Monomer's residuals test elimination for Soft Acrylic Buttons

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Abstract

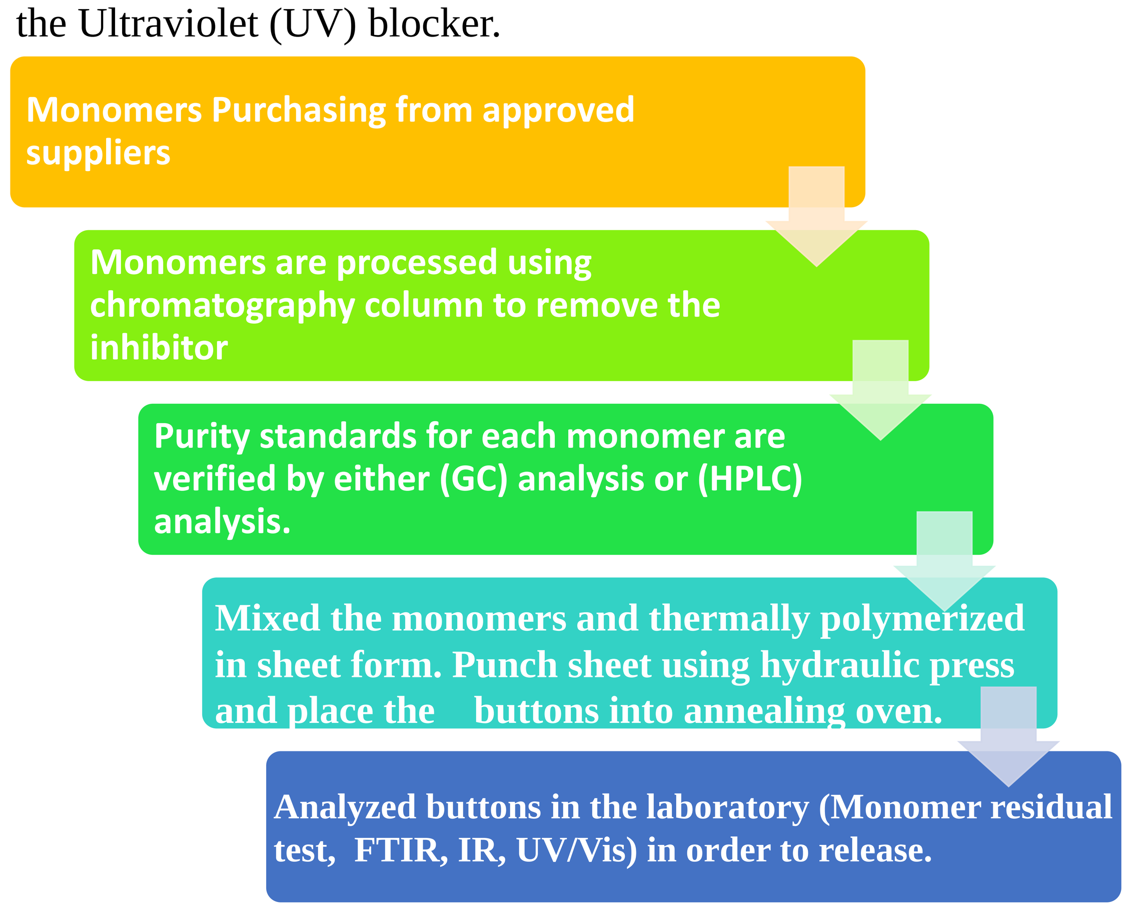
In the cataract surgery, the natural lens in the eye is replace with an Intraocular Lens. Five monomers (EA/EMA, TFEMA, EGDMA, UV Chr) are mixed to produce the soft acrylic lens. Residual monomer testing measures the amount of monomer and crosslinker not polymerized or removed by annealing process. During the last years residual monomer testing become a high-cost test due to equipment maintenance, chemical purchases, and spare parts cost. Historical data was collected from the residual testing for Optiblue from January 2019 up to May 2020 and Opal from June 2018 up to May 2020. DMAIC methodology was used in this analysis. Process Performance Index (Ppk) value varies from 5.62 to 49.52 for Opal and 2.09 to 30.00 for Optiblue, which confirm annealing process is a capable and is in statistically control. Trend analysis was performed, and no negative trend was observed. Therefore, the monomer residual test can be eliminated.

