Quality Control Laboratory Improvements

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Abstract

Sanper Pharmaceutical is an inhalation anesthesia manufacturing plant. Its main products are Elim and Marile. Currently, the delay in laboratory analyses hinders the Finished Drug Product release time, increasing the final release cycle time. Thus, it is difficult to comply with the delivery agreements made with customers. By the end of this project, Quality Control (QC) Laboratory will minimize the analyses release time by 20% or more. This will enable the site to be more agile in the delivery of its products.

Description

The importance of this study is to minimize the time required for Chemical Analysis to release the final product to the market. The longer the product release process takes, the longer it will take to reach the customer. This affects the relationship with customers, increases back orders and minimizes the ability to acquire new markets. In addition, it also affects the relationship with internal customers.

Objectives

- Improve Quality Control Laboratory analyses cycle time
- Standardize Priorities Management and daily job plan
- Align internal goals with client's needs.

Methodology

Six Sigma is the methodology used in improvement projects. Its main component is the discipline, which is an acronym for defined as: Define, Measure, Analyze, Improve and Control.

Results and Discussion

Define Phase

The first step of the project was the development of the Project Charter. This tool helped in the definition of Problem Statement, Project Scope and Business Case.

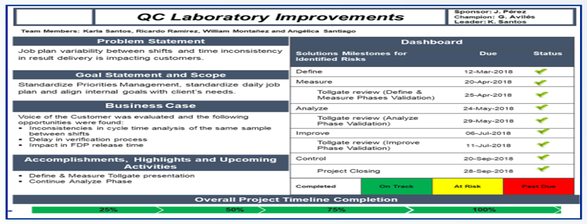

Figure 1: Project Charter

A SIPOC diagram was used to identify all relevant elements of a process improvement project before work begins. It helps define a complex project that may not be well scoped.

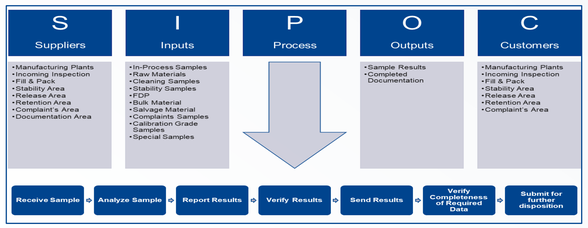

Figure 2: SIPOC

Results and Discussion

Measure Phase

To work with our first point, data obtained from the LIMS electronic system was evaluated. These reports provided the exact time between the date and time that each sample arrived at the laboratory and the date and time when the release process was completed. Figure 3 presented the Raw Material and Bulks analysis that need improvements to comply with the Finished Drug Product Release Cycle Time (Ideal Scenario).

Product	Minimum	Maximum	Average	Median	Internal Goal	QC vs. Goal	Goal	QC vs. Goal
Amine	4.1	11.4	9.2	11.4	5.0	6.4	2.0	9.4
Bottles	0.3	6.1	6.1	6.1	5.0	1.1	2.0	4.1
Cabosil	0.4	6.9	3.5	4.7	5.0	-0.3	2.0	2.7
Caps	0.2	9.6	3.4	3.9	5.0	-1.1	2.0	1.9
Hexafluoroisopropanol	1.4	7.9	3.9	3.5	5.0	-1.5	2.0	1.5
Sevomethyl Ether	0.2	4.1	2.3	2.4	5.0	-2.6	2.0	0.4
Elim Bulks	1.5	9.5	5.3	5.7	5.0	0.7	3.0	2.7
Marile Bulks	1.3	8.7	5.0	5.0	5.0	0.0	3.0	2.1

Figure 3: Data Collection

The understanding of the Bulk Analysis Process was studied using a Value Stream Map. Its development, provided the time required, step by step, for the analysis of Elim and Marline Bulks, respectively. In addition, the waiting time between each step could be identified.

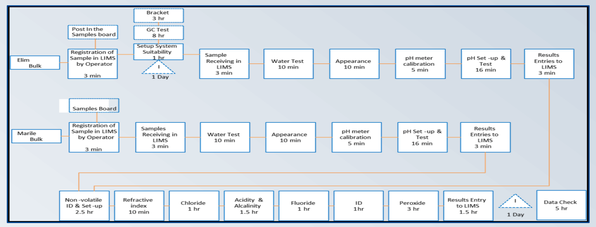

Figure 4 : Value Stream Map (VSM)

Analysis Phase

After the evaluation of data collected from the LIMS electronic system, we identified that the most impacted analyses were the ones for Raw Materials and Bulks for Elim and Marile Products.

