Increase Quantity Per Production Orders for OBI Intraocular Lenses

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Abstract - *The right order quantity can often drive your costs down and the quality up. This is because larger orders tend to give you more influence and control at a factory level. Factories are rarely totally independent and often rely on other people and services in the supply chain that often influence the focus of a factory. Smaller quantities can almost never really give you the necessary attention to both reduce costs as well as improve quality [1].*

To pursue the increase in production order size and to have a structured change management, the DMAIC methodology was used. As know it, DMAIC is a data-driven quality strategy used to improve processes. The term DMAIC stands for the five main steps in the process: Define, Measure, Analyze, Improve and Control.

To make business more competitive it is important to ensure higher utilization of the resources because can reduce unit costs [2].

Key Terms *– CQA, CPP, increase, IOL.*

INTRODUCTION

Intraocular Lenses are medical devices that are implanted inside the eye to replace the eye's natural lens when it is removed during cataract surgery [3] [4]. A cataract is a clouding of the normally clear lens of the eye. Product OBI is one of two model part of the initial manufacturing process of Intraocular Lenses (IOLs). OBI product increase arises with the launch of new IOLs designs. The new IOLs designs represent an innovation for the customers (patients) necessities for cataract surgery treatment and eye conditions.

It is requested to increase model OBI production orders from 675 units to 3465 units. This represent a benefit for the process in terms of more outcome quantity, time of processes and many others. Planning forecast for next year of this model will require approximately the double of the current production.

Problem Statement

The main objective of this design project is to present a strategic and cost-effective production order increase for the OBI material for the IOLs Medical Device Industry. This increase in production orders quantity is a business need due to the launch of new product.

Research Description

This project will be conducted to the implementation of an increase in production orders quantity. A balanced chemical composition is important to ensure that the product outcome met Critical Quality Attributes (CQAs). Current chemical composition weight a total of 700 grams to reach the increase projection a composition weigh of 3500 grams. With this quantity increase, manufacturing will be five times the current quantity with the same process and manpower.

Research Objectives

This project aims to achieve an increase in base formulation mixing that meet and maintain current financial yield of 83.5. This increase in base formulation means up to 40% more than the actual with the same manpower

Research Contributions

This project supports a business needs of a product increase to sustain manufacturing of new IOLs designs. OBI model production orders output increase from current 675 units to 3456 units. Satisfy an increase in demand of this model due to the introduction of new IOL designs.

LITERATURE REVIEW

This project will be conducted to increase the capacity of produce OBI model. Changes include increase formulation volume used to in the process of OBI acrylic material. Current formulation mixing is 700 grams. This change is to scale up the formulation mixing amount to 3,500 grams.

The intent of this project is to increase process efficiency and capacity for the generation of OBI Intraocular Lenses (IOLs). The increase in the formulation quantity only intends to expand the quantity for the OBI acrylic material. There is no impact to the formulation component, product ingredients and the percentage of the final materials composition. Material amount will increase but material composition will need to remain the same to comply with CQA established to release the OBI IOLs. Increase shall be as show in Table 1.

Table 1

Current Formulation amount vs. Proposal Increased amount

Monomer / Reagent	Base Formulation	Current Amount (g) 700 grams	Proposal Amount (g) 3500 grams
1. UVAM	0.35 % wt	2.45 ± 0.05	12.25 ± 0.05
2. UV	1.49 % wt	10.43 ± 0.10	52.15 ± 0.50
3. YD	0.20 % wt	1.40 ± 0.03	7.00 ± 0.03
4. EA	56.80 % wt	397.60 ± 0.40	1988.00 ± 2.00
5. EMA	27.55 % wt	192.85 ± 0.20	964.25 ± 1.00
6. TFEMA	9.77 % wt	68.39 ± 0.15	341.95 ± 0.75
7. EGDMA	3.73 % wt	26.11 ± 0.15	130.55 ± 0.75
8. TI	0.110 % wt	$\text{Amount of Thermal Initiator Required} = (0.770g)\,\frac{(6.7\%)}{\text{Actual percent activity}}$	$\left(3.85\ x\ \frac{6.7\%}{Actual\ \%AO}\right) \pm 0.07$