Introduction

Cataract is a cloud that cover the normal clear lens in the eye affecting the visibility of the person. This cloud is produced as result of tissue breakdown and protein clumping. During the cataract surgery, the natural lens in the eye is replace with an Intraocular Lens (IOLs) [1]. Medical devises companies that produce IOLs are focused in develop a large variety of IOLs such as refractive IOLs, Torics, Monofocals, Multifocals among others.

Background

There are two types of soft acrylic lens : Opal (clear buttons), and Optiblue (yellow buttons) Soft Acrylic Sheets. The Soft Acrylic Button is a cross-linked multi-constituent polymer used to produce Acrylic IOLs. Five (5) monomers (EA/EMA, TFEMA, EGDMA, UV Chr) are mixed to produce the soft acrylic lens (Opal). The Optiblue contain the same 5 monomers of Opal and additionally two (2) more additives (Yellow Dye, UVAM) to add the Ultraviolet (UV) blocker.



Problem

The monomer residual test during the last years become a high-cost test due to equipment maintenance, and spare parts cost. Now a day, the release time of the productions orders can be defined for the waiting time for the equipment's: High-Performance Liquid Chromatography (HPLC) or Ultra High-Performance Liquid Chromatography (UHPLC) results.

Methodology

DMAIC methodology will be used for this analysis [2]. In the measure phase, residual results from January 2019 to May 2020 were evaluated for Optiblue and for Opal residual results were evaluated from June 2018 to May 2020.

The sampling size was determined using data previously collected and analyzed using Minitab Power and Sample Size technique, assigned a 0.5 of standard deviation for the difference, and 95% for confidence interval (CI). The historical data used for Power and Sampling Size analysis was Optiblue, based on test failures [3].

A process capability analysis was performed using Minitab 18 to analyze the gathered data. The Process Performance Index (Ppk) was determined using Process Sigma and Yield for the 5 main monomers (EA/EMA, TFEMA, EGDMA, UV Chr), a Process Capability were analyzed to compare Process Performance Index (Ppk).

Additionally, a trend analysis was performed to analyze any negative trend. It is important to highlight that EA/EMA is analyzed using the average of the residuals obtained from both monomers as established in the procedure and in the corresponding method validation.

Results and Discussion

Process capability analysis was performed to analyze the historical data collected from January 2019 to May 2020 for Optiblue, Opal from June 2018 to May 2020 was evaluated. For sampling size, a Power and Sampling size technique was used with a 95% of Confidence level, and 0.5 of standard deviation of the historical data for the difference. The sampling size according to the Power and Sampling size analysis was 105. A total of 2,037 samples points was collected. Each PO consist of 5 sheets for Optiblue buttons and 16 sheets for Opal buttons [4].

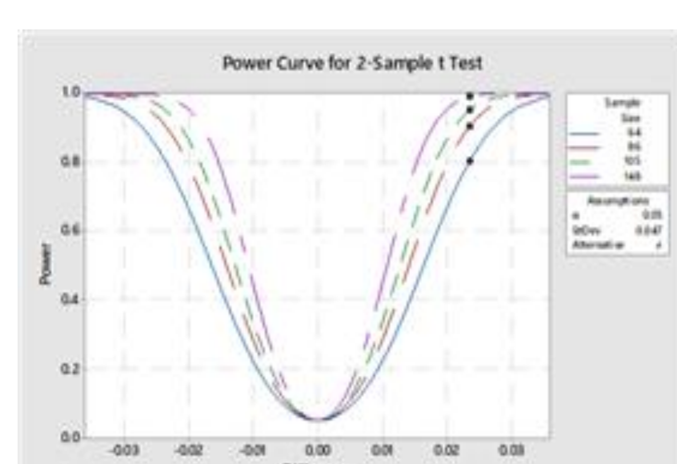


Figure 1. Power and Sample size graph

The Process Performance Index (Ppk) was determined using Process Sigma and Yield for monomers EA/EMA, TFEMA, EGDMA and UV Chr, a Process Capability were analyzed to compare Process Performance Index (Ppk). For the five monomers (EA/EMA, TFEMA, EGDMA, UV Chr) there are no defects in samples, with the efficiency of 100% and high process sigma confirms that process is capable and meet its predefined requirements [4].

