DERMABOND Topical Skin Adhesive Sampling Plans Optimization Project between Ethicon San Lorenzo & Cornelia

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Abstract *— This project investigates the optimization of sampling plan for DERMABOND Topical Skin Adhesive products, focusing on reducing lead times for the Critical to Quality attributes: viscosity, purity, and packaging peel strength. Currently, each raw material and finished goods lot undergoes extensive testing, which this study proposes to evaluate for potential reductions based on product homogeneity. Through the application of statistical techniques, including Mann-Whitney tests and Two-sample T-tests, the research aims to establish the feasibility of reducing testing frequency. The goal of this study is to achieve a 75% reduction in lead times by Q4 2025, which would improve product release timelines and customer satisfaction. The expected outcomes recommend a streamlined quality assurance process in Ethicon, decreasing testing time by two hours per lot and reducing overall lead time by 20.5 days. This study highlights the importance of data analysis in enhancing manufacturing sampling plans and improving the cost of quality.*

Keywords *—Cost of quality, Critical to quality Attributes, Manufacturing Sampling Plans, Statistical Techniques.*

PROBLEM STATEMENT

DERMABOND Topical Skin Adhesive is a designed for rapid wound closure following surgical procedures, and it comes in three product families: Prineo, Advanced, and High Viscosity Dermabond (HVD). The primary formulation is manufactured at Ethicon's facility in Cornelia, GA, where it undergoes rigorous testing for viscosity and purity before processing at San Lorenzo into Finished Goods (FG) lots. These lots are then sterilized and returned for final testing.

This research focuses on optimizing the testing of Critical to Quality (CTQ) attributes—viscosity, purity, and packaging peel strength. It proposes reducing redundancy in testing by conducting a homogeneity evaluation that allows for a subset testing strategy based on raw material formulations. Furthermore, the study aims to correlate pre-sterilization and post-sterilization peel strength data to streamline quality assurance processes.

The project's main objective is to achieve a 75% reduction in FG testing lead time by the end of Q4 2025, improving operational efficiency and enhancing customer satisfaction. The key contributions include reducing processing time by 2 hours per lot and decreasing the lead time for FG lot releases by 20.5 days.

LITERATURE REVIEW

In today's competitive market, organizations must continuously improve product and service quality to maintain success. A systematic approach utilizing Statistical Process Control (SPC) tools is essential for enhancing the quality of mass production and minimizing costs. Customer satisfaction is vital, and variability in product specifications must be eliminated through Process Capability Analysis, which assesses the accuracy of production processes.

The process capability analysis is a vital framework for assessing and improving production processes to ensure consistent quality and reliability. The key steps in this analysis begin with the selection of quality characteristics, where attributes that significantly correlate with product performance are identified. Following this, a measurement system analysis is conducted to evaluate the effectiveness and accuracy of the measurement systems used for these attributes,

ensuring that they capture the necessary data accurately. Once the measurement system is established, data collection occurs over a sufficient period, capturing all relevant sources of variability affecting the process. It is crucial to validate the data through verification of prerequisites, which involves statistical tests to confirm the normality and independence of the data sets. The analysis continues with the calculation of capability indices such as Cp, Cpk, Pp, and Ppk, which are used to compare process performance against established product tolerances. Finally, the process culminates in statistical inference, where sampled data is analyzed to make broader conclusions about the production process through hypothesis testing. By systematically following these steps, organizations can enhance their manufacturing processes, reduce variability, and improve overall product quality [1] [2] [3] [4].

METHODOLOGY

The methodology for this project focuses on implementing the Six Sigma DMAIC framework at Ethicon Cornelia and San Lorenzo to achieve a 75% reduction in the lead time for DERMABOND products. This framework consists of five key phases: Define, Measure, Analyze, Improve & Innovate, and Control [5].

- **Define Phase:** This phase identifies the problem and objectives while highlighting the impact on customers and processes. A project charter is created, outlining the project's scope, with a SIPOC diagram (Suppliers, Inputs, Process, Outputs, Customers) to provide an overview of the process. The Voice of the Customer tool is utilized to gather insights into customer needs regarding timely testing and product turnaround.
- **Measure Phase:** A comprehensive data collection plan is developed to gather historical data on the purity, viscosity, and peel strength of DERMABOND products over a two-year period, reflecting the products' shelf life.
- **Analyze Phase**: This phase employs graphical tools, such as probability plots and process capability analyses, to evaluate the historic data. Assessing the normality of the data allows for the application of standard statistical techniques, facilitating a determination of process capability to inform testing frequency reductions.
- **Improve Phase**: The improvements from previous phases are implemented and tested. A new sampling plan will be developed with input from Subject Matter Experts (SMEs) and other relevant stakeholders, resulting in multiple change orders to refine procedures, test methods, and specifications.
- **Control Phase:** This phase ensures the sustainability of improvements by updating procedures, methodologies, and documentation. Training will be provided for associates in the San Lorenzo manufacturing facility and QA Lab in Cornelia, alongside integrating audit control checks into manufacturing systems to maintain compliance and quality assurance prior to product release.

