Quality Alerts Notifications Evaluation and Response Solution for Sites to Communicate Computer Systems Potential Issues in an Alignment Form and Integrated Process

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Abstract *— The Quality Alert Process is used to communicate IT or computer system related situations that have the potential to adversely impact regulatory requirements (e.g. product quality, patient safety, record integrity and privacy) as well as potentially impacted sites/areas. In addition, the pharmaceutical industry is a highly and strictly regulated environment. Therefore, the data generated in this process are important in order to demonstrate compliance to the external agencies and patient safety. The Quality department is accountable for this process and, with the technology changes across the world, many business decisions are driven thru this department. A commercial off-the-shelf (COTS) software was identified to standardizing a global practice and replace/eliminate the manual and local process in the sites. This software helps communication to all the sites at the same time, with the same information, increasing and improving the process experience. To develop a global solution, Lean Six Sigma methodology were used to identify and implement the requirements to this process.*

Key Terms *— Compliance, Quality Alerts, Response, Simplify, Standardize, Sustainable*.

INTRODUCTION

The current manufacturing processes are working more fast and faster than in the past years. In addition, the information is taken a most important position in order to take final decisions. Also, the information thru the Quality systems is handled by computer systems in order to have the complete information and data integrity (e.g., batch records, process performance, stability samples).

The content of the Quality Alerts notification will provide enough information to determine if the site does not have any impact from the start, like for example, Quality Alerts for systems not being used at the site. Therefore, the information technology (IT) and departments as Quality are working closely and more integrated to each other.

In the current times one of the most important aspect in the business environment is the Quality Assurance Management (QA). The QA department has in its hands the final disposition of the product (final/intermediate/raw material) for manufacture as well as to distribute. Therefore, QA department has also in its hands the patient safety with the decisions they took in order to release a product. In order to comply with patient and regulatory agencies expectations and requirements, all information must follow the ALCOA principles (attributable, legible, contemporaneous, original and accurate), and current technology allow us the ability to comply with it not only in paper or manual records, but in computer systems too.

This project was implemented in a global pharmaceutical company, that provides products worldwide (for confidentiality purposes referred as Company). This Company has different systems to handle the Quality Alerts in the sites and all the process are people dependent, as well as manual. After several evaluations, it was concurred to standardizing the processes and provide a single solution across the sites. This solution is a big initiative since need to establish a strategy for implementation, data migration from previous process and comply with ALCOA, as well as process archival of previous process by site.

PROBLEM STATEMENT

The Quality Alerts evaluation is a people dependent process that require a Subject Matter Expert (SME) availability. Normally, the SME resources is represented by QA department, and typically are the same resources. This represent a problem because sometimes there's no visibility of the SME's workload, and lack of ownership from impacted areas, since undestands that the evaluation responsibility is from Quality department (that needs to be part of the process for impact evaluation). In addition, the Quality Alerts evaluation is different from sites. Each site handles the evaluation in a different way and use different systems to document it. This situation shows a lack of procedure for the process, as well as the need of a requirement for globally standardization.

Research Description

This research pursues simplify the Quality Alert process with a reduction of at least a 30% in the cycle time to evaluate and document the alert impact. In addition, this research has the north to standardize the Quality Alert process and convert it in a sustainable and no people dependent.

Research Objectives

This project pursues to reduce by 30% the cycle time to perform the Quality Alert impact evaluation. In addition, this initiative will be a global solution in order to improve the current process as well as sustain it. Lean Six Sigma methodology will be used as well as thinking criteria for the deployment of the Quality Alert handling solutions.

Research Contributions

Contributions of this research project will be noticed in cycle time process reduction in the Quality Alerts evaluation and responses and higher quality and standardized processes. In addition, the process will be more simplified and sustainable. This process enhancement will be implemented by the collaboration of Global Quality Partners with IT Teams in order to work together. The inversion of capital for this initiative implementation will be zero (0) since the quality tool is an existing one at the Company and distributed globally.

The standardization of the process to evaluate, document and archive Quality Alerts across at the sites will help to avoid ambiguity in procedures across the sites, as well as pursue into the answers same or similar responses and implementation plan with a globally overview.

LITERATURE REVIEW

Quality Alerts Process under the Quality Management is a wide-ranging concept, which covers all matters, that individually or collectively influence the quality of a product. It is the sum total of the organized arrangements made with the objective of ensuring that products are of the quality required for their intended use. Quality Alerts process; therefore, incorporates Good Manufacturing Practices.

