Optimization of the Registration Process of Products on the Pharmaceutical Industry of Puerto Rico

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Abstract *— Registration Process for pharmaceutical products in Puerto Rico has unique requirements for the marketing, sale, and distribution of the products. The Organizations must be approved before they can market, sell or distribute the product. The estimated products without registration on the organization are 4,800 products; these products belong to 2016, 2017 and 2018 years. Under this scenario, the organization decides to implement a standardized process using the tools of Lean and Six Sigma Methodologies. The cycle time reduction after the implementation process is 95.9%. After the implementation of the improvement process is 55 products in 405 minutes. The organization can register after the improvement process 1,100 products for a month with only one resource. The reduction of the cycle time allows increasing, quality, customer satisfaction and reduction of the inventory of unregistered products. This reduction of stock allows releasing products for marketing, sales, and distribution faster.*

Key Terms *— Cycle Time Reduction, Lean Six Sigma, Standardization.*

PROBLEM STATEMENT

The register process of prescription drugs and non-prescription drugs approved by the United States Food and Drug Administration (FDA), on the Department of Health of Puerto Rico demand a series of requirements and steps to follow. Different than the states, Puerto Rico has unique requirements when marketing, distributing or selling pharmaceutical products. Each prescription drugs and non-prescription drugs approved by FDA must be registered with the Department of Health before it may enter the island. As well, any entity passing title to controlled substances to any customer on the island must be licensed by the Puerto Rico Department of Health, Office of Investigations (formally ASSMCA). The registration of a drug requires a series of steps and attached documentation that are not structured. The optimization of the registration process is essential to reduce the cycle time of the drug product on the drugstore. The cycle time can be defined as the time we spent manufacturing an order. The time starts counting since the system place the order request; the system instantly assigns a date that the request must be released. The application should be completed with all the requirements that it needs to be released. Cycle time is one of the metrics that it is crucial for the industry. Its information allows collecting data of how the processes are being executed. This research enables structuring the registration process using the Methodologies of Lean Manufacturing and Six Sigma. Also gives the opportunity to create a continuous process free of wastes, improving quality and performance. The optimization allows to deliver a high-quality product, reduce costs, the organization must be competitive in the market and increase customer satisfaction.

Research Description

The registration of prescription drugs and non-prescription drugs are not a continuous process. The poor registration process increases inventory and holds the release of the products.

Research Objectives

- Reduce the cycle time of registration process of prescription drugs and non-prescription drugs by 10%
- Create a structured and continuous process.
- Identify and eliminate wastes.

- Identify possible improvement opportunities
- Evaluate and prioritize the alternatives identified.
- Increase quality and customer satisfaction.
- Implement identified improvement opportunities.

Research Contributions

The main contributions of the research work are the following:

- Less time to register the products
- Cost reduction
- Increase the efficiency of the process
- Guarantee quality and performance of registration process and all the changes
- Have product on time in the market
- Eliminate waste
- Establish Lean and Six Sigma methodology
- Increase profits of the organization
- Eliminate non-value-added activities
- Increase customer satisfaction
- Complies with the regulatory requirements

LITERATURE REVIEW

The process to register prescription drugs, non-prescription drugs approved by the United States Federal and Drug Administration (FDA) on the United States and territories are ruled by different laws and depend on the state and region. [1] The Food and Drug Administration (FDA or USFDA) is a federal agency of the United States of America the Department of Health and Human Services. [1] The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation's food supply, cosmetics, and products that emit radiation [2]. Currently, Puerto Rico, Massachusetts, and Alaska are the only states that do not have non-resident licensing programs to regulate the shipping of drugs and devices into their states. [2] However, if organizations are selling controlled substances to a Puerto Rico facility or prescriber, organizations must apply for and maintain a Puerto Rico controlled substance license [2]. The registration can be done only through a Puerto Rico licensed representative agent. The law of pharmaceutical is known as “Ley Núm. 247; Ley de Farmacia de Puerto Rico, según enmendada” and the rule is known as “Reglamento de la Secretaria de Salud Número 156 para la Operación de los establecimientos dedicados a la manufactura, distribución y dispensación de Medicamentos de Puerto Rico”. Both are created to guarantee an excellent health service to Puerto Rico citizens. [3] The Pharmacy Law 247 was created to regulate the exercise of the profession of pharmacy and occupation of pharmacy technician; create the Board of Pharmacy of Puerto Rico, determine its organization and functions; regulate the manufacture, distribution and dispensing of medicines in the Commonwealth of Puerto Rico [4]. The regulation was also created with the purpose to regulate and control the operation of organizations and companies who manufacture, distribute and market medications in Puerto Rico. The process of the registration of medications in Puerto Rico has steps and requirements. [2] Unlike the mainland states, Puerto Rico has unique requirements when marketing or selling pharmaceutical products in that each pharmaceutical product must be registered with the Puerto Rico Board of Pharmacy, Department of Health before it may enter the island [2]. As well, any entity passing title to controlled substances to any customer on the island must be licensed by the Puerto Rico Department of Health, Office of Investigations (formally ASSMCA.) [2] Unlike the northern states, a company does not merely apply for a license and start shipping. [2] In Puerto Rico, a company must make sure all products being sold and shipped are registered and that the company passing title will designate a licensed representative agent on the island. [2] The products that must be registered are: Human and Animal Prescription Drugs, Human and Animal OCT Drugs, all controlled substances, List one chemicals, Dietary

