Cost Improvement Process CIP LAL Sample Selection Procedure

Author: Frank Alvarez Delgado
Advisor: Rafael Nieves Castro, PharmD, Mechanical Engineering Department

Abstract

The Cost Improvement Process for LAL Sample Selection Procedure was identified with the purpose of reduction of cost and increase in revenue. This process was analyzed and overviewed, estimating an annual saving of over $50k. This was all done eliminating the need for use of end-items for testing and using scraped parts instead.
DMAIC project methodology was used to attack this project. This methodology was used to develop a new strategy and new process steps in order to make the use of scraped parts possible. This process underwent changes in various stations, including documentation and layout of the manufacturing process. The steps added to this process attack the LAL sample selection, while introducing new instructions on how to handle material and how to obtain the most out of the lot and out of the line. Implementation of this project is within compliance of the regulation agencies requirements, from the employees engaged with this process and with the technicians performing the LAL testing in the laboratory.

Project Description

Limulus Amebocyte Lysate (LAL) is a qualitative test for detection of Gram-negative bacterial endotoxins. This test is performed in order to ensure that manufactured product at BD Humacao is not compromised. LAL testing is performed in the laboratory using ten (10) samples retrieved from the lot after quality inspection. This procedure is critical due to bacterial growth called Pyrogen that may cause a fever reaction in humans and could be fatal, which could compromise the product. Given the fact, these ten (10) samples are selected from every manufactured lot. Three to four lots are manufactured per month. This is a 30 to 40 product loss each month. Which intend, this translates to loss of revenue and increase in expense.

Objectives

The main objective is to develop a Work Instruction for daily extraction of scraped product that can be used for LAL testing and represent the lot. This includes specified instructions for the operator to follow and successfully complete the sample selection process. It also includes specific instructions on how to manage these samples in order to maintain them segregated from the lot and how to complete the manufacturing process as described in the MP. Revenue increase will be the focus while maintaining the process between MP lines and in line with the requirements provided by the FDA. A $50K yearly saving is projected and a better handling of the lot.

Methodology

Sample Selection

- Scraped product will be placed in enclosed bins, prepared for LAL sampling to ensure no debris or any particles come in contact with the scraped product. After the shift has ended and all documentation is finished on good product, the operator will continue to follow to step 15 on the LHR Traveler and start with the LAL Sample Selection procedure. The operator will then select samples to be used for LAL testing following the WIM0307 (Work Instruction).

Manufacturing Procedure

- Following this same work instruction, the scraped product selected for LAL testing will undergo Zero Load Clip Installation, Strap to Tray Installation and Package seal. This process will be under the same instructions and same parameters as the good, manufactured product. The operator at package seal must inspect every sample to ensure all manufacturing processes have been correctly performed and that the sample is qualified for LAL testing following the SOPQ0065 and WIM0307.

Inspection Procedure

- Inspection procedure will consist of the same parameters. A new table will be added in the LHR Traveler for the purpose of selection and inventory. This table will include quantity of samples for LAL selected from scarped parts as well as quantity of samples selected from the lot if the scraped parts do not meet the amount of ten minimum samples needed for LAL testing.

Proposed Analysis and Implementation

- A DMAIC process improvement analysis will be performed to select the best strategy to achieve and implement this project. Utilizing these principals to ensure that $50K savings is met and exceeded.

Results and Discussion

Define Phase

Final Selection for LAL Samples is done in the inspection process. In every lot the inspection specialist withdraws 10 pieces from the lot to take them to the laboratory for LAL testing. This method of selection takes End-Items that could be sold to the customer. The purpose of this project is to change this method within what the SOP of sample selection allows. Change in this method could affect other stations and other documentation.

Measure Phase

As part of this phase, measurements from recorded data over a year was observed. Every lot that was produced this past year was taken into consideration to have real and concrete data to be used. It was found that during this past year 30 lots where manufactured, in which 10 End-Items form the manufacturing line were taken for LAL testing. Cost per part was obtained and a Cost Analysis was generated to have a projected cost/savings report. This analysis will be shown in Figures 3, 4 & 5.

	Lot Serial Number	Quantity	Shipment Day
Fixation 15 Tacks	HUDW1901	430	11/4/2019
	HUDX1555	425	12/13/2019
	HUDY0404	470	12/20/2019
	HUDZ0175	415	1/31/2020
	HUDV2032	100	2/13/2020
	HUDY0630	425	2/21/2020
	HUEP0700	450	3/27/2020
	HUEV0187	220	8/27/2020
	Total Lots	8	

