Enhancement of CAPA's and Audits Responses in a Medical Devices Industry

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Abstract *— In the regulated industry of medical devices, different issues can compromise regulatory certifications. The CAPA and Audit system were presenting a situation regarding the submission of responses; Timeliness. One of the objectives was to reduce the quantity of extensions requested. During the collection and presentation of data using DMAIC, 24 CAPA's and 7 audits were analyzed. Identifying the quantity of extension and its justifications. The majority of justifications were about complete a criticality assessment in CAPA's and incomplete trainings in audits. After a difficulty impact analysis, workload and decision making could be two of the principal contributors for timeliness. 25% of CAPA's exceed the general rule of requesting only two extensions. The audits does not have a rule. One of the suggested improvement was the implementation of a tracking system, which could facilitate the process. Continuous monitoring should be performed to ensure the effectiveness and the reduction of extensions requests.*

Key Terms *— Audit, CAPA, Medical Device, Timeliness.*

PROJECT STATEMENT

In the regulated industry of medical devices, products with Non-conformance normally initiate an investigation; to find the root cause of the nonconformance. The manufacturing industry must follow federal regulations and Standard Operations Procedures (SOP's) to maintain investigations comply with established requirements. A variety of aspects are audited, timeliness of Corrective-Action/Preventive-Action (CAPA) system and Audits observation is one of them.

Research Description

This research wants to analyze, evaluate and improve the timeframe for completing a CAPA and observations response of an audit, which in most cases is not on time. In the majority of the cases an extension is requested by the auditee or CAPA coordinator to schedule a new due date. The problem found regarding the responses of an audit observations and CAPA investigations is that more than two extensions are requested. Most of the cases and the investigation/audit cannot be closed, on the due date based on the priority that the project has. Some of the possible causes are that the time limit for the CAPA investigations or audit responses is not enough, Quality Improvers had a large quantity of tasks or assignments, the implementation of corrective or preventive actions are complicated.

Research Objectives

The expected objectives of this research to be accomplished are:

- Reduce quantity of extensions requested;
- Maintain quality of the procedure of CAPA investigations, audits and improved systems;
- Develop a platform that helps close investigations of CAPA or audits procedures on time.

Research Contributions

With this project the company will improve their CAPA system review and audits by closing their investigations on time. In addition also create tools for the quality improvers to have a perspective of how to work with the problems in a shorter time and comply with the regulations.

LITERATURE REVIEW

The 21 Code of Federal Regulations (CFR) part 820, International Standardization Organization (ISO) 13485:2003 and Standard Operations Procedures (SOP's) property of the

company are used to establish standards with the purpose of fulfill the requirements. These standards help to ensure that non-conformance investigations comply with the established requirements of an organization. During an audit conducted in a regulated industry by internal or external parties, the auditor can audits a variety of systems but one related aspect to the system can be timeliness. Timeliness is considered a projected timeframe commensurate with the risk and magnitude of an issue and considered reasonable by a company to finish an investigation [1]. This opportunity of timeliness can be linked to the Corrective-Action/Preventive-Action (CAPA) systems or to the response of an observation from an audit.

CAPA is a systematic approach that includes actions needed to correct, avoid recurrence, and eliminate the cause of potential non-conforming product and other quality problems. A CAPA investigation begins with analyzing the process, investigating the root cause, identifying corrective and preventive actions, verifying and/or validate CA and PA prior to implementation, implement CA and/or PA and finalize with the evaluation of the effectiveness. Most of the times, regulatory actions taken by FDA and foreign regulators, are linked to inadequate CAPA systems [1].

Timeframes for completing CAPA actions must be established based on the risk of the situation under investigation; four weeks for low-risk situations, three weeks for medium-risk situations, and two weeks for high-risk situations [1]. Different timeframes can be established for each phase of the investigation. When an investigation is reaching its time limit, management often increases the pressure on investigators and reviewers. The result is that most investigations can be inadequately completed but closed without exceeding the time limit [1]. Also the extension requests are available if the investigation cannot be on time; the majority of the investigations, request more than two (2) extensions during the CAPA life cycle.

Regulatory agencies also took into consideration Internal Audits. An audit is a systematic, independent and documented process for obtaining evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled [2]. Audit process includes: opening meetings, data collection and analysis of evidence, exit meeting providing final report of observations made through the audit and follow up activities. Findings and nonconformities are identified by the auditor through corrective action request; the auditee acknowledges the request and submits a plan to correct the deficiencies [2]. The primary concern with timeliness is the completion and verification of the effectiveness of the corrective action.

