Syringe Filling Line Changeover Time Reduction by CIP Recipe Overlap with Product Transfer Recipe

Ernie Figueroa Perez
Advisor: Héctor J. Cruzado, PhD
Graduate Program in Engineering Management

Abstract

In a biopharmaceutical company, the syringe filling process is thru one of two filtration trains that must be previously washed with a cleaning in place and sterilized with sterilization in place. Therefore, while one train is transferring and filling product, the other train is preparing it with cleaning and sterilization. It was identified that when lots of 70,000 units or less and lots of Product R were filled, the stipulated changeover time of 4.75 hours was not met. A procedure stipulated that a transfer recipe could not run in parallel with a cleaning in place cycle causing a delay in the lot-to-lot changeover. An analysis by the automation department certified that the system was capable of handling both processes in parallel. The procedures were revised allowing the operator to perform both processes at the same time. After the changes, the stipulated changeover time was fulfilled and an increase of 3.3 million of additional units is projected for this year.

Introduction

The syringe filling line has a stipulated lot-to-lot changeover time of 4.75 hours. A Standard Operation Procedure stablished that the CIP recipe could not be performed during product transfer phase. Due to this fact, two types of lot-to-lot changeover were affected, small lots of 70,000 units or less and Product R lots. Figure 3 shows data from the third quarter of 2021 where the exceeded changeover time of the two types of lots can be observed.