1. Table information gather from Site Manufacturing Instructions

General Concepts of Six Sigma

Six Sigma is a method that provides organizations tools to improve the capability of their business processes. This increase in performance and decrease in process variation helps lead to defect reduction and improvement in profits, employee morale, and quality of products or services [5]. The Six Sigma process includes measurement, improvement, and validation activities [6].s many companies in the medical device industry and many other types of industry customer satisfaction is the number one priority. JJSV Credo that our first responsibility is with patients, doctors, mothers, and fathers when they used our products. meeting their needs with a high-quality standard therefore the use of lean methodology will help reducing mistakes and defects in processes. Moreover, Six Sigma focuses on quality more than speed.

DMAIC

Following the methodology and tools provided by Six Sigma, DMAIC is a problem-solving tool who help to screening between project to pick the right one for a process improvement. Regarding that this is a measurable project this is the ideal tool to demonstrate efficiency results. Since this project is a measurable project this tool will be of great help to demonstrate results.

DMAIC tool is describe as follow:

-Define: Is how the business need can be solved? This phase the project core team create a project charter, this include Problem Statement, Objective, Scope and Boundaries, Risks, Financial Impact, Critical to Quality (CTQ)/Final Project Objective (FPO) Metric of Success, Stakeholders, Milestone Timing, and Resources.

-Measure: Which is the current process flow and the proposal. The current process flow will allow to understand the process benefits and drawbacks. This phase has two focuses: reducing lead time and/or improving quality [7].

-Analyze: This phase will determine what is causing the problem. Root causes of the problem are defined in this phase, hypothesis of what and why the problem exists are develop. In the analysis, the team can't pretend to find solutions; this is an opportunity to brainstorm about the issue, but it is required to work to prove with data.

-Improve: Here is where the changes where done. Hypothesis are accepted or discarded in this phase. Improve phase move pilot processes to production, brainstorms get solutions, implemented solutions are lastly.

-Control: The Control section is all about putting processes and procedures in place to make sure the implementation of the new solution runs smoothly and can be tracked and optimized over time [8]. In this phase is how the process improvement is sustain and repetible.

PROJECT METHODOLOGY

The DMAIC methodology will be used to develop the formulation process increase for the OBI model.

In the Define phase, the problem statement and objective are established. The Scope and Boundaries, Risks, Financial Impact, Critical to Quality (CTQ)/Final Project Objective (FPO) Metric of Success, Stakeholders, Milestone Timing, and Resources requirements are determined and stated. This phase will align the current and proposed process path.

A feasibility test has been run to challenge the process CQA and established base on statistic procedure the requirements to move into process operational and performance qualification. This feasibility test helps to run a capability analysis of current CQA of the process to demonstrate data normality.

In the Analyze phase, data gather from the operational qualification will provide a behavior of the change challenging the worst-cases. Data gather from the performance qualification will give the objective evidence that the process is reproducible and repeatable under nominal conditions.

In the last phase, Control, the improved process will be monitored and evaluated against the overall yield expectation that is 83.5%. In addition, the most notable changes in the process will be observed for zero nonconformities through the quality system.

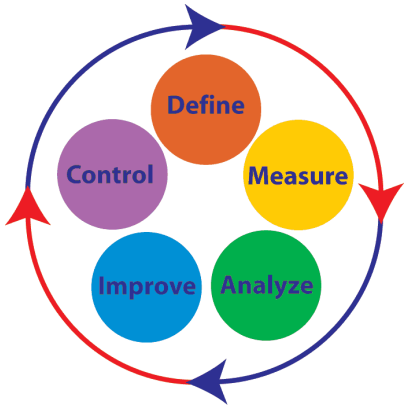

Figure 1

DMAIC

DISCUSSION AND RESULTS

As mention in the Methodology section, in this phase it will be describe how the DMAIC tool helps in the execution and implementation of this project.

