New Flow Route for the Delivery of the to be Cleaned Filling Equipment for the Lot-To-Lot Changeover Optimization Using the Lean Manufacturing Methodology

Karina Y. Cruz Martínez
Master in Manufacturing Competitiveness
Rafael Nieves, Pharm D.
Industrial and Systems Engineering Department
Polytechnic University of Puerto Rico

***Abstract* —** Management demand to reduce downtime in manufacturing had increased in recent years. This led manufacturing to use the Lean Methodology and Six Sigma tools to optimize the process. Focused on process improvement and downtime reduction an initiative started to reduce the lot-to-lot changeover for filling areas. A new flow route was added to the Standard Operating Procedure to deliver the used filling equipment. This new flow route resulted in a reduction of 33% in movement waste and a 58% benefit of time spent on task for the Syringe Filling Line, and a 43% in movement waste and 67% time spent on task benefit for the Vial Filling Line. The ergonomic risk was calculated for the task, and it was lowered from a Moderate to a Low Risk after implementing administrative ergonomic controls in the Job Hazard Analysis. These results yielded a positive impact in time reduction for both filling lines.

Key Terms — Flow Route, Lean Manufacturing, Lot-to-Lot Changeover, Process Improvement.

PROBLEM STATEMENT

The commercial demand in the filling areas of a pharmaceutical located in Juncos has been on increase on the last years. The high commercial demand produced a demand by Upper Management to reduce downtime in the filling areas, specifically on the changeovers between batches, called lot-to-lot changeovers. This motivated the increase of process improvement projects using Lean Manufacturing and Six Sigma tools and techniques. Changeover can be defined as a change from using one system, machine, method, etc. to another [1], in this case the change that occurs is one filling batch to another filling batch. The lot-to-lot changeover in the filling areas have different tasks that need to be performed, and between these tasks is the delivery of the to be cleaned equipment to wet component preparation area. The to be cleaned equipment is the equipment used during the filling batch that needs to be delivered to wet component preparation for it to be cleaned. The filling equipment is transported inside of a Rapid Transfer Port (RTP), this is a device used to securely transfer materials from one place to another while preventing the contamination of the product. There are two stablished flow routes (Route 1 and Route 2) in Vial Filling and one flow route (Route 1) in Syringe Filling for the to be cleaned equipment delivery and they are defined in the Standard Operating Procedure (SOP). The stablished equipment routes make the operators move the equipment from classified Grade 8, an area with particulate control of <100 CFUs, to Control Not Classified (CNC), an area with Heating, Ventilation and Air Conditioning (HVAC) system designed to reduce airborne contaminants below the level of the ambient environment [2]. Moving the equipment from one area to another converts the task from a one operator job to a two-operator job, because an operator from CNC must pick up the equipment and finish delivering it. This means less operators performing the changeover in the filling rooms and more equipment handling, as well as a motion and transportation waste during the lot-to-lot changeover process.

This project looks to implement a new to be cleaned equipment flow route from the filling areas to wet component preparation staff. The new flow route has to be shorter and reduce the number of operators required for the task.

Research Description

The research to be performed during this project will regard the application of Lean Manufacturing and Six Sigma tools in the filling areas to reduce the wastes of transportation and motion during the lot-to-lot changeover. The research will also cover the review and update of the Job Hazard Analysis (JHA) and Standard Operating Procedures (SOP) of each filling area, Vial Filling and Syringe Filling. Discussing the Lean Manufacturing and Six Sigma tools to be implemented, process improvement, Spaghetti Diagrams, and standardization.

Research Objectives

The research objectives for this project are to successfully implement a new shorter flow route for the delivery of the to be cleaned equipment from the filling rooms to the wet component preparation room for the improvement of motion and transportation during the lot-to-lot changeover. Reduction of the ergonomic risk in the handling of the equipment during the transportation. Reduction of the transportation and motion waste by a 30% during the lot-to-lot changeover.

Research Contribution

This project helps reduce the downtime caused by lot-to-lot changeovers in the filling areas and improve the production time in them. This project also contributes to the scheduling by generating more time on a long-term basis to add more filling batches to the production schedule or giving a buffer of time if a delay occurs during the process. The project primarily contributes to comply with the demand of Upper Management of reducing downtime.

RESEARCH BACKGROUND

The industry under study is a pharmaceutical industry, which is in constant search of process improvements. The goal of process improvement is to improve efficiency or productivity, which allows an organization to produce with reduced effort. Pharmaceuticals have a need to reduce their cycle times by eliminating waste from their process, which can result in process improvement. To comply with the goals of process improvement, the process and its procedures need to be revised and optimized. It can even require new processes and re-training of the operators.

