"The use Six Sigma in a Computer System Validation Project in A GMP environment"

Author: Tania Ramos
Advisor: Jose A. Morales Morales
Industrial Engineering Department

Abstract

Computer Systems Validation is a process used to test, validate, and formally document that a regulated computer-based system does exactly what it is designed to do in a consistent and accurate manner that is secure, reliable and traceable. This this is done under a very regulated environment. Biopharma industries uses computerized systems like The DeltaV™, that is an automation system that simplifies operational complexity. "The DeltaV™ is an easy-to-use system that simplifies operational complexity and lowers project risk. Six sigma is "business management strategy used by different industries to improve the quality of products or services produced by the business through the removal of defects and errors. The six-sigma methodology is to improve a process with a positive implication on quality of product or like in this case a service in the Information System Department to reduce the Computer System Validation delays in the IS Department to cero days in a GMP environment

Introduction

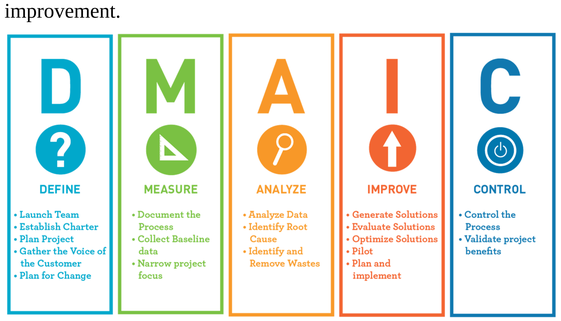
The Federal Drug Administration have a "General Principles of Software Validation guidance" and specified that Based on the intended use and the safety risk associated with the software to be developed, the software developer should determine the specific approach, the combination of techniques to be used, and the level of effort to be applied. "(FDA, 2002) All changes related to the system need to be validated withing the Information System/ Automation department because this system (DeltaV™,) is classified as GXP system in the Biopharma. Changes in the code will be validated in an off-line testing environment and once the validation is approving the Automation Engineers will download the code to the production environment.

Problem

In order to reduce Computer System Validation delays will be investigating all deviation created in a period to analyze root causes to determine and implement a solution and to improve download to production withing the Automation department to production.

Methodology

The six-sigma objective is to improve a process with a positive implication on quality of product or like in this case a service in the Information System Department (IS). Six Sigma techniques and tools is a common approach to continuous improvement in a business sector and often include a framework tool called DMAIC that outlines a method of identifying and challenging sources of poor quality, and inefficient processes, looking for opportunities for improvement.



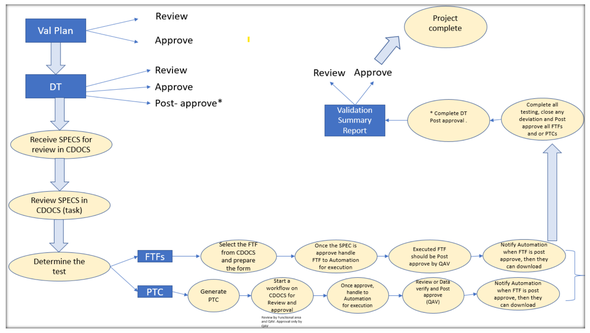
Results and Discussion

Define Phase

Project Charter	
Project Name	The use Six Sigma in a Computer System Validation Project in A GMP environment"
Business Case	**Scope, Constraints, Assumptions**
To reduce Computer System Validation delays will be investigating all deviation created in a period to analyze root causes to determine and implement a solution and to improve download to production withing the Automation department to production.	All deviation from the validation of DeltaV system in Q1
Problem/Opportunity	**Team Members**
Delays downloading a validated code into production environment	Computer System Validation Engineer — Team Leader
Goal	Quality Assurance Validation — Team Member Quality Assurance Validation — Team Member
Reduce Computer System Validation delays in the Information System/Automation department to cero days by Q3 2022.	Automation Engineer — Team Member Quality Manager — Stakeholder Automation Manager — Stakeholder IT Manager — Sponsor CSV Manager — Sponsor
Primary Project Plan	

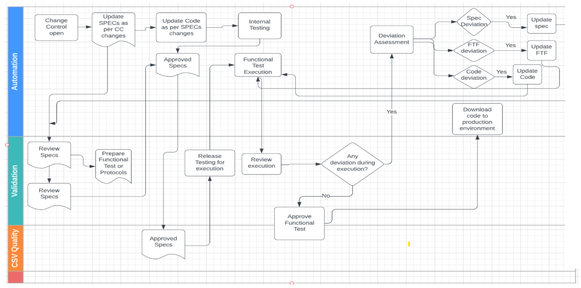
Project Charter

Measure Phase



Process Map

Analyze Phase



Value Stream Mapping

0 No relationship between the input and the outputs
1 Slight relationship between the input and the output
3 Average relationship between the input and the output
9 Direct relationship between the input and the output

