YIELD IMPROVEMENT FOR ANESTHESIA PRODUCT AT FILLING & PACKAGING LINE

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Abstract

In the manufacturing process of anesthesia, the yield for Fluxane product, manufactured at ANESTHER Healthcare, is consistently performing lower than target (2.785 bottles/kg) from tank F-SV-001 in comparison to tank F-SV-002. Based on a 12-months data review, the yield is not met for 77% of the manufactured lots, resulting in an annual loss of $115,000. The DMAIC methodology was used to determine the possible causes for the low product yield results in BDP tank F-SV-001. The following causes were identified: (1) the venting system of the tank F-SV-001 was not working efficiently due to pressure valve malfunction, causing evaporation of the product; (2) calibration classification was not appropriate for load cells causing tolerance errors; and (3) lack of a standardized yield reporting method. During control phase, yield data was collected for one (1) month and results were equal to or greater than 2.785. The objective of increasing product yield in tank F-SV-001 to approximately 2.785 bottles/kg was achieved.

Introduction

The Filler Machine at Line 1 is dedicated to the filling of Fluxane product, which is feed from two (2) storage tanks: F-SV-001 and F-SV-002, located at the Vessel Room in the Packaging area. The product yield from storage tank F-SV-001 is consistently performing lower than the target 2.785 bottles/kg. Based on a 12-months data review (01-Jun-2018 to 31-May-2019), a 77% of the time, the yield is not met, resulting in an annual loss of 6,989 bottles of Fluxane, at a cost of $115,000, and consequently, the site does not meet the customer demands based on the bottles produced.

Objectives

The objectives of the investigation are:

- Increase product yield in bulk drug product (BDP) storage tank F-SV-001 from 2.772 bottles/kg to approximately 2.785 bottles/kg or by 5,940 bottles equivalent to 85% annual increase by December 2019.
- Achieve a state of control for BDP tank F-SV-001 filling process.

Background

The process yield, also known as first-time yield (FTY) is defined as the percentage of units coming out of a process free of defects [1]. It is an indication of performance measures for the manufacturing of a product that signals the causes of variation of the process [2].

$$Yield = \frac{Quarantine\ (bottles) + QA\ Samples\ (bottles)}{Net\ Weight\ (kg)}$$

Methodology

The DMAIC methodology was used to determine the possible causes for the low product yield results in BDP tank F-SV-001 (refer to Figure 1).

Define — Problem statement, determine the scope and establish the goals.
- SIPOC Diagram (Supplier, Input, Process, Output, and Customer)
- Is/ Is Not
- Stakeholder Analysis

Measure — Examine the current state and establish a baseline.
- Process Map
- Data Collection
- Basic Statistics

Analyze — Analyze the current state and find measures to reach the goal.
- Root Cause Analysis
- Determine critical X's

Improve — Implement improvement measures.
- Brainstorming for ideas
- Kaizen events

Control — Monitor sustainability of the changes for effectiveness.
- Monitor product yield for one (1) month after the implementation of the corrective and/or preventive actions.
- To measure the effectiveness of the changes implemented, the project should render an increase in product yield for bulk drug product (BDP) tank F-SV-001 from 2.772 bottles/kg to approximately 2.785 bottles/kg or by 5,940 bottles (85% annual increase) by the end of the year.

Figure 1: DMAIC Methodology [3]

Results and Discussion

Define

Problem Statement

A historical discrepancy exists between two similar Fluxane Bulk Drug Product (BDP) Tank Yields. The yield target is 2.785 bottles/kg: Tank F-SV-001 is performing at a mean of 2.772 bottles/kg based on 12 months data review and Tank F-SV-002 is performing at a mean of 2.786 bottles/kg during the same review period.

A SIPOC diagram of the process is illustrated in Figure 2.