To ensure product quality, safety, and efficacy for customers, it was designed a quality system that meets or exceeds the regulatory requirements of the countries in which the products are distributed. This quality system, with the help of IT group, is a framework for achieving the stated quality requirements through the management of resources, processes, and data. Identifying, understanding, and managing interrelated processes as a system strengthens with the ability to meet its objectives and to effect continual improvement in operations. This quality system represents a scientific based philosophy that ensures drug products, processes, systems, and devices consistently meet or exceed customer needs.

For systems as well as devices, the quality system design must take into consideration the risk class and the type of system/device. The overarching philosophy articulated in both the current Good Manufacturing Practices (cGMP) regulations and in robust modern quality systems is that quality should be built into the product and testing alone cannot be relied on to ensure product quality.

Implementation of the Quality Alert System is the responsibility of senior management and requires

the participation and commitment of staff in various functions at all levels, both within the company and by the company's suppliers and distributors (since include external devices and computer systems). All parts of the quality system must be adequately resourced with qualified personnel and suitable and sufficient premises, equipment, and facilities. Management is responsible for establishing the quality systems structure appropriate for the specific organization, and provides the leadership needed for a successful quality system.

Is highly important to take into consideration that the Pharmaceutical Industry is one of the most regulated workplaces across different manufacturing industries. Therefore, attend any situation quickly will avoid situations with drug products as well as patient safety.

General Information of the Methodology Used "DMAIC"

The DMAIC technique is the project's methodology to be used. DMAIC is an acronym for Define, Measure, Analyze, Improve, Control. DMAIC is the Six Sigma process methodology used for improving existing processes [1]. All the steps of DMAIC will be described with the required tool used.

Define: Define the Customer, their Critical to Quality (CTQ) issues, and the Core Business Process involved. Define who customers are, what their requirements are for products and services, and what their expectations are. In addition, define project boundaries, the stop and start of the process as well as define the process to be improved by mapping the process flow.

Measure: Measure the performance of the Core Business Process involved. Develop a data collection plan for the process. Collect data from many sources to determine types of defects and metrics. Compare to customer survey results to determine shortfall.

Analyze: Analyze the data collected and process map to determine root causes of defects and opportunities for improvement. Identify gaps between current performance and goal performance. Prioritize opportunities to improve. Identify sources of variation.

Improve: Improve the target process by designing creative solutions to fix and prevent problems. Create innovative solutions using technology and discipline. Develop and deploy implementation plan.

Control: Control the improvements to keep the process on the new course. Prevent reverting back to the "old way". Require the development, documentation and implementation of an ongoing monitoring plan. Institutionalize the improvements through the modification of systems and structures (staffing, training, incentives).

PROJECT METHODOLOGY

DMAIC methodology will be used for this project in order to achieve the project goals. In addition, Lean Thinking will be pursuing for all the projects steps. Therefore, each one of all project steps will be defined from the quality management as well as IT standpoint when applicable**.**

Define: In this phase it is expected to define a clear scope of the project. Therefore, a project charter will be developed in order to state: Project Goal, Project Participants, Stakeholders, Requirements, Constraints, Milestones, Communication methods and Deliverables. In this phase the Voice of the Customer (VOC) as well as Voice of the Business (VOB) will be evaluated to understand the real customer/business requirements.

Measure: The Measure phase will include a Value Stream Mapping (VSM) of the Current Process with the objective of identifying real output (Process Time Estimate) from the customer as well as requirements. With this information obtained and gathered from the customer a Critical to Quality (CTQ) tree or analysis will be conducted. In addition, business requirements will be defined. In this project the customer represents one of the plants or sites where the solution will be implemented. This will include a team of Quality Personal, Information Technology (IT) and Quality Management.

Analyze: as part of this phase, the data and information obtained from the Measure phase will be evaluated, in order to establish the necessary approach for implementation. Also, in this phase will help how to concentrate the efforts to accomplish deliverables of the project. In addition, weekly meetings were arranged, including representatives from the site as well as the core team members of the global solution.

Improve: In this part of the project phase, an implementation of the project will be taking place of the process improvement as well as the tool to be used in all the company sites. Therefore, deployment plan needs to be approved by global as well as the SME's impacted as per process improvement and modifications with the require trainings.