Lean Manufacturing focuses on designing a robust production operation that is responsive, flexible, predictable, and consistent [3]. Lean Manufacturing not only creates an operation focused on continuous improvement through self-directed workforce that is driven by the output aligned with the customer's criteria, but it also develops a workforce with the ability to utilize the lean tools and techniques necessary to satisfy all expectations. The pharmaceutical industry has adopted the lean manufacturing methodology to promote continuous improvement for the elimination of waste in the process, therefore obtaining operational excellence and optimization.

The core principle of Lean Manufacturing is the reduction of non-value-added activities [4]. Non-value-added activities, also called process waste, are the performance of unnecessary work because of errors, poor organization, or communication. There are seven (7) primary forms of waste in the lean manufacturing methodology:

- Defects – product deviating from the standards of its expectation.
- Overproduction – making things not required by the customer or having an excess of product in inventory.
- Waiting – wasted time due to slowed or halted production in a step of the production chain while a previous step is completed.
- Transportation – moving materials or products from one position to another. Transportation itself adds no value to the product so minimizing this cost is necessary.
- Motion – all the motion made by a machine or person that could be minimized.
- Inventory – waste produced by unprocessed and excess inventory.
- Overprocessing – components of the process of manufacture that are unnecessary. It is

essentially, to add more value than it is required by the customer.

In this study a lot-to-lot changeover reduction time is being proposed by the addition of a new and shorter route to deliver the to be cleaned equipment to wet component prep area. Changeover is defined as the total process of converting a machine, line, or process from running one product to another [5]. Changeover can be divided into three (3) major parts, called the 3Ups [5]:

- Cleanup – is the removal of materials, components, and equipment from the previous lot. The research will focus on this part of the changeover.
- Setup – consists of the physical conversion of the machinery to run the next products.
- Startup – is the period after cleanup, setup, and all other changeover tasks have been performed but before the line begins producing. It is characterized by stoppages for adjustment.

In a manufacturing environment the lot-to-lot changeover can be defined as the elapsed time from when the last unit is stoppered in a fill batch to the first filled unit from the next fill batch. Therefore, the Lean Manufacturing and Six Sigma tools, like spaghetti diagrams, process improvement, and process standardization, will help achieve the objectives for this research.

METHODOLOGY

The first step to achieve the research objectives for this project was to analyze the equipment delivery process and the stablished flow routes. The Standard Operating Procedures (SOP) has a different route for the delivery of filters to be cleaned from the filling equipment. The filters are delivered to wet component preparation area by using a wall Pass-Thru that connects the Grade 8 corridor to the Grade 9 Wet Component Prep Area.

This route was chosen as the proposed flow route (PFR) for the filling equipment because it reduces the handling of the equipment and the staff needed to perform the task of delivery. Currently, this route and Pass-Thru is only used for the delivery of the used filters, which is a waste of transportation. Using this Pass-Thru for the delivery of the filling equipment, and filters, allows for additional flexibility in the lot-to-lot changeover.

To ensure that the proposed flow route (PFR) is the flow route for the delivery of used filling equipment a spaghetti diagram will be created to measure the steps and time used for each stablished route (Vials Route 1, Vials Route 2, and Syringe Route 1), and the proposed flow route (PFR). The spaghetti diagram will be created because is the easiest and most visual way to understand the movement in all the routes, this data will help understand if the proposed route is the better option.

Ergonomic and security aspects are going to be considered with the proposal of this new flow route. Therefore, the measurements of volume inside the Pass-Thru and the equipment dimensions are going to be taken to determine if it is possible to place the equipment inside the Pass-Thru. and sketch will be made to calculate the area of the Pass-Thru and the filling equipment to confirm that the filling equipment can fit inside the Pass-Thru without any safety issue.

An ergonomic evaluation by the Environment, Health and Safety (EHS) department of the Pass-Thru height, and filling equipment weight and handling will be conducted and a comparability with the ergonomic guideline design (Figure 1) will be performed. This step will ensure the safety of the staff while handling the filling equipment.

The last step to achieve the research objectives is the review, update and approval of the equipment and material flow route Standard Operating Procedure (SOP), in conjunction with Plant Quality Assurance (PQA), to add the new flow route for the to be cleaned filling equipment. This step helps ensures compliance with the established regulations by the pharmaceutical and regulatory agencies.

