Strategy for the Reduction of False Rejects in the Visual Inspection of Injectable Drug Products

Author: Edgardo R. Rivera Torres

Advisor: Rafael Nieves Castro, PharmD Graduate School – Manufacturing Competitiveness

Abstract

A hundred percent visual inspection is performed as part of the manufacturing process of injectable drug products as a regulatory requirement to detect and remove units with defects to protect the patients. The rejection of acceptable drug products in the visual inspection process increases waste and manufacturing costs. The analysis of historical data identified three vial defect types with a trend of high false reject rates. A second inspection step method with reference standards was designed as a strategy to reduce false rejects in the visual inspection process. The experimental results obtained showed a significant reduction in false rejects during the visual inspection process. The reduction of false rejects translates into fewer financial losses as waste for the organization.

Introduction

In a pharmaceutical company dedicated to manufacturing injectable drug products, a sustained increasing trend of non-conformances with reject rate limits was observed during visual inspection. Results of laboratory analyses identified a high number of false rejects as a major contributor to this problem. A second inspection step for the evaluation with a reference standard can be a cost-effective strategy to reduce false rejects as a major source of additional costs in the manufacturing of injectable drug products.

Background

The COVID-19 outbreak in addition to the development of more biological treatments for chronic health conditions has increased the demand for the manufacturing of injectable products, such as the delivery of pre-filled syringes for vaccines and other critical treatments [4]. Furthermore, there is a consolidated demand from distributors and healthcare providers to pharmaceutical companies to reduce the costs of injectable drug products [5].

On the other hand, there are several unavoidable factors in the manufacturing process of injectable products that can contribute to contamination and primary container functional defects [1]. The United States Pharmacopeia in alignment with European Pharmacopeia and Japanese Pharmacopeia requires a hundred percent visual inspection before the final packaging process with the intention to protect the patients [8] – [11]. The two principal methods for visual inspection are manual inspection, which is performed by highly trained persons, and automated inspection which involves the use of machinery [6]. Still, factors such as maintenance, mechanical problems, and ejected units from the automated process demand human intervention for manual visual inspection [1].

As part of the acceptance criteria for visual inspection, each batch must comply with established statistically acceptable quality limits such as a statistical acceptance sampling plan and reject rate limits [3]. Regulatory standards require a thorough investigation and Corrective Actions and Preventive Actions on any batch that fails to meet one or more of the established Acceptance Quality Limits during visual inspection to be authorized for further processing [7]. All these factors represent challenges for pharmaceutical companies such as higher manufacturing costs and a lead time delay, which can lead to public health threats such as the shortage of treatments for critical health conditions [2].

Problem

A high number of false rejects was identified as a major contributor to non-conformance investigations due to exceeded reject rate limits during the visual inspection. The additional negative impact on manufacturing costs and the supply chain reduces the company's capability to meet the demand for on-time delivery of products at an affordable price to its patients. The company aims to implement a method into the visual inspection process as a strategy to reduce the rejection of acceptable units of injectable drug products by 50%.