Control: This project was pursuing since quality management require a better tool to follow-up and track the quality alerts into the sites. However, the group of Information Technology (IT) will be providing support in this step, they will be accountable for the support of the process after project implementation. For this phase, the site or plant should expect: Unified transition, IT support and Reports.

RESULTS AND DISCUSSION

DMAIC approach was used to complete the evaluation as well as the implementation of this project. In addition, the standardization and the deployment of the Quality Alert evaluation and its notification across Global. Following a summary of the steps taken during project evaluation and final implementation.

Define – A project charter [2] was prepared in order to identify requirements, required personnel and stakeholders. As part of the Define step, the Voice of the Customers (VOC) and the Voice of the Business (VOB) was taken into consideration (results shown in Figure 1). In addition, a SIPOC (Supplier, Input, Process, Output and Customer) exercise was made (refer to Figure 2).

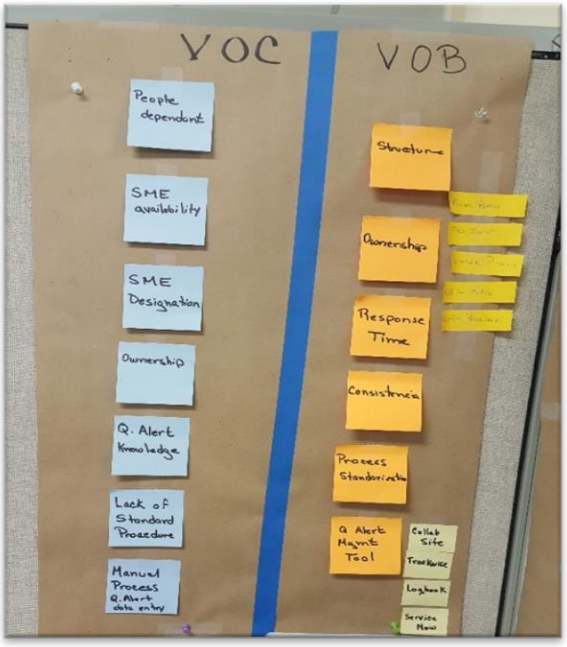

Figure 1
VOC/VOB

Project Charter

- Problem Statement: Quality Alerts provides the means to communicate issues and potential issues with computerized systems servicing the sites.
- Plant 1 (local site) tracks the Quality Alerts using logbooks and the local deviation procedure, to escalate any issues that have an impact to the site.
- Plant 2 (local site) tracks the Quality Alerts using a local computer tool as well as the local deviation procedure for this site, to escalate any issues that have an impact to the site.

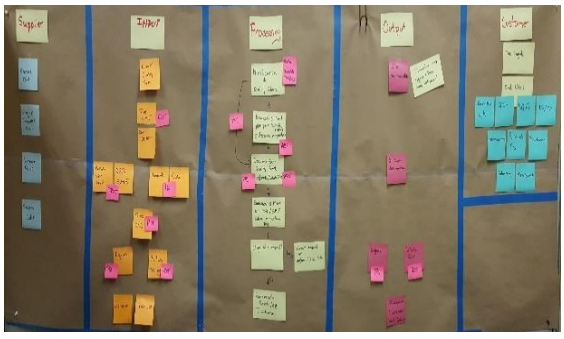

Figure 2
SIPOC

- Sites outside Puerto Rico and the United States, tracks the Quality Alerts using a local computer tool as well as logbooks. In addition, if detected any situation, they escalated it using the deviation procedure for the applicable site. Logbooks and computer systems used to document and evaluate the Quality Alerts, calls different sections and evaluate different aspect of the issue.
- In order to maintain a state of compliance and to simplify the process, it is required to harmonize the management of Quality Alerts among the sites.
- Goal Statement: Simplify, standardize and make sustainable the management of Quality Alerts among the sites in order to achieve a 30% of Cycle time Reduction.
- Project Benefits: As a result of achieving this goal, the Quality Alerts evaluation, documentation and resolution will be completed in a more harmonized and simplified manner.
- Local (Non-Financial): This project is intended to maintain a compliance status and no financial outcome is expected.
- Local, Global, Strategic Benefits: Efficiency, 30% of Cycle time Reduction.

With the Voice of the Customer/Business, was obtained a better idea of the requirements (needs) [3]. In addition, this tool will help to organize all these requirements, the current compliance of them and identify any Lean opportunity.