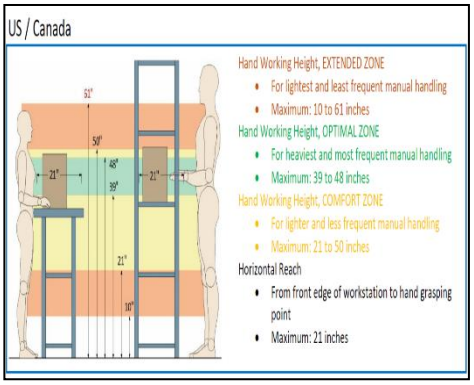

Figure 1
Ergonomic Guideline Design

RESULTS AND DISCUSSION

This section summarizes the results of obtained from the steps described in the methodology section to ensure the Proposed Flow Route (PFR) is the optimized flow route for the delivery of the used filling equipment. The Proposed Flow Route (PFR) is the actual flow route to deliver the used filters by using a wall Pass-Thru that connects a Grade 8 Corridor to Grade 9 Wet Component Prep room.

Spaghetti Diagram

To ensure that the Proposed Flow Route (PFR) is the optimized route, two spaghetti diagrams were created, one for the Vial Filling Line (Figure 2) and another for the Syringe Filling Line (Figure 3). The spaghetti diagrams gave a better understanding of each route, how many operators are needed for the task, and the equipment handling. It revealed that the stablished flow routes by the Standard Operating Procedure (SOP) have more equipment handling than the proposed flow routes, each green and red dot represents the start and end movement of the filling equipment from a single operator. This means that the stablished flow routes need at least two operators to deliver the used filling equipment, meanwhile the Proposed Flow Routes (PFR) only need one operator to complete the task. A Proposed Flow Route (PFR) had to be design for each filling line, the spaghetti diagram helped recognize the necessity of creating a Proposed Flow Route (PFR) for the Syringe Filling Line and another for the Vial Filling Line.

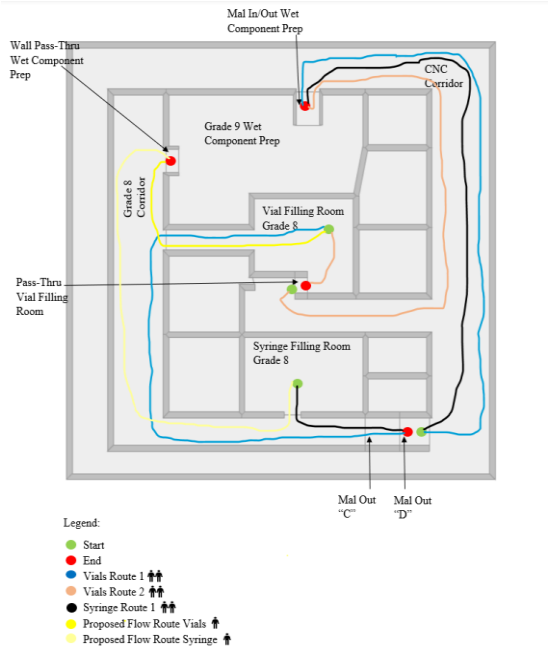

Figure 2
Spaghetti Diagram with Stablished Routes and Proposed Flow Route

Steps Taken, Time Spent, and Benefit

The time and quantity of steps were evaluated and tabulated for each stablished route (Vials Route 1, Vials Route 2, and Syringe Route 1) and the Proposed Flow Routes (PFR) for Syringe Filling Line (PFRS) and Vial Filling Line (PFRV) (Table 1). In Figure 3 and Figure 4, the difference between the quantity of steps and time of each route can be appreciated. In this analysis, the Proposed Flow Route (PFR) for both filling lines provide a greater benefit to the lot-to-lot changeover with four (4) minutes and one-hundred ninety-two (192) steps for the Vial Filling Line and five (5) minutes and three hundred (300) steps for the Syringe Filling Line.