The Value Stream Map developed in the Measure Phase, helped in the understanding that the current analysis process can reduce the delivery time of the QC Laboratory analysis results. One of the causes identified by which laboratory analysis has become a stopper for the Finished Drug Product release cycle process is the organization and distribution of laboratory activities on a day-to-day basis.

An evaluation of QC Laboratory Value-Added and Non-Value-Added activities was performed. The following points were identified as major offenders:

- A total of 16 reports are made without apparent functionality.
- After each analyst audits their logbook, it is audited again, for a total of 28 audits.

Results and Discussion

Improvement Phase

Throughout the project, we have demonstrated that the organization and distribution of laboratory activities were possible root causes for the delay in laboratory results. For this reason, a Core Group was designed. This group of analysts is in charge of working on Raw Material, Bulks and Finished Drug Products. The analysts who stay in the regular shifts, are in charge of the in-process samples and tasks of laboratory maintenance.

	Position	Responsibilities
Core Group (Day)	Group Leader	- Personnel Deployment, support SOP revisions, support Investigations, Tier attendance, C/R
	All Group Responsibilities	- BDS, BDP, FDP, Stability of all 3 Products - Raw Materials - Working Standard and Solution preparation - System Suitability / Cleaning / Special Samples - C/R - Safety Inspection / Safety Talk / Quality Talk - Personnel Development - Calibration Program Support - SOP Revision / Investigations / Instrument Troubleshooting - Cross training / New Hire Training

Figure 5: Core Group Responsibilities

	Position	Responsibilities
Shifts A, B, C & D	Supervisor	- Primary Responsibilities: Personnel Deployment, Verification: In-process samples, FV-1344, FDP (all three products), Equipment Daily Verifications
	2 Analysts: Plant I & II	- Primary Responsibilities: In-Process Samples, Equipment Daily Verifications
	1 Analyst: Wet Area	- Primary Responsibilities: FV-1344, Previous Shift Documents Verification, Equipment Daily Verifications, BDP (appearance, pH, water

Figure 6: Regular Shifts Responsibilities

After implementation of the Core Group, a significant reduction in the time required for laboratory analysis was observed. The difference observed was from 1.0 day to 4.0 days less in the execution and release of laboratory analysis.

Products	Lots Before Implementation (Days)	Lots After Implementation (Days)	Difference
Amine	4.9	1.7	3.2
Bottles	5.5	1.5	4.0
Cabosil	2.1	0.6	1.5
Caps	3.1	2.1	1.0
Hexafluoroisopropanol	1.7	0.7	1.0
Sevomethyl Ether	3.0	1.1	1.9
Elim Bulks	5.0	2.9	2.1
Marile Bulks	5.0	2.6	2.4

Figure 7: Raw Materials and Bulks QC Lab Release Time

All laboratory activities were evaluated. Those that were non-value added to the process, product or regulatory aspect were eliminated. Opportunities were identified, through electronic reports, to cover different reports in one. As a result, 59% of the tasks were eliminated, all of them Non-Value Added activities..

Control Phase

To be able to have control over the implemented changes, the following actions were taken:

- A Standard Worksheet was generated for Core Team and Shift Teams.
- A Schedule for receiving of Raw Materials was established. They will be received from Monday to Wednesday and the analysis and disposition will be completed from Tuesday to Friday, every week.

Results and Discussion

Control Phase Cont.

A visual aid was designed to establish a Visual Control of the Manufacturing Process with the priority of all samples under normal process conditions. It includes a scale of priorities from 1 to 5.

- Everyone involved in the process received proper training, including, Laboratory personnel and all internal customers.

Conclusions

The project carried out each of the established objectives. With the new organization of work shifts, it was obtained:

- Decrease in release time of Raw Materials up to 27% and
- Up to 48% in the Marile Bulks product, exceeding the initial expectation of a 20% reduction.

Standardization Management:

- An agreement was reached with the Supply Chain area, in which Raw Materials will be received from Monday to Wednesday and analyzed and dispatched from Tuesday to Friday, every week.
- A Standard Worksheet was designed for rotating shifts and another one for the Core Group.
- A total of 59% of the tasks were eliminated, all of them Non-Value added activities.

Finally, although during the execution of the project, the financial aspect was not considered, we were aware that it was positively affected. The importance of this study was to minimize the time required for Chemical Analysis to release the final product to the market. The longer the process of releasing the product, the longer it will take to reach the customer. This affects the relationship with customers, increases pending orders and minimizes the possibility of acquiring new markets. In summary, the more satisfied customers are, the more sales the company will generate.

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