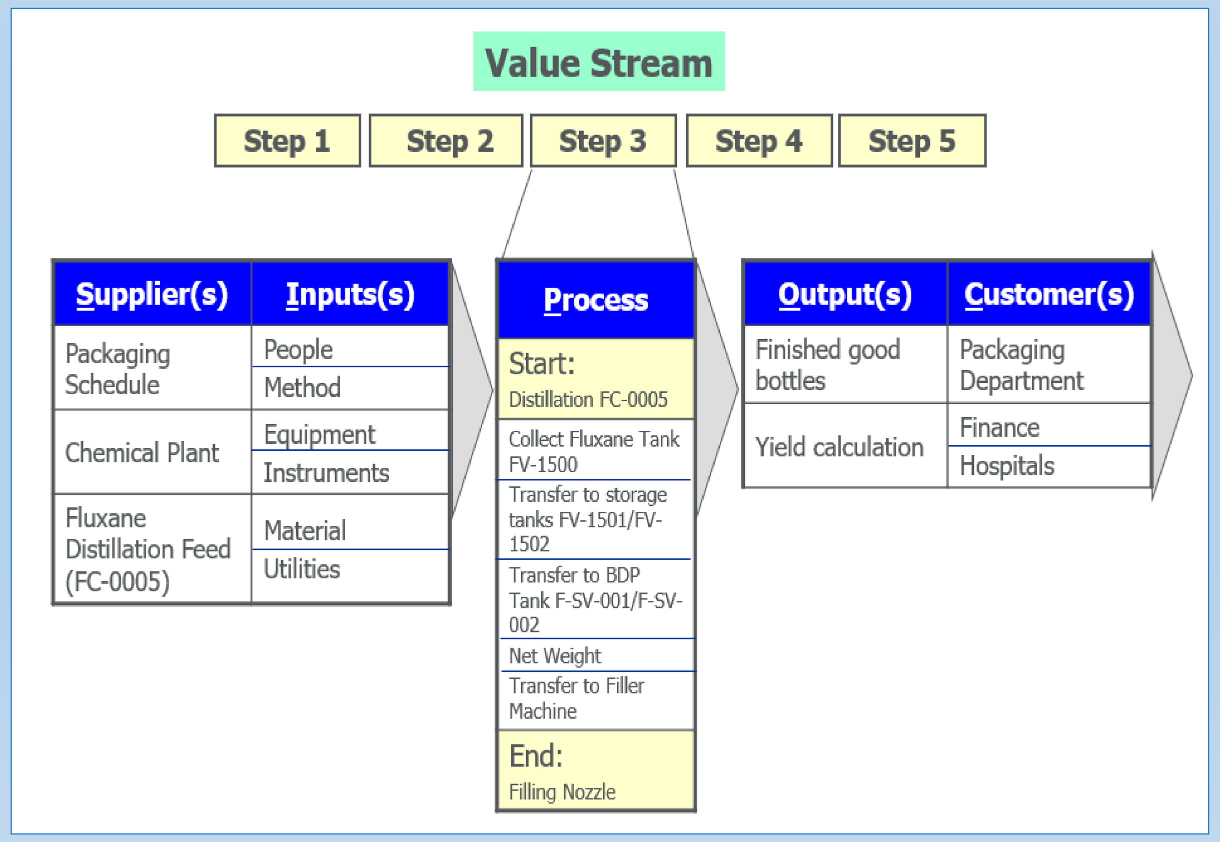

Figure 2: SIPOC Diagram

The scope of the project is the product transfer of Fluxane BDP storage tank F-SV-001 from the chemical plant (drug product formulation) to the Filler machine reservoir.

Results and Discussion

Measure

A process map was performed to establish the sequence of steps for the process within the scope of this project (refer to Figure 3). The process includes the final steps of the synthesis of the anesthesia and ends with the starting point for filling the anesthesia product into bottles.

