Improve service and efficiency of LAL Kinetic Chromogenic Method for a Combine Manufacturing Product

Author: Sheila M. Reyes Donatiú
Advisor: Rafael Nieves, Pharm.D.
Graduate School Polytechnic University

Abstract

A new supplier is now validated according to the requirements on the USP <85> Bacterial Endotoxin Test, USP <161>, ANSI/AAMI ST72:2011. This validation is conducted in order to comply with manufacturing and customer needs. This company has been dedicated to producing medical devices and advancing the delivery of healthcare for over a hundred (100) years. Considering this information, it is necessary to be persistent on our deliveries and to comply with the validation of Supplier 2. This validation becomes a positive outcome when shortening time testing thus making the documentation process easier and faster. This is also reflected as an economic yield.

Introduction

The essence of every Company is to deliver the best product. When working in a manufacturing environment, you need to follow procedures. Actions that the operator perform must be included or mentioned in these documents. The suppliers that are provide to companies must be validated and be included in procedures according to regulations. It is important that procedures provide more than one supplier for products the operator needs to assemble. The same thing occurs with laboratory tests in order to perform the tests, that confirm the excellent quality levels of products. For everything the test needs, procedures shall have more than one supplier. An opportunity is found in one of our procedures due to a distribution service inefficiency according to business needs. A new supplier shall be validated to eliminate waiting time, back orders and stopping the manufacturing line works. This promotes a better work efficiency and comply with our goal of advancing the delivery of healthcare.

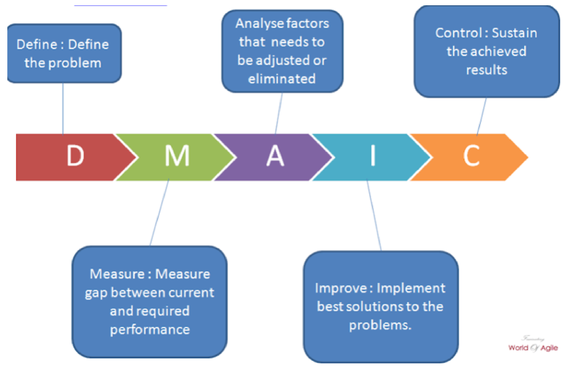
Problem

Supplier 1 distribution service inefficiency, delivery not on time based on business necessities and quality issues. Needs to look for an alternate supplier, the plant was limited to only one approved supplier. Supplier 1 (Actual Validated Supplier) notified no reagents will be received until near May 2018. The Manufacturing Company service to our customers will be affected by at least six (6) months. Our Combine manufacturing product reagents will be affected for testing of LAL (Limulus Amebocyte Lysate -LAL) Kinetic Chromogenic (KQCL) for raw material, in-process water and final product.

Methodology

The research methodology DMAIC on this project consist on the following steps. The implementation of DMAIC which is a six sigma methodology is show in figure 1 below.

Methodology



Figue 1. DMAIC methodology diagram.
EPMC Nurturing Careers, «Effective Project Management Consultancy,» [Online]. Available: http://www.effectivepmc.com/blog/lean-six-sigma/what-is-dmaic. [Last access: 29 09 2018].

Results and Discussion

As established on methodology; using the six sigma process DMAIC, a Supplier 2 validation process were performed and the results is shown below.

Define

The supplier 1 service inefficiency, their quality issues was solved by the validation of Supplier 2 and their approval on procedures when the release process was completed.

Measure

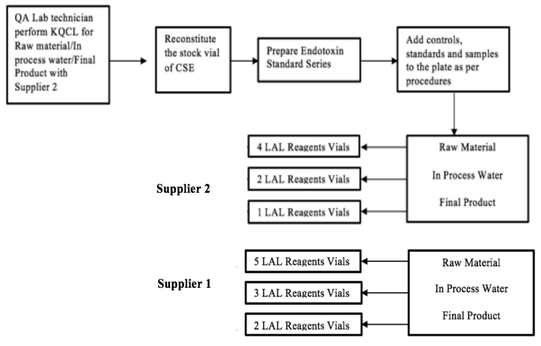


Figure 2. Supplier 1 vs Supplier 2

Results and Discussion

Analyze

When analyzing the process from start, yield reduction on time is 12 minutes shown on table 1 below.

