Handling and Managing of Vial Rejects

Author: Gilmaris Santana Vargas
Advisor: Rolando Nigaglioni, Ph.D.
Engineering Department

Abstract

A large accumulation of filled vial rejects generated in an aseptic filling line of a parenteral medication was identified to be in the custody of the Quality Assurance department indefinitely. Using the DMAIC methodology the current vial handling practices and the batch records from the lots manufactured from 2019 until August 2021 were evaluated. Two (2) root causes were identified for storing all rejected filled vials indefinitely: (1) vials were needed for the visual inspection qualification defect library and (2) no formal procedure was established for the handling and management of rejected vials. New procedures were designed and implemented to provide guidance on how to evaluate and onboard rejected filled vials to the defect library or to discard the vials per waste regulations.

Introduction

A large accumulation of rejected filled vials was observed to be in custody of the Quality Assurance department. This accumulation of rejected filled vials started in 2019, when the facility received authorization for commercial manufacturing and transitioned from the commissioning and qualification phase. No formal process was in place to determine next steps after the rejected vials were collected from the manufacturing area or how to manage this inventory.

Background

Ludwig [1] states that “injectable products must be manufactured using the highest quality active drug substance and excipients. Parenteral products must be sterile, pyrogen free, and free from visible particulate matter and remain so throughout shelf life”. Errors in manufacturing can result in material to be rejected if it does not meet the established acceptance criteria. As explained by Raghavan [2], "in an aseptic process, the drug product, container, and closure are first subjected to sterilization methods separately, as appropriate, and then brought together.“

The inspection of parenteral products is driven by the need to minimize the introduction of unintended particulate matter to patients during the administration of injectable medications. Toler [3] describes that visual inspection also allows the opportunity to detect and reject other categories of nonconforming units. When designing the qualification for the inspection process the visible particles that come from the filling process and its predecessors shall be considered and incorporated in the program. Visual inspectors must demonstrate acumen in particle detection to ensure that containers containing visible particles are identified and rejected from the lot.

Problem

A large accumulation of filled rejected vials was observed in the Quality Operations cage. These vials were generated from product lots filled from calendar year 2019 until present that were not being discarded or repurposed after they were collected from manufacturing.

Methodology

To understand the current state and to implement a solution(s) linked to the underlying causes and establishing best practices to make sure the solutions stay in place, the DMAIC methodology will be employed in this research project. As described by George [4], DMAIC is a structured problem-solving methodology widely used in business. The letters are an acronym for the five (5) steps of Six Sigma improvement: Define, Measure, Analyze, Improve, Control. Several six sigma tools will be employed throughout the execution of the DMAIC methodology.

Results and Discussion

Define: To understand the problem, a process map, depicted in Figure 1, was created to clearly define the process inputs and outputs.

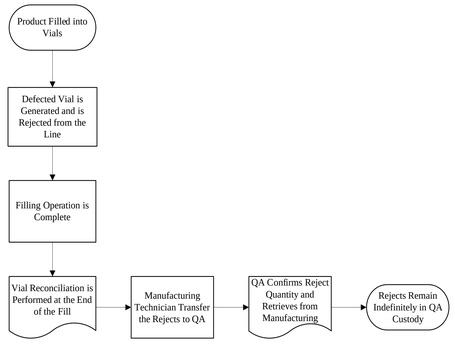

Figure 1
Process map- Current state

Measure: A times series plot, shown in Figure 2, was created to show the quantity of rejected vials produced from 2019 until the start of this project on August 9th, 2021. This data was divided into filled vial rejects (blue) and empty vial rejects (orange).

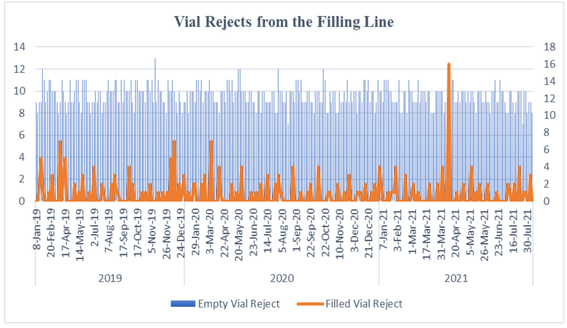

Figure 2
Rejected Vials from 2019 until the August 9th, 2021

From the batch record evaluation, it was observed that each fill lot will generate empty vials rejects but not every fill will generate filled vial rejects. Quantity of rejects also varies per fill lot.