With the information obtained during the SIPOC exercise (Figure 2) was summarized the Global Process of the communication of the Quality Alerts to the Sites. This tool included the information that they require (Quality Alert Producer), the information that they provide, when and where the information came and the sites/services impacted (from global perspective).

Measure – A Value Stream Mapping (VSM) was created to assess all the current process to evaluate and document the impact (if any) [4] of the Quality Alert Notifications into the Site. With this tool was obtained an overview of information flow to complete the Quality Alert Evaluation. In addition, the tool focused on the customer requirements and help to understand where the sites depart one from each other. Refer to Figure 3 for the VSM created for this project.

Analyze – For the analyze phase, a Cause and Effect Diagram [5] was prepared, shown in Figure 4. After identifying the value steps in the Quality Alerts Notification Process, it was understood how the current controls from sites were to notify, evaluate and respond the Quality Alerts impact. It started to show that the process improvement will be achieved. In this diagram was captured the required resources like personnel (SME's), procedures and documentation tools (computer systems). In addition, a benchmark was performed to obtain and evaluate the tools that the global sites used to make the Quality Alert evaluation and the responsible personnel for this action.

Figure 3
Value Stream Map

Improve – In this Phase a Flow Chart was created with the new Quality Alert Management Process (refer to Figure 5). With the proposal of the new management process to evaluate and document the Quality Alerts notifications, was obtained a cycle time improvement from 20 days to 8 days. Improvement in the process can be observed in the assignment of a coordinator that has the responsibility of receive the Quality Alert, log in the computer system (global system) and assign it to the corresponding SME. Then the SME evaluates and document the Quality Alert and send it to the quality assurance (QA) representative to review the response and determine if an observation is required. In Table 1 can be observed the required actions to be completed in order to implement the project. It was important that these actions were completed at the target due date since the new process was scheduled to deploy in all the company sites at the same date.

Control – To assure process sustainability, a global procedure was put effective, required personnel trained (e.g., SME's, Coordinators, Owners, QA representative) and the new mechanism defined to document the evaluation and final resolution of the notification. In this phase, IT group supported all sites coordinators and SME's in order to assure the proper use of the computer tool and assist in any doubt that arise during the Quality Alert notification and documentation.

- Improve phase was completed on September 14, 2020 with the implementation of a procedure *in all Sites: Quality Alert Management*.
- Only one Quality Alert has been generated and processed through the new mechanism defined in the procedure.
- The first Quality Alert Event under the new format was notified by the Global Computer System QA group on October 13, 2020.
- By October 19, 2020, Quality Alert and corresponding addendums were evaluated and documented by the SMEs, as well as verified by the Computer System QA Representative at both sites (Plant 1 & Plant 2) with a total process time of 6 days. Similar results were obtained from Global Sites.

Table 1
Actions for Project Implementation

Action	Description	Due Datee
Identify a Coordinator Resource/Back Up assignment	This Coordinator will be a Quality Representative and the tasks are: • Receive Quality Alert Notification. • Log Quality Alert in Trackwise Review Management module, if applicable. • Assign action to SME for the evaluation of the Quality Alert impact.	May-13-2020
Identify the SME Resources & Back-Ups Confirmation (Update Key Contact List Documents)	The Subject Mater Experts will be responsible of: • Evaluate Quality Alert from the area of their expertise to determine impact to the site. • Document evaluation of impact in the Computer System Action record. • Generate (Open) an observation record in Trackwise if the Quality Alert impact needs to be further investigated. The SME's identified to perform this evaluation, their names with the technology that they support in the Key Contact List of each Site.	May-17-2020
New Procedure Generation & Approval.	The Quality Alert Process is used to communicate IT or computer system related situations that have the potential to adversely impact regulatory requirements (e.g., product quality, patient safety, record integrity and privacy) or the Company brand to potentially impacted sites/areas. Therefore, a procedure is required to assure that all the sites included in the Quality Alerts Notification and impact perform the evaluation with the same instructions.	Jun-16-2020
New Procedure Assignment Curriculum	Assure that local personnel as well as global sites personnel are assigned with the corresponding training to the people impacted with the Quality Alerts Notification and Evaluations. This activity includes any process school across all sites in order to assure proper implementation.	Sep-04-2020
Procedure Effective	The new process will be start when the Quality Alert Procedure are Effective in all sites.	Sep-14-2020