Table #1
Process Performance Index (Ppk) Indexes for Opal

Component Name	Specification (%)	Average Value (%)	Ppk (Process Sigma and Yield)	Ppk (Process Capability)
EA/EMA	≤ 0.3	0.013	32.83 / Yield:100%	18.27
TFEMA	≤ 0.05	0.002	32.83 / Yield:100%	5.62
EGDMA	≤ 0.1	0.001	32.83 / Yield:100%	32.84
UV Chr	≤ 0.3	0.001	32.83 / Yield:100%	49.52

Table 1 shows the process Performance Index (Ppk) values of Opal that varies from 5.62 to 49.52 for the Process Capability analysis. Refer to Figure 2 to Figure 5 for Normal Plot. The five monomers are in statical control and meet the requirement of Process capability of ≥ 0.657, this value was obtained using a Statistical Interval Excel Calculator Opal.

Table #2
Process Performance Index (Ppk) Indexes for Optiblue

Component Name	Specification (%)	Average Value (%)	Ppk (Process Sigma and Yield)	Ppk (Process Capability)
EA/EMA	≤ 0.3	0.043	32.83 / Yield:100%	2.09
TFEMA	≤ 0.05	0.007	32.83 / Yield:100%	2.12
EGDMA	≤ 0.1	0.001	32.83 / Yield:100%	11.08
UV Chr	≤ 0.3	0.00	32.83 / Yield:100%	30.00

Table 2 shows the process Performance Index (Ppk) value of Optiblue that varies from 2.09 to 30.00 for the Process Capability analysis. Refer to Figure 6 to Figure 9 for Normal Plot. The five The five monomers are in statical control and meet the requirement of Process capability of ≥ 0.671, this value was obtained using a Statistical Interval Excel Calculator Optiblue.

