Reduction in Dye Test Failures Incidence for Cartridges Manufacturing Process in the Medical Device Industry

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Abstract *— The medical device industry is known to be regulated by regulatory agencies across the world. Every year, a significant number of Non-Conformances (NCs) and Corrective Actions Preventive Actions (CAPA's) are generated to investigate the incidences where the product specifications are not aligned with company requirements. In coated cartridge manufacturing process, 63 Non-conformances were generated from January 2022 to October 2022 in where 22 non-conformances correspond to Dye Test Failures. This incidence of Dye Test Failures triggers the generation of one CAPA to investigate and identify actions to reduce the incidence of Dye Test Failures associated to human errors, equipment malfunctions and method. Kaizen Methodology and 6M's Tool were applied for the investigation and implementation phases. A total of 5 actions were successfully implemented. An Effectiveness Monitoring (EM) was established for a 9-month period where a maximum of 9 Non-conformances will be permitted to declare successful the reduction as part this Dye Test CAPA.*

Key Terms *— Cartridges, Dye Test, Coating, Non-conformance.*

PROBLEM STATEMENT

Cartridges are used in conjunction with handpieces to assist the insertion of the Intraocular Lens (IOL) in the eye capsular bag during cataract surgery. The cartridges are coated with two different solutions. The basecoat is dispensed first to assure adherence to the porous internal cartridge surface. The topcoat application serves as a lubricant agent to reduce friction between Intraocular lens (IOL) and cartridge tube through which the IOL travels during insertion. All the Production Orders are challenged with the Dye Test which consists of collecting determined sample units. The Dye test consists of inserting the cartridges on dye solution (purple substance) that is adhered to the cartridge interior surface when it has presence of topcoat solution. The objective of the Dye Test is to demonstrate that cartridges had an uniform coating coverage throughout the cartridge interior surface.

In 2021, the first CAPA was created to investigate the incidence of 5 consecutive Non-conformances generated due to Dye Test failures identified in that year. After investigation and actions implemented, the Effective Monitoring for this CAPA was established with the goal of reducing the incidence of Dye Test failures in a 50%, which results in a 10 Non-conformances or less in a 9-month period (from August 21, 2021, to July 21, 2022) after completion of CAPA actions. However, in the 9-month period, a total of 22 Non-conformances were generated due to Dye Test failures.

Due to these events reported, a second CAPA was generated to perform a robust investigation and determine why Dye Test failures occurs with a high frequency on coated cartridges affecting the quality and compliance profile, adding workload to available resources and potential disruption to company strategic products, while keeping the operations with an increased degree of uncertainty in the process, leading to reworks, additional inspections, and delays in demand delivery.

In the last 3 years, the volume of coated cartridges has increased significantly, and the company invested in four new manufacturing lines to satisfy the increment in the market demand. The incidence of Dye Test failures also raises in

proportion with the increment on manufacturing lines as shown on Table 1.

Table 1
Coated Cartridges Production Plan per Year

Period	Coater Qty.	Cartridges Unit (yr.)	Dye Test Failures
Jan 2021 to Dec 2021	4	6,576,436	25
Jan 2022 to Dec 2022	6	8,912,241	26
Jan 2023 to Aug 2023	8	9,505,644	16

Even that previous CAPA implemented actions, they were not enough to reduce the incidence of Dye Test failures and require an exhaustive investigation to established effective actions that can assure a reduction in Dye Test Failures

RESEARCH OBJECTIVES

The second CAPA was generated to evaluate different aspects of the coating cartridge manufacturing process to identify what factors can contribute to the high incidence of dye test failures. Two different lean manufacturing tools (Kaizen Methodology and 6M's Tool) were used to investigate the manufacturing process and reduce or eliminate waste. After completing both exercises, the results were analyzed to identify the potential contribution factors that can cause the Dye Test failures. The actions are determined and discussed with leadership, to decide which actions will be pursued for the reduction of Dye Test failures incidence. The actions negotiation includes budget identification, resources required and timeline of activities to complete each action among others.