Supplements, Herbal Products and Remedies, Cosmetics containing Active Ingredients, Devices (currently only drug-related devices), Agricultural items, such as pesticides. The process of registration can be performed on a digital platform that the Department of Health develops. It is a slow system and can delay the release and distribution of the products.

Operational Excellence is being continuously used as a strategic tool to improve processes. The Toyota Production System is unique. The Toyota way approach to the basis of Lean Manufacturing production with Six Sigma. The goal is to eliminate waste and variations in the process and make improvements. Their tools help to improve the process and identify waste on them. Some of the tools are the seven wastes and the DMAIC (Define, Measure, Analyze, Implement and Control). The seven waste is identified as Overproduction, Waiting, Transporting, Inappropriate Processing, Unnecessary/Excess Motion, Unnecessary Inventory, and Defects. The used of Lean Manufacturing and Six Sigma methodologies for the process registration will improve the process, reduce costs and quality and the most important improve customer satisfaction.

METHODOLOGY

The objectives submit to this research project will improve the registration process for products by using methodologies and tools. Six Sigma methodology and Lean Manufacturing and principles are the tools that will be used for the research project. The five phases of Six Sigma are:

- Define - It is the most crucial phase. Establish the problem or issue and define a goal statement. Some of the tools that can be used are Suppliers, Inputs, Process, Outputs, and Customers (SIPOC), the "Voice of the Customer" (VOC) to understand the requirements of them. The identification, definition and structured the process are essential to understanding the registration process. Those requirements will guide the research to design a continuous flow process. The Define phase will be developed a Project Charter.
- Measure - Collection of data. Visual data to identify potential contributors to problems in the process.
- Analyze - This phase allows to identify potential cause's contributors to the problem.
- Improvement - This phase consists of establishing the improvements to the process, based on the analysis performed on the data collected with the tools used.
- Control - Performed audits with a fixed frequency to measure, maintain and control the improvements implemented. Continue to collect data, use quality controls process charts, etc. The creation of Standard Operation Procedure to assure the control of the Registration Process and 5's.

Some of the tools that can be used from Lean Manufacturing Methodology are Value Stream Map, Time observation, Production Control Board, Standard Work in Process, 5's, etc. The non-value activities and value-added activities will be identified. A brief description of how some of Lean Manufacturing tools can improve the process and can help of the reduction of cycle time is as follows:

- Value Stream Map - Identify waste and prioritize where action should start to improve the process. Collect information about product business results. Can help to improve procedures, reduce inventory, reduce the variation of the process.
- 5's - Improve the area to change it on effective workplace and standardize work procedures. Simplify work environment. Helps to improve discipline, quality, productivity, and safety.
- Standard Work - Allows achieving consistency of the process if we can establish a baseline of tasks completed. Helps to review the Standards Operating Procedures and align them to improve the process.

- Production Control Board - Allows us to have a visual goal. Helps to compare the actual production with the purpose of reducing cycle time and improve the process. Allows a clear view of the process.
- Time observation - Measures the time on a sheet that the technicians are performing.

The project charter and the Registration Process Data Sheet will be used on the design project The Gantt Chart was developed to ensure we comply with the time stipulated for the DMAIC phases and guide the team through the process. The Gannt Chart, Figure 1 was created taking into consideration the time proposed for the design project.