RESULTS AND DISCUSSION

In the Define phase, the project’s purpose and scope were established through the development of a project charter, which aligned management and team expectations and clarified roles and responsibilities. This charter served not only as a guiding document but also ensured that the project was consistent with the organization’s strategic priorities, fostering accountability and decision-making. To further refine the project boundaries, a SIPOC diagram was used to map the process, clearly defining the start and end points, which helped prevent scope changes and ensured a common understanding among all stakeholders. Additionally, the Voice of the Customer (VOC) analysis highlighted the necessity for timely testing and rapid product turnaround, identifying key issues affecting customer satisfaction. Historical data was gathered to confirm that process

parameters were statistically controlled, emphasizing the critical need for effective communication regarding testing deviations.

In the Measure phase of the research, three critical-to-quality attributes (CTQs) for DERMABOND products—Purity, Viscosity, and Peel Strength—were assessed to evaluate product stability and performance. The study employed validated bulk chemical batch processes to ensure uniformity in composition and performance throughout the production cycle. Homogeneity testing established that if worst-case attributes met standards, other components could also be deemed homogeneous, allowing for reduced sampling in future tests.

Purity and Viscosity

To determine stability of the data for Dermabond Products, Purity and Viscosity were subjected to review through use of an individual's control chart compared to the respective specifications for each product families (Prineo 22/42/60, Advanced and HVD/ HVD mini). The chart shows a stable representation of one of the product families of the HVD testing values shown in Figures 1 and 2 for HVD Purity and Viscosity. In the 2-year time span used from historical data, no failures occurred. A two-year time span is also most appropriate as it represents the shelf life of the Dermabond product line.

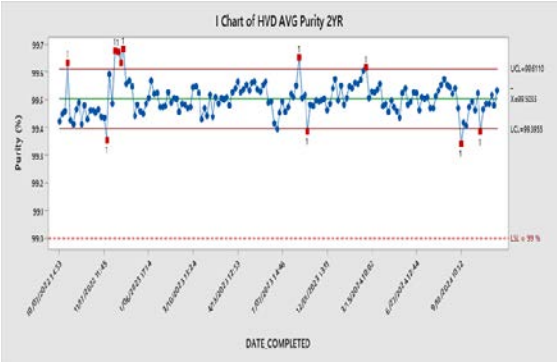

Figure 1
I-Chart for HVD Purity

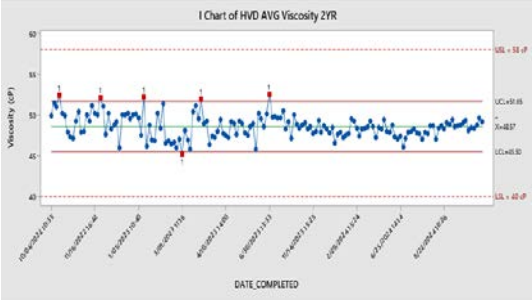

Figure 2
I-Chart for HVD Viscosity

Historical data for Purity and Viscosity was subjected to a capability review. The results obtained for HVD Purity and HVD Viscosity of 2.94 and 2.03 respectively demonstrate a high process capability (Ppk) in meeting the specifications. A Ppk value of 1.36 or greater for a class 1 defect is deemed to have a process robustness level of a very high per production sampling plans procedure. Refer to Figures 3 and 4 for process capability reports.