Define

The business needs can be solve using an operational qualification protocol as follows: Operational Qualification (OQ) protocol is to establish documented evidence that the critical process parameters (CPPs) identified for the OBI formulation process increase will result in a product that meets all predetermined CQAs under anticipated worst-case conditions. Also, a Performance Qualification (PQ) was executed to demonstrate that the process is reproducible and repeatable under nominal conditions.

Table 2

Project Charter

Project Name	
OBI Increase Project	
Problem Statement	
Actual capacity of OBI needs to be increased to support future forecast. Projections are that OBI demand will be increase as current Principal Product demand.	
Objectives	
Current process outcome is five sheets projection is to increase up to sixteen sheets per production order. Also, this means a standardization in the manufacturing processes executing in this area.	
Scope and Boundaries	
• OBI product Only • Develop an increase in base formulation mixing • Operational/Process Qualification • Verify equipment validations. • Modify equipment as required and re-qualify if necessary • Room re-layout if necessary • Test Methods Assessment	
Risks	
If the formulation process development failed actual capacity cannot support future forecast for OBI. Alternate project to increase capacity will require major capital investment for additional equipment and constructions.	
Milestones Timing	
Key Deliverables	**Due Date**
ET19-0045 technical report	12-12-19
CR Approval/Release	11-27-19
VP, QQ Protocol approval/release	01-24-2020
PQ Protocol approval/release	02-28-20
QQ Protocol Execution Completion	03-13-20
PQ Protocol Execution Completion	03-30-20
Regulatory Agencies Submission	N/A
Procedure Update	04-30-20
Stakeholders	
Site Leader, Engineering Director, Operations Directors, Planning Director	
Core Team	
Project Leader (Linda Cordero-SME), Quality Engineer, Operations Area Supervisor, R&D, Regulatory Affairs, Scientist	

Table 3

Critical Process Parameter (CPP) established

Process Equipment	Process Parameter	Unit	Process Range	Nominal
Curing Bath	Temperature	ºC	76 - 80	78
	Curing time	Hours	17.5 – 18.5	18
Curing Oven	Temperature	ºC	87 - 93	90
	Curing time	Hours	21.5 – 22.5	22
Annealing Oven	Temperature	ºC	54 - 66	60
	Vacuum pressure	Torr	0 - 5	N/A
	Annealing cycle	Days	10-11	11

Table 4

Critical Quality Attributes (CQA) to be measure

CQA#	Quality Feature
CQA1	Thickness
CQA2	Cosmetic Inspection
CQA3	Haze
CQA4	FTIR
CQA5	Monomer Residuals
CQA6	UV-Vis
CQA7	Refractive Index

Measure

In Table 1 the proposal amount of the increased formulation (total 3500 grams) was used in this phase for the operational qualification with a total of nine production orders (3 per condition). Production Orders was executed as follow to challenge the worst-case amounts to comply with the qualification protocols:

Table 5

Qualifications Conditions

Monomer / Reagent	Base Formulation	Target amount (g) 3,500 grams	Low	Nominal	High
UVAM	0.35 % wt	12.25 ± 0.05	12.20	12.25	12.30
UV	1.49 % wt	52.15 ± 0.50	51.65	52.15	52.65
YD	0.20 % wt	7.00 ± 0.03	6.97	7.00	7.03
EA	56.80 % wt	1988.00 ± 2.00	1986.00	1988.00	1990.00
EMA	27.55 % wt	964.25 ± 1.00	963.25	964.25	965.25
TFEMA	9.77 % wt	341.95 ± 0.75	341.20	341.95	342.70
EGDMA	3.73 % wt	130.55 ± 0.75	129.80	130.55	131.30
TI	0.110 % wt	$\left(3.85\ x\ \frac{6.7\%}{Actual\ \%AO}\right) \pm 0.07$			

In addition, three more production orders were executed and analyzed under nominal condition as part of the performance qualification.