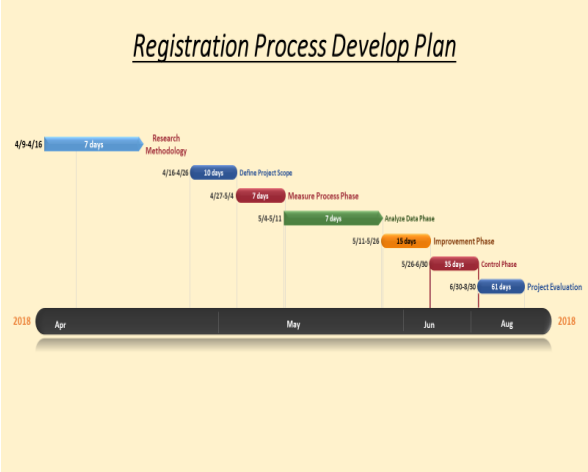


Figure 1
Gantt Chart

RESULTS AND DISCUSSION

The Registration Process for Prescription Products and Non-Prescription Products (OTC) was causing situations in the organization.

Define Phase Analysis

Through the years the inventory was increasing since the process was not structured. The organization has an inventory of 2016, 2017 and 2018 accumulated. Refer to Figure 2. The lack of a structure registration process, guidelines, procedure, and controls contribute to the accumulation of 4,800 products in the warehouse area. The accumulation of inventory for lack of registration increase costs, decrease time release of the orders and decrease customer satisfaction. Therefore, the organization is looking for new initiatives to structure and establish guidelines to standardize the registration process to reduce inventory, cost and comply efficiently with the rules and regulations.

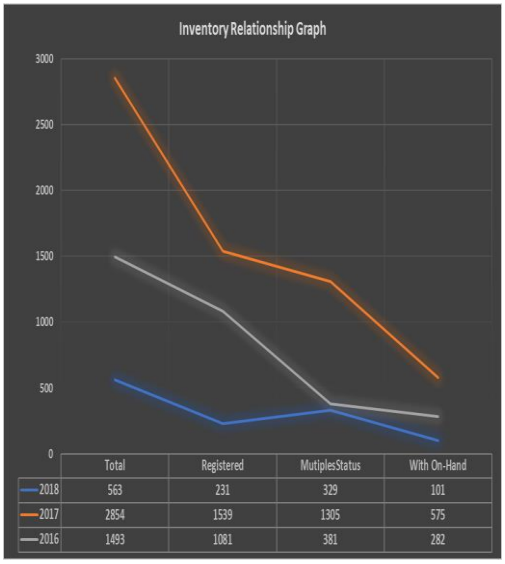


Figure 2
Inventory Relationship Graph

The goal of the process is to reduce and structure registration process to decrease inventory and increase quality and customer satisfaction. The project scope includes the optimization of the Registration Process of Prescription and OTC products on the Platform of the Department of Health of Puerto Rico, also the reduction of the cycle time to improve the registration process. The focus will be on the unregister products of the years 2016, 2017. Products that must prioritize are on-hand from major to minor demand, second Rx products, third pending products that have orders to sell and last blocked products that are not allowed to sell. The project team members include Quality Director, Supervisor of Control Drug products, Sr. Data Coordinator, Engineers, Engineer student and temporary resources. The Voice of the Customer Diagram was created to identify our external and external customers, customers' requirements and customers' expectations. Standardization of the

process and reduction of the cycle time are the essential requirements for the registration process and customers. Refer to Voice of Customer (VOC) Diagram on Appendix A. The Project Charter tool was performed as a guide for team members to see whether the project is conducted in the correct direction as proposed and the goals have been achieved in time. The Project Charter was developed, as shown in Figure 3.

PROJECT CHARTER

1. General Project Information	
Project Name:	OPTIMIZATION OF THE REGISTRATION PROCESS OF PRODUCTS ON THE PHARMACEUTICAL INDUSTRY OF PUERTO RICO
2. Project Team	
	Department
Project Manager:	Quality Director
Team Members:	Supervisor of Control Drug Products
	Sr Data Coordinator
	Engineer
	Compliance Supervisor
	Engineer Student
	Temporary Resources

3. Scope

Optimization of the Registration Process on the platform of the Department of Health of Puerto Rico

4. Project Goals

Project Purpose

Reduce the cycle time registration process to decrease inventory and increase quality and customer satisfaction.