Figure 3: Fixation 15 Count Lot Review

	Lot Serial Number	Quantity	Shipment Day		Lot Serial Number	Quantity	Shipment Day
Fixation 30 Tacks	HUDU1760	565	9/9/2019	Fixation 30 Tacks	HUEN1872	475	6/24/2020
	HUDU1761	570	9/13/2019		HUES0749	440	6/24/2020
	HUDU1762	570	9/16/2019		HUES0748	370	7/2/2020
	HUDU1763	550	9/26/2019		HUES0750	415	7/10/2020
	HUDV2034	425	10/18/2019		HUDZ0174	440	7/24/2020
	HUDV2035	435	10/28/2019		HUDX1553	405	7/24/2020
	HUDW1899	455	11/4/2019		HUET1709	340	7/24/2020
	HUDX1554	465	12/9/2019		HUET1636	420	7/31/2020
	HUDW1900	460	1/27/2020		HUDZ1222	455	7/31/2020
	HUEQ0334	445	4/3/2020		HUEU0693	394	8/11/2020
	HUDZ1933	440	5/1/2020		HUEU0693	390	8/20/2020
	HUEQ1490	395	6/15/2020		HUEU0696	450	8/21/2020
	HUEN1508	435	6/19/2020		HUEU0694	430	8/31/2020
	Total Lots	13			Total Lots	13	

Figure 4: Fixation 30 Count Lot Review

	Item Number	Qty of Lots	Qty for LAL	Total Samples	Standard Cost	Cost per Item	5% Scrap
Cost Analysis	0113315	8	10	80	$ 270.90	$ 21,672.00	
	0113330	26	10	260	$ 300.82	$ 78,213.20	5% Yield
	Annual Cost			Projected Cost/Savings For this Year			$ 63,260.63
	0113315 + 0113315	$ 21,672.00 + $ 78,213.20	= $ 99,885.20	$ 99,885.20 / 12	$ 8,323.77 x 8	= $ 66,590.13	

Figure 5: Cost Analysis for Fixation 30 Count & Fixation 15 Count

This data analysis was taken in order to know the current status of the process. The current cost for sampling is an average of 100k yearly. This shows that there is enough data and enough value to implement a new Sample Selection process to reduce those costs and improve efficiency. This analysis also shows the projected savings for this current year. This project is being implemented in February 2021, BD currently closes the year in October, there are 8 months left in this year to obtain the projected savings of 50k. Shown above is the projection for this year coming up to 70k.

Analyze Phase

During this analyze phase the root cause of this process will be addressed. Using a fishbone diagram (Figure 6) to show the differences and the cause-and-effect analysis. As part of this analyze phase, potential causes identified in the fishbone diagram will be prioritized on their critical level. Critical level legend will be shown on Table 4.

Table 4: Critical Level Legend

Critical Level	Scale
(1)	Low
(3)	Medium
(5)	High

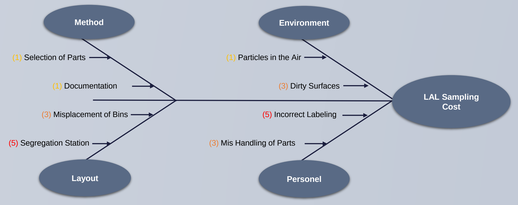

Figure 6: Fishbone Diagram for Cause-and-Effect Analysis

Analyze Phase

As part of the Analyze Phase, Each assessment will be evaluated individually and verified to select which continue to the next phase. This step ensures that these causes will be accessed, and they will not affect the finished method. All 8 will undergo verification to reduce the probability of issues due to effects causes in the manufacturing process. Refer to Table 5 for details on the critical component analysis (Cause-and-Effect Analysis).

Table 5: Cause-and-Effect Analysis for Critical Components

Cause	Effect	Effect on Project?
- Selection of Parts - Documentation	Error in Documentation	NO NO
- Segregation Station - Misplacement of Bins	Manufacturing Mix-up	YES YES
- Particles in the Air - Dirty Surfaces	Contamination on Product	NO YES
- Incorrect Labeling - Mis Handling of Parts	Product Mix	YES YES

Improve Phase

Each critical and high alert element was analyzed and evaluated in to understand each one and find the best way to tackle it. This is another critical component of this assessment and must be verified carefully. Within this analysis various components were taken into consideration. These include organization, labeling, segregation, cleanliness and mis-handle of product. All variables for each component were analyzed and only the critical components were included in this assessment. Table 6 shows each critical component of the new method being implemented along with a brief description and its proposed improvements.