Analyze

For the analysis of the feasibility of this change test was executed obtaining the following results:

1.1 The individual and overall yields were within normal trend.

1.2 In terms of process capability, sheet/button *Thickness* was evaluated according to the criteria in statistical procedure. The process capability analysis for two-sided, variable data with an RQL of 10.0% and 95% confidence, n=42 ($P_{pk} \geq 0.680$) was performed. This analysis was completed in Minitab and resulted in P_{pk} values that met all specifications.

1.3 *Haze* was evaluated using 210 buttons and resulted in zero failures. This was compared against an existing validated test method.

1.4 *Refractive Index* was also evaluated following the criteria under the statistical procedure. The process capability assessment for two-sided, variable data with an RQL of 3.0% and 95% confidence, n=42 ($P_{pk} \geq 0.897$) was performed. The analysis was completed in Minitab and resulted in a P_{pk} values that met all specifications.

1.5 *Monomer Residuals* were also evaluated according to the criteria under statistical procedure. The process capability analysis for one-sided, variable data for RQL of 3.0% and 95% confidence, n=42 ($P_{pk} \geq 0.794$) was performed. The process

capability results for each of the residual monomers in the 10-day and 11-day annealed samples met the P_{pk} specification.

1.6 Regarding to *Cosmetic Inspection*, *FTIR*, and *UV-Vis* tests were compared with pass or fails criteria against established parameter. All results were complying with the established.

Once all CQA's were evaluated against the already existing validated criteria, the next step was to execute the operational/performance qualification to present with objective evidence that the increase process is an improvement for the current process maximizing the resources utilization to obtain a greater output with the same man power

Improve

To demonstrate that the increase in the production orders amount is an improvement for the manufacturing process productions orders has been challenged against existing parameter and results has been statistical analyzed.

For *Thickness* test each sheet was measured in six locations. Measurements for all sheets were within the specification range (2.1 – 3.0 mm). Results are reported per formulation condition, all conditions met acceptance criteria.

Table 6

Thickness Results

OQ Run	Production Order	n	Mean	Spec. Range	Acceptance Criteria	P_{pk}
1	9-1844477	84	2.47	2.1 - 3.0	$P_{pk} \geq 0.653$	0.82
2	9-1844478	90	2.49			
3	9-1844479	96	2.52			
4	9-1844480	90	2.39			0.79
5	9-1844481	78	2.41			
6	9-1844482	90	2.49			
7	9-1844483	90	2.47			0.67
8	9-1844490	96	2.37			
9	9-1844491	96	2.32			

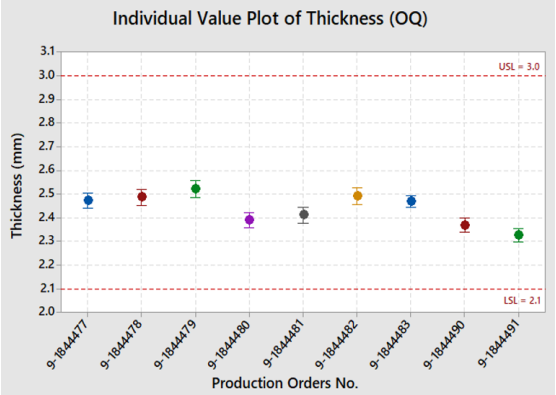

Figure 2

Individual Value Plot

For *Cosmetic Inspection* evaluation yield results exceed the current target, 83.5%. All sheets from each production order (PO) were visually inspected for the presence of fractures, bubbles, lakes, concave shape, or cloudiness within the usable region of the sheet. The results are summarized in Table 7. Yield results are reported per formulation condition, all conditions met acceptance criteria.

