Fill and finish Production Line End Effectors Improvements for Reducing Rejected Units due to Robot Pickup Failures

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Abstract *— Since the production of parenteral is more regulated and complicated, it makes the manufacture investment cost higher in comparison with other dosage forms. As result, is important to apply lean tools in order to reduce the waste through the manufacturing process. The manufacturing process of a parenteral fill and finish facility can be divided in four (4) principal stages: Formulation, component preparation, filling and packaging. As the process goes forward, the waste cost increment since at each step, work if invested on the product. For example, filling and packaging waste are more expensive than component preparation or formulation. This research will evaluate the factors which cause pickup failures during the filling process and provide mitigations in order to reduce the quantity of waste related to such events.*

Key Terms *— End effectors, grippers, lean, parenteral.*

PARENTERAL MANUFACTURING

Parenteral is a type of drug administration that the drug is administered through an injection or infusion. Injections can be administered intravenous (into a vein), subcutaneous (under the skin), and intramuscular (into muscle). In the other hand, infusions are typically are given by intravenous route. The parenteral dosage forms may be solutions, suspensions, or emulsions, but they must be sterile, if they are to be administered intravenously. As result, parenteral drug manufacture process usually involves more process complexity, quality attributes and engineer controls among others in comparison with other administration route manufacture process. The parenteral manufacturing facilities requirements are stricter and complex in comparison with other pharmaceuticals dosage form facilities. As result, the production costs of have a tendency to be higher due the controls that are required to ensure the compliance and quality of the final product. The food and drug manufacturing is regulated on United States (US) by the Food and Drug Administration (FDA) through federal regulation and rules. The US Government has developed the "Code of Federal Regulation" (CFR) are codification of general and permanent rules created to regulate the industries among its territory. The CRF has been divided in 50 chapters and are update on an annually basis. The Food and Drug Administration (FDA) have developed the CRF chapter 21 which regulated the Food and Drug business. According to the 2011 CRF 21.42 (CRF 2011 revision, Chapter 21, section 42) explain the design and construction features which are required in a drug manufacturing environment i.e. Aseptic processing requires a system that monitors the environmental condition. Such continuous monitoring system increase the production cost of every manufacturing stage in the fill and finish facility and is proportional the criticality of the room classification. For example, the monitoring costs in a class 100K rooms is less than a class 100 (Aseptic environment). [3]

Manufacturing Process

The manufacturing process at the fill and filling facility include many process steps such as: Drug Dispensing, Formulation, Filling and packaging. At the dispensing area, usually the active ingredient is transferred from a bulk facility and is then measure according to the product final specification and recipe. Once the product is

dispensed into the manufacturing area, is then transferred to the formulation area where the buffer solution is mixture with the active ingredient. Once the formulation and filtrations are completed, the product to be filled is transferred to the filling area. The filling area is where the product is filled into empty syringes or vials. As result, the product is exposed during the filling process and the area required stickier environmental and process control in order to guarantee the product quality and efficacy. During this process the product is exposed to the room environment and as result it requires an aseptic process. In order to minimize the human intervention with the process, many companies update the process with several component and equipment such as robots to create an automatic filling process where humans only interact with the equipment such as robots programed to support the filling process.

MANUFACTURING AUTOMATION ROBOTICS

The requirement of high-precision operation in manufacturing area settings gave the opportunities to develop robots capable to have higher precision in comparison with a human. Also robots are not susceptible to human factor characterizes such as sneezing, undesirable moments, trembling and emotions. In the manufacturing environment, robots are programmed to perform a specific task at determine series of instructions.

Robotic Automation: History and Development

The field of robotics has been among us over several millennia but it was until the early 20th Century when it was referenced as robots. In 270 B.C., the Greek physicist and inventor Ctesibus of Alexandria created a water clock, which was powered by the rising water and employed a cord attached to a float stretched across a pulley to track time. This invention was called the clepsydra, or "water-thief". The name was given since the contraption entertained many people who pass by and stay focus watching the time pass, and as result it "Steal" the time of the people who were watching. Posterior invention were created by the France Joseph Jacquard who in 1801 invented a loom that used a series of punches cards to controls the patterns used to weave cloths and carpets. Charles Babbage in early 19th Century Britain created an automatic calculator later by adapting Jacquard's invention. Babbage's principles later led to the development of computers and computer programming. In 1892, Seward Babbitt created the motorized crane that uses a mechanical gripper to remove ingots from furnace. 70 years after Babbitt's invention, General Motors was the first industry to use similar concepts in its manufacture. Many similar inventions were created among the years; on 1979 the Selective Compliance Assembly Robot Arm (SCARA) was created as a result the joint forces of Yamanashi University in Japan, IBM and Sankyo. The SCARA was the first automation device with revolute joints that had vertical axes, thus providing stiffness in the vertical direction. The equipment has grippers, which can be controlled in compliant mode, or using force control, while the other joints were operated in position control mode. These inventions are the base and fundamentals of the robotic automation, which is used on the modern parenteral manufacturing process. [4]