Table 6: Critical Elements Assessments

Cause	Description	Proposed Improvement
Misplacement of Bins	Bins are paced under the tables without any coverage. Scarped parts often receive debris and other particles which are not tolerated by the laboratory for LAL testing.	Bins shall remain in their designated location and shall be labeled. Selected bins for scraped samples must have a lid and a bag. This will ensure protection of the samples from any debris or anything that could compromise the part and the testing.
Dirty Surfaces	Surfaces must remain clean; contamination of product is not acceptable. This will cause loss of product and increase in work.	Operators will perform line clearance before each sampling selection to undergo final stations. Every table and tool must be cleaned following the respective SOP, and this will include cleaning and maintaining the bins in optimum conditions.
Cause	Description	Proposed Improvement
Segregation Station	Currently all of the samples used for LAL testing are selected at the end of the Shift/Lot in the inspection section of the manufacturing process. Given the fact that these are good products, no labeling needs to be used until this point. For the proposed method, the selection will be in the same station but, the product will already be scraped before it arrives to the inspection section.	Segregating the parts is a must. For this reason, once the parts are scraped the first thing that the operator will do is place a red label of Manufacturing Stop and a label of LAL sample to the part. This label will go directly on the handle, where it is most visible to ensure that no mix-up happens during the manufacturing process and no part scraped leaves the manufacturing line with the lot. After the samples are sealed, another label will be placed on the outside of the pouch containing the lot number information, the reason of scrap and specifically identifying the part for LAL testing with a yellow label. Station designated for storage of these samples shall be clearly marked as LAL Samples and shall not be together with the lot.
Incorrect Labeling	Incorrect label placement can result in a major issue. Regulated industries like BD cannot afford to have any product go out of the facility and ship if it is not meant to be for human use. This will cause a major recall and several regulation actions including the possibility of shut down. These mishaps could cause a regulatory event with the FDA or other agencies. Which could lead to a serious investigation and even shutting down the facility.	This is a very delicate part of the entire process, and it is one that should be verified with much care. Labels will be placed on each sample, inside and outside to make sure there are no issues. The process will also select these samples at the end of the shift or at the end of the lot. This way the supervisor can make reconciliate and know how much manufactured product there is and verify that quantity to the one at the end of the lot with all the scraped parts accounted for. This way there is very little room for any mishaps.
Mis-Handling of Parts	Adding scraped parts to the manufacturing line while it is running is not allowed. This could cause a major mix-up with the lot and samples could be added to the final lot by mistake.	Process documentation will specifically state that the sample manufacturing process will be performed at the end of the shift or at the end of the lot. Once the supervisor has reconciliated all manufactured product and the only remaining product is the scrap to be used for LAL testing.

Control Phase

After applying the improvement plan, the final process for the Sample selection of LAL Test Samples reduces the quantity manufactured products to be used. The operation adds a new step to the entire process. This step helps the operator identify scraped product that can be used for testing, and it also shows how to select it, segregate it and finish it. As part of this control phase, the Log History Record Travelers (LHR traveler) were updated to include information regarding this new step and the new method selection. Detailed tables have been added with specific information and instructions regarding the sample selection process per Work Instruction (WIMXXXX). This Work Instruction has also been created to provide more detailed information of the process and assure the process is accomplished according to the instructions. In this work instruction, important information like specific values and timing is determined in order to maintain control of the entire process and assure the documentation practices are done correctly. Non-conformances are not acceptable and attach a bad review to the product. FDA regulations require testing for this product, part of this control phase is to ensure that all regulations are met, and the product delivered to the customer is within spec and up to BD standards.

Conclusions

After the successful implementation of the LAL Sample Selection Procedure, the manufacturing line is running smoothly and effectively. Following this implementation plan, the cost was updated to the exact cost of production until the extraction point from the line. The projection of cost reduction/saving for the remainder of the year 2021 is of approximately $60,000. Refer to Figure 6 and Figure 7 for the projection data and savings analysis.
By eliminating the need of selection of samples from end-items per applicable SOP, a savings projection of approximately 60K is acquired. This projection places the Company above the established goal of 50K for the year. All ten (10) samples passed the testing performed by the lab technicians.
Currently the new method has been used in the last lot manufactured in February and the 4 lots manufactured on March and a current 100% of the samples selected for LAL testing have been selected from the scrap of the manufacturing line. A total of 50 samples have been used from the scrap of the line. This provides a savings of $10,925.70 for the first two months of production with the new method. No quality events have been generated nor any MRR's, method is working accordingly, and all staff is executing the tasks in order as per WIMXXXX.

	Lots to be Manufactured per Month							
Month	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Fixation Device 15	0	1	1	1	1	1	1	1
Fixation Device 30	1	3	3	3	3	3	3	2

Figure 7: Projection of Lots to be Manufactured

	Item Number	Qty of Lots	Qty for LAL	Total Samples	Standard Cost	Cost per Item	Projected Saving (2021)
Cost Analysis	0113315	7	10	70	$ 200.81	$14,056.70	
	0113330	21	10	210	$ 222.94	+ $46,817.40	= $ 60,874.10

Figure 8: LAL Related Savings Projection 2021

References

[1] Lonza.com. (2020, Nov 22). *An Introduction to Bacterial Endotoxin Testing*. [Online] Available: https://bioscience.lonza.com/lonza_bs/PR/en/endotoxin-testing

[2] Advena. (2020, Nov 9). *Medical Device Definition (MDD/IVD)*. [Online]. Available: https://www.advenamedical.com/medical-devices/definition-mdd/

[3] T. McCarty, L. Daniels, M. Bremer, P. Gupta, J. Heisey, and K. Mills, "Introduction to the DMAIC Process Improvement Methodology," in *Six Sigma Black Belt Handbook (Six Sigma Operational Methods)*, McGraw-Hill, 2005. [E-Book] Available: McGraw-Hill Access Engineering https://ezproxy.pupr.edu:2053/content/book/9780071443296

[4] K. Terry (2020, Nov 27). *What is DMAIC* [Online]. Available: https://www.isixsigma.com/new-to-six-sigma/dmaic/what-dmaic/