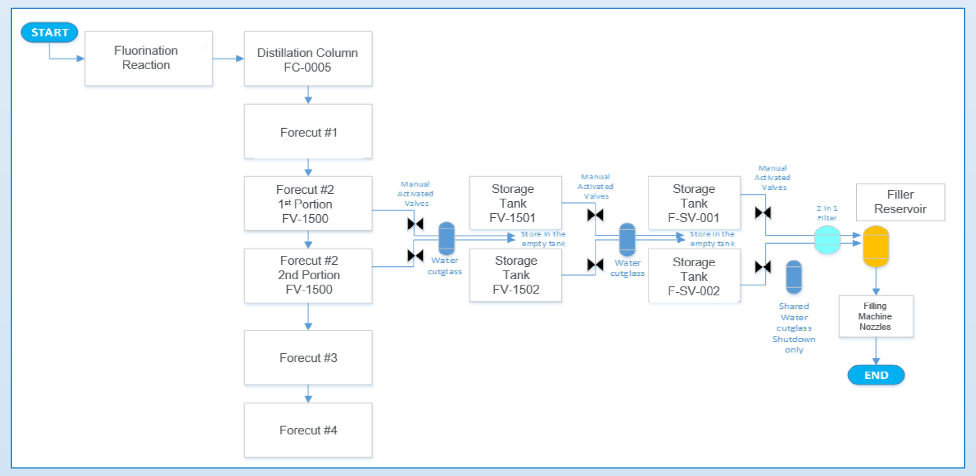

Figure 3: Fluxane Process Map

The data of yield was collected for the period June 2018 to May 2019 (12-month period), resulting in high variability and fluctuations in the yield results obtained from tank F-SV-001.

Analyze

A fishbone (root cause) analysis was performed to determine the direct and/or most probable cause of the low yield results obtained in tank F-SV-001, as illustrated in Figure 4.

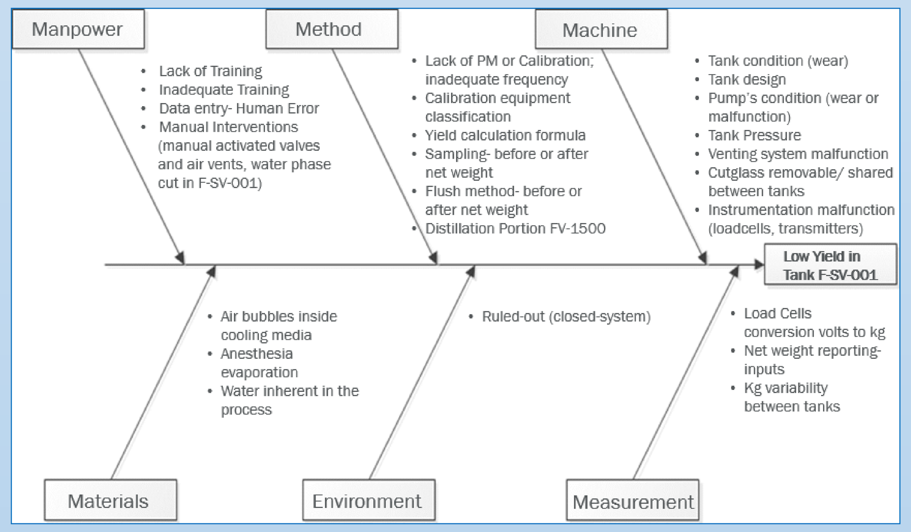

Figure 4: Fishbone Analysis for Low Yield in Tank F-SV-001

An increase in tank pressure was observed for lots F-19-059 to F-19-075 (2.45 psiag to 4.50 psiag in average), resulting in low yield, as shown in Figure 5. The pressure in tank F-SV-001 (3.12 psiag) was higher in comparison to tank F-SV-002 (2.72 psiag) for the period between March 2019 and May 2019.

The pressure venting valve of storage tank F-SV-001 was found not sealing properly causing product to evaporate. Since the net weight data used for yield calculation is obtained from the tank release label, product evaporation is not considered and results in a misleading yield result.