Objectives

Reduce Inventory, Reduce Costs, Identify and eliminate waste, reduce cycle time, increase quality, increase customer satisfaction.

Schedule

DMAIC	Start Date	End Date	Days
Define	4/17	4/26	9
Measure	4/27	5/4	7
Analyze	5/4	5/11	7
Implement	5/11	5/16	5
Control	5/26	6/30	35

Business Benefits

Implementation of a standardize registration process and reduce cycle time. The product will be on time to satisfy customers.

Figure 3
Project Charter

Measure Phase Analysis

The measured phase is the collection of data. The purposes of the Design Project for Registration Process are to develop a SIPOC and Flow Diagrams. The SIPOC created will help to identify the relationship between the suppliers, input product, process, output, and customers. Refer to Appendix B for the SIPOC Diagram. The following Process Map is created to optimize the Registration Process. The Process Maps were generated based on the requirements needed by the Organization. The process map will be used as requirements and needs of the Organization. Three process maps were developed. Process Maps helps to guide the registration process.

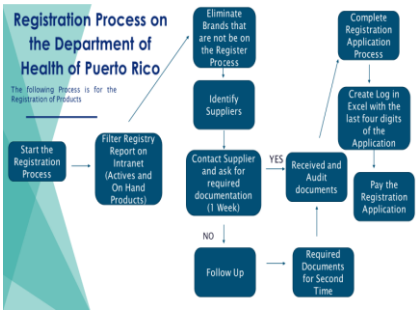


Figure 4
Registration Process Map

Analyze Phase Analysis

The focus in this phase is about identifying opportunities for improvement within the current registration process. The first step is to analyze all measured data and collected results. Next is to understand all viable causes that affect registration process by performing a Fishbone Analysis and set priorities among them discovered causes. As presented in the measured phase, the relationship graph shows the current inventory for the years of 2016, 2017, 2018. The Total Inventory for 2016 is 100% divided by registered, and unregistered products. Refer to Current Inventory Graphs Figure 5, Figure 6, and Figure 7. The graphs show the lack of standardization on the process.

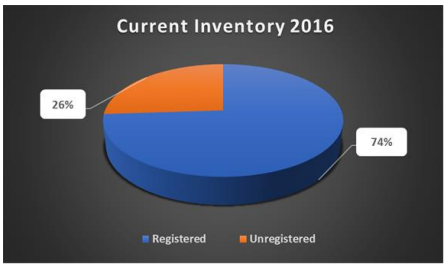


Figure 5
Current Inventory 2016

Figure 6
Current Inventory 2017

Figure 7
Current Inventory 2018

Using Lean Methodology, the Waiting and Unnecessary Inventory waste were identified in the registration process. The products are waiting for registration documents. The ERP program cannot generate new orders because of the status of the products. This status creates the waste of unnecessary inventory. The products are using space and don't have a continuous flow. The organization takes the risks that the products can reach the expiration date, be discontinued, or don't have the market to sell them. The value-added activities and non-value-added activities were identified. The used of 5's philosophy focus on creating an effective registration process for the organization. The development of standardizing work procedures helps to improve the registration process. It reduces waste and non-value-added activities while improving discipline, quality, and productivity.

- Sort - Identify the steps of the registration process and activities related to the process.
- Set in Order - Shared folder created to organize all the data collection required for the documentation process. Process Maps were created as a visual strategy to perform the registration process. Also, is used to establish control. Standard Operating Procedure was designed to comply with regulations applicable and as a guide for the registration process.
- Shine - Shared folder to collect data. Table Log to enter registered products.
- Standardize - Temporary and organization colleagues were trained and qualified in the process. Responsibilities were assigned for colleagues that performed the registration process. The established of frequency-time for data collection from Suppliers. The fee will be applied if the data do not arrive on time for the registration process. Minimum quantity of registration data was established daily. Resources performed evaluation and measurement of the process.
- Sustain - Audit of the process will be performed monthly to ensure the registration process have a continuous flow and complies with the strategies establish. A measure of the registration process will be completed, and the organization designees will analyze and release the results. Procedure, guidelines, and process maps will be reviewed periodically.