Robotic End Effectors (Grippers)

Bedsides the robot itself, the most critical device in a robotic system is the end effector (gripper). The design of the end effector depends of the application that the robot which is being used, since there is a great number of robotic application. The end effectors must be an integrated part of the robot process designs. The end effector design depends on the type of robot being used, objects to be grasped, tasks to be performed, and the robot work environment. Parenteral manufacturing facilities have special system environmental requirements that directly impact the robot and end effector design. In parental filling areas, robots must operate in clean room conditions. End effectors must be selected for compatibility to the

class of clean room (class 100) in which the robot will operate and perform the assigned task. It is important that the end effector do not generate particles in order to ensure the quality of the product being filled. As result, the end effectors must be designed with all surfaces to be either stainless steel, polymer plastic or a material to be coated with a clean room acceptable material (such as an anodized aluminum surface or a baked-on powder coat). In addition, polymer washers and bearings should be used in the end effector operating mechanisms surfaces friction do not wear or generate particles. In some circumstances, mechanisms must be enclosed with seals or bellows in order to isolate the mechanism from the aseptic environment. [4]

Among the design considerations of the robots vary from robot size and payload capacities, since robot are designed for many operations. For example, some robots are designed for specific, singular tasks such as materials handling, painting, welding, cutting, grinding, or deburing and as result, these robots use specific tools as end effectors. The primary considerations for end effector designs is to understand the tool, orientation, and tool control for effective processing but not forgetting the robot payload capacity. In the other hand, robots designed for general purposes and material handling required additional engineering detail in end effector design. In both cases, tasks and the robot environment must be considered while designing the appropriate robot and end effector. In order to understand and properly design the end effector device is important to have a process flow diagram describing the tasks and how it will be accomplished poor the end effector design. [4]

The process work flow diagram will clarify how the object required to be handled and which functions are required to be performed by the device or the entire system. In the work flow diagram is also required to define the roles of the robot, system controller, peripheral devices, end effector, and specialized tools used to perform the task. From the activities necessary to complete the process, the end effector design requirements and specifications are created. During the design phase, is required to contemplate several aspects of the process, since they could affect the design of the end effectors and characteristics. Usually even with having robot, process, system requirements and specifications are not enough information available to be provided regarding the process. For example, process variables cannot necessary be available at the design stage and could potentially affect the operation of the end effectors in the further. Weight, uniformity, surface, orientation, friction coefficient, spacing, dimensions and dimension tolerances are example of factors that could potentially affect the design of the end effectors. If the design considerations aren't carefully evaluated the operation of the end effectors could potentially contribute to rejects (in process waste). Rejected units during the filling process are categorized as one of the seven type of waste defined by lean thinking. [4]

LEAN MANUFACTURING

"Lean" is a concept created and deeply rooted in the Toyota Production System. In its purest form, Lean thinking is about the elimination of waste and the increase of speed and flow of a determine process of facility. A highly level oversimplification of the ultimate goal of lean is to eliminate waste from all process. The waste can be defined as an activity that consumes resources but it does not have value to the costumer. The costumers are not willing to pay for an activity that has no meaning to them. Ironically, in most of the business, the processes that actually create value for the costumer are a small percent of the total activity cost. [1]

Although the elimination of waste may seem like a simple subject it is noticeable that waste is present among all manufacturing process and in some cases is seeing as an inherent aspect of the process. The elimination of such waste is the goal of lean, and Toyota Production System divides the waste in seven types: Waiting, Overproduction,

Rejects, Excess motion, over processing, Excess Inventory and Transportation. In order to properly reduce the value of a product, the company must eliminate the seven (7) wastes of lean in order to reduce costs, increase profits, improve employee engagement, reduce rework and improve delivery time. [5]

COMPANY X IN-PROCESS WASTE EVALUATION

Since the product have move through the process from dispensing, formulation to filling areas, the product cost filling area have greater cost in comparison with previous stages. The production costs of each intermediated stage are added to the product through the process. As effect, the filling area process waste is relative expensive in comparison with previous stages since its carrying the production cost from previous stages. As result, is mainly important to reduce as possible the waste among the filling process in order to improve the effectiveness and lowered the product costs. The waste among the filling process of Company X was evaluated and filled unit waste was identified as the mayor offender.