Table 1
Steps Quantity and Time Spent for the Stablished Routes and the Proposed Flow Routes

Equipment Flow Route	Quantify of Steps	Time Spent (min.)
Stablished Vial Route 1	579	17
Stablished Vial Route 2	338	12
PFRV	192	4
Stablished Syringe Route 1	451	12
PFRS	300	5

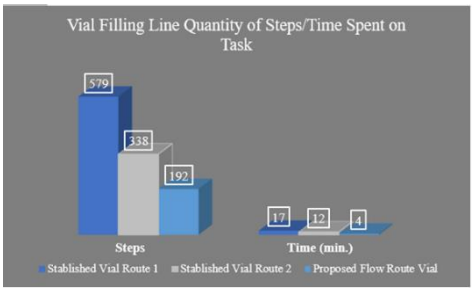

Figure 3
Vial Filling Line Quantity of Steps/Time Spent on Task

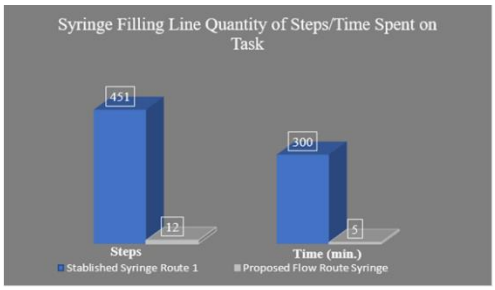

Figure 4
Syringe Filling Line Quantity of Steps/Time Spent on Task

Using the data from Table 1 the benefit obtained comparing the stablished routes with the Proposed Flow Route (PFR) in time spent and steps taken performing the task of delivering the used filling equipment for both filling lines was calculated (Table 2). The obtained time benefit for the Vial Filling Route 1 was 67%, for the Vial Filling Route 2 was 4%, and for the Syringe Filling Route 1 was 33%. The obtained benefit from the steps taken in the Vial Filling Route 1 was 67%, Vial Filling Route 2 was 43%, and Syringe Filling Route 1 was 33%. These are significant benefits that makes a difference when performing the lot-to-lot changeover.

Table 2
Benefit Obtained Comparing Time Spent and Steps Taken

Filling Equipment Flow Route	Time Benefit%	Steps Benefit%
Vial Filling Route 1	76%	67%
Vial Filling Route 2	67%	43%
Syringe Filling Route 1	58%	33%

Safety

To consider the security aspect of this new delivery point, the measurement from the interior of the Wet Component Preparation Wall Pass-Thru were taken and the filling equipment dimensions (Table 3). Using the measurements on Table 3 a sketch was made with the area calculated and it confirmed that at least four (4) Rapid Transfer Ports (RTP), which has the filling equipment inside, can fit inside the Wall Pass-Thu without any safety issues (Figure 5).

Table 3
Measurement from Interior of Wall Pass-Thru and Filling Equipment Dimensions

Interior Wall Pass-Thru	
Long	32" ¼"
Width	27"
High	27"
Rapid Transfer Port (RTP) Dimension	
Diameter	12" ¾"
Height	21" ½"
Height with Valve	23"
Diameter with Handle	19"

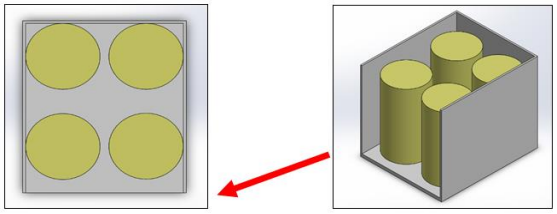

Figure 5
Sketch of Filling Equipment Inside of Wall Pass-Thru

Ergonomic Evaluation

An ergonomic assessment was conducted by the Environmental, Health and Safety (EHS) department for the handling of the Rapid Transfer Ports (RTPs) at the Wet Component Prep Wall Pass-Thru to analyze and risk rank manual handling activities. The task was evaluated using the Humantech System. The Wet Component Prep Wall Pass-Thru has a height from floor to base of 39", which is inside the optimal working zone specified in the ergonomic guideline on Figure 1. The overall Risk Priority Score (RPS) of the task was 20.8, presenting a Moderate Risk (Table 4), due to identified potential risk factors of bent wrist, twisted back, overhead reach, horizontal reach, awkward neck, and heavy lifting. The RPS can be reduced to 8.9, which presents a Low Risk, with the implementation of recommended administrative ergonomic controls. These administrative ergonomic controls were to update the Job Hazard Analysis (JHA) to include good ergonomic practices when handling the filling

equipment and ensure rotation of tasks to reduce time exposure to heavy lifting.

