# *Research in the Requirements for Reducing the Blood Transfer Device Complains for Air Bubbles and Leakage*

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***Abstract*** *— An increase on complain trigger a company Quality department raising a flag for further investigation of a product Nonconformance. Using Lean Six Sigma tools and DMAIC methodology a multidisciplinary team work together to found possible root cause that create robust process and brings back customer confident. Following the Existing Process Failure mode analysis and customer experiences, a route to follow was created to pursue some corrective action activities that address the failure study. Design of experiment and process validation prove that there was some process opportunities that's needs to be implemented. Also during the Analyze phase some recommendation were found to pursue as a long term solution.*

***Key Terms*** *— CAPA, Complains, DMAIC, Lean Principals.*

## INTRODUCTION

On a medical device environment a company is dedicated to automated assembly blood transfer devices. A manufacturing department currently is working with three manufacturing lines that are responsible to manufactures a volume around one hundred and fifty (150) millions units per years. The Blood Transfer Device is a single use, sterile product designed to provide safe and convenient transfer of venous blood from Syringes to Collection Tubes and Blood Culture Bottles. This device reduces the risk of transfer related injuries while maintaining the specimen integrity required for accurate disease diagnosis. An increase in complaints above normal Complain by million on to blood leakage and/or under-fill were received on a Medical device Company Customer complaints describe blood leakage or splatter while using the blood transfer device resulting in inadequate tube filling, foaming or air entering the tube, violent flow leading to hemolysis as well as hissing and whistling sounds team members, decrease the confusion and downtimes between steps. Gaining all these improvements, the split case department will be more productive and will provide the shipping department a faster service that will finally meet the customers' need, having the correct product at the exact moment that they need them to have.

### Research Description

This research will bring a comprehensive study for the possible causes of the specified defect of Blood leakage on the blood transfer device. It will allow a better understanding of the factors on the process or characteristics of the product that influence more on the occurrence of the blood leakage.

### Research Objectives

A situation Analysis was open by the manufacturing Plant in order to establish an investigation that brings effective corrective actions. The research objectives are the identification of the contributor's factors and possible corrections actions to reduce the complaint rates for the specified product defect.

### Research Contributions

It is expected that this research would help to reduce the company complains rates, as the exposure from the client to hazards and customer dissatisfaction. The application of the corrective actions will lead to a better machine/process creating

a robust environment engaging the company quality standards.

## LITERARY INFORMATION

In order to understand the requirements for Reducing the Blood Transfer Device Complaints for Air Bubbles and Leakage is important to define what is consider a leak issue. A leak issue is consider when the customer experienced significant blood splatter on their person during the normal operation of the device. It is consider as a moderate on a severity ranking level which have a potentially significant impact on Quality System and Regulatory Compliance.

### FDA

As been located on Puerto Rico and sell product to US and international the company involve in the current study is a regulated one by the Food Drug Administration (FDA) [1] and International Standard Organization (ISO). The Food and Drug Administration is responsible to protect the public heath assuring that products and medical devices intended for human use are safe and effective. FDA define medical devices based on the risk associated with the device. Devices are classified onto three categories class I (low risk), class II (medium risk) and class III (high risk). The blood transfer device on study are consider as a class II medical device. As part of the quality system regulation FDA have define different codes. Those codes establish some basic rules to follow on different manufacturing and management aspects The Code of Federal Regulations that applies to the class II device is the CFR (21) Part 820. CFR 21 Part 820 outlines the current good manufacturing practices (CGMP) that govern the methods used for all finished devices intended for human used.

### ISO Regulations

As requirement for the international sales the company has to comply with the ISO 9000 certification [2]. Certification to the ISO 9000 standard can enhance an organization's credibility by showing customers that its products and services meet expectations.

The standard that is design to be used by the organization is the ISO 13485 that involve in the design, production, installation and servicing of medical devices and related service. ISO 13485 is described as follow:

"ISO 13485:2016 specifies requirements for a quality management system where an organization needs to demonstrate its ability to provide medical devices and related services that consistently meet customer and applicable regulatory requirements. Such organizations can be involved in one or more stages of the life-cycle, including design and development, production, storage and distribution, installation, or servicing of a medical device and design and development or provision of associated activities (e.g. technical support). ISO 13485:2016 can also be used by suppliers or external parties that provide product, including quality management system-related services to such organizations.

Requirements of ISO 13485:2016 are applicable to organizations regardless of their size and regardless of their type except where explicitly stated. Wherever requirements are specified as applying to medical devices, the requirements apply equally to associated services as supplied by the organization.