If the corrective actions are completed on schedule is considered to be timely. There are times when delays occur that are beyond the auditee and continual request of extensions are made to fix the problem, conclude a phase or answer an audit observation. One of the most important contributions of the CAPA system and internal Audits in this case is that it continuously improves the effectiveness and efficacy of its Quality Management System [2].

METHODOLOGY

In this design project, DMAIC will be used in order to accomplish and present the expected objectives.

Figure 1
DMAIC Process

- ***Define*** **–** consist in identifying opportunities for improvements, defining objectives and determining project scope or problem statement and his contributions to the industry.
- ***Measure*** – is where the majority of evidence is collected, to establish an activity process map of the process performance.
- ***Analyze*** - consist in identify the possible root causes that can affect the value stream of the researched situation.
- ***Improve*** – is the phase which consists in design and implement potential solutions to eliminate the root cause.
- ***Control*** - during this phase the expected objectives are proved to be efficient. Also that can be further improved to maintain the new design aligned with the quality requirements for the process being improved.

RESULTS AND DISCUSSION

The results obtained during this investigation are presented in this section.

Define Phase

This research in a medical devices manufacturing industry wants to analyze, evaluate and improve the timeframe for completing a CAPA review process and observations response of an audit, which in most cases is not on time. The problem found regarding the responses of an audit observations and CAPA investigations is that more than two extensions are requested in most of the cases and the cases cannot be closed on the due date based on the priority that the project has.

The expected objectives of this research to be accomplished are:

- Reduce quantity of extensions requested;
- Maintain quality of the procedure of CAPA investigations, audits and improved systems;
- Develop a platform that helps close investigations of CAPA or audits procedures on time.

With this project the company will improve their CAPA system review and audits by closing their investigations on time, but managing adequately performed and implemented strategies to the process or system being improved

Measure Phase

In order to facilitate the understanding of the process of CAPA and Internal Audit, the collection of data helps to known each stage and what is performed during each phase. In the figure 2 and 3 CAPA Process Flow and Audit Process Flow respectively is presented each one of the stages of a CAPA Investigation and Audit Investigation.

Figure 2
CAPA Flow Process

Figure 3
Audit Flow Process

A summary of each phase will be presented in order to understand the CAPA process.

- Evaluation phase- is when an issue or a potential problem is identified and can initiate a CAPA, the CAPA Board members decides if a CAPA needs to be open.
- Initiate phase- the resources or CAPA coordinator is assigned. The situation is identify and documented also containment actions are executed in order to establish primary controls.
- Under Investigation phase- is where a proposed implementation plan is establish and presented to the board. After the previous phases CAPA Board members have the responsibility of review the report and approve the presented plan.
- Implementation phase- is where Corrective and Preventive actions are implemented.
- Effectiveness Review phase- is where the monitoring of each one of the implemented corrective or preventive actions is performed. Performing a new analysis of the process during this phase it will determine if the root cause of the problem was controlled.
- Closure phase- a summary report should be completed and approved by the CAPA Board members to consider the CAPA closed. Approximately from 14 – 60 days are the timeframe in calendar days to perform the Initiate phase through the investigation report in the Under Investigation phase. Depending of the CAPA severity the investigation phase could not exceed 30-60 days.

Each phase of an audit will presented next to understand the process.

- Audit planning- is where, the schedules of the areas to be audited around the year are stipulated, coordinate the audit agenda, audit plan, scope, objectives and checklists are determined.
- Audit execution- opening meetings are held to announce the purpose of the audit and what will cover. Also the audit is conducted in the audited area. After that phase is complete a report is created in order to present the findings and improvement that can be perform to ensure compliance with the regulations. After the report is delivered to the responsible of the area the auditee must provide evidence of the corrections plan to be implemented within 30 days after the report date. And if the corrective actions cannot be achieved during the days for each action needed they should request an extension.
- Closing- is when the auditor revise the effectiveness and implementation of corrective actions with the intended purpose of eliminate any situation that can affect a process and not comply with a regulation.

In the Medical Device (MD) industry the CAPA and Audit process flow is very similar to the found in the references. During each one of the phases the CAPA coordinators or auditees should address on time each one of the responses during the proposed completion dates. In figure 4 it is presented the process which the CAPA and the Audits follow in the industry.

Figure 4
CAPA & Audit Flow in Medical Device Industry System

Performing data research of past's CAPA's and audits and interviews were the tools used to collect the information required to perform this project. From October 2013 through March 2015 twenty-four (24) CAPA's and for the audits the year 2014 with a total of seven (7) audits were choose to be analyzed. The interviews were performed to help understand the process by the point of view of the employees who work directly with each one of the process.

In figure 5 CAPA's Source it shows the major contributors for opening new CAPA's. Were customers' complaints was the major offender with a 33% and internal audits with 25%. Also in the collected data, the majority of new CAPA's were opened during December 2013 with a total of seven (7), following with three (3) November 2013 and January 2014. In the next months the opening of new CAPA's fluctuate between one and two per month, for a total of twenty four (24) new CAPA's, as show in figure 6. Twenty four CAPA's were categorized by the phase or stage that they were. Two (2) Under Investigation, five (5) on Implementation, one (1) in Effectiveness Review, eight (8) Closed and the last eight (8) were Cancel.

During the audit data collection all the audits from the 2014 excluding third party audits were took for the research. In figure 6 Audit Status from a total of seven (7) audits a 43% of the audits were In Process and a 57% Completed. Each audit can have more than one observation in different areas or repeat the areas. The data also demonstrate that the majority of the observations were three (3) in a variety of departments. The total of observations for the seven (7) audits were nineteen (19). During the interviews of the employees key elements that were discusses are categorized such as:

- Complexity;
- Daily Tasks;
- Training;
- Timeframes;
- Resources;
- Decision Making;
- Format for Extension Request and
- System

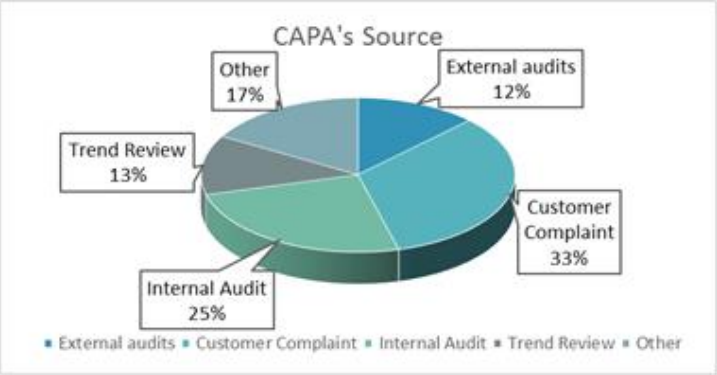

Figure 5
CAPA's Sources

Figure 6
Audit Status

Analyze Phase

During this phase the primary goal is to identify possible causes for the timeliness in the CAPA's and Audits responses. During the CAPA life the request of extension were categorized in the times an extension was requested. In figure 7 Extension Requested during CAPA Life presents that a total of nineteen (19) extensions were requested for the period of October 2013 through March 2015.

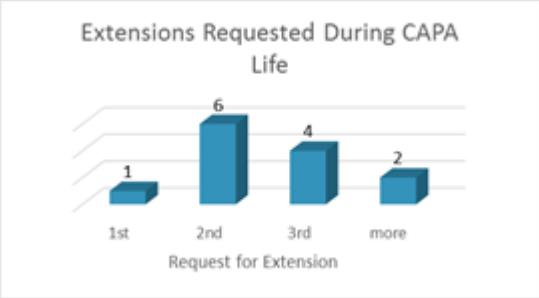

Figure 7
Extensions Requested during CAPA Life

One (1) extension was requested for the first time, six (6) for second time, four (4) for third time and two (2) for the fourth or fifth time that are classified as more. Another analysis performed were the Quantity of Extension per CAPA life. It was identified that the PA AA has five (5) extension and the CAPA AB four (4). Two CAPA's and two PA's have three (3) extensions each one of them. Six (6) CAPA's and PA's only have two (2) extensions, only one CAPA have one (1), eleven CAPA's and PA's does not have extensions. The PA AA and CAPA AB were identify with the most quantity of extensions; both were classify as Customer Complaint type and Normal type which both have 60 days for the Investigation phase.

In each extension request a reason or justification for the request of extra time and change the due date is required. In figure 9, Reasons for Request a CAPA's Extension are identified the most common reasons. The graph demonstrate ten (10) request extensions for time to complete a Criticality Assessment also ten (10) extensions to complete activities which can include a variety of activities for example during the implementation or other phase.

Taking into consideration all the reasons to justify the request of an extension for the due date, having as major offenders Time to Complete Criticality and Time for completion of activities the reasons will be used to analyze using a Cause and Effect Diagram. For the Audits part in figure 8 shows, that eight (8) extensions were requested during an audit life.