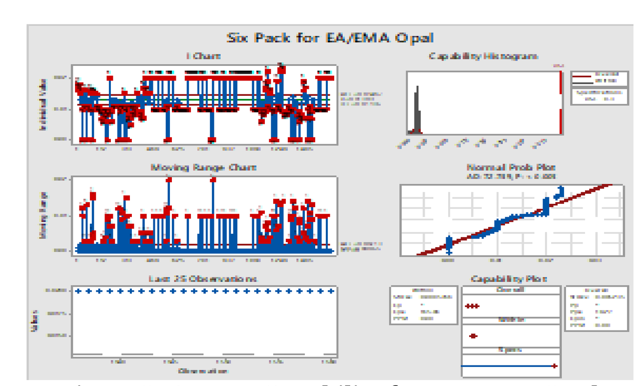


Figure 2. Process Capability for EA/EMA Opal

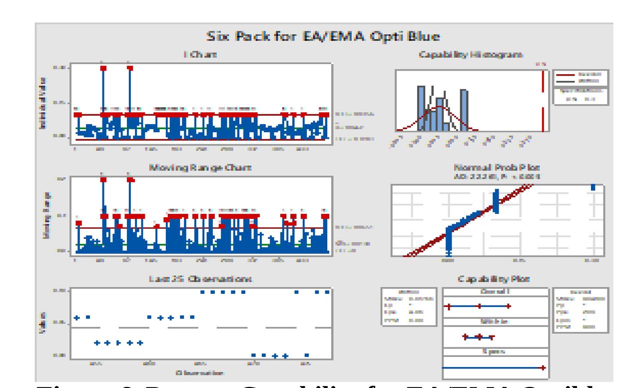


Figure 6. Process Capability for EA/EMA Optiblue

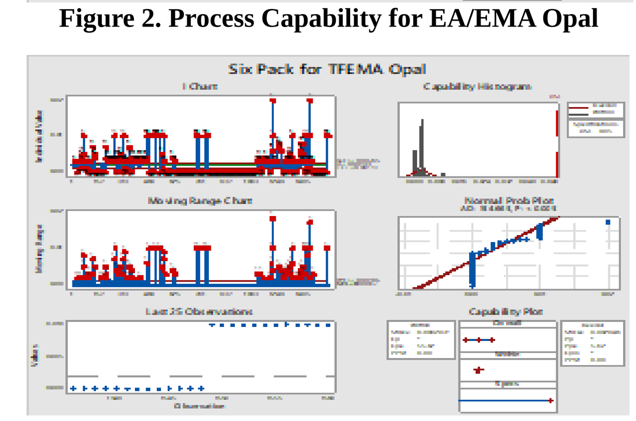


Figure 3. Process Capability for TFEMA Opal

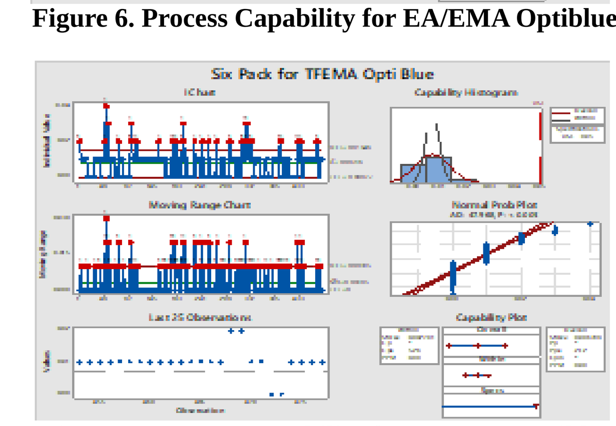


Figure 7. Process Capability for TFEMA Optiblue

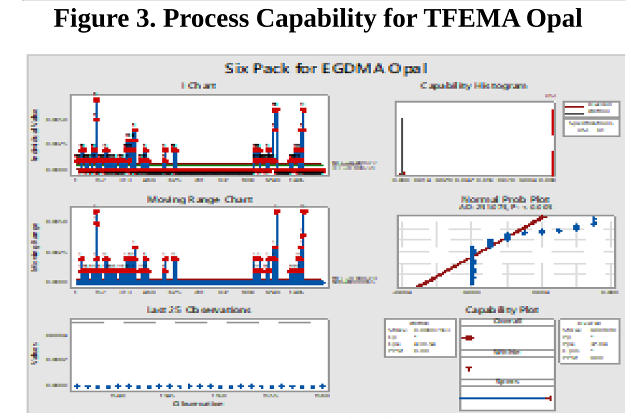


Figure 4. Process Capability for EGDMA Opal

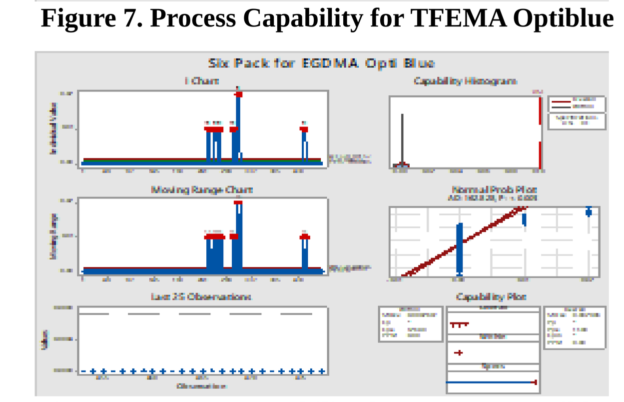


Figure 8. Process Capability for EGDMA Optiblue

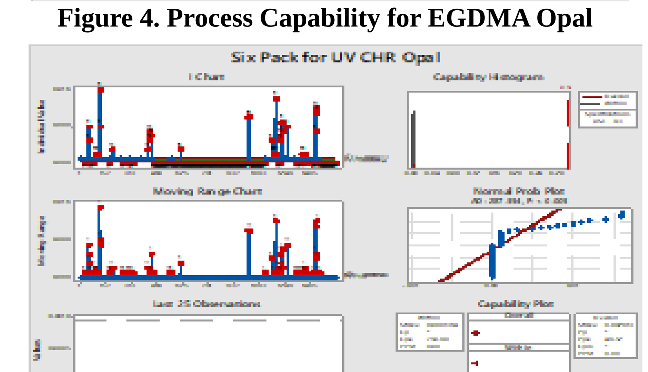


Figure 5. Process Capability for UV Chr Opal

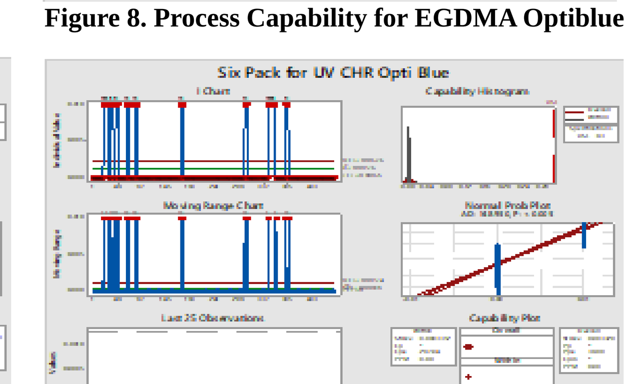


Figure 9. Process Capability UV Chr Optiblue

Conclusions

Process Performance Index (Ppk) value varies from 5.62 to 49.52 for the Opal and 2.09 to 30.00 for Optiblue, which confirm annealing process is a capable and is in statistically control. According to Statistical Sampling for Validations procedure, with a Severity Level of (3) from the "Sensar Sheet Casting and Lens Button Process FMEA Summary Report", the minimum required Process Performance Index (Ppk) value for opal is 0.657, for Optiblue the minimum Ppk is 0.671. No negative trend was observed in any of the components. No OOS, ERs or NRs were generated during the time frame evaluated (from June 2018 to May 2020 for Opal and January 2019 to May 2020 for Optiblue).

Following review of applicable process step and hazard risk assessment using "Sensar Sheet Casting and Lens Button Process FMEA Summary Report", there is no impact foreseen in the test elimination. Even if testing will be eliminated, every Production Order in annealing oven run will be analyzed and if material is not completely polymerized it