Table 7

Cosmetic Inspection Results

PO P - Pass F - Fail	Sheet																Raw Data Attachment	Yield (%)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16		
9-1844477	P	P	P	P	P	P	F	P	P	P	P	P	P	P	P	F	B	93.7
9-1844478	P	P	P	P	P	P	P	F	P	P	P	P	P	P	P	P	C	
9-1844479	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	D	
9-1844480	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	F	E	91.6
9-1844481	P	P	P	P	F	F	F	P	P	P	P	P	P	P	P	P	F	
9-1844482	F	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	G	
9-1844483	P	P	P	P	P	P	P	P	P	F	P	P	P	P	P	P	H	97.9
9-1844490	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	I	
9-1844491	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	J	

Haze test was conducted on buttons sampled from each production order. No buttons exhibited a haze level of 5 or greater and all production orders met the specification. It was concluded that the increase in the formulation amount had no observable impact on button haze.

Table 8

Haze Results

OQ Run	Production Order	Specification: No buttons with a haze level 5 or greater				
		Haze Level 1 Button Qty	Haze Level 2 Button Qty	Haze Level 3 Button Qty	Haze Level 4 Button Qty	Haze Level 5 Button Qty
1	9-1844477	0	35	58	20	0
2	9-1844478	0	17	45	51	0
3	9-1844479	0	28	53	32	0
4	9-1844480	0	19	57	37	0
5	9-1844481	0	27	65	21	0
6	9-1844482	0	17	53	43	0
7	9-1844483	0	38	65	10	0
8	9-1844490	0	47	51	15	0
9	9-1844491	0	27	59	27	0

Fourier Transform Infrared Spectroscopy (FTIR). FTIR spectra were obtained for each production order. Hundred thirteen samples from each production order was analyzed. The data indicate that all test samples conform to the reference spectrum and the minimum required correlation factor of 0.9900.

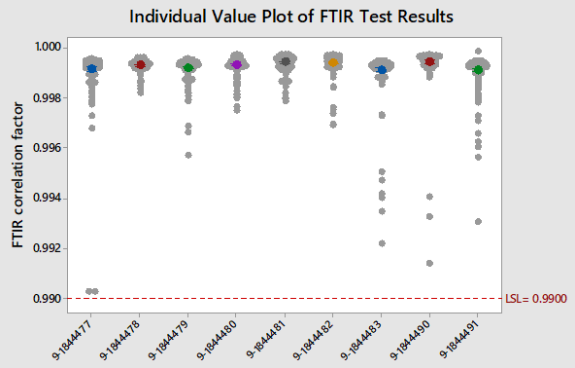

Figure 3

Individual Value Plot FTIR

Monomer Residual testing was conducted per established validated test method all production orders met the specification. Figure 4 shows the residual levels of each monomer component.

