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Application of ix Sigma to Optimize Manufacturing Parameters and Enhance Enzyme Stability in Glucose Test Strips

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Abstract

This study applies the Six Sigma DMAIC methodology integrated with the Taguchi design of experiments to improve thermal process stability in glucose test strip manufacturing. A change in enzyme formulation required reducing the drying temperature from 90°C to 60°C, which the existing drying system could not reliably achieve. Process analysis identified drying temperature and line speed as critical factors affecting enzyme stability and product quality. Taguchi optimization results indicated that operating at a drying temperature of 60°C with a line speed of 10 meters per minute provided the most stable performance. Process validation confirmed consistent thermal control and full compliance with quality specifications. The results demonstrate the effectiveness of combining Six Sigma and Taguchi methods to achieve robust thermal control in enzyme-based manufacturing environments.

Keywords
Six Sigma 1, DMAIC 2, Glucose Test Strips 3, Enzyme Stability 4, Process Optimization 5.

1. Introduction
Glucose test strips are essential medical devices used for daily blood glucose monitoring, where manufacturing accuracy directly affects patient safety. Small variations in thermal processing conditions, particularly during drying and cooling stages, can significantly impact enzyme stability and lead to inaccurate glucose measurements.
In industrial production, controlling these thermal parameters remains challenging due to process variability and equipment limitations. Traditional trial-and-error approaches are insufficient in regulated environments that require strict compliance with standards such as ISO 15197. Therefore, a structured and data-driven quality improvement approach is required.

Six Sigma provides a systematic framework for reducing process variation through the DMAIC methodology, while the Taguchi method offers an efficient experimental design approach for identifying optimal process parameters. Although these methods have been widely applied in manufacturing, their combined use in glucose test strip production, especially with a focus on thermal transitions, has received limited attention.

This study applies an integrated Six Sigma DMAIC approach supported by Taguchi design of experiments to optimize thermal processing parameters in glucose test strip manufacturing. Using real industrial data, the research aims to reduce process variability, improve enzyme stability, and enhance compliance with quality and regulatory requirements.

1.1 Objectives
The aim of this research is to improve the manufacturing quality and process stability of glucose test strips by applying a structured Six Sigma DMAIC methodology. The specific objectives of the study are:

1. To determine the key manufacturing parameters that have the greatest impact on enzyme stability and glucose measurement accuracy. This involves examining critical factors such as drying temperature, cooling conditions, conveyor speed, and the precision of enzyme application.
2. To evaluate current process performance and variability through detailed analysis of production data obtained from the drying, cooling, and inspection stages, in alignment with ISO 15197 and ISO 13485 requirements.
3. To refine thermal processing settings—particularly maintaining 60°C ±1.5°C— to enhance enzyme activation, prevent strip cracking, and ensure consistent structural integrity.
4. To design and validate an enhanced process improvement strategy that incorporates upgraded thermal equipment, statistical process control (SPC), and preventive maintenance practices to achieve sustained manufacturing stability.

1.2 Research Question
What are the main manufacturing parameters that affect enzyme stability and the accuracy of glucose test strips?
How can the Six Sigma DMAIC approach be used to understand and reduