Computer System Validation Cycle Optimization

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Abstract *— The concept of the project involves the optimization of a current Computer system validation cycle in an active project in the biopharma industry. The root cause for the problem was the excessive amounts of deviations that were being received due to a deficient document generation process. This has been solved by identifying a gap in the review process and putting in place an engineering subject matter expert to review the documents. The end state is reducing the amount of deviations obtained by document at the Quality Assurance level or during the execution. Upon verification, the implementation of technical engineering review layer deviations were reduced to the point of having significant savings towards project managing events. Thus confirming that by having a technical review after generation of the document gaps were reduced to half of what was expected originally.*

Key Terms *— Computer System Validation (CSV), General Manufacturing Practices (GMP), Food and Drug Administration (FDA)*

INTRODUCTION

In a world where everything gets regulated or scrutinized, healthcare products are not the exception. The intent of this project is to optimize the documentation aspect a Computer System Validation cycle in an ongoing project. This project is taking data from an active project in a biopharma manufacturing site. The objectives for this project are:

- Minimize deviations- The Intend driving this optimization is the reduction of deviations found during the documentation process to include testing.
- Have budget savings- By optimizing the documentation process there will be some savings that can be utilized for further activities.

LITERATURE REVIEW

Background

Back in the day, medicine was considered whatever was sold as the "miracle elixir", the "cure all". This caused a lot of tragedies during the early years of the 1900s. One mayor event kick started the entire regulatory mentality in the industry. The publication of The Jungle helped exposed the unsanitary conditions and the terrible conditions in which the meat packing industry dealt business: unsanitary conditions, dead rats mixed with ground meat, and rotten meat that was sold to the public as "good" or "fresh". This created pressure from the public to Pass the Pure Food and Drug Act of 1906 which covered and protected the public from events like the Chicago Meat Packing. This act also covered the correct and accurate labeling of medicine in the containers to avoid any misbranding or false statements regarding the potency of the medicine. Shortly after this events, the federal regulatory agency that it is now known as the FDA came to existence. In the 1930s, the FDA included cosmetics in the regulated articles since a lot of women were experiencing ill effects after applying the products. During the 1960s, more critical cases were registered involving medicine to treat morning sickness and sleeplessness. This medicine created secondary effects on fetuses creating deformations. In more recent years the FDA has continue to provide regulatory controls to provide safer and more effective medicine [1]. These regulations encompass what is called the CGxP in which the "x" represent manufacturing, clinical and laboratory.

Current Good Manufacturing Practices (cGMP)

The way of FDA ensures the population that the Food and Drugs to be consumed are to standard is by the implementation of the cGMP. These practices contain the minimum requirements for companies to follow. These include methods, types of facilities, controls used in the manufacturing of the food and drugs while covering processing and packing of the products. The entire concept behind the cGMP is to deliver a safe and consistent product to the consumer or patient. There are multiple regulations that are covered in the Code of Federal Regulations and the FDA is governed by the Title 21. which included sub regulations like 21 CFR Part 11, Electronic Record and Electronic signatures and 21 CFR Part 211 Current Good Manufacturing Practice for Finished Pharmaceuticals [2].

Documentation Cycle

Computer System Validation (CSV) is a highly regulated process in which the system gets documented and tested according to requirements. They go in detail by providing services to comply with the different aspects of the validation cycle as well as the different regulations that govern the CSV process. CSV is the process of ensuring that any technology component (software or hardware) is fulfilling its purpose in line with the regulatory guidelines for a certain industry. It is especially crucial in FDA-regulated industries like biotech and pharma, since products from these sectors impact public health and safety [3]. It follows the Good Automated Manufacturing Practice Model 5 or GAMP 5 [4]. See Figure 1 for documentation and testing correspondence in the cycle.

The documentation is the backbone of the CSV cycle. It holds in black and white all of the aspects of the systems. In this project the focus is to optimize the document generation process, the generation of a high quality document that accurate represents the functionality and configuration of the system. Following Figure 1, the project is targeting the Functional Specification and Design Specification Documents so that when the Validation team conducts the proper testing Deviations are minimal.

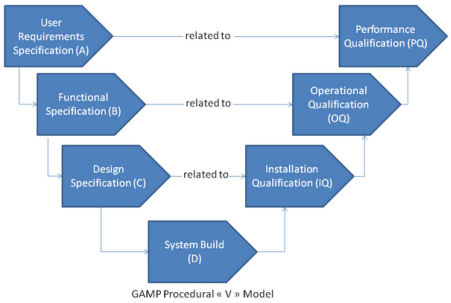

Figure 1

GAMP 5 Model

Deviations

Deviations are any event or finding that fails to reflect the expected. These could be anything from missing information, having a discrepancy in parameters while testing, bad wording, unapproved changes or not properly documenting changes. Once a deviation is found proper investigation need to follow to determine the root cause of the deviation and the impact on not only the document but also the process.

The effects of the deviation vary depending on the type. A quality impacting deviation will have effects on quality, purity and strength of the product. A quality non-impacting will not have the impact on the quality, purity and strength of the product.

The further prevent deviations sites my implement a CAPA or Corrective and action Plans. This is a management program that will focus on investigations of paste events or problems that had cause deviations in the past and the ones that can potentially prove critical to the events. They are very systematic and if used properly this tool can eliminate deviations by providing preventive actions [5].

ENGINEERING ANALYSIS

Methodology

The Implementation of the Engineering review layer; following the corrective actions of

implementing a layer of engineer technical review it can be determined that documents being generated were lacking a lot of the technical details. These details were missing because the document generator lacks the experience or knowledge to identify gaps in the information edited in the document regardless of functionally or design. This layer was implemented after the March 22, 2018 test that resulted in six (6) deviations. These deviations included lack of data in tables, failure to portray complete configuration and typographical errors in parameter transcripts from the production code.

Deviation Analysis

During the investigation it was found that in a period of 28 documents before the implementation, 8 documents produced deviations for a total of 10 deviation total in different events. These deviations triggered revision to the documents that fine-tuned the details and content of the original document.

Turnaround time

During the deviation analysis it was also found out that the engineering team took multiple days for the review and correction of the content in the documents. It is clear that during the day the engineer performing the review will not commit his/hers full day to this activity. For the most part the engineer will commit around 2 hours performing review by day since there are other activities that will continue the progress of the project to include coding and hardware configuration.

Investment cost for rework

To determine the total investment in the rework it's imperative to determine the contingency engineer team. This team consists of four (4) members that are part of the workflow in the approval of a document. The first member is a COOP, his/her role is the generation of the document, and this activity will be followed by the engineer performing the content review. After the document has been reviewed for content a QA engineer will review the document for formatting errors and compliance with site procedures. Lastly, the document will go to the document controller which will upload the document and start the approval process all over again for the new version.

RESULTS

After the initial assessment, multiple things were noticed. Sample size was not equal, only 28 documents were recorded before the implementation. The threshold stated by the Project Manager was 40%. This forecast was higher than what was encountered and 8 documents contained deviations out of the 28 documents, as seen in Figure 2.

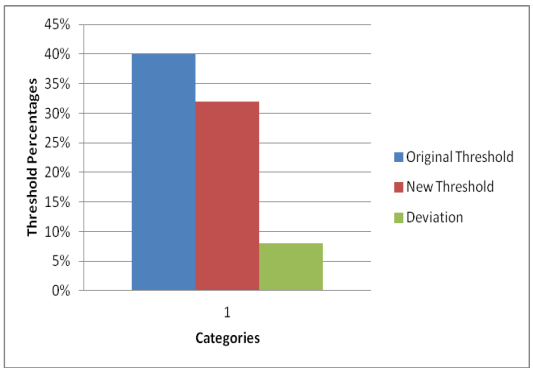

Figure 2

Before Implementation Deviation Thresholds

After the implementation, it was surprising to see that documents receiving deviations were lower than expected. Only 4 deviations were recorded surpassing the percentage of expected threshold by 7%, as seen in Figure 3.

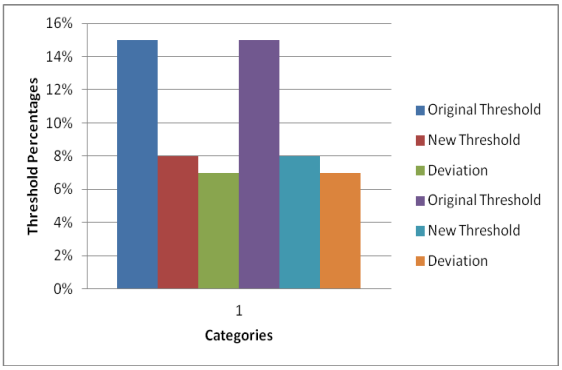

Figure 3

After Implementation Deviation Thresholds

Before implementation, the average turnaround was 14 days, but in reality engineering working on that document was 2 hours at the most per day. After the implementation, the turnaround average was 11.75. It went down a little, but for the most part it was not as significant change from the expected. The main reason for taking that many days per document review is that engineering is still working on the official code and most of their time is allocated to accomplish milestones in the automation department. To properly determine if it was used properly, the Project manager had to account for these events while balancing automation tasks without impacting the next level of activities.

Savings of the implementation

The Project manager was able to justify the implementation due to the large reduction of costs per document with deviations. With the exercise the project manger had an estimate of over $29,000 in savings as seen in Figure 4. These saving were calculated utilizing a Base salary per hour of $40 per document optimization team member multiplied by 2 hour of document review per turnover day.

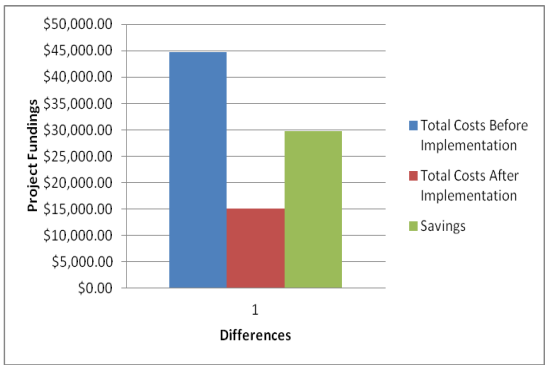

Figure 4

Cost analysis and savings

DISCUSSION

Following the analysis and the results obtained it can be determined that the implementation of this layer provided a better quality product that the validation team can rely on and that the company can utilize as a new standard of requirements across the board for the new system implementation.

CONCLUSION

For Capital Projects, proper planning is not only critical but imperative. Having a team that understands the task and have the technical knowhow of the system can prove crucial in the allocation of key players and the generation of the project schedule. This schedule has to account for not only the milestones, but also need to represent the reality of the expectations. Having someone in the team with the real knowledge can provide the PM with a real understanding of the activities that can and will affect the progress regarding system proper documentation and testing activities. Setting the documentation requirements from the beginning and creating a standard the team can follow effectively and smoothly during the duration of the project.

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