Results and Discussion- *Continued*

Analyze: A fishbone or cause and effect diagram, depicted in Figure 3, was created to summarize the potential root causes to our problem divided into categories (6Ms).

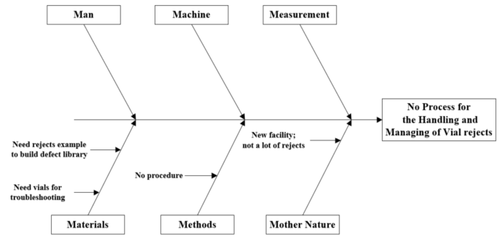

Figure 3
Fishbone Diagram

Potential root causes identified n the fishbone were evaluated using the 5-Why methodology, see Table 1.

Table 1
5-Whys to Identify the Root Cause

		No procedure	Vials needed for defect library
01	Why?	Haven’t needed to discard any vials yet	All rejected vials are being kept in QA custody
02	Why?	Did not identify the quantity needed for reject library	Until now there are not enough vials for training
03	Why?	New facility, still assessing needs of defect categories	Still assessing needs of defect categories
04	Why?		Planned to keep rejects for training
05	Why?		New facility still generating this library

Improve: After identifying the root causes the PICK chart tool was used to evaluate the proposed improvements, see Table 2.

Table 2
Improvement Selection- PICK Chart

Prioritize Improvements		Select Improvements		
1. Create procedure for how to document the receipt of rejected vials and designate a location for them 2. Create procedure for how to evaluate rejects on if they should be kept and how to discard remaining vials	Benefit	High Benefit	Implement: Improvement 1, Improvement 2	Challenge
		Low Benefit	Possible	Kill
			Low Effort	High Effort
			Effort	

Control: Twenty (20) days were used for monitoring in the Control phase, starting on September 6th, 2021, and ending on September 26th. To determine adherence to the new procedures the batch records, the logbooks, and the ERP (enterprise resource planning) system were evaluated. During this evaluation it was confirmed that the empty vials were being discarded via nonhazardous waste and that the filled vial rejects were being kept in the designated quarantine area and were evaluated for onboarding into the defect library or if they were rejected via hazardous waste.

Conclusions

In the Define stage it was determined that no formal process for the managing and handling of rejected vials was in place. Data gathered in the Measure phase further supported this statement where a large accumulation of rejected vials was observed dating back from 2019 until present. Two (2) root causes were identified in the Analyze phase for the large vial accumulation, (1) rejected vials were being kept to be used in the defect library for the qualification of visual inspectors, (2) no procedure was established to dictate how to manage the rejected vials. In the Improvement phase an SOP, two (2) job aids, and one (1) logbook were generated to provide guidance on how to manage these vials and to have the correct documentation of the process to remain compliant. Twenty (20) days were used for monitoring the process in the Control phase. During this time, it was observed that the empty rejected vials were being discarded and the filled vial rejects were being collected by Quality Assurance representatives. The filled rejected vials are now being kept in a designated locked cage that only QA personnel can access. Inventory records of these vials is generated to have visibility of the quantity, lot number, and location of vials. The inventory is further adjusted after the vials are either onboarded to the defect library or discarded via hazardous waste.

Future Work

The DMAIC used in this research project focused on the process after a rejected vial is retrieved by Quality Assurance representatives. Further evaluation in the visual inspection qualification area will be needed to determine if the improvements from this DMAIC are still valid. The assessment should include,

- Evaluation of storage capacity
- Efficiency of vial reject evaluation for onboarding
- Digitalization of logbook
- Managing of the replacements of defects in a set

Acknowledgements

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References

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