The standard work tool was a key to the registration process. It helps for the identification and elimination of waste. The process maps or diagrams were created taking into consideration the needs of the organization to reduce cycle time and backlog. Registration Control Board was created to have a view of the actual registered and unregistered products weekly, monthly, quarterly, and annually. Registration Data Require Sheet was developed to contact suppliers to send the data needed for the registration of the product. The time observation table sheet was created to record the elements and measured the registration work and activities that the resources assign performed. A cause-effect analysis was performed shown in Figure 8, to find these possible causes. These are the leading potential causes in the fishbone diagram that affects cycle time registration.

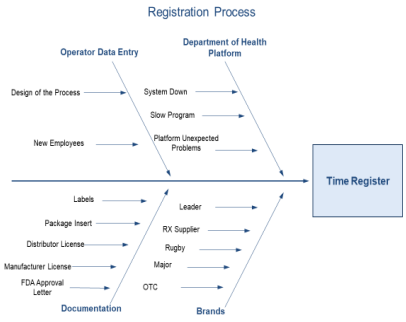


Figure 8
Cause and Effect Diagram

The measure of the registration process was performed. The Registration Data Sheet was used to collect the data. The four reasons that can influence the accumulation of inventory were evaluated. The registration process was performed first without guidelines or procedure, and the data were collected at the time they performed the registration process. The results show that the time performing both processes together don't improve the process. The lack of standardizing work, guidelines, and controls increase the time significantly as shown in Figure 9. No more samples were taken because of the time (3 hrs. or more) spent measuring each sample.

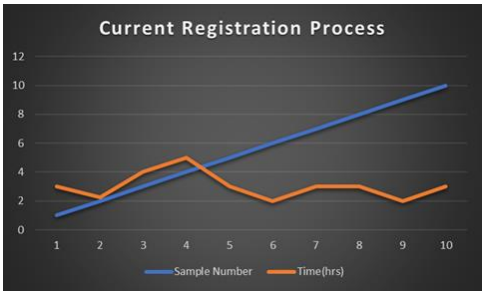


Figure 9
Current Registration Process

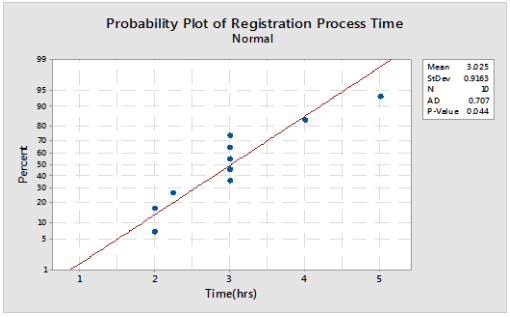


Figure 10
Current Probability Plot of Registration Process

The results of the registration process with standardize work shows improvement of the cycle time registration. To reduce the cycle time, Sr Data Coordinators were instructed to follow the Process Maps applicable. The Standard Operating Procedure and the Shared folder were created to collect the data of the products. The collection of data was performed before to enter the registration platform. Sometimes data takes more than one week (1 week) to be collected. More than 30 product data were collected before registration process begin. Samples register 60.

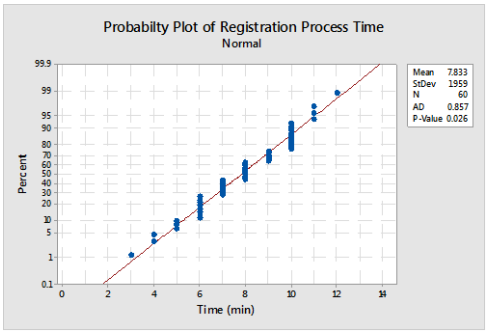


Figure 11
Probability Plot Registration Process after Standardize Work Implemented

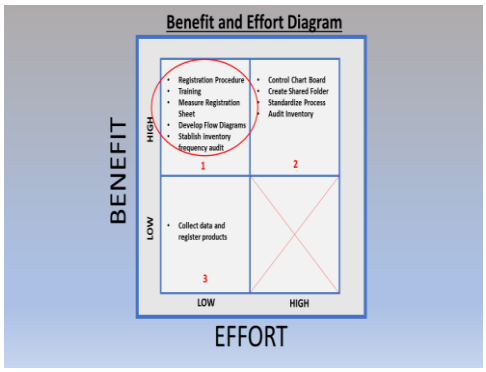


Figure 12
Benefit and Effort Diagram

The Benefit and Effort diagram, Figure 12 were defined regarding production benefit/effort of reduction of variations and implemented a standardize registration process. Regarding benefit Low/High refers to the benefits the organization gain with the initiatives premises proposed and discussed by the team members. The effort Low/High refers to the efforts the organization must put on developing the initial premises. The discussion of the results provides the tool to prioritize the premises proposed as shown in Figure 12. The discussion of prioritization assign ascends numbers. In which 1 is the first square to be work. The effort must be high, but the benefits will help to the reduction of the cycle time of the process. Although the square number 2 has a high effort, the benefits of the process and the organization are essential. The shared folder, the control chart, standardize the process and audit inventory is tools

that are key to the development of the project. The square number 3 was proved in the measured phase it not viable initiative for the organization because of the time consuming and is identified as waste.