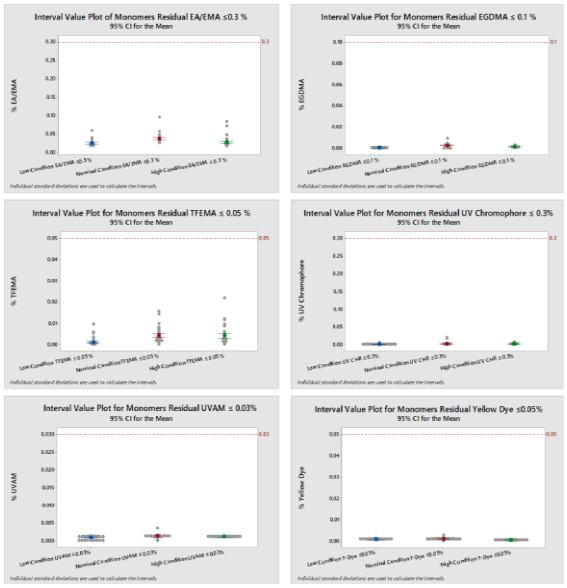

Figure 4

Monomer Residual levels

Table 9

Summary of OQ Residual Monomer Results

Condition	Monomer	n	Mean (%)	Spec (%)	Acceptance Criteria	P_{pk}
Low	EA/EMA	48	0.0249	≤ 0.3	$P_{pk} \geq 0.781$	2.01
	EGDMA	48	0.0004	≤ 0.1		141.19
	TFEMA	48	0.0011	≤ 0.05		1.27
	UV	*1	*1	≤ 0.3		*1
	YD	48	0.0001	≤ 0.05		3.10
	UVAM	*1	*1	≤ 0.03		*1
Nominal	EA/EMA	48	0.0376	≤ 0.3		1.14
	EGDMA	48	0.0025	≤ 0.1		1.74
	TFEMA	48	0.0044	≤ 0.05		1.23
	UV	48	0.0029	≤ 0.3		1.58
	YD	48	*2	≤ 0.05		*2
	UVAM	48	0.0012	≤ 0.03		1.46
High	EA/EMA	48	0.0278	≤ 0.3		2.25
	EGDMA	48	0.0016	≤ 0.1		43.35
	TFEMA	48	0.0042	≤ 0.05		1.81
	UV	48	*3	≤ 0.3		*3
	YD	48	0.0004	≤ 0.05		123.12
	UVAM	48	*3	≤ 0.03		*3

Notes for table 9: *1 P-Value for UV, and UVAM, is below 0.05 for Low Monomers Condition. Most of the data obtain is near 0, therefore there is no normal distribution of the data. Also, a distribution test for non-normal data has performed and none of the distribution available fits

to get a P-value > 0.05. In conclusion no process capability analysis can be perform, but data still acceptable for the process specifications.

*2 P-Value for YD is below 0.05 for Nominal Monomers Condition. Most of the data obtain is near 0, therefore there is no normal distribution of the data. Also, a distribution test for non-normal data has performed and none of the distribution available fits to get a P-value > 0.05. In conclusion no process capability analysis can be perform, but data still acceptable for the process specifications.

*3 P-Value for UV, and UVAM is below 0.05 for High Monomers Condition. Most of the data obtain is near 0, therefore there is no normal distribution of the data. Also, a distribution test for non-normal data has performed and none of the distribution available fits to get a P-value>0.05. In conclusion no process capability analysis can be perform but data still acceptable for the process specifications.

UV and Visible (UV-Vis) Spectroscopy was performed on samples from all sheets of each production orders

Table 10

Summary of UV-Vis Results

OQ Run	PO	Sample															
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
		Spec. (% T from 200-410 nm ≤ 1.0% and from 500-800 nm ≥ 80.0%)															
1	9-1844477	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
2	9-1844478	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
3	9-1844479	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
4	9-1844480	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
5	9-1844481	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
6	9-1844482	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
7	9-1844483	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
8	9-1844490	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
9	9-1844491	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass

Refractive Index values were measured per established specification of 1.473nD to 1.475nD. One sample per sheet was analyzed. All sheets met the specification requirements. Figure 5 shows a plot of the measurement results for the OQ production orders.

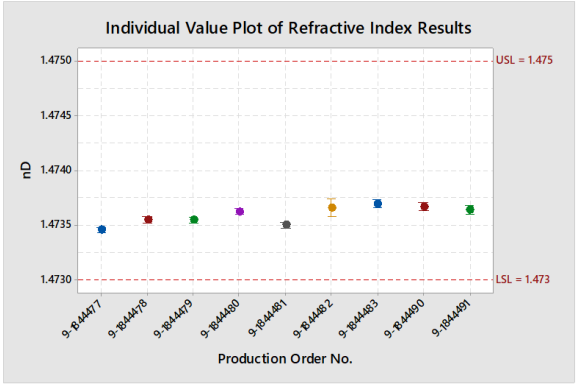

Figure 5

Individual Value Plot

Table 11

Summary of Refractive Index Results

OQ Run	PO	n	Specification (nD)	Acceptance Criteria	P_{pk}	OQ Result
1	9-1844477	48	1.473 - 1.475	N = 48 $P_{pk} \geq 0.882$	1.74	Pass
2	9-1844478					Pass
3	9-1844479					Pass
4	9-1844480	48			1.04	Pass
5	9-1844481					Pass
6	9-1844482					Pass
7	9-1844483	48			1.10	Pass
8	9-1844490					Pass
9	9-1844491					Pass