Methodology

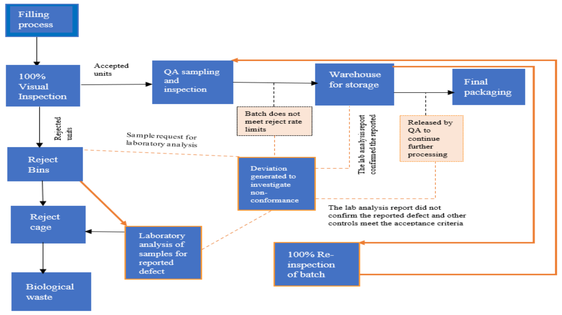

Figure 1
Visual Inspection Process Map Diagram

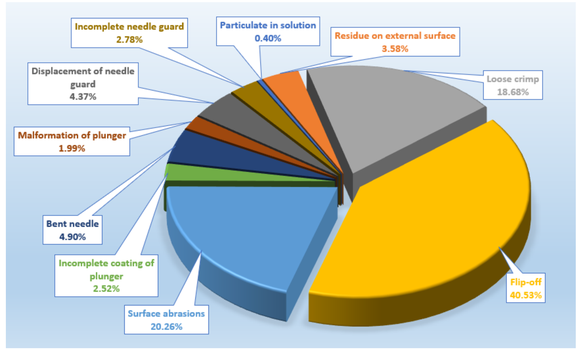

Figure 2
False Reject Rate by Defect Type Distribution Pie Chart

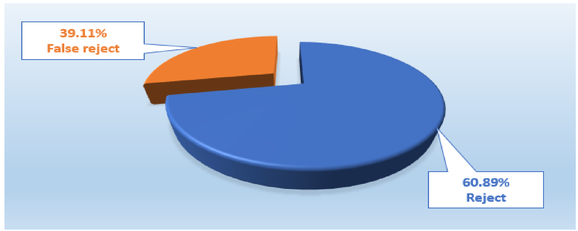

Figure 3
Pie Chart of Historical False Reject Rate Identified as Baseline

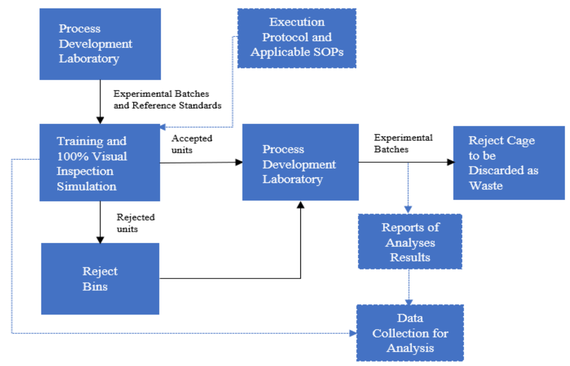

Figure 3
Experimental Visual Inspection Simulation Flow Diagram

Results and Discussion

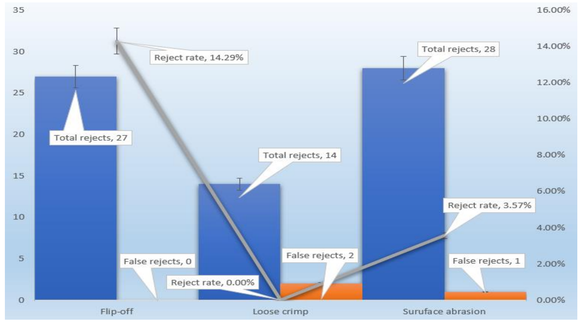

Figure 3
Experimental Reject Rate Results by Defect Type

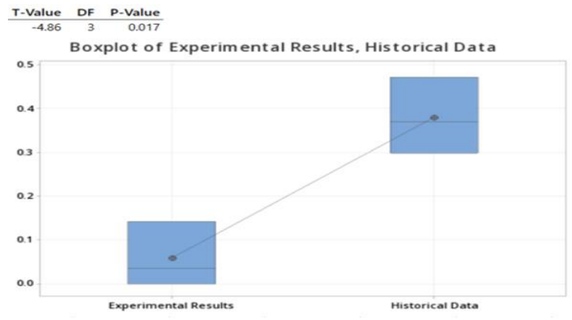

Figure 4
Two-Sample T-Test Result of Comparative Statistical Analysis

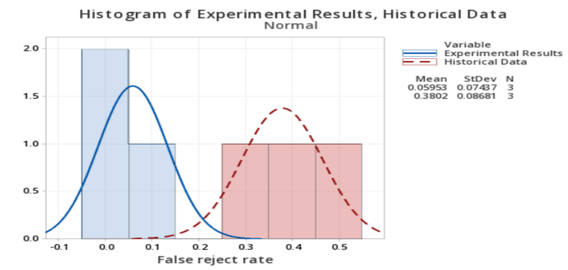

Figure 5
Historical vs Experimental False Reject in a Normal Distribution Histogram

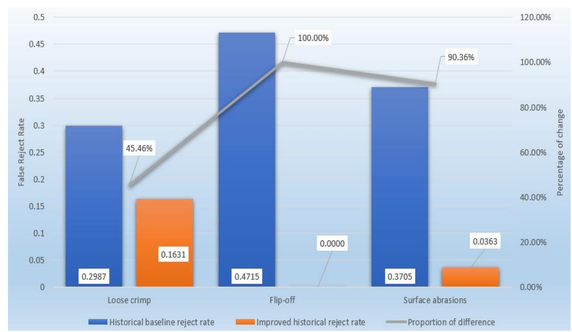

Figure 6
Bar Chart of Historical Data vs Historical with Improved False Reject Rates Results

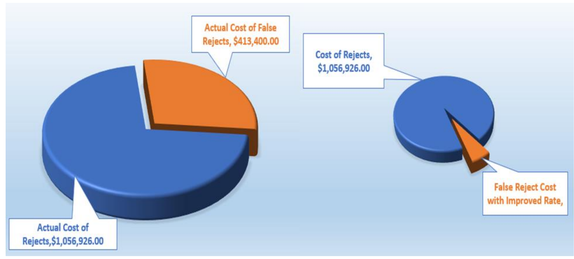

Figure 7
Comparative Cost Analysis Pie Charts

Conclusions

False rejects are a significant contributor to non-conformance deviations that generates additional waste increasing the manufacturing costs of injectable drug products. The implementation of an additional step using reference standards to confirm specific conditions improves the visual inspection process output, reducing false rejects by more than 50% during the visual inspection process. Additionally, the improvement of the false reject rates reduces the opportunity for non-conformances with the reject rate limits which prevents other activities such as investigations and re-inspections trigger as consequence. The preventive approach of this method is the greatest advantage over the CAPAs actions deployed as a reactive approach. This strategy is a significant contributor to the company's objective of cost improvement of the visual inspection process for the next year, in addition to enhancing the company's competitiveness and marketplace.

Future Work

Is recommended an implementation project with a holistic cost analysis, and an effectiveness check plan for this method. Furthermore, is recommended to increase the frequency of evaluation of the visual inspection process output to identify defect types with a trend of high reject rate including results inside the accepted reject rate limits.

Acknowledgements

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