### Complains

A Complain [2] is define by the company as any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a product after it is released for distribution. As soon as the company become aware of an alleged product deficiency /performance issue, the following information should be collected (if available) from the customer for further investigation and better understanding of the event: faster changes with higher benefits with lower efforts.

## DMAIC PROJECT METHODOLOGY

In order to achieve the objectives of this project the DMAIC [3] methodology will be executed. The Continues Improvement department would help engineering team to run the process improvement project effectively executing the five steps efficiency approach that brings DMAIC


**Figure 1**
**DMAIC Methodology**

The **Define** phase is the first of the DMAIC process and would establish the route to follow. By integrate associates from different department it would allow to understand the process and product malfunction or error. A CID (CAPA Initiation determination) process would start and a CAPA [4] number will be assigned if needed. The use of a consistent, objective evaluation method to identify the potential risk of quality issues based on severity and occurrence factors should be performed as part of the define phase. All the contingent activities required should be evaluated to control the use of potentially non-conforming products materials or process. A description and characterization of potential hazard needs to be define during this phase

The **Measure** phase would be used by the team member to collect all the data about the related complains during the affected period. Samples of the related complains should be collected and analyzed. The amount of affected product on plant /or market should be define in this phase.

All the Data collected should be **Analyze** during the third phase to determine root causes of defects and opportunities of improvement. Team should identify the actions that's rectifies immediate problem only (does not prevent recurrence - repair, rework) and possible actions to eliminate the root cause of a potential quality issue (leakage) in order to prevent its occurrence. Those action needs to be prioritize in order to identify which would be executed first. Visualization tools as Cause and effect diagrams and paretos would help during this phase for categorizing the potential causes of the investigation problem in order to identify root causes An evaluation of process or product redesigned should be performed during these phase. Process documents and validation procedures also needs to be considered.

During the **Improve** Phase the team should target all the solutions to fix and prevent the current investigated incidents. A commitment of the Management is required to support the improvement actions. Time of manufacturing lines for validation and testing needs to be discussed with the manufacturing management team. Also possible future expenses should be considered and discussed with finance team. Any possible solution should have an owner and due date and should be assigned during this phase.

Finally the **Control** phase should prevent the reverting to the "old way". Team should define an effectiveness method to define that the CAPA root causes have been addressed. Predefine the acceptance criteria should also needs a due date. All the procedures changes implemented during the improve phase should be added into each involve associated curricula to be retrained on the define time frame. If effectives is not meet during the control phase team needs to decide if the CAPA needs to be re-open and back to investigation again

## RESULTS AND DISCUSSION

All the DMAIC phases were covered as part of the Lean Blitz Activities.

### Leakage Blitz - Define Phase

Quality Department assign the increase of complains as an event to be discussed on the Quality Data trending's meeting and a CAPA initiation process was performed. A review of the Complains per millions trend was executed. It was decide to

open a CAPA to further investigate and address this event. It was determine that the CAPA was a medium risk one and classify as a corrective CAPA type.

### Severity Assessment

In the scale of the company quality statements the Capa was classify with a Severity level of S3. This ranking level describe that the defect could be harm to patient user causing some injury, which may include significant discomfort, minor non-permanent injury and/or temporary disability. This injury usually required medical interventions. As a quality compliance S3 is describe as an issue having significant impact on Quality System /Regulatory Compliance.

### Occurrence Ranking

Specifically, blood splatter defect occurs once every 20 million units shipped and broken & leakage at hub defects occur once every 41 million units shipped. On the occurrence ranking Capa was define as an O3 level. Specifically, blood splatter defect occurs once every 20 million units shipped and broken & leakage at hub defects occur once every 41 million units shipped. On the occurrence ranking Capa was define as an O3 level.

### Leakage Blitz – Measure Phase

Starting the data collection, complains trending were discussed. A total of Fifty-nine (59) complaints have been received between October 2015 and May 12, 2017. Figure 4 describe on details the complaints trending.

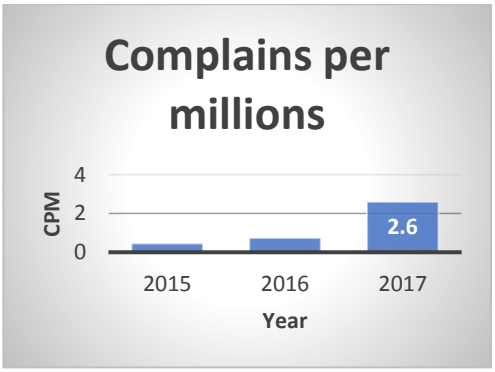


**Figure 2**
**CPM Trend**

The estimated complaints per million (CPM) for Fiscal Year 2017 is based on forty eight (48) complaints received through mid-May from twenty nine (29) affected lots with an average batch size of 259,850 devices. The complaints per million for FY17 is significantly higher compared to prior years (FY2015 - 0.46CPM and FY2016 – 0.73CPM).As a containment action team define the amount of possible affected product.