Figure 8
Extension Request during Audit Life

The request for first and second time were four (4) and zero (0) requests for the third or more time.

With the requested extensions the reasons should be provided also each extension can have more than one reason. In figure 10 Reasons for Request an audit extension are presented. The major reason for request an extension were Training and Complete Changes founded in four (4) extension each one, following were Identify Impacted Procedures, Identify Resources with three (3), Return to previous phase with two (2) and with one (1) Additional Changes after Approval, Approval Process and Complete Implementation.

After executing the measure phase were all the stages were identified, possible triggers considered to be attached to root causes of our main problem *Timeliness* were established. The root causes will be presented in a Cause and Effect (Fishbone) Diagram figure 11 and figure 12 for CAPA's and Audit respectively.

After collecting a considerable amount of data and perform an analysis; the majority of the requested extensions don't provide enough justification for the lack of completeness for the activities. Also the differences between the CAPA

and Audit extension justification should be very similar in reality they weren't. Taking into consideration the Impact Difficulty Analysis Table 1 and Table 2 both were very similar.

In High Difficulty and High Impact the cause was Workload on both, which can be diminish delegating and creating support groups and decision making. These quality systems are truly connected in the way that the improvements can be very similar or the same.

Table 1
Impact Difficulty Analysis for CAPA's

	Low Impact	High Impact
High Difficulty	Lack of Tracking	Decision Making Workload
Low Difficulty	SOP's Reports	Training Lack of time Investigation Reviews

Table 2
Impact Difficulty Analysis for Audit

	Low Impact	High Impact
High Difficulty	Lack of Tracking	Workload
Low Difficulty	Priorities SOP's	Training Lack of Time

In CAPA's the 25% exceed the general rule that no more than two (2) extension should be requested or submitted through all the period of the CAPA. In the Audits responses, there is not a general rule which could limit the request of extensions. Even that only eight extensions were requested having nineteen (19) observations during seven (7) audits.