The filling process at company X is fully aromatic and continuously by using several equipment. Two positive pump displacement fillers and four stoppering placement units are the main components in charge of the filling and stoppering process. In the process, there is also a series of conveyor used to transport the components along the process and robots that move the unfilled and filled components through the different stages. At the stoppering stage, the robot pickup the filled syringe tub and transport it to a temporally holding station where the robot pickup only the syringe nest and place it inside the stoppering unit. After the stoppering process is complete, the robot pickup the syringe nest from the stoppering unit and return it to the tub, where the robot pickup the tub and transport it to the exiting conveyor. Figure 1 shows the robot movement during the stoppering process cycle.

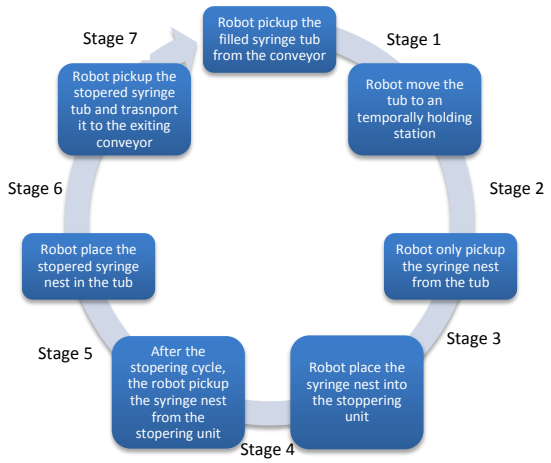


Figure 1
Robot Operation a Stoppering Cycle Process

At the Company X, the mayor contributor was identified to be pickup failures. The pickup failure event is produces during the robot process stage 1 and stage 7 (refer to figure 1). As result, the entire syringe tub is discarded producing 100 syringes of waste. This contributor was analyzed using several lean tools such as: five why and fishbone analysis in order to evaluate the conditions, which create the failure and properly identified possible corrections. Figure 2 and 3 showed the five why and fishbone analysis created for the pickup failure event analysis respectively.

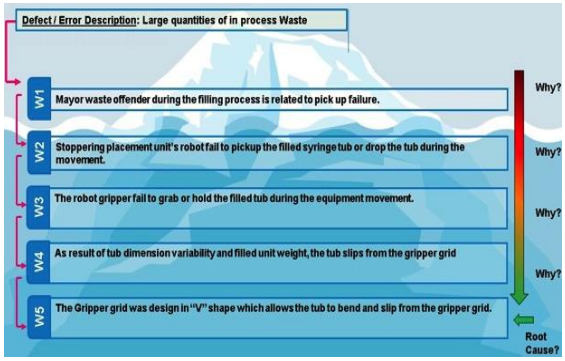


Figure 2
Five (5) Why Analysis

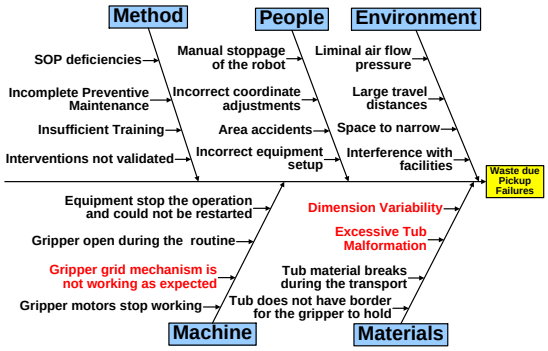


Figure 3
Pickup Waste Fishbone Diagram

On the Fishbone analysis (Figure 3) possible causes for filling waste due pickup failures were identified. Among the evaluated possible root causes categories (Method, equipment, environment, material and people) the only confirmed causal factors were: Gripper mechanism not working as expected, tub dimension variability and excessive tub malformation. The gripper mechanism is design to grab the tub edges and move the tub between conveyors and holding stationary centers. When the mechanism doesn't open or close as expected, the robot fails to grab the tub and as result the tub is discarded. The last two causal factors identified (tub dimension variability and excessive tub malformation) are related to material issues. The lean tool of five why was used to specific determine the root cause of pickup failures and properly determine the modification that could improve the process. During the five why evaluation, it was determined that gripper grid design was mayor responsible of the pickup failures event. The gripper grid actual design have a V shape which reduce the contact area of the tub edges and in the event that tub edges shows variability or malformation it will fail to properly secure the material during the transport. Refer to figure M and N, which shows a representation of the gripper grid and tub edges interaction respectively.