### Leakage Blitz – Analyze

In order to confirm the complaint verbatim multiple actions have been taken. A visit to customer site was completed to understand the failure mode and samples were brought back which had failed in the field during use. Return samples from customers have been decontaminated and examined on site. Functional and leak testing has been performed in order to replicate the failure. When performing a leak test through a quick check method developed by Japan air escaping can be visualized. (Method: holder is filled with water and air filled syringe is connected, when the syringe is depressed air bubbles may be seen in the water-filled holder if there is a path for air to travel through).

Functional testing involves using the product in a simulated use with Vacutainer tube and either sheep's blood, water, or colored water filled syringe and observing for normal or abnormal tube filling. When testing the same decontaminated samples the defect was not always confirmed. This may be explained by possible residual clotted blood which has occluded a leak path.

Furthermore, these samples were analyzed with microscopy and OGP in order to obtain dimensional data and images to see if any defects could be observed or measured. Five parts were measured from each lot 3165306, 3304147 and 3304154 for Tab O.D., Hub O.D., and I.D. Taper; all measurements met specifications. Pictures taken of the hub show varying degrees of what appears to be cracks or residual adhesive glue. Also, it is known that the molding process results in certain demarcation lines which can also be seen in images taken of the parts.

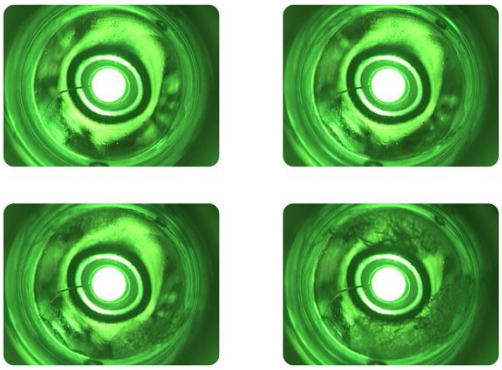

**Figure 3**
**Molding Cracks**

Process Failure Mode Effects Analysis (FMEA) was evaluated for the affected products and manufacturing lines and the possible cause of the defect is Hub/Holder joint that could fail and patient's blood could leak onto the medical practitioner leading to possible blood exposure.

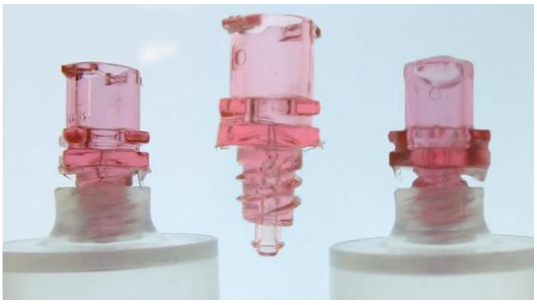

**Figure 4**
**Parts Joined on the Automated Process**

### Design of Experiments and Engineering Studies

A design of experiments and other studies were executed on site on May 1st. The protocol outlines the engineering study composed of three (3) parts: Max torque application, Design of Experiments (DOE) matrix and adhesive dwell time characterization. The objective was to study these input variables as they relate to the output of leakage, the failure mode associated with these complaints. Other output variables examined include torque to break, and hub to holder gap.

### Max Torque Application

Here, the purpose was to prove the failure may be caused by high RPM and high torque clutch setting (the effective torque is a function of RPM and torque clutch setting). It was observed, however, that excessive torque led to the hubs stripping the threads on the holder.

### Design of Experiments (DOE)

A multilevel factorial design was created with key process input variables (KPIVs) being torque clutch (2 levels: 2.3 in-lbs., 2.7 in-lbs.) and RPM (4 levels: 180, 220, 260, 300) settings with two replicates of each run. Additionally, these runs were repeated by slowing down the chassis speed from twenty seven (27) cycles/min to ten (10) cycles/min.

### Adhesive Dwell Time

Adhesive Dwell Time was examined as a factor by decreasing the chassis speed from the nominal twenty seven (27) cycles per minute to thirteen (13) cycles per minute, seven (7) cycles/min, and three and a half (3.5) cycles/min and running a select combination of the DOE conditions at these speeds.