RESEARCH CONTRIBUTIONS

The Effective Monitoring of this CAPA requires a 60% percentage of reduction which consist of generating 9 or less Non-conformances in a 9-month period. The reduction in Dye Test failures incidents reduces the investigators workload designated for these investigations. The company profit increases because it saves the budget invested in investigation effort and the product scrap costs are significantly reduced. With less Dye Test failures, the operations area had the opportunity to increase volume and deliver the product in compliance according to the planning schedule which also benefits the yield program.

LITERATURE REVIEW

The Dye solution is also known as Toluidine Blue Dye penetrant solution and is prepared by the operator once per week or when is fully consumed. Each Production Order is challenged with the Dye Test and consists of collecting a determined sample size of 32 units for production orders of 6,000 cartridges and 50 units if production order is of 12,000 cartridges. The sample units are collected from tray and are submerged in dye solution for a minimum of 3 minutes, units are cleaned with purified water and dried with deionized air. Then, units are placed in the oven for a minimum of 15 minutes at 60±5°C. Refer to Figure 1 for cartridge sections diagram.

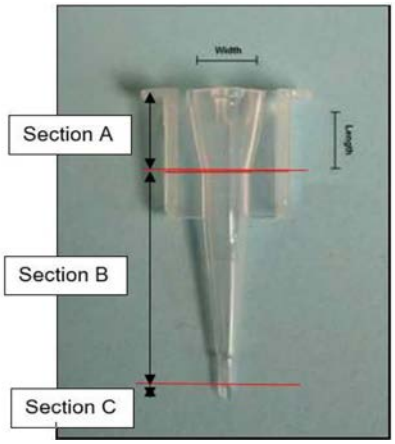

Figure 1
Cartridge Sections

The Dye Test is declared fail if one of the following conditions is identified:

- Cartridges contain voids in Section A that do exceed a minimum of 0.100” wide and 0.250” length.
- There are gaps or missing purple dye in section B and C.
- Cartridges that do not show presence of basecoat and/or topcoat.

The 22 Non-conformances covered on Effective Monitoring failed, were analyzed, and shown that the assignable causes were distributed between man omission error, machine malfunction and method as shown on Figure 2.

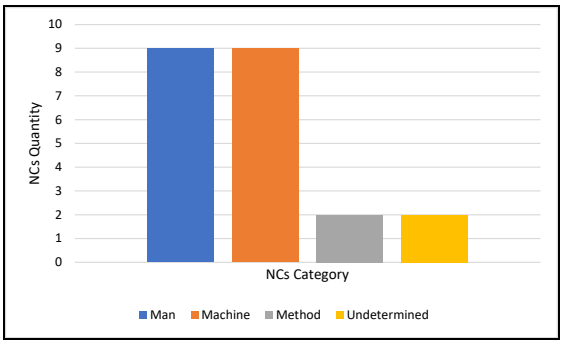

Figure 2
Dye Test Failure Assignable Causes of NC’s

A total of 9 Non-conformances revealed that most of these dye test failures were attributed to operator omission errors. The investigations show that operators skipped or did not follow the instructions established on the coating manufacturing procedure. The second incidence demonstrates that 9 failures were attributed to coater machine malfunction when processing the production orders on coater machines. The coater machine is an equipment used to dispense the basecoat and topcoat solutions to coated cartridges. The third incidence corresponds to method with 2 Non-conformances. In both Non-conformances investigations was demonstrated that manufacturing procedures instructions were not clear and caused confusion to operator during coating process execution. In addition, 2 Non-conformances were evaluated, however, a root cause was not possible to determine due to the unique failure detected.

The coater machine is a complex equipment and composed of a needle washer, vacuum system, dryers, dispensing pumps, alarm system and dispensing mechanism. Due to the complexity of equipment and difficulty understanding when it presents a malfunction, equipment is intervened through Corrective Maintenance Work Orders (CMWO). The Corrective Maintenance Work Orders generated from January 2022 to October 2022 for these coater machines were analyzed to determine which equipment has the highest incidence of failure and identify any tendency of failures per coater machine associated to dye test failure. Refer to Figure 3 for CMWO generated per coater machine.