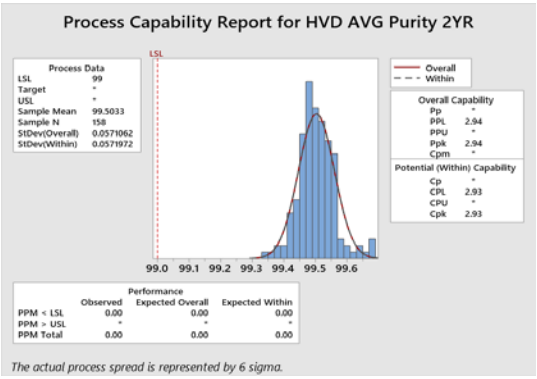

Figure 3
Process Capability Report for HVD AVG Purity

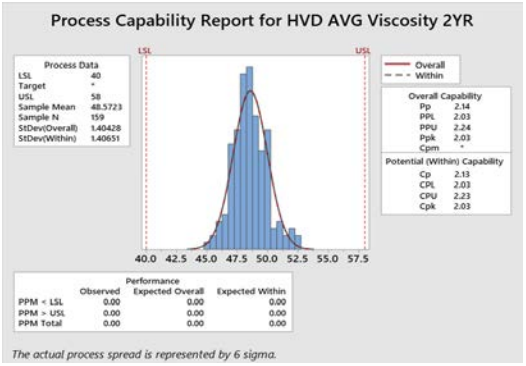

Figure 4
Process Capability Report for HVD AVG Viscosity

Table 1 shows the process capabilities for all Dermabond Product families.

Table 1
ppk Values for Purity & Viscosity for Dermabond Families

Dermabond Family	Ppk Purity	Ppk Viscosity
HVD	2.94	2.03
HVD Mini	3.39	1.70
Advanced	3.45	1.75
Prineo 42	2.62	2.04
Prineo 22	2.60	2.06
Prineo 60	2.59	2.01

Based on the process capabilities summary, all ppk values for purity and viscosity for all Dermabond product families are greater than 1.33 is typically considered indicative of a capable process that is performing well and consistently producing outputs within specifications.

Peel Strength

To determine stability of the data for HVD, peel strength was subjected to review through use of an individual's control chart compared to the respective specifications. The chart shows a stable representation of the testing values shown in Figures 5 and 6.

Figure 5
2 Years of Data of HVD AVG Peel Strength from San Lorenzo, PR Pre-Sterilization

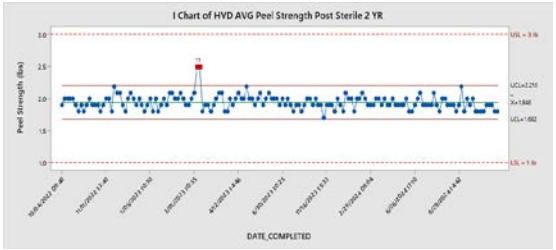

Figure 6
2 Years of Data of HVD AVG Peel Strength from Cornelia, GA Post-Sterilization

Historical data for peel strength was subjected to a capability evaluation for both pre and post sterilization. The results obtained for Dermabond HVD pre-sterilization and post-sterilization resulted in a value of 2.77 and 3.02 respectively, demonstrating a high process capability (Ppk) in meeting the specifications. demonstrating a high process capability (Ppk) in meeting the specifications. A Ppk value of 1.36 or greater for a class 1 defect is deemed to have a process robustness level of a very high per production sampling plans procedure. See Figures 7 and 8 for process capability reports.

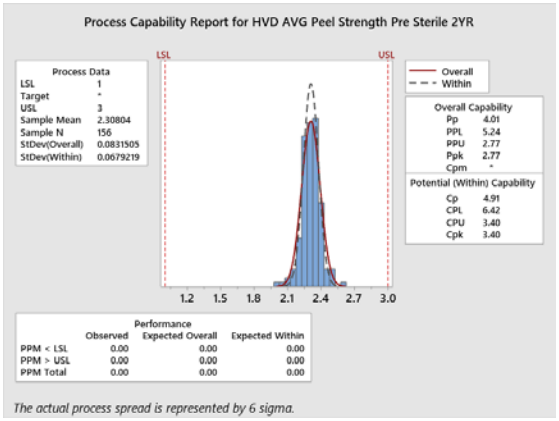

Figure 7
2 Years of Data of HVD AVG Peel Strength from San Lorenzo, PR Pre-Sterilization

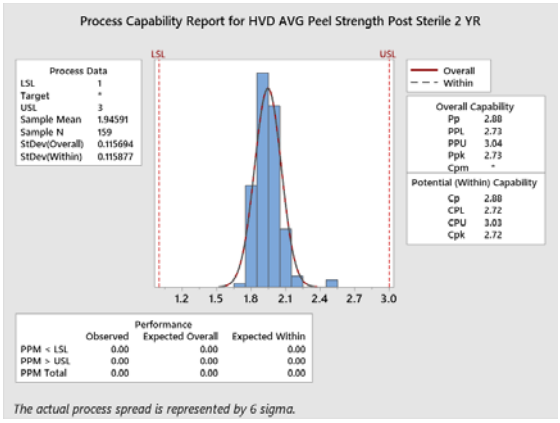

Figure 8
2 Years of Data of HVD AVG Peel Strength from Cornelia, GA Post-Sterilization

Table 2 shows the process capabilities for the Dermabond Product families for peel strength pre-sterilization and post-sterilization.

Table 2
ppk values for Purity & Viscosity for Dermabond Families

Dermabond Family	Ppk Pre-sterilization	Ppk Post sterilization
HVD	2.77	2.73
HVD Mini	3.02	3.05
Advanced	3.78	1.50
Prineo 22 &42	2.16	2.74
Prineo 60	1.79	2.49

Based on the process capability summary, the pre- and post-sterilization Ppk value indicated strong performance and capability to maintain seal integrity after sterilization for all Dermabond product families. The ppk value above 1.33 should be a minimum target to ensure product reliability.

In the Analyze phase of the research, the attributes of Purity, Viscosity, and Peel Strength for DERMABOND products were thoroughly evaluated. Ethicon validated bulk chemical batch processes to ensure uniformity in composition and performance throughout the production cycle. It was demonstrated that if the worst-case attributes showed homogeneity, other components could also be considered homogeneous, allowing for reduced sampling in subsequent tests.

Purity and Viscosity

Purity and viscosity results were obtained for all finished good lots made using the same parent formulation lot. The FG lot results were divided, randomly, into two groups to complete the Mann-Whitney test to determine if there are any differences statistically between the two groups. This can be determined through the P-Value that the Mann Whitney tests outputs.

A P-Value of or below 0.05 indicates that there is a significant difference between the two groups of data. On the contrary, a value above 0.05 indicates that there is no statistically significant difference between the two groups being compared. This analysis was completed for five randomly chosen formulation lots. The analysis performed on the five randomly chosen formulation lots indicates the purity and viscosity results for the FG lots produced using the same formulation lot are representative of each other. In the five Mann-Whitney tests performed, all of them resulted in a P-Value above 0.05, thus proving homogeneity. The Table 3 shows the hypothesis test results of Mann-Whitney Test for all the Dermabond Product families.

Table 3
Ppk Values for Five Formulation Lots for Dermabond Families

CTQ	Dermabond Family	pvalue Lot 1	pvalue Lot 2	pvalue Lot 3	pvalue Lot 4	pvalue Lot 5
Pur	HVD	1.000	0.245	0.470	0.312	0.676
Pur	Advanced	0.699	1.000	0.699	0.245	0.699
Pur	Prineo	0.395	0.582	0.343	0.340	0.177
Vis	HVD	1.000	0.245	0.245	0.773	0.531
Vis	Advanced	1.000	1.000	0.245	1.000	0.699
Vis	Prineo	0.940	0.960	0.209	0.986	0.356

Based on the summary above, purity and viscosity tests can be conducted on only one finished good lot per formulation parent lot for all Dermabond product families since the P-Value are above 0.05.

Peel Strength

The data for the peel strength was taken from both pre and post sterile samples over a time span of two years for Dermabond HVD and HVD Mini products. With the data being divided into two groups, pre and post sterile, they were compared using a two sample T-test to see if there was a significant difference between the two groups. This can be determined through the P-Value that the two sample T-Test outputs. A P-Value of or below 0.05 indicates that there is a significant difference between the two groups of data. On the contrary, a value above 0.05 indicates that there is no statistically significant difference between the two groups being compared. The result of the two sample T-Test was below 0.05 which signifies that

there was a significant difference between the two groups as shows in Figures 9 and 10.

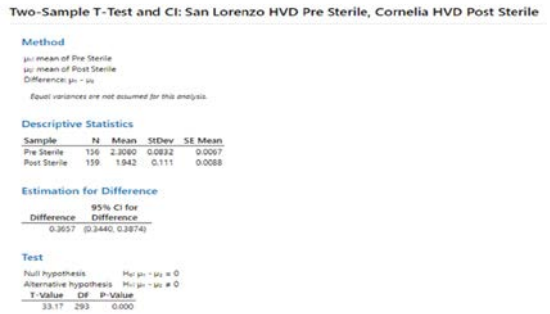

Figure 9
Two-Sample T-Test Results for HVD AVG Peel Strength Pre vs. Post Sterile