Table 4
Risk Priority Score (RPS) Levels

Score Level	Risk
0 - 9	Low
10 - 30	Moderate
> 30	High

To proceed with the next step in the methodology, which is the Standard Operating Procedure (SOP) review and approval, the administrative ergonomic controls recommended by the Environmental, Health and Safety (EHS) department were implemented. The Job Hazard Analysis (JHA) for the Vial Filling Line, Syringe Filling Line, and Component Preparation were revised and updated with the activity of Rapid Transfer Port (RTP) handling. The administrative control added to follow the Good Ergonomic Practices; which are to be aware of awkward postures, to maintain neutral postures, use tools to minimize material handling (carts), keep materials close to the body to reduce overhead and horizontal reach, and to move feet instead of torso to avoid twisting; was added to the activity. Rotation of tasks to reduce time exposure to heavy lifting was already in placed on the manufacturing floor but as a precaution it was also included on the Job Hazard Analysis (JHA) as an administrative control. Job Hazard Analysis (JHA), for the three areas, were updated and approved by the Environmental, Health and Safety (EHS) department.

Standard Operating Procedure (SOP)

The last step in the methodology section to implement the new delivery flow route for the to-be-clean filling equipment was the reviewal, update and approval of the Standard Operating Procedure (SOP). The Proposed Flow Routes (PFR) were added as alternative delivery routes to the equipment and material flow route Standard Operating Procedure (SOP). The stablished flow routes were kept as backup if the Proposed Flow Routes (PFR) are not available. The Standard Operating Procedure (SOP) was reviewed and approved by the Standard Operating Procedure (SOP) owner and Plant Quality Assurance (PQA).

When the revised version of the Standard Operating Procedure (SOP) became effective an official notification was sent to the affected areas with the new delivery instructions for the to-be-clean filling equipment.

Conclusion

The main objective of this project was to successfully implement a new shorter flow route for the delivery of the to be cleaned equipment from the filling rooms to the wet component preparation room for the improvement of motion and transportation during the lot-to-lot changeover. To accomplish this objective lean manufacturing tools were used to reduce the time spent delivering the filling equipment. The spaghetti diagram determined the optimal Proposed Flow Route (PFR) needed for both filling lines to deliver the filling equipment. It was discovered, through the spaghetti diagram, that the Proposed Flow Routes (PFR) not only take less time than the stablished flow routes, but they also have less equipment handling and need less operators to complete the task.

The transportation and motion waste reduction by a 30% during the lot-to-lot changeover was accomplished by counting the steps and time spent on each flow route to deliver the to-be-clean filling equipment. The Syringe Filling Line had a reduction of 33% in movement waste and a 58% benefit of time spent on task. Meanwhile, the Vial Filling Line had two stablished flow routes and the transportation waste reduction comparing with the best stablished route was 43% and had a 67% time spent on task benefit.

The objective of reducing the ergonomic risk in the handling of the equipment during the transportation was accomplished by having the Environmental, Health and Safety (EHS) department perform an Ergonomic Evaluation of the task. The evaluation determined that the overall Risk Priority Score (RPS) of the task was 20.8, presenting a moderate risk but it was reduced to 8.9, presenting a

low risk, with the implementation of the recommended administrative ergonomic controls. Job Hazard Analysis (JHA) for both filling lines (Vials and Syringe) and Component Preparation were revised and updated with Good Ergonomic Practices as administrative controls.

The new and optimized flow routes will serve as standards for future process improvements. Using Lean Manufacturing and Six Sigma methodology helped made the development of this project a more standardize process, as well as helped increase the manufacturing capacity by lowering the time spent on lot-to-lot changeover, reduce transportation and motion wastes, and increased the productivity of the line process.

REFERENCES

[1] Cambridge English Dictionary (2022). Changeover. [Online] Available: www.dictionary.cambridge.org/us/dictionary/english/changeover.

[2] G. Farquharson and N. Goldschmidt. (2022, June 10). *Understanding Cleanliness Classifications for Life Science Facilities* [Online]. Available: www.ispe.org/pharmaceutical-engineering/march-april-2017/understanding-cleanliness-classifications-life-science.

[3] W. Feld, "Lean Manufacturing: A "Holistic" View", in *Lean Manufacturing: Tools, Techniques, and How to Use Them (Resource Management)*, 1st ed. Florida: Taylor & Francis Group, 2000, Ch. 1, pp. 6.

[4] N. Torres, "Process Optimization by the Application of Lean Manufacturing Principles." Polytechnic University of Puerto Rico, 2020. PUERTO RICO CLOUD REPOSITORY (PRCR): POLYTECHNIC UNIVERSITY OF PUERTO RICO, hdl.handle.net/20.500.12475/1050.

[5] J. Henry, "Introduction" in *Achieving Lean Changeover Putting SMED to Work*. 1st ed. New York: Taylor & Francis Group, 2013, ch 1, pp. 21-22.