Customers
Retail Customers	Orders from suppliers	Media Prep	Money received	Managers Department
Same company in other states	Product demand	Purification Prep	Data entry	Product Quality
Other buildings	Amount of money	Assembly team	FDA metrics	Safety
Contractors		Up stream		

Figure 6
SIPOC Diagram

As a third step is the process; this step describes what kind of development is being carried out to create a manufacturing product. As a fourth step, are the outputs such as data, orders, among other things; and finally, the focus on service. This is the most important factor or one of them to carry out this whole process, as it is the demanding part that requires some parameters that you want to be met, where as a manufacturing process is achieved to meet certain metrics or goals of quality products.

3. Analyze Phase

In this next phase, researcher will explain in more detail the different reasons why the deviations during the different processes affect so much the quality and integrity of the products that are carried out during the processes of this one. Currently, there are about 13 deviations per year causing a loss of $406,250 dollars. It has been found that within that number of deviations between seven or eight are caused by human error. Some of the main causes that affect this process are due to unwanted components that were introduced by mistake into the product being manufactured such as plastics, glass, tools, PPE, gaskets, among other factors, that affect the integrity of our products.

With this research it is expected to be able to reduce this percentage of losses by 54% of the costs.

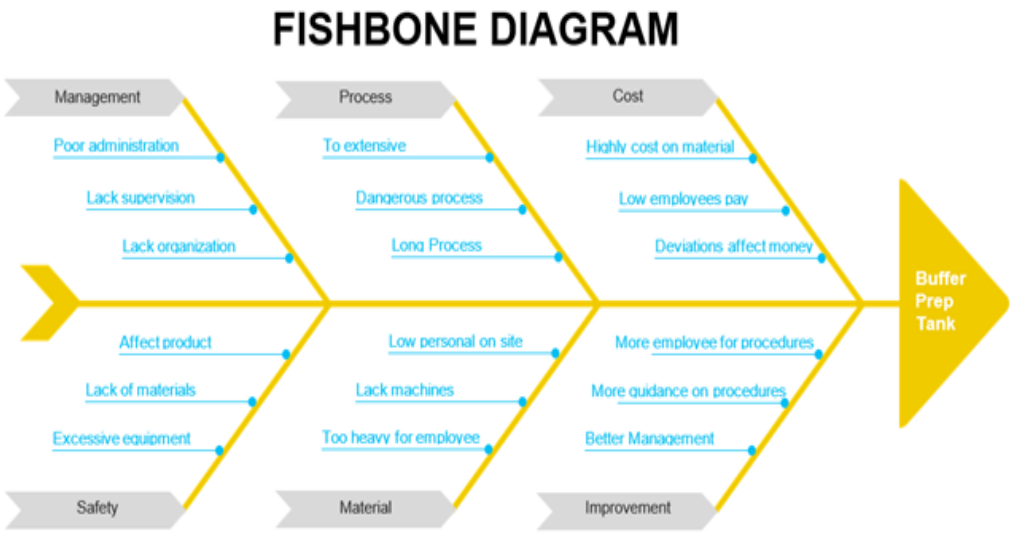

Figure 7
Fishbone Diagram

To analyze the possible problem of causes and effects of this research and how it is affected by the different deviations that are seen and found impacting the products and quality, an explanatory diagram was made in Figure 7, which explains all the causes that directly affect the performance of creating a buffer when it is being performed. Now, each of these causes or problems has a possible solution; however, this is a biopharmaceutical company that has been operating for about 30 years, and the opportunities for growth or change have been few as described in the image presented. Next, Table 1 shows the improvements that can be made to improve this process.

Table 1
Root and Cause Table

Title: Improvement solutions for Unidirectional Flow Gasket			
Number	Source	Potential Root Cause description	Improvement Solution
1	Man, error problem	Management	Leadership is vital in each of the processes that are carried out for this reason it is a point of opportunity to improve being a very poor one in the plant.
2	Man, error problem	Low employees pay	Pay is often an important factor when it comes to employee performance.
3	Man, error problem	Long process	12-hour workdays can affect the various processes that are performed daily.
4	Man, error problem	Lack organization	Organization is an important factor so that everything can flow within an organization to avoid future mistakes.
5	Man, error problem	Dangerous procedures	Many of the tanks that are made use aseptic chemicals that can affect the health conditions of the employees/operators.