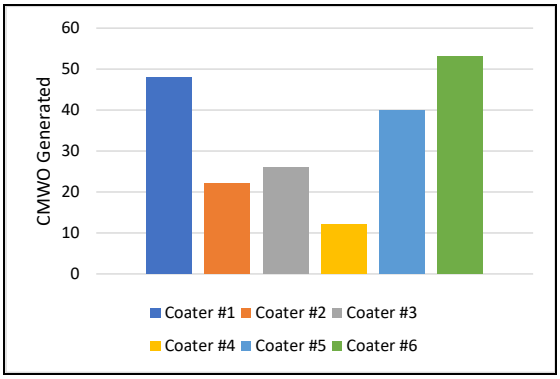

Figure 3
Dye Test Failure Assignable Causes of NC’s

- The coater #1 has a total of 48 CMWO generated, where the major incidence corresponds to axis error with 20 CMWO events. The axis errors are distributed in X, Y and Z axis. Due to the complexity of the equipment, it only has the capacity to reflect an axis error, however, the root cause is different in each CMWO. The second incidence is the cosmetic defects with a total of this 13 CMWO that are detected by coater operator. When operator identifies a significant trend of “overflow” “tip” or “plugged” condition on cartridges, equipment is verified by technician and cartridges with cosmetic defects are discarded as part of normal manufacturing process. The third incidence corresponds to needle washer problems with a total of 6 CMWO. These events are related to misalignment of needle washer on equipment

during the changeover or any other incidence during execution.

- The coater machine #2 has a total of 22 CMWO, where the major incidence corresponds to axis error with 10 CMWO events. The axis errors are distributed in X, Y and Z axis. The second incidence is cosmetic defects with a total of 6 CMWO that are detected by coater operator. The third incidence corresponds to atypical events with a total of 3 CWMO. These events are different in each case and cannot be related.
- The coater machine #3 has a total of 26 CMWO, where the major incidence corresponds to axis error with 13 CMWO events. The axis errors are distributed in X, Y and Z axis. The second incidence is cosmetic defects with a total of 6 CMWO that are detected by coater operator. The third incidence corresponds to atypical events with a total of 5 CWMO. These events are different in each case and cannot be related.
- The coater machine #4 has a total of 12 CMWO, where the major incidence corresponds to cosmetic defects with a total of 6 CMWO that are detected by the coater operator. The second incidence is related to atypical events with a total of two 2 CWMO. These events are different in each case and cannot be related. The third incidence corresponds to axis errors with a total of 2 related to Y axis. Due to the complexity of the equipment, it only has the capacity to reflect an axis error, however, the root cause is different in each CMWO.
- The coater machine #5 has a total of 40 CMWO, where the major incidence corresponds to cosmetic defects with a total of 13 CMWO that are detected by coater operator. The second incidence is related to Vacuum System events with a total of 9 CWMO where chiller of the vacuum system was replaced and required re-validation activities. The third incidence corresponds to atypical events with a total of 8 CWMO which includes problems with manifold misalignment and pumps failures.
- The coater machine #6 has a total of 53 CMWO, where the major incidence corresponds to axis error with 39 CMWO events. The axis errors are distributed in X, Y and Z axis. In this equipment, most of these events were associated to X axis error where slider and motor of this axis were replaced as part of the troubleshooting and required re-validation activities execution. The second incidence is cosmetic defects with a total of 5 CMWO. The third incidence corresponds to needle washer problems with a total of 4 CWMO. These events are related to misalignment of needle washer on equipment during the changeover or any other incidence during execution.

The CMWO includes details of events and dates generated. This information allows to relate the events per coater machine with failures on Non-conformances included in the bounding of this CAPA. From data analyzed, only 4 CMWO coincides with 4 Non-conformances. For this reason, the Kaizen methodology and 6M tool were developed and focused on evaluate how mitigate the human error, to reduce the high incidence of equipment malfunction and facilitates the identification of root cause when an event related to equipment malfunction is presented.