will fail other identification test in the downstream testing (Haze, FTIR, RI or UV/VIS). There is no change to the form fit or function of the material / product, and no changes to material composition or further inspections, based on that there is no new severity or changes in the risk to eliminate this test method.

Future Work

Based on this assessment findings and retrospective data collected, it is recommended to:

Eliminate the Post Annealing Monomer Residual Test for EA/EMA, TFEMA, EGDMA, UV Chromophore. This evaluation confirm that the annealing process is a capable and is in statistically control. Every annealing oven run will be analyzed and if material is not completely polymerized it will fail other downstream identification test (Haze, FTIR, RI and UV/VIS). With Post Annealing Monomer Residual Test elimination, it can reduce the release time for each production order and reduce exponentially HPLC's and UHPLC equipment spare parts and maintenance cost and waste.

Acknowledgements

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References

[1] Boyd, K. (2021). *IOL Implants: Lens Replacement After Cataract*. [American Academy of Ophthalmology]. [Online] Available: https://www.aao.org/eye-health/diseases/cataracts-iol-implants.

[2] DeFeo J. A. (2020). *DMAIC Process & Methodology: An Essential Guide*. [Juran]. [Online] Available: https://www.juran.com/blog/dmaic-attaining-superior-quality-sustainable-results/

[3] Pena, M. "Monomers residuals data summary and evaluation for OptiBlue Soft Acrylic Buttons". Revision 02. JJSV, Anasco, Puerto Rico, 2020.

[4] Vargas, B. "Monomers residuals data summary and evaluation for Sensar and Sensar UV² Soft Acrylic Buttons". Revision 01. JJSV, Anasco, Puerto Rico, 2020.