6	Man, error problem	Material too heavy for employee	Many of the materials to be used as salt solutions have a weight of about 35 lbs. This is a factor that can be corrected by distributing the weight over a larger number of bags.
7	Man, error problem	Low personal on site	The staff in the area is not sufficient to cover all the tasks that are seen daily in the field, increasing the employee rate decreases errors which avoids cost losses.

4. Design Phase

Figure 9 presents a prep buffer tank, which is composed of many parts, but the most vital are listed within the image being five pieces of our interest.

1. Valves that control the pressure of the tank and connections made to carry out. It should be noted that this is an extremely important safety factor due to the amount of pressure that can be found within these systems, where it is around 15-24 psi of pressure.
2. Spray Ball, the purpose of this small one is simply for the tanks of greater volume, when the cleaning of these, can be done in a uniform way, because its large size makes it impossible to be cleaned autonomously as the other tanks that work, being this a vital tool for this process of CIP.
3. Hatch is the focus of this research, because in this section employees would be placing researcher design to improve the system when applying different substances or chemicals inside the tank.
4. Agitator is the piece that is responsible for homogeneously mixing the product so that the integrity of it meets the standards of the SOP as stipulated by the quality process, after making the readings of PH or conductivity.
5. Sampling collection, in this section researcher collect the result of the analyzed tank to be read after having standardized our equipment, so that in the process of delivering it to the quality team, it complies with the parameters of the EBR (process that is necessary to determine if the process carried out was correct).

It should be noted that each of the tanks performed have a cost between $50,000- $100,000 dollars; this varies depending on the volume of tank capacity.

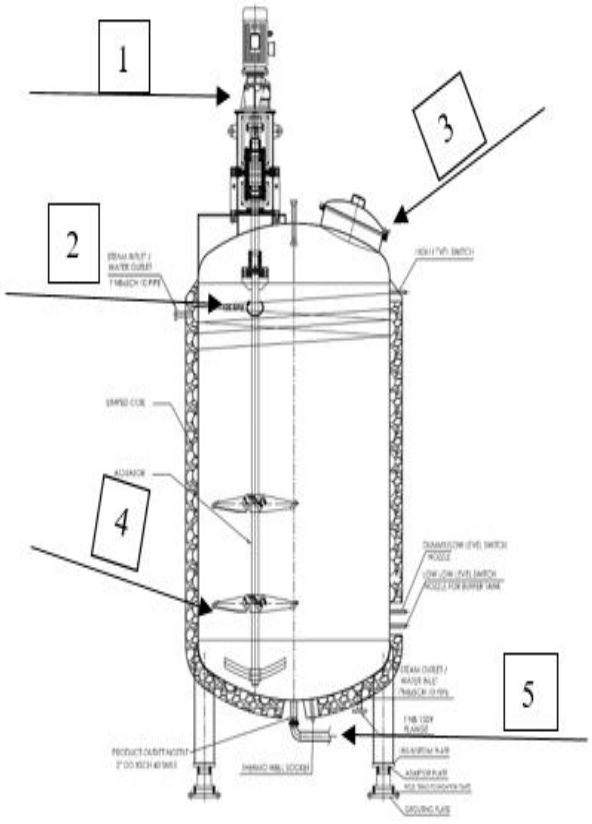

Figure 9
Buffer Tank Prototype [1]

The following design represents the piece that is desired to implement to reduce the number of deviations being this a generalized piece, because the dimensions of the tanks that are used varies according to the volume of the same. Kreft [2] discusses the properties that benefit the product being used to select the correct material.