Figure 4
Actual end effector design

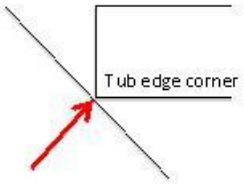


Figure 5
End Effector/Tub Surface Contact Area

A change on the gripper grid design that improves the contact area between the gripper grid and the tub edges will minimize the effects of the tub variations or malformation. Knowing a possible solution to minimize the pickup failures events in the filling area, a PDCA (Plan, Do, Check and act) diagram was created in order to prepare a plan and implement a solution. The PDCA diagram is an iterative four-step management method used in business for the control and continuous improvement of processes and products. Figure 6 shows the PDCA for Company X filling waste minimization by gripper improvement. [2]

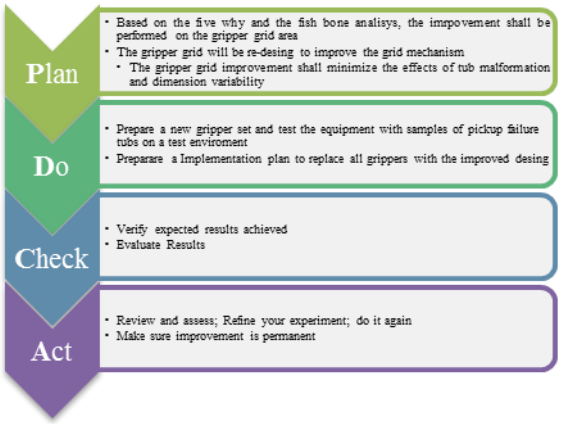


Figure 6
PDCA Diagram

METHODOLOGY TO REDUCE COMPANY X PICKUP FAILURES EVENTS

The mayor waste contributor among the filling process was determined to be the pickup failures trigger by the clean room robots. The syringe tub malformation or dimension irregularities contribute to the pickup failures since the robot gripper actual design does not compensate for the changes related to variability. The first milestone of this project is to document the quantity if filled units rejected due pickup failures. The information documented will support as baseline in order to determine the effectiveness of the new design. Concurrently with this activity, the actual gripper will be evaluated in order to determine the improvements requirements to the grid area. The surface contact between the grid and the tub is required to be increased in order to minimize the effect of tub malformation in the transport operation. Figure 7 shows the path flow required to create and propose the new gripper design.

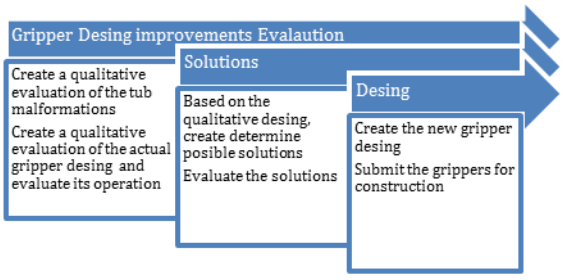


Figure 7
Gripper Design Evaluation Workflow

Once the grippers are delivered to Company X, they will be tested on a test environment room, to determine if the installation requirements were archived and introduce the new design as an equivalence replacement to the quality organization. Once the new design grippers are approved by the quality organization, planning and maintenance organization will obtain the require installation windows. Figure 8 shows the planning maintenance workflow.