METHODOLOGY

To define and establish the action to mitigate the incidence of Dye Test failures, a Kaizen methodology and 6M's tool were performed. The Kaizen methodology comes from Japanese and is define as a "continuous improvement" [1]. It is characterized by the implementation of small improvements that require low investment and work effort to be completed. For the Kaizen exercise, a multifunctional group was involved. Resources of Quality Engineers, Manufacturing and Process Engineers, Operations, Technicians, and a SME Contractor who works in the company as

R&D employee and was part of the coated cartridge development process participates in the Kaizen exercise. The Kaizen includes a Gemba walk to the manufacturing area. Gemba is a Japanese terminology which means “the real place” and is used in the Lean Manufacturing methodology [2]. A Gemba walk is an exercise where the lead group visits the manufacturing area to evaluate the workplace and identify areas for improvements and to eliminate waste. The Gemba walk was focused on the coating dispensing process and after 4 hours evaluating the process, all the participants identified 40 actions that can improve the coating process. All the 40 actions were evaluated by the group and established a number based on the effort that required to be implemented (based on resources, monetary investment, time consuming and benefit) and value added for the manufacturing process. Refer to Figure 4 for “Effort versus Value” matrix. The “Effort versus Value” matrix is divided into 4 groups: Strategic, Gems, Quick Hits and Re-think. A total of 5 actions were categorized as re-think, which results in major effort to complete the actions with the less value added. 8 actions were categorized as germs, which add significant value with a low effort of implementation. There were 21 actions identified as quick hits which requires low effort, but the value added is low. The remaining 6 actions were categorized as strategic, which required significant effort to be implemented and the value added is significant. Based on this distribution, two diagonal limit lines are made to determine which actions should be implemented.

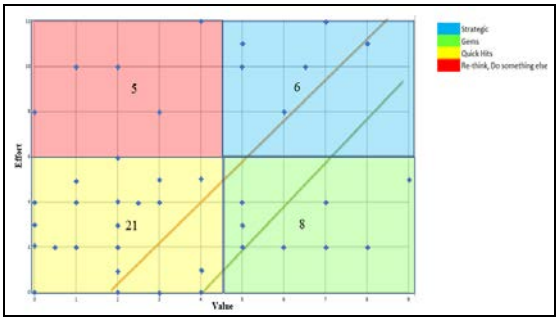

Figure 4
“Effort versus Value” Matrix

As shown in Figure 4, only 8 actions fall between the desire zone identified are those described with the most positive impact added with a lower cost of investment. Of those 8 actions, only 6 actions were considered because were directly related to Dye Test failures and implementation will not require much effort or support from different functional groups. These 6 actions are described below.

1. Add inspection step after a changeover to assure that cartridge clamp is aligned with the nesting tray.
2. Update manufacturing procedures to include tray flatness verification and ensure all screws are in place. (3 manufacturing procedures)
3. Install vacuum lines with negative slope posture to avoid manifold misalignment.
4. New tool design to avoid tilt of basecoat solution jar and avoid air bubbles on lines. Also include a poka-yoke identification of solution limit.
5. Implement the use of dummy cartridges when cartridge is dropped or discarded.
6. Implementation of analytic balance for dye test solution preparation.

As part of the CAPA investigation process, to support the finding of the Kaizen, a 6M Quality Tool was performed to evaluate the factors identified as root causes for Dye Test Failures. The 6M’s is a tool that evaluates 6 most important categories that can contribute to development of a product, the 6 categories are the following: Man, Method, Machine, Measure, Material and Mother Nature/Environment [3]. The 6M was also focused on the coating process since is the step directly related to inconsistency on coated cartridges. The actions identified on Kaizen exercise were evaluated as part of the 6M. The evaluation of 6M is summarized below.

1. Man:
    a. Vacuum lines filled with coating solution.
    b. Loose tubing (connects the needles tubing with solution jar) stuck to solution jar wall.

2. Method:
    a. Inadequate loading of cartridges on trays.
    b. Tilt mechanism of solution jar.
3. Machine:
    a. Balance improvement for dye test solution preparation
    b. Coater walls and doors covered with stains of solutions affecting operators' visibility during dispensing process.
    c. Vacuum system whitening condition.
4. Measure:
    a. Lack of inspection after a changeover.
    b. Unavailable the measure of coating solution limit in basecoat jar.
5. Material:
    a. As part of the controls in place, cartridges pass through an Incoming Inspection prior processing component through the Cartridges manufacturing process. The cartridges raw material is challenged against the specifications delineated on parts drawing. All batches of cartridges raw material under Non-conformances raised in 2022 passed through Incoming Inspection and were satisfactorily released as they met specifications delineated in drawings.
6. Mother Nature:
    a. The Cartridge Manufacturing Room is monitored for temperature and relative humidity on a daily basis. The cartridge manufacturing process initiated after confirming room temperature and relative humidity is within specifications. Room environmental conditions are monitored through chart recorder. For dye test failures events raised in 2022, travelers were assessed as part of the Non-conformances investigation, and it was confirmed that all Production Orders (POs) were manufactured with temperature and relative humidity within specification. For this reason, based on investigation performed as part of 6M's, there is no evidence identified on mother nature that can be associated dye test failures.