Improvement Phase Analysis

After improvement phase, the registration process reduced cycle time process significantly. The registration process was measured without the standardized process, showing the results are a waste of time. After the implementation of the standard operating procedures, process maps to guide the Sr. Data Coordinator, the cycle time of the registration process reduces. After evaluation of the data the average to perform the registration process on the platform is eight minutes (7.8 minutes). The registration process measured to determine that 55 registrations can be performed over 6.5 hours of work per day. Always taking in consideration other causes that can influence on the working hours. The calculations performed shows that 95.9% was the cycle time reduction for this process.

Cycle Time Reduction		
	Total of Registers	Time of Register(min)
	1	180
Cycle Time Before	Every 180 Minutes	
After Improvement	55	405
Cycle Time After	Every 7.4 minutes	
Improvement	Time was of 173 minutes, which is 95.9% of reduction	

Figure 13
Cycle Time Reduction Table

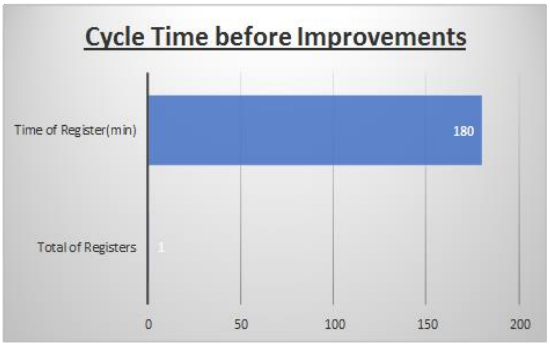


Figure 14
Cycle Time before Improvements

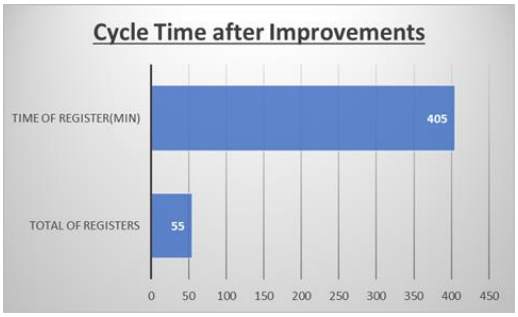


Figure 15
Cycle Time after Improvements

The results show that a total of 1,100 registers can be completed for a month with one resource, after the training of personnel the accumulation of the inventory can be reduced in a minimum period. It is essential that the data of the products to be registered be available in the shared folder created.

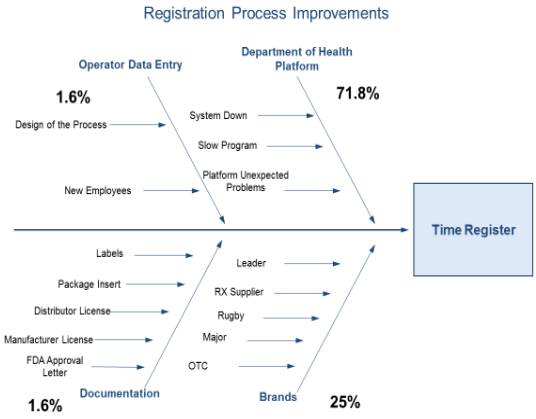


Figure 16
Cause and Effect Diagram after Improvements

The registration process was affected most by the platform and documentation. The creation of a shared folder increases the number of registers performed per day. This improvement reduces the time Sr Data Coordinators spent searching for the data. The process mapped guide and established the time required to follow up documents to maintain the continuous flow of the process. Cause and effect diagram in Figure 16, shows the results of which are the leading causes that affect the registration process. The Department of Health Platform is 71.8% the primary cause that affects the registration process. Some recommendations will

be suggested to the organization to work with the situation.