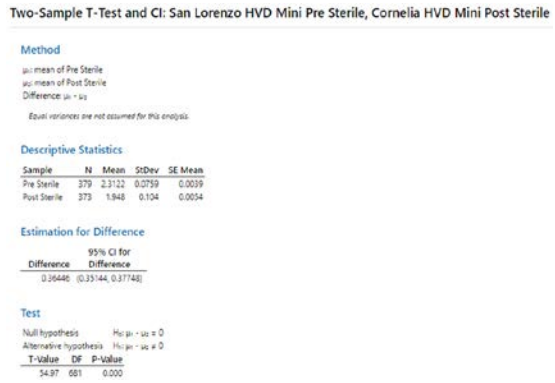

Figure 10
Two-Sample T-Test results for HVD Mini AVG peel strength Pre vs. Post

An evaluation of Dermabond HVD and HVD Mini historical data from October 2022 to October 2024 shows the process is stable and operating at a high process capability for peel strength both pre and post sterilization. An evaluation of the data demonstrates that the peel strength of the Dermabond HVD and HVD Mini finished good lots pre sterilization performed slightly better than they did post sterilization. Also, with the results from the two sample T-tests we can see that there is a significant difference in the data sets with the pre sterile samples averaging stronger seal strengths for both HVD and HVD Mini. It is recommended that peel strength testing for Dermabond HVD and HVD Mini be conducted on only during the manufacturing process in San Lorenzo, PR. Table 4 shows the hypothesis test results of T- Test results for all the Dermabond Product families.

Table 4
Ppk Values and Mean for Pre and Post Sterilization Results for Dermabond Families

Dermabond Family	Pre vs Post P-values	Mean pre-sterilization	Mean post-sterilization
HV	0.0000	2.3	1.9
Advanced	0.038	2.3	2.3
Prineo	0000	2.3	2.5

Based on the Hypothesis test summary, we can see that there is a significant difference in the data sets with the pre sterile samples averaging stronger seal strengths for all product families. Therefore, it is recommended that peel strength testing for Dermabond be conducted on only during the manufacturing process in San Lorenzo, PR

In the Improve phase of the DMAIC methodology, nine new sampling plan rationales were developed for various product families in collaboration with Subject Matter Experts (SMEs), Quality Engineers, Quality Compliance personnel, Technical Operations, Research & Development, and Regulatory teams. This collaborative effort resulted in one change project and nine change orders, each supported by a memo outlining the rationale behind the modifications. Additionally, redlined applications were created to update impacted procedures and testing methods. This structured, change management process ensured that all stakeholders were informed and aligned on the updates, facilitating the effective implementation of improvements that enhanced overall process efficiency and compliance. The analyses and documentation generated during this phase will serve as crucial references for future initiatives and decision-making processes.

In the Control phase, the focus was on sustaining the improvements made during the project by ensuring effective implementation of modifications to procedures, test methods, material specifications, and quality documentation. The updated testing requirements based on Critical to Quality (CTQ) parameters were integrated into the Manufacturing Execution System (MES) and the Laboratory Information Management System (LIMS). Additionally, change management initiatives included training for associates at the San

Lorenzo manufacturing site and the Quality Assurance Lab in Cornelia. To prevent any critical testing from being overlooked before product release, audit control checks were implemented within both MES and LIMS. This comprehensive approach to monitoring and training ensured the long-term sustainability of the process improvements, ultimately enhancing the overall quality and compliance of manufacturing operations.

CONCLUSIONS

The evaluation of historical data for Dermabond products over a two-year period indicates that the manufacturing process is stable and demonstrates a high process capability in terms of purity, viscosity, and peel strength testing. Analysis of homogeneity showed that the purity and viscosity of finished goods produced from the same parent lot are consistent from lot to lot. Consequently, it is recommended that purity and viscosity testing for Dermabond product families be conducted on only one finished good lot per formulation parent lot. This change would reduce testing time in Cornelia, GA, and streamline the overall lead time for the lot.

Furthermore, the data evaluation revealed that the peel strength of Dermabond Advanced finished goods for post-sterilization showed improved performance compared to pre-sterilization, exhibiting higher average peel strength but lower Ppk values. Results from two-sample T-tests also indicated a significant difference, with post-sterile samples demonstrating stronger seal strengths on average. Therefore, it is advised that peel strength testing for Dermabond product families be performed only during the manufacturing process in San Lorenzo, PR. This recommendation would further decrease testing time in Cornelia, GA, reduce overall lead time by 20.5 days, and eliminate the need for destructive testing of saleable products.

In summary, this research has made significant contributions to the Dermabond end-to-end process. By implementing the proposed changes, the lab capacity in Cornelia, GA, can be increased, resulting in a reduction of testing time by 2 hours for Dermabond lots and a more efficient production process overall. However, limitations of this study include potential variability in testing conditions and the reliance on historical data, which may not account for future changes in processes or materials. These findings lay the foundation for optimizing operations and enhancing product quality in the Dermabond production process.

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