Standard Endotoxin	
Supplier 1	**Supplier 2**
E. coli O55:B5	*E. coli* O113:H10
Vortex CSE solution for at least 15 minutes at a high speed.	Vortex CSE solution for at least 5-10 minutes at a high speed.
The reconstitution volume will yield a CSE concentration of 50 EU/mL	The reconstitution volume will yield a CSE concentration of 1,000 EU/mL.
Dilute CSE stock to the appropriate standard concentrations, vortexing each glass tube for 60 seconds prior to making the next dilution.	Dilute CSE stock to the appropriate standard concentrations, vortexing each glass tube for 30 seconds prior to making the next dilution.

Table 1. Time analysis for the reconstitution of CSE per Supplier.

A similar analysis was conducted with Limulus Amebocyte Reagent; yield conduction is now reduced by 16 hours. Analysis is shown on table 2 below.

Limulus Amebocyte Lysate reagent	
Supplier 1	**Supplier 2**
Reconstitution volume before use with 2.6 ml of LAL Reagent Water (LRW) per vial.	Reconstitution volume before use with 3.2 ml of LAL Reagent Water (LRW) per vial.
Reconstituted reagent is stable for 8 hours at 2-8 ℃ or can be stored at -10 ℃ for up to two weeks.	This solution is stable 24 hours at 2 - 8 ℃ or for two weeks at -20 ℃.

Table 2. Analysis for the reconstitution volume and stability time of LAL reagent per Supplier.

Improve

The qualification/ validation activities for KQCL assay with Supplier 2 were performed according to procedure ANSI/AAMI ST72:2011, USP <85>, and our procedures and the results were found satisfactory. Refer to Table 3 below for results.

Results and Discussion

Product Description	Item No	Lot No	Maximum Validation Dilution	Product Dilution	Positive Product Control (PPC) Recovery	Acceptance criteria	Meet Acceptance criteria YES (Y) or NO (N)
Raw material Sample	1X	X	Calculated per ISO	1:10	All values results within acceptance criteria per regulations and our procedures.	50%-200%	Y
				1:100			
				1:1,000			
				1:10,000			Y
In Process Water	1X	X	Calculated per ISO	1:10		50%-200%	
				1:100			
				1:1,000			
Final Product	1Y	Y	Calculated per ISO	1:10		50%-200%	Y

Table 3. Results of Inhibition/ Enhancement/ Screening for raw material, in process water, and final product using KQCL Method with Supplier 2 Reagents.

Also an economic evaluation was performed and we have a favorable variance of $52,842.57 in a total of 183 lots that was tested.

$$Cost\ Saving = (183\ lots)(\$286.79) = \$52,482.57$$

Control

Procedures were updated to reflect a new supplier Acceptance Criteria and implementation of usage of Bacterial endotoxin test/KQCL method using Supplier 2. The results for our combined manufacturing product with Supplier 2 is a reduction on cost and the reduction on scrap materials.

Conclusions

The qualification/validation of this new supplier was made considering the necessities of the company and the manufacturing line requirements to comply with customer needs. This project was designed initially to have an alternate supplier instead of depending on only one. Afterwards, an economic evaluation was performed and a yield reduction on test time and cost was reflected. The yield reduction on test time helped the manufacturing line and receipt and product release was faster and there was continuity with their manufacturing steps.

Future Work

With this new validated supplier, future projects could be conducted. For the same manufacturing product, we realize a pH assay and we have only one validated extraction solution. In the future we could validate a new supplier with another extraction solution for the final product.