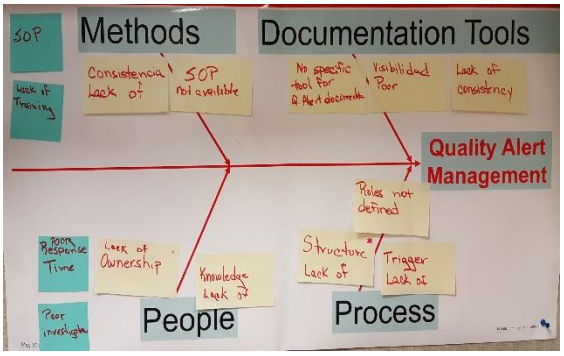

Figure 4
Cause and Effect Diagram

- This example represents a total reduction time of **70%** when compared to the estimated most efficient process time of 20 days calculated during the Measure phase.
- Additional Quality Alerts were notified during the period of September 14, 2020 thru October 31, 2020 with an average process cycle time of 7 days.
- Although some Quality Alert is not enough to demonstrate a solid control of the process, it indicates that the solution provided had a positive impact in terms of cycle time improvement along with the harmonization of the evaluation and documentation process from a compliance point of view.

CONCLUSION

The Quality Alerts Evaluation and response was improved in local plants (Puerto Rico) as well as Global Sites. As a result from the project it was established a standardized mechanism that allow the sites to evaluate the Quality Alerts notifications in the same way using the same tools and the evaluation performed by the corresponding SME's of the impacted areas.

As part of this project, can be concluded, and was demonstrated, that the correct use of the Lean Six Sigma methodology provides optimization and continues improvement. In addition, help the users to think out of the box and maximize the tools available at moment to use it at their convenience. In this project the cycle time to evaluate and response a Quality Alert to Global group was reduced from 20 days to an average of 7 days, but the tool used (Computer System) was an existing system by local sites as well as global ones.

The objectives pursued in this project were successfully fulfilled. Therefore, the customer and business requirements were achieved with the help of the correct project staff, since the strategy, evaluation and modifications were defined using the knowledge from the SME's.

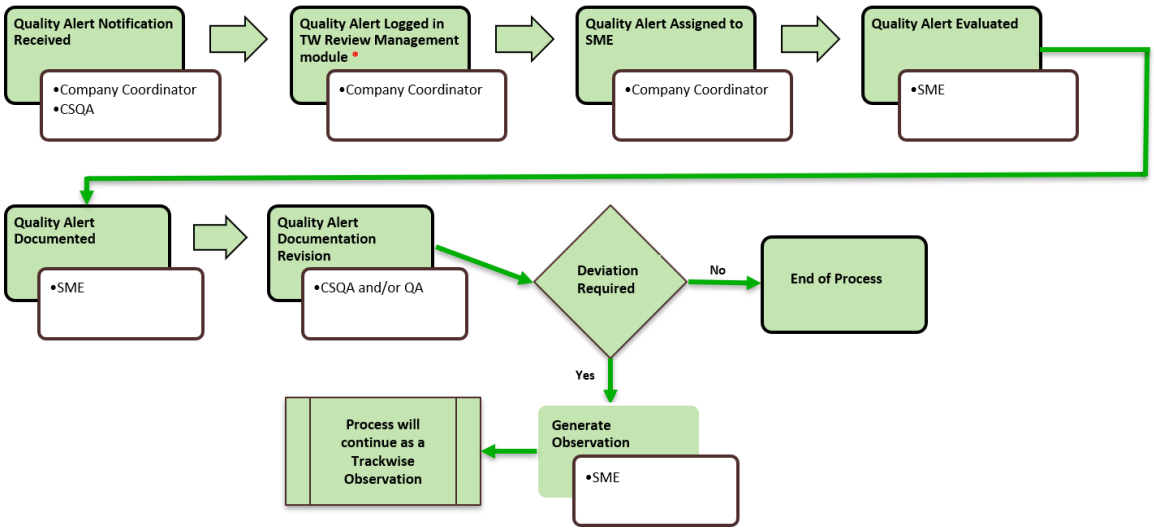

Figure 5
Company's New Quality Alert Management Process

The use of Lean Six Sigma and DMAIC methodology helped to implement this project in a structured and correct way. Also, it improved the compliance and commitment to the patient safety in local and global sites evaluating and responding more faster adverse situations related to computer systems (data, process performance, etc.). Finally, harmonization was produced when all sites with the same problem situation take the correct implementation and implement the same corrections.

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