After evaluation of Kaizen and 6M's results, the leadership determined to pursue 6 actions since requires low resource investment with a highly improvements to reduce the dye test incidence. The actions that were approved are:

1. Adding a cartridge inspection step after running the first two trays on the coater machine. This strategy will help to identify any cosmetic defect on cartridge related to coater component misalignment or inconsistency during dispensing process. This action will allow to intervened equipment with a CMWO proactively, reducing the impact on the remaining units of production order.
2. Update manufacturing procedures to place the required screws on nest trays to assure cartridges are placed correctly on their poke yoke position and reduce cartridge movement during coating dispensing process and vacuum process. If cartridges are not introduced completely on nest tray, the vacuum process would not be capable of removing the excess of basecoat and/or topcoat.
3. Install and validate an analytic balance for the preparation of Dye Test solution. This analytic balance will improve the measurement of reagents used for this solution. In this way, it can be guaranteed that each Dye Test solution has the same concentricity independently of which operator prepares it.
4. Develop and implement a new tool fixture to assure all basecoat tubing's are submerged on basecoat solution. The intention of this tool is to avoid the air bubbles in tubing and eliminate contact with tubing ends with jar walls which interrupts the dispensing process. Also, the new tool fixture will have a base that serves as a poke-yoke to indicate the lower limit level of basecoat solution. This action will eliminate the risk of tilting the jar to consume the maximum basecoat solution.

5. Update the Preventive Maintenance Work Orders (PMWO) performed to coater machine in a weekly basis to replace the vacuum hoses. The basecoat and topcoat solution are corrosive and if vacuum hoses are not constantly drained, the solution solidifies affecting the suction pressure to eliminate the excess of coating from cartridges. Also, the solidification triggers a whitening condition on vacuum hoses, affecting the operator's visibility to identify when is required to drain them.
6. Install clear protective film to coater machine acrylic walls and doors resistant to the corrosive basecoat and topcoat solutions. The clear protective film permits operator to have a clear visibility during the coating dispensing process and helps to keep the coater machine clean.

After a deep investigation with Kaizen and 6M's tools, it was identified that the root cause is Method, Man, and Machine since there is lack of instructions during the Coating process that does not permits operator execute properly each step of coating operation. In addition, some equipment and/or tools used to perform the manufacturing process and dye test requires to be analyzed and updated to pursue and obtain better performance results. Both analyses were presented to the leadership and as per management decision, it was approved the budget and resources to proceed with the following actions.

1. Add an inspection after completion of changeover to assure that cartridge clamp is aligned with the nesting tray.
2. Update the Preventive Maintenance of coater machine to assure vacuum hoses are replaced weekly and assure a negative slope position to avoid misalignment of manifold.
3. Install and validate an analytic balance for dye test solution preparation.
4. Update manufacturing procedures to add and clarify the requirements of screws during coating process.
5. Install coater machine clear protective film resistant to corrosive coating solutions.

RESULTS AND DISCUSSION

The approved actions were successfully implemented between August 2022 and August 2023. A full description of each action implementation is described below with results obtained.

1. The inspection implemented after performing a changeover helps to identify setup problems after processing the first 2 trays on the coater machine. Once the 2 trays complete the coating process, a dye test inspector examines the cartridges to capture any defect condition like tip, overflow or excessive coating which can contribute to dye test failures. If any of these conditions are identified, cartridges are rejected on coating operation and will not be selected for dye test routine sample. A new form was developed to document the inspection. This form resides on each production order and coating manufacturing procedure was updated to include the instructions to perform this new activity. Once the incidence of defect condition is detected in this inspection, a technician intervened the coater machine to fix the issue to reducing the extended impact on remaining trays of production order to be processed. This action helps to reduce the incidence of cosmetic defect during coating operator. A daily monitoring is performed to this inspection per coater machine to identify any tendency related to operator or equipment malfunction.
2. The Preventive Maintenance was updated to include the instruction of vacuum hoses replacement on a weekly basis. This constant replacement mitigates the accumulation or solidification of coating solution that affects the suction pressure of vacuum system to remove excessive coating on cartridge. The installation position of the vacuum hoses was clarified to assure all technicians place the

vacuum hoses with a negative slope (curvy position) to facilitate the movement during coating process and avoid the manifold misalignment. An awareness was provided to technicians for clarification on new instructions and ensure that all install the vacuum hoses in the same manner.