Other factors that were considered include the torque clutch position (samples were kept traceable to their clutch head position 1-12).

## RESULTS

Torque to break testing did not correlate with the changes in the process settings, for the part I of the DOE all samples tested passed. For the adhesive dwell time study the torque to break averages were lower than the DOE samples and there were two failures overall. A summary of the leak testing overall is shown below. There was a strong correlation between increased dwell times resulting in an increase in number of failures (Table 4). Additionally, when longer adhesive dwell times occurred with higher RPM settings more failures were observed.

**Table 1**
**Leak Testing Results Summary Overall**

| Study Section | Chassis Speed (cycles/min) | Est Dwell Time (s)* | Sample Size | No. Failures | % Failed |
|---|---|---|---|---|---|
| Part II | 27 (Nominal) | 36 | 1158 | 3 | 0.26 |
| Part III | 13 | 61 | 180 | 12 | 6.67 |
| Part IIB | 10 | 75 | 576 | 16 | 2.78 |
| Part III | 7 | 100 | 360 | 19 | 5.28 |
| Part III | 3.5 | 175 | 90 | 2 | 2.22 |

### Root Cause

Experiments on-line at local site shows that decreasing chassis speed resulted in increased failure rates. It is hypothesized that the cause is the adhesive has more time to attack and degrade the hub material.

It is likely there are interactions between the factors, for example high RPM combined with adhesive dwell time resulted in higher failures rates for the engineering study executed. Assembly Product and production specifications/ control plans will be updated to add leakage as a product requirement based on established deign Input requirements. The rpm for the required assembly process will be revised and validated.

### Leakage Blitz – Improve Phase

Based on the analyze phase the following action needs to be addressed to reduce / eliminate the cause of the leak failure.

### Corrections

Dwell time was reduced from ninety (90) seconds to three and a half (3.5) seconds at assembly process machine.

The RPM settings at assembly process machine (Torque station) was lowered at the end side of the validated window.

### Corrective Actions

Decrease RPM range and revalidate the machine assembly process. Update control plan documents and Product Specification(s).

### Preventive Action

Implement the Leak Test Method as part of inspection process for product.

Following the results of the DOE a validation process was perform in order to a follow the statements describes on the corrective actions

### Process Validation

As a requirement for the Process qualification a total of lot three (3) lots were run.

### Effectiveness Plan

After the implementation of actions, the leak test data will be analyzed for the next five (5) BTD lots to demonstrate effectiveness of the actions. Acceptance Criteria will be based on the meet of all values describe on specification procedures.

### Leakage Blitz – Control Phase

A total of sixteen (16) lots have been manufactured since the implementation of the corrective actions on 09JULY2017. Only one (1) event was reported on the lot number 4171905 (after eight lots manufactured) manufactured on 06/26/2017. For this event, NCMR 2014-06-057 was completed concluding that the event was related to UV system equipment at assembly machine. Correctives action were defined and implemented under on 23JULY2017. After this implementation, a total of six (6) lots have been manufactured with pass results. Complaint trend was evaluated on 20AUG2017and no complaints related to Leak, Bubbles or Incomplete Fill has been received after the corrective actions implementation.

## CONCLUSIONS

Based on the comparison of results against the Performance Qualification acceptance criteria, the validation of the Blood transfer device Assembly Machine with the new Torque Station parameter for the affected products was satisfactorily completed as per Validation Plan. It can be concluded that the process will be released for production and the PQ products can be released for sale after the approval of this completion report and the completion of all engineering change requirements. Based on the latest Nonconformance material repost (NCMR) and complaint Data, leak events has been improved by 94% with the actions implemented through the DMAIC process.

During the execution of the Process Qualification most of the failures occurred when chassis speed was decreased which means increasing adhesive dwell time. Results of leak testing also suggest that failure rates increase with higher RPM

settings. Most likely there is an interaction between these factors which may amplify failure occurrence. Lack of process procedures and inspect did not allow manufacturing team to observe adverse condition on products as it happen with the leak issue.

Since some environmental stress cracking (ESC) was observe on some failed samples, which push the material well beyond its yield stress ,as a long term solution further investigation should be pursue with the hub (molded part) modification to avoid hub cracking and failure. This was challenge on material samples which showed severe cracking in surprising short time. This time are equivalent to process dwell time found on the assembly equipment. Redesigned Hub should reduce thread interference and stress substantially.

## REFERENCES


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