Control Phase

This phase has been started to be evaluated once process was release for manufacturing. These are the yields obtains after process implementation.

Table 12

Yield results since project implementation per operations

Operation	Values Sum of Processed	Sum of Confirmed	Sum of Yield	
10	286848	286848	100.00%	
20	286848	286848	100.00%	
30	286848	279936	97.59%	
40	279936	279936	100.00%	
50	279936	260280	92.98%	
60	304317	304317	100.00%	
70	304317	301794	99.17%	
80	238140	238140	100.00%	
90	173010	173010	100.00%	*Overall Yield*
Grand Total	**2440200**	**2411109**	**98.81%**	89.99%

Table 13

Rejects % per Code

	CRK	HTK	LAK	LTK	MPS
Jul	0.88%	0.02%	0.13%	0.13%	0.11%
Aug	0.26%	0.00%	0.09%	0.00%	0.74%

Mayor offender are Cracks as reflected before implementation of the increase project; this is more related to manual handling. The increase in MPS for the month of August was for 2 PO discarded due to the natural events (Isais Storms). If this 2 PO are removed from the sum the overall Yield should be 92.21% instead of 89.9% (target 83.5%). Regarding for this impact, it can be mention that the process is in control and complying with the historical manufacturing yield target.

CONCLUSION

This project indirectly reduces the lead time of the final product because the output of the initial step increase. Therefore, there will be no shortage of OBI buttons supply. Expectations for flawless implementation were accomplished because yield target is complying without any major or unknown process defects/issues.

REFERENCES

[1] Sourcing Allies Global, "Why small manufacturing orders increase costs," 2019. [Online]. Available: https://www.sourcingallies.com/blog/minimum-order-quantity. [Accessed September 17 and 19, 2020].

[2] A. A. Thompson, "Strategies for Staying Cost Competitive,", "Harvard Business Review Home Review, January 1984," Harvard Business Publishing Copyright © 2020 Harvard Business School Publishing. All rights reserved., [Online]. Available: https://hbr.org/1984/01/strategies-for-staying-cost-competitive. [Accessed October 4, 2020].

[3] "Johnson & Johnson Vision," 2018. [Online]. Available: https://jjvision.com. [Accessed August 26, 2019].

[4] A. Debrowski,, "All About Vision," AAV Media, LLC. ©, Sept 2020., [Online]. Available: https://www.allaboutvision.com/conditions/cataract-surgery.htm. [Accessed October 13, 2019].

[5] "American Society of Quality (ASQ) "What is Six Sigma,"," American Society of Quality. All rights reserved, 2019. [Online]. Available: https://asq.org/quality-resources/six-sigma. [Accessed October 13, 2019].

[6] "Quality-One International, "Six Sigma," Quality One International, 2020.," Quality-One International - All Rights Reserved, 2015. [Online]. Available: https://quality-one.com/six-sigma/. [Accessed September 26, 2019].

[7] "Go Lean Six Sigma.com, "DMAIC five basic phases of lean six sigma,", n.d.," [Online]. Available: https://goleansixsigma.com/dmaic-five-basic-phases-of-lean-six-sigma/. [Accessed September 17, 2020].

[8] A. Henshall, "DMAIC, the complete guide to Lean Six Sigma in 5 key steps",, "PROCESS.ST, Nov 4, 2017," [Online]. Available: https://www.process.st/dmaic/. [Accessed October 16, 2019].