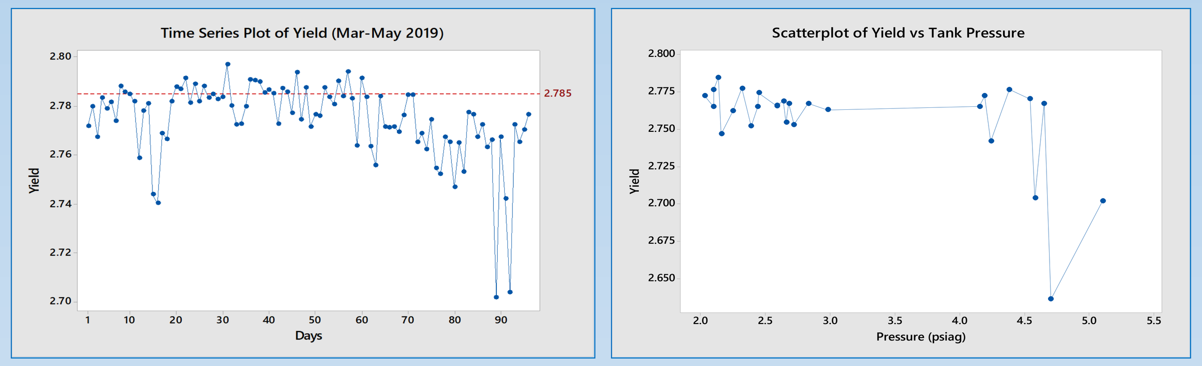

Figure 5: (a) Time Series Plot of Yield (Mar-May 2019)
(b) Scatterplot of Yield vs. Tank Pressure

Results and Discussion

Improve

- A preventive maintenance (PM) record was for inspections of pressure valves in tanks F-SV-001 and F-SV-002.
- Tank F-SV-001 was calibrated with satisfactory results.
- Calibration classification for the load cells of the tank were re-classified as a critical instrument.
- Tank pump was replaced from Wilden to a Centrifuge type to improve product transfer.
- A permanent cut-glass was installed to minimize the loss of product.
- A standardized yield reporting method was developed in an electronic database to reduce data entry errors.

Control

From a total of 15 bulk lots manufactured from storage vessel F-SV-001 during a 1-month period, the target yield of 2.785 was met for 14 lots, as shown in Figure 6. The average yield result for the 14 lots (that is eliminating the outlier) was 2.788 (above target).

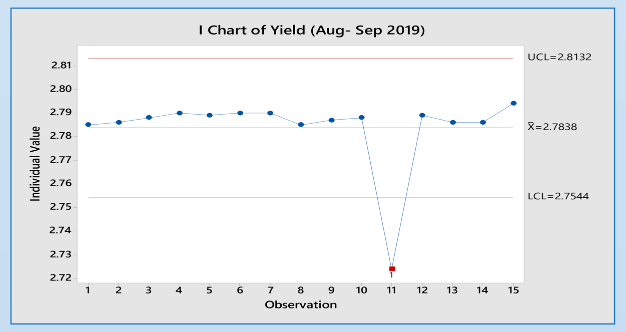

Figure 6: Control Chart of Yield (Aug-Sep 2019)

Conclusions

The objective of the project was to increase product yield in bulk drug product (BDP) storage tank F-SV-001 from 2.772 bottles/kg to approximately 2.785 bottles/kg or by 5,940 bottles equivalent to 85% annual increase by December 2019. Based on the data collected and investigation results, improvements on the equipment (tank F-SV-001) and yield calculation method were implemented. One-month yield data was monitored and evaluated after implementation of actions, and results demonstrated that the increase in product yield for BDP tank F-SV-001 was achieved. The bulk lots monitored resulted in a yield equal to or greater than 2.785 (target). Also, a reduction in data variability was observed. The increase in product yield results in a financial benefit of approximately $207,900 by the end of the year.

It is recommended to continue the monitoring of process yield up to December 2019. Also, the impact of multiple lot presentations for a bulk in yield results should be investigated in order to identify opportunities that will assure a product yield within or above target.

References

[1] G. Brue and R. Howes, McGraw-Hill 36-Hour Course: Six Sigma, McGraw-Hill, 2006.
[2] R. T. Westcott, Process Management, American Society for Quality (ASQ), 2006.
[3] T. Pzydek, "Six Sigma Infrastructure," Quality Digest, 2003.