3. The analytic balance was successfully installed and validated. It has been used for the preparation of Dye Test solution. This analytic balance had a precision of five significant figures to guarantee all Dye Test solutions contain the exact quantity of reagents. The analytic balance was installed in a fume hood and placed over a granite table to avoid any environmental disruption that can affect the solution measurement.
4. The manufacturing procedures were updated to include the requirements and quantity required of screws needed to guarantee cartridges are placed in correct position in the tray. The tray requires 4 screws to assure correct position of cartridges for coating procedure. An awareness to coating operators was provided to reinforce the knowledge and importance of the screws use.
5. The walls and doors of all 8 coater machines were covered with transparent protective film. This protective film is resistant to basecoat and topcoat solution and helps to maintain clean the coater machine.

After successful implementation of these 5 actions, an Effective Monitoring (EM) was established on the Dye Test CAPA to monitor the incidence reduction of dye test failures. This Effectiveness Monitoring started on August 21,2023. A review of Non-conformances for a 9-month period will be performed. The data gathered from the 22 Non-conformances covered on previous CAPA were analyzed in a period of 1 year (October 2021 to October 2022) considering the major quantity of coater machines in manufacturing production service. Each Non-conformances were evaluated in detail and were categorized as described in Table 2.

Table 2
Root Causes Categorization

NCs Root Cause	Qty of NCs	Mitigated by CAPA Actions	Mitigation Rate
Man	9	2	2/22=01.0
Machine	9	9	9/22=0.40
Method	2	2	2/22=0.10
Undetermined	2	0	0
			=0.60*100= **60%**

The Effectiveness Monitoring established a 60% of Dye Test failures reduction as the acceptance criteria based on analysis described on Table 2. The actions implemented cover the root causes identified in these Non-conformances evaluated. This 60% reduction consists of reporting 9 non-conformances or less to accomplish the EM goal in a period of 9 months. The nine months period was established considering that a significant quantity of production orders is manufactured in this timeframe and covers the variability of coated cartridges models, material inventory and environmental condition behavior.

CONCLUSION

The Effectiveness Monitoring started on August 21, 2023, there is not enough evidence to demonstrate that Effectiveness Monitoring has been accomplished. However, during the elapsed period, there is no Dye Test failure reported. With the implementation of these 5 actions, the coating process performance increases and operators demonstrate more confidence during coater machine setup and coating process.

The leadership made the compromise to continue with manufacturing improvements and implement 1 additional action as part of the Aim for Zero effort for 2024. This action is pursuing the development of a new tool for the dispensing process of basecoat solution. This action will mitigate 3 issues, identify the minimum volume

required for the basecoat solution, eliminate the incidence of air bubbles in basecoat lines and will eliminate the tilt mechanism to consume the maximum basecoat solution in jar. An engineer resource is partially assigned to the tool development. Once the prototype is delivered to the company, additional resources will be added to test, validate, and implement the new tool in all coater machines. Also, technician training will be provided in the middle of 2024 for technicians across the company to temper the theoretical information and mechanical practice to reinforce and align the techniques during troubleshooting and equipment alignment.

The leadership has the engagement to continue with improvements to maximize the manufacturing operations in compliance with company quality system and regulatory agencies requirements. The generation of 22 Non-conformances in 9 months period due to Dye Test failures (2.5 Non-conformances per month), represents to the company an investment of approximately $65,000 for these investigations. Having cero Non-conformances in the first month of the Effective Monitoring represents a reduction of an approximate of $7,500. Even that Effective Monitoring is in at the beginning, the non-generation of Dye Test failures in this first month demonstrates that actions implemented were successful to mitigate the inconsistency coating solution adhered on cartridges internal surface.

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