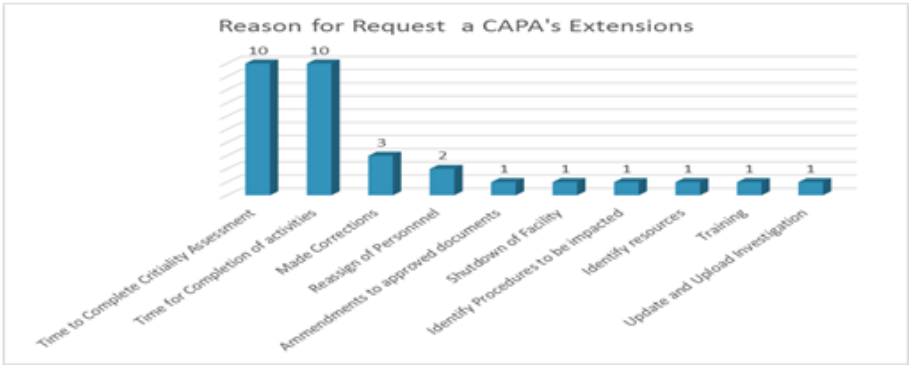

Figure 9
Reasons for Request CAPA Extension

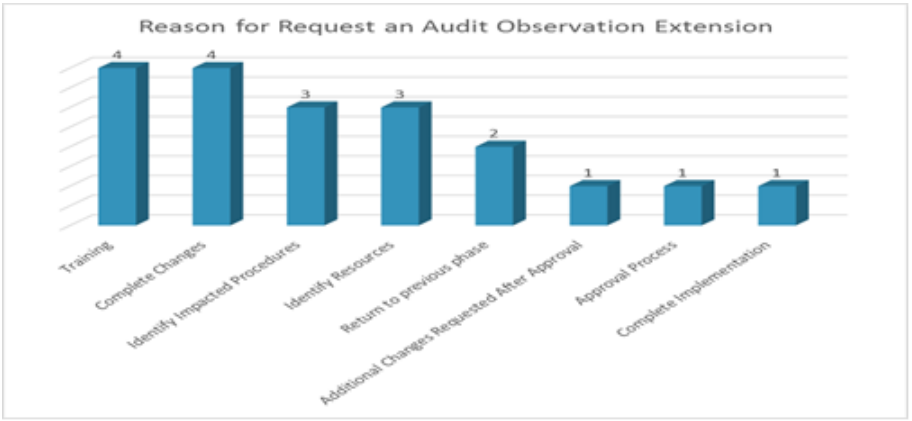

Figure 10
Reason for Request an Audit Extension

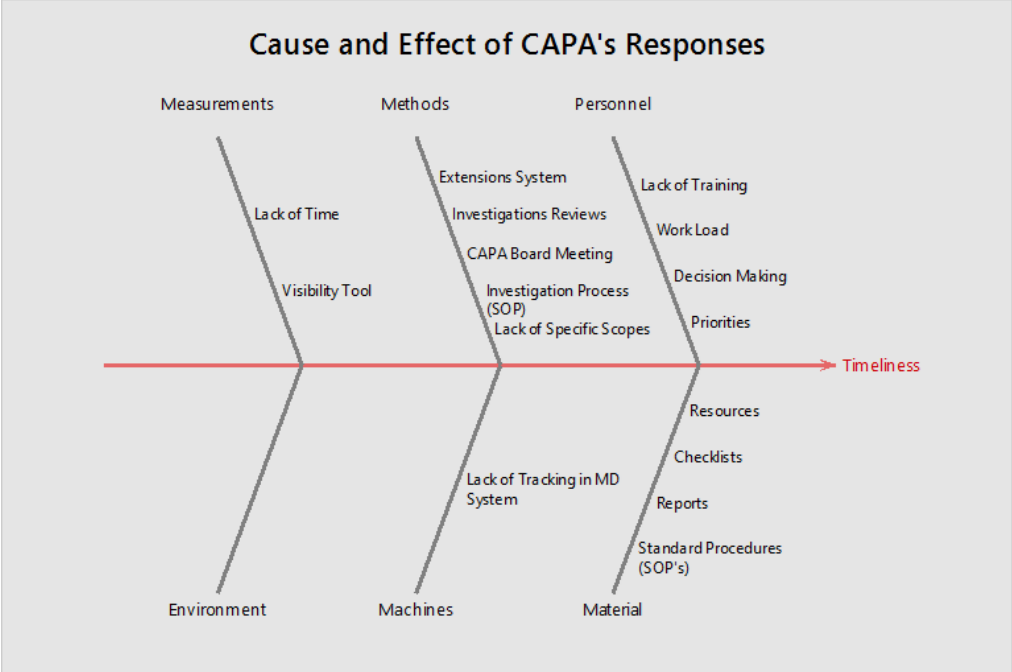

Figure 11
Cause and Effect of CAPA's Responses

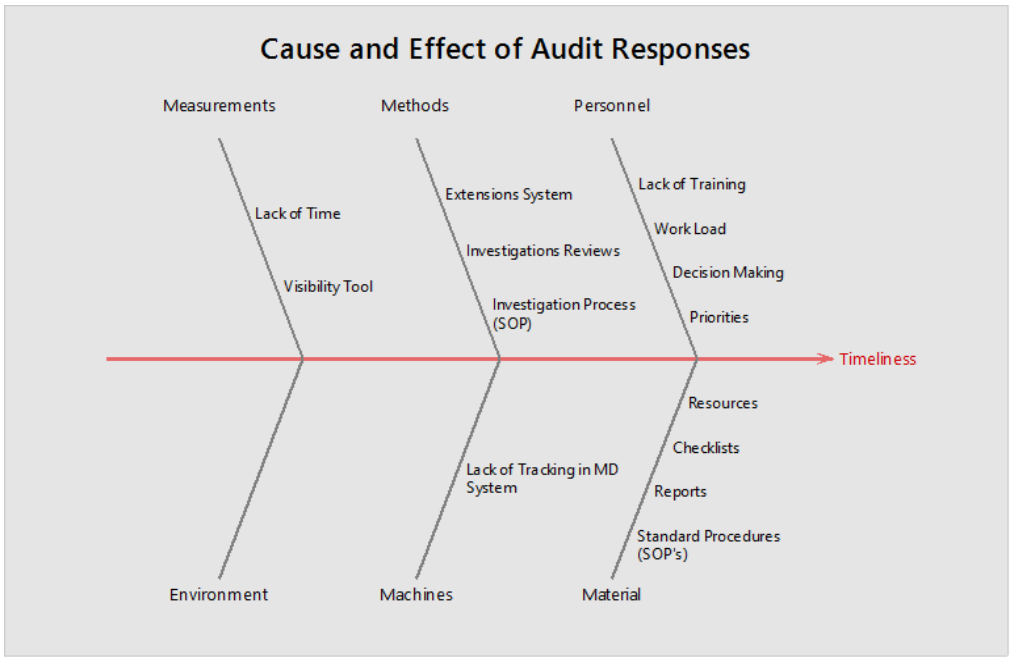

Figure 11
Cause and Effect of Audit Responses

Improvement Phase

During this phase the goal is to design and implement potential solutions to eliminate the root cause of the problem, based in the data gathered and analysis performed during the previous phases.