Modeling and simulation of heat production in a local heating installation including a batch-fired straw boiler with a buffer tank. The material selected to be able to develop the piece was Alloy 316, since it is sought to implement a piece that will withstand the different chemicals such as acetic acid, being a

resistant metal alloy this problem of decomposition of the piece will not be one that has to be contemplated with so much frequency. The purpose of this design is as follows:

- Prevent PPE equipment from entering the tank
- Plastics
- Tools (pliers, torque wrenches, among others)
- Glass (larger than 2x2 inches in size)
- Straps
- Gloves

Figure 10

Unidirectional Flow Gasket Solid Works

5. Validate Phase

In Figure 9 a 5S diagram process is carried out, which is composed of a series of 5 phases (1) Sort, (2) Set in order, (3) Shine, (4) Standardize, (5) Sustain. This process helps to define a process within a close loop to maintain a system in constant improvement.

For the first phase **SORT** it is necessary to establish what will be the objective or problem to be solved. In this case to reduce the number of deviations that occur annually, to reduce costs, increase product quality, and the amount of safety that is required to comply with the products aimed at patients.

SET IN ORDER, this procedure helps to establish based on a series of SOP guide for the employee or operator to reduce the number of possible errors when carrying out the implementation of this research.

The third phase **SHINE** consists of being able to maintain parts to avoid possible damage to it, because if the correct maintenance does not occur, it would imply another type of deviation since the different particles that can adhere to the part can affect the quality factor of our product and its integrity.

STANDARDIZE is that phase or process that explains in detail each process that must be carried out so that in detail the operator or employee can carry out without committing faults. When using the design tool that is implemented in the design area and shown in Figure 8, it is expected that the staff can carry out a protocol with a series of steps that serve as a guide to define a process. In the case of this research this process should be done in the second stage of creating the buffer, specifically in the part of adding materials or chemical solutions, which should be placed on top of the tank as specified in Figure 9 of the design part so that it can fulfill its purpose of avoiding future deviations or the integrity of our tanks is affected.

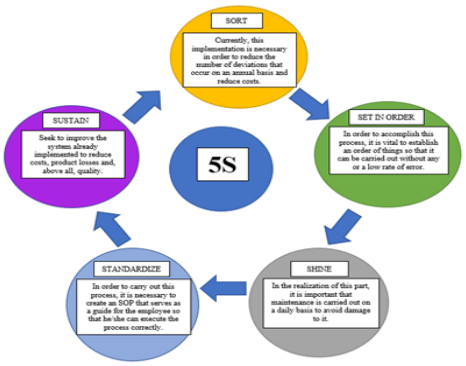

Figure 11

5 S Diagram [1]

The last phase of **SUSTAIN** consists of maintaining the process functional with the possibility of establishing improvements within the implemented system to reduce the number of deviations that occur annually, i.e., they will always see opportunities for continuous improvements that can benefit this product, both in costs, as in the safety factor, and even lead time processes. This 5S system will help to maintain a system focused on continuous improvements constantly following a series of guides that directly help the employee to follow a series of instructions to carry out a process correctly and avoid the different errors that are found during this type of buffer creation processes [3].

CONCLUSION

The "Unidirectional Flow Gasket" has been identified as a tool for continuous improvement during the buffer creation process, according to the different studies carried out. This system using the DMADV methodology (design, measure, analyze, design, and validate) using as reference the Lean Six Sigma practices and its different practices, we showed a result in improvements of up to 54% of decrease in the deviations caused by human errors. Now the other 46% is due to problems occurred using the OIT system of which the implementation to be carried out is not directly correlated. Now when talking about cost, a significant savings of $218,750 was seen, creating savings of $15,444 in cost per operator on an annual basis, having a decrease in lead time of 65 hours. With this information we can say that the reduction of deviations has decreased to the amount of 6 deviations annually at a cost of $187,500, considering the original value factor of $406,250.

Limitations

During the process of this investigation, there were some setbacks that directly affected the investigation as many of the permits requested from the entity or company were denied performing data collection among other things. According to dialogue with plant engineers it is understood that the following implementation in the buffer tank systems would be an excellent one for the different benefits that this brings at the time of realizing the same ones. With the information provided within the investigation it can be determined that it was a successful one and meets the requested parameters as had been stipulated from the beginning the scope of our work.

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