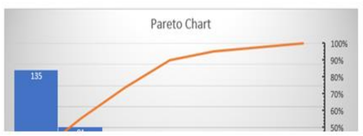
Voice of Customer (Rating of imp to customer)

Output (y)	Download on time	No deviation	No re execution	Total Value	Total Value %
Priority (Output rating)	9	3	3		
Input (x)					
Validation Plan approval	1	0	0	9	2%
SPECs review and approval	9	0	0	81	21%
Testing assessment	1	0	0	9	2%
Execution	9	9	9	135	35%
Testing approvals	2	9	9	72	18%
Deviations assessment	3	9	3	63	16%
Validation Summary report	1	3	1	21	5%
				390	

Cause and Effect Matrix

Root Cause Analysis		
Area	**Effect**	**Root Cause**
Delays in Specs review and approval	Testing delay	Different priorities from approvers Communication Schedule not updated
Execution	Testing delay impact the code download window	Re testing as per specs fails Re testing as per code fails Re testing as per execution errors

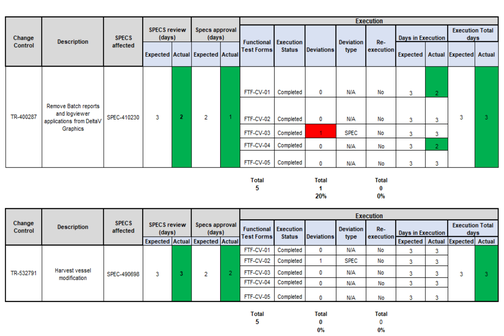
Root Cause assessment



Cause	Correlation Score	Total Value
Validation Plan approval	9	2.0%
Testing assessment	9	2.0%
Validation Summary report	21	5.0%
Deviations assessment	63	16.0%
Testing approvals	72	18.0%
SPECs review and approval	81	21.0%
Execution	135	35.0%

Process Data Collection

Improve Phase



Implemented Solutions	
Priorities	PM assigned, timelined monitored
RE-executions	Automation Eng. Include revisions in their internal testing
Executions	Validation eng included during the executions as a verifiers
Deviation Tracker	Validation Eng creates a Smarsheet including all the execution steps, tracking any delays. Smarsheet monitored by the PM

Post Implementation
Process Data Collection

Method

σ_1: standard deviation of Pre Implementation
σ_2: standard deviation of Post Implementation
Ratio: σ_1/σ_2

Descriptive Statistics

Variable	N	StDev	Variance	95% CI for σ
Pre Implementation	12	0.996	0.992	(0.455, 2.606)
Post Implementation	12	0.389	0.152	(0.158, 1.148)

Ratio of Standard Deviations

Estimated Ratio	95% CI for Ratio using Bonett	95% CI for Ratio using Levene
2.55930	(0.619, 13.125)	(*, *)

Test

Null hypothesis $H_0: \sigma_1 / \sigma_2 = 1$
Alternative hypothesis $H_1: \sigma_1 / \sigma_2 \neq 1$
Significance level $\alpha = 0.05$

Test

Method	Statistic	DF1	DF2	P-Value
Bonett	1.97	1		0.161
Levene	1.82	1	22	0.191

Variance
Test Analysis

Control Phase

Deviation tracker
- Responsible: Validation Engineer
- Description: Create, update and share with Team members and stakeholders
- Method: Smartsheet
- Frequency: Weekly

Priorities
- Responsible: Project Manager
- Description: Create schedules with cross functional department input
- Method: Standup meetings, Project Meetings
- Frequency: Each Change Control

SOP and Work Instruction
- Responsible: Automation Engineer
- Description: Update SOPs and Work Instructions guidelines to include internal reviews requirements
- Method: Documents
- Frequency: Before the project closure

Conclusions

The problem stated in this project has been solved: as shown in 5 the Six Sigma methodology section implemented with the DMAC tools represent consequent stages within Six Sigma implementation roadmap to reduce the delays in the coding the download to production in the Information System/Automation department.

Most important findings

- Internal testing is key in the process. Taking time for testing before the actual validation made a difference.
- Adding resources to the process like including a verifier demonstrate that deviations and time reduce significatively.
- Tracking tools – robust tracking tools and monitoring them helped the Automation department to had visibility on the time
- Project Manager - facilitates the project timeline to reduce any delays.

Future Work

There are some gaps in our knowledge around the Computer System Validation delays in research that follow from our findings, and would benefit from further research, including realist evaluation to extend and further test the theory we have developed here:

- In-depth exploration of how Change control can influence in the code downloading delays.
- Research could explore the types depending on the system change, that can include, parameters, graphics, recipes, formulas o phases and how these changes may impact the coding. Opportunity to explore the implementation of the finding solutions to another system beside this one (DeltaV), Logmate, RT reports or any other computerize system. Research could explore which systems may adapt to implement Sig Sigma in their process.

Acknowledgements

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