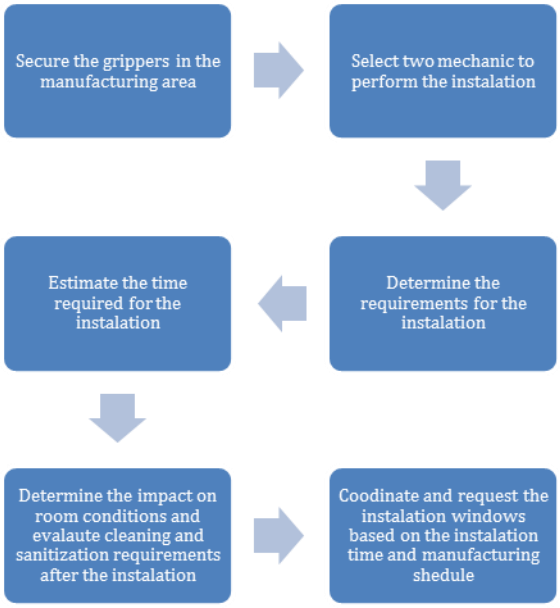


Figure 8
Planning and Maintenance Scheduling Workflow

After the gripper installation, the robot coordinates will require modification in order to mitigate the changes of the gripper dimensions. Once the coordinates are corrected, the equipment operation will be tested in order to ensure that the equipment was left in normal operating conditions. After the robot grippers are replaced, the pickup failures will be evaluated in order to determine the effectiveness of the new gripper design. The evaluation will cover a comparison between the pickup failures reject rate before and after the new gripper implementation design.

RESULTS AND DISCUSSION

The mayor waste contributor among the filling process was determined to be the pickup failures trigger by the clean room robots. As discussed previously, tub malformation or dimension irregularities contribute to the pickup failures since the robot gripper actual design does not compensate for the changes related to variability. The first milestone of this project is to document the quantity if filled units rejected due pickup failures. The information documented will support as baseline in order to determine the effectiveness of the new

design. Table 1 shows the summary of pickup failures rates per filling batch.

Table 1
Pickup Failures Rates per Filling Lots

Month	Pickup Failure rejects quantity (units)	Batch filled (Quantity)	Pickup failure/Batch
January 13	12931	27	478.93
February 13	11966	32	373.94
March 13	10729	34	315.56
April 13	12448	25	497.92
May 13	5624	40	140.60
June 13	9376	32	293.00
July 13	9015	32	281.72
August 13	12210	41	297.80
September 13	13228	38	348.11
October 13	14324	26	550.92
November 13	5815	19	306.05
December 13	8319	21	396.14
January 14	11146	33	337.76
February 14	12670	42	301.67
March 14	12199	38	321.03

Concurrently with this activity, the actual gripper will be evaluated in order to determine the improvements requirements to the grid area. The surface contact between the grid and the tub is required to be increased in order to minimize the effect of tub malformation during the tub transport operation. Based on the five why analysis and the fish bone diagram developed (Figure 2 and Figure 3 respectively), The installed grippers were evaluated in order to determine which characteristics are contributing to the pickup failure events in Company X. Table 2 shows the evaluation performed.

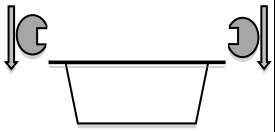
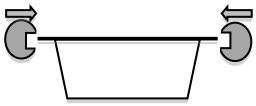
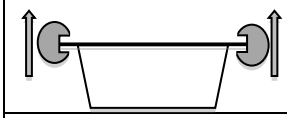
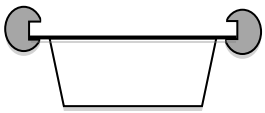
Table 2
Current Installed Gripper Evaluation

Gripper characteristic	Contribution to pickup failure	Improvement proposal
Material of construction	• The material of construction is Stainless steel. • The material of construction was not identified as a possible contributor to pickup failures.	• No improvement related to material of construction was identified.
Gripper grid position	• The gripper grid position is design to grab the tub from the center. • The gripper grid position was not identified as a possible contributor to pickup failures.	• No improvement related to gripper grid position was identified.
Gripper grid shape	• The gripper grid "V" shape allows the tub to slip in certain cycles since he contact area between the tub edge and gripper grid is limited (Refer to figure 4) • The gripper grid shape was identified as a causal factor of pickup failures.	• The gripper grid shape shall be redesign to provide a better surface contact area. • Replace the gripper grid shape with a "C" instead the "V" shape.
Gripper operation	• The gripper open and close with the support of a stepper motor. When the gripper close and reach the tub edge, the force exerted on the motor produce certain level of current which indicate the robot when to stop closing the mechanism. • The gripper operation was identified as a causal factor of pickup failures.	• No improvement related to gripper operation was identified.

Based on the analysis performed on Table 2, the solution is to redesign the gripper grid in order to change the grid share from "V" to "C". The "C" shape will provide more surface contact between the gripper grid and the tub edges. Also as the robot move vertically, the tub edges will rest on the gripper grid allowing minimizing the effect of tub malformation or dimension variations. The rest of the gripper design will remain the same in order to

maintain the same gripper operation. The gripper operation can be summarize in four operations described on Table 3.