- Implement an automatic tracking system which could send CAPA's coordinators, approvers

and auditees, messages with due dates. In order to eliminate the manual tracking system sending individual emails to remind due dates;

- Classify the CAPA's and audit observation responses in accordance to the complexity and adjust timeframes;
- For Audit purpose determine the quantity of extensions permitted to be requested and evaluate the justifications presented to request extensions in both cases;
- Estipulate very concise a timeframe of days in every phase, especially for approval process, identify with each approver the quantity of days they could use to review and approve in the work flow;
- Training was an issue that constantly repeats, improve in the department better ways to help approve during process;
- Educate the persons that an Internal Audit has its purpose and have relevancy even that is not external;
- Try to reduce the opening of new CAPA's or Audits near the date of shutdown in the facility;
- Establish a group of each unit as resources to work in the investigations;
- Take into consideration the quantity of tasks for the investigators or auditees, help to create a way to delegate tasks through the culmination of the investigations;
- Improve the CAPA Training, creating groups to teach and refresh the knowledge of how to conduct a proper investigation, write reports or preparedness for interviews of third party audits;
- Timeframes that are not sufficient by the complexity, create a team of persons which could be CAPA Board members to evaluate timeframes;
- Create groups dedicated to the CAPA investigations, to help assure the knowledge of all the parts including approvers and limit the back and forward between parts and will help in the decision making;
- In the extension requests the phases are not contemplated, revise extension request format and include validate justifications in the format;
- The perspective of concluding an investigation first, before perform an excellent investigation is present, implement a new way of thinking by giving trainings related the theme.

With the implementation of the possible solutions previously presented the CAPA and Audit system can be improved. Various solutions are oriented to educate the employees, so it would be challenge the culture and perspective of some of them, always willing to improve systems and the company.

Control Phase

During this phase the expected objectives are proved to be efficient. Also that can be further improved to maintain the new design aligned with the quality requirements for the process being improved. To achieve the effectiveness of each one of the solutions previously suggested, a plan should be created with the purpose of monitoring each one of the effectiveness. A continuous evaluation of the quantity of the extensions requested in CAPA's and Audits should be address to help understand the reasons for request. A continuity in the education of the employees will help to ensure the compliance of the quality systems previously analyzed. Monitoring is the key of success to help diminish the incidence of timeliness present in CAPA's and Audits.

CONCLUSION

This research in a medical devices manufacturing industry wants to analyze, evaluate and improve the timeframe for completing a CAPA review process and observations response of an audit, which in most cases is not on time. During the Define phase the identification of the research objectives result in three (3) objectives: reduce quantity of extensions requested; maintain quality of the procedure of CAPA investigations, audits

and improved systems; and develop a platform that helps close investigations of CAPA or audits procedures on time. In the measure phase, a variety of offenders which could affect the responses of CAPA and audits were identified. After the identification of the potential causes of timeliness in the CAPA and Audit systems, the suggestions of improvements were made. In order to help ensure the compliance of the systems with the standards provided by regulatory agencies and the company standards.

Some of the suggested improvement to improve the CAPA and Audit systems were the implementation of an automatic tracking system which could send CAPA's coordinators, approvers and auditees, messages with due dates; Classify the CAPA's and audit observation responses in accordance to the complexity and adjust timeframes; determine the quantity of extensions and review the justifications to request more time; identify the quantity of days that a reviewer or approver should complete the process, evaluate timeframes; create groups to be dedicated to each CAPA limiting the back and forward during the process previous CAPA Boards meetings; continuous education to the employees, seeking the commitment between them and the improvement of the systems among others. Also monitor continuously the systems to ensure that systems are not with timeliness problems.

Understanding the CAPA and Audit systems in a Medical Device Industry granted the knowledge to help improve the systems. The suggested improvements and control techniques will help ensure compliance with regulations and with the organization standards. These systems are one of the most critics in an industry, because they treat critical or problematic situations that can harm the company certifications by regulatory agencies. The research objectives are considered accomplished after the improvement and control phase.

REFERENCES

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