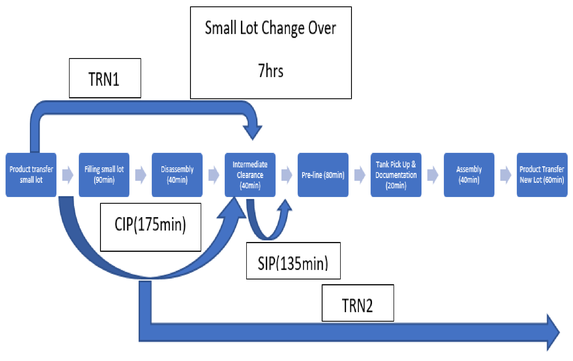

Figure 1: Small Lot Changeover Before Improvement

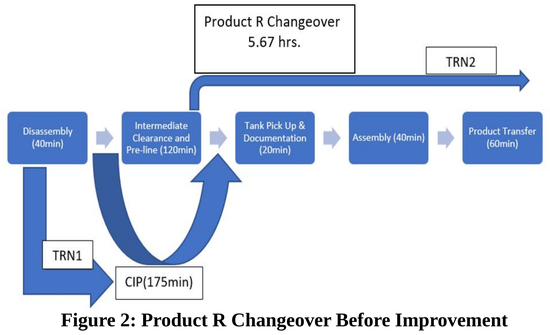

Figure 2: Product R Changeover Before Improvement

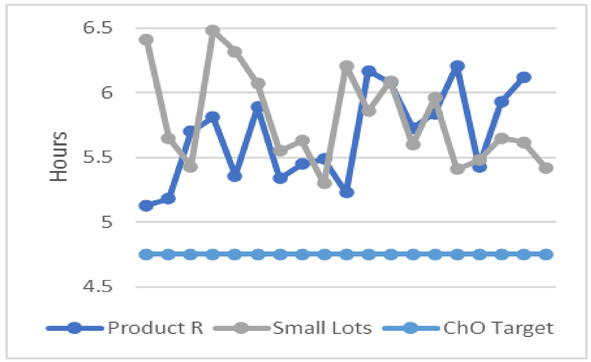

Figure 3: Product R and Small Lot 2021 Third Quarter Lot-to-Lot

Problem Improvement

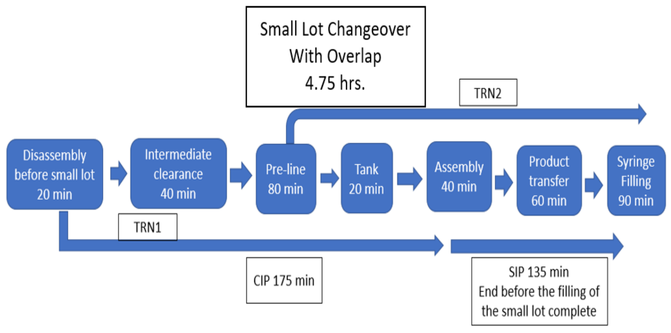

Figure 4: Small Lot Changeover After Improvement

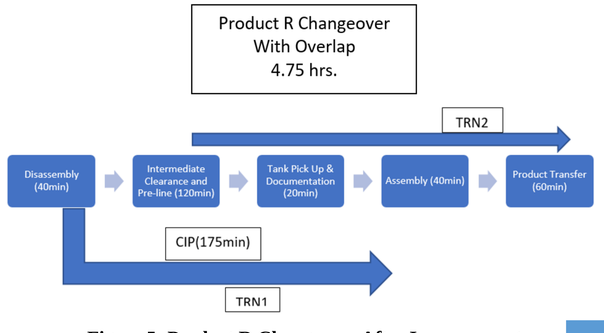

Figure 5: Product R Changeover After Improvement

Methodology

DMAIC (Define, Measure, Analyze, Improve, Control) methodology was used to develop and implement this project, as follow:

- Define – The SOP for the CIP and SIP process established that the product transfer recipe cannot be performed in parallel with a CIP recipe. This has an area of opportunity to decrease or eliminate the downtime between lots of 70,000 units or less, and Product R lots that exceed the target time of 4.75 hours.
- Measure – Data analysis confirmed that Product R lots and lots of 70,000 units or less exceeded the stipulated 4.75 hours of changeover target. The total lots of Product R and lots of 70,000 units or less were more than 160 lots for 2021 representing the 35% of total manufactured lots.
- Analyze – After an assessment of the automation engineer team, it was certified that the filling systems are capable to run both processes (the CIP recipe and the product transfer recipe) in parallel.
- Improve – The SOP was modified to allow the CIP process to be performed during the product transfer recipe.
- Control – The syringe filling system has process and engineering controls like the post fill pressure hold test and the pressure hold test before the start of the CIP recipe.

Results and Discussion

Figure 6 shows the direct results of the implementation of this initiative. The changeover of four out of five lots of Product R were below the target time of 4.75 hours and the three small lots were also below the target changeover time.

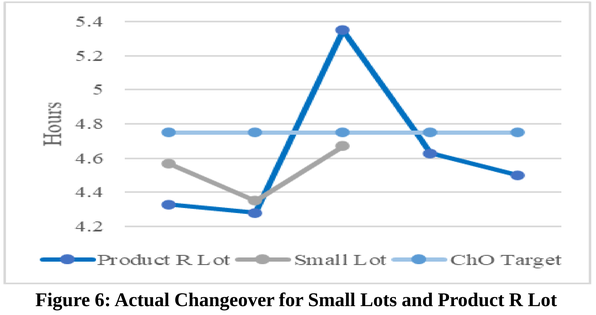

Figure 6: Actual Changeover for Small Lots and Product R Lot

Table 1: Projections of Project Benefit for Syringe Filling Line

Lots	Changeover average per lot (Actual) hrs.	Changeover average per lot (proposed) hrs.	Benefit Changeover average per lot %	Benefit Hours per Year	Units that could be absorb
Product R	4.91	4.07	17%	217	3.3 million
Small Lots	5.07	3.46	32%		

Conclusions

The implementation of this project allows all lots manufactured in the syringe filling line to comply with the stipulated changeover time of 4.75 hours. One of the goals of the production department was to absorb an increase in lots and volume of units filled, and as Figure 2 shows, this can be achieved by having the product transfer recipe in parallel with the CIP recipe. According to the analysis of the industrial engineering department, the syringe filling system is capable to adsorb an increase of 3.3 million of additional units, since this initiative has a flexibility of 26% utilization, which is equivalent to 217 hours per year.

Future Work

The process engineering department are engaged with the continues improvement program developing new ideas to be more efficient, reduce downtime and eliminate other process waste. Identification of other project to increase capacity in the manufacturing filling lines are under evaluation with process development scientist, manufacturing team and management. Therefore, the vial filling line is being evaluated since the filling process is like the syringe line and could benefit from the implementation of this project.

Acknowledgements

- Dr. Hector J. Cruzado (Advisor)
- The syringe filling line multidisciplinary team composed by the departments of; manufacturing staff, operational excellence, automation engineer, industrial engineer, quality control, environmental health and safety department.