Table 3
Material Pickup Operation

Gripper operation diagram	Gripper operation description
	Step 1: Robot positioned the open grippers over the tub edges and performs a vertical movement to lower the grippers until the grid is in the tub edges range.
	Step 2: Once the robot reaches the preset coordinate, the grippers start to close until the grid reach the tub edges.
	Step 3: After the gripper have close, the robot move vertically to remove the tub from the conveyor.
	Step 4: The robot moves the tub to the next process stage were the tub is moved.

Once the grippers were constructed, a quality and operation inspection was performed to ensure the like for like replacement. During the inspections, construction and operation parameters such as: Material of construction, Dimension, Gripper grid modification and operation testing among other criteria were evaluated. Table 4 shows the acceptable criteria established for Company X.

Table 4
Acceptance Criteria

Characteristic	Acceptance criteria	Acceptable or not acceptable
Material of construction	•Stainless steel 316 Electro polish <15RA	☑ Acceptable ☐ Not acceptable
Dimensions	Gripper dimension must be the same as installed grippers	☑ Acceptable ☐ Not acceptable
Gripper grid	Gripper grid in "C" Shape	☑ Acceptable ☐ Not acceptable
Operation testing	•No pickup failures reported while operating the gripper in a test environment with new material •No pickup failures reported while operating the gripper a test environment with material that caused pickup failures during process	☑ Acceptable ☐ Not acceptable
Quantity	Receive a total of eight (8) pairs of grippers	☑ Acceptable ☐ Not acceptable

Once the grippers characteristic were verified and approved, the grippers were deliver to the manufacturing aseptic were they remain storage until the installation window. The installation was performed by two mechanics who replace the grippers and tune the robot coordinates as required. After the gripper installation and verification the pickup failures reject information was used to evaluate the project effectiveness. Table 5 shows the defect rate average before and after the implementation of the new grippers.

Table 5
Pickup Failure Defect Rates Before and After the Gripper Modification

Pickup failures defect rate of the first 7 batches of May 2013 (unit/Batch)	Pickup failures defect rate of the first 7 batches of May 2014 (unit/Batch)
256	33

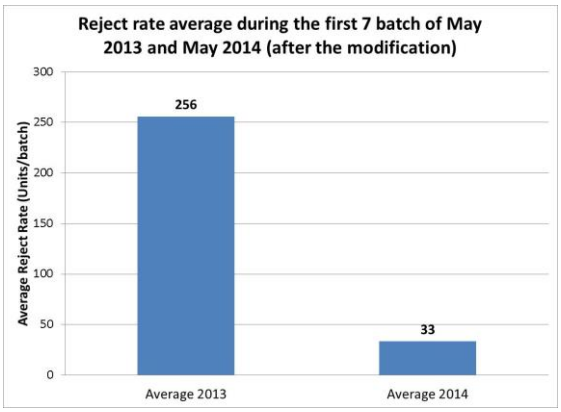


Figure 9
Reject Rate Average during the First 7 Batch of May 2013 and May 2014 (After the Modification)

CONCLUSION

At Company X, the mayor contributor to the waste during the parenteral filling process was the robot pickup failures. The grippers with the new design were installed on 4/25/2014 and the reject quantity due pickup failures was gathered through the filling process to confirm the effects due the new gripper design. As showed on figure 9, the first seven (7) batches filled with the new gripper design, a reduction of the pickup failures rejected units was observed. The reject rate was reduced from 256 to 33 units per batch.

In addition, the manufacturing associates reported that the pickup failures reported after the implementation, were related to an excessive tub malformation. Based on the defect rate measure after the implementation of the new gripper design, the engineering solution was considered a success.

REFERENCES

[1] Goldsby, T., & Martichenko, R., *Lean Six Sigma Logistics: Strategic Development to Operational Success*, Boca Raton, FL, US: J.Ross Publishing, 2005.

[2] Liker, J. K., & Meier, D., *The Toyota Way Field Book*, McGraw-Hill Ed., New York, NY, US, 2005.

[3] U.S. Government, (June 1, 2013). *Code of Federal Regulations Title 21*, Retrieved 3 1, 2014, from Federal Food and Drug Administration (FDA): http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=211.

[4] Wesley, S. L., & Hodge, J., *Robotics and Automation Handbook*, (T. R. Kurfess, Ed.) Boca Raton, FL, US: CRC Press, 2005.

[5] Womack, J. P., & Jones, D. T., *Lean Thinking*, New York, NY, US: First Free Press Edition, 2003.