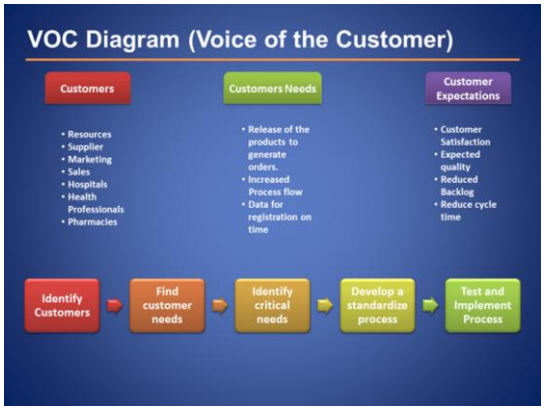
Control Phase Analysis

The focus of this stage of DMAIC is to assure that the action item created in the Improve phase is well-implemented and maintained. Some tools are used in this phase to ensure that the process is within limits. The control of the process after the implementation of the improvements are Standard Operation Procedure, VOC, Visual Control Board, Registration Measure Audit Sheet, 5's tool and Process Maps. The procedure will act as the tool to guide and train the personnel in the registration process. The 5's tools are used to identify possible waste, added and non-added value activities, maintain a continuous flow, and standardize work in the registration process. The control of the process is essential to maintain the continuous flow and don't allow the accumulation of inventory. Some tools were developed during the design project are Process Maps and Registration Audit Sheet. Refer to Appendix C. The Voice of Customer tool will still on the registration process to audit if customer demands and requirements are satisfied. Visual Control Boards will be created to help the organization to know how the registration process is running. The control board will allow making the adjustments and improvements necessary for the success and the maintenance of the continuous flow of the registration process. All successful implementation must include constant training, revision, and audits frequently.

CONCLUSION

The Lean and Six Sigma Methodologies were crucial for the design and improvement of the project. The cycle time reduction objective was 10%, but the improvement of the process after the design project is 95.9%. The goal was achieved making a structured process, identifying, and eliminating waste, identifying possible improvement opportunities, evaluating, prioritizing and assigning responsibilities and finally implementing improvement opportunities in the process. The tools increase customer satisfaction and reduce inventory allowing the release of products. These also will enable the increase of space and the distribution of the products before they can reach the expiration date or lose the demand on the market. Some contributions of the design project are the reduction of cycle time to register the products, cost reduction, increase the efficiency of the process. Also, guarantee quality and performance of registration process and all the changes, have product on time in the market, eliminate waste, establish Lean and Six Sigma methodologies, eliminate non-value-added activities, increase customer satisfaction and complies with the regulatory requirements. The process still needs improvements. Some recommendations to the organization for the registration process are registered products by brand; it can reduce more the cycle time, collect and maintain the shared folder data updated, revised and audit the registration process frequently. The analysis and results show that the major problem is the platform of the Department of Health of Puerto Rico. The recommendation for the organization is to send a letter to the Department to let them know the experiences of the representative agents with the platform. Last, always work as a team to improve the process, quality, and customer satisfaction.

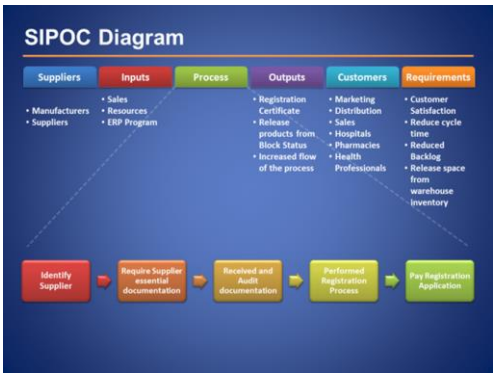
Appendix A



Voice of the Customer Diagram explain the requirements of the customers. The detail of

requirement is essential for the organization to puts the efforts to improve those areas to satisfy external and internal customers.

Appendix B



Appendix C


Auditor or Designee: _____ Date: _____

Registration Process Audit Sheet

Brands	Start	End	Total Time	Platform	Documentation	Operator Data Entry

Comments:

Auditor or Designee Signature:

Approved by:

REFERENCES

[1] US Food and Drug Administration (FDA). (2018, March 28). *About FDA - What We Do* [Online]. Available: https//www.fda.gov/aboutfda/whatwedo/default.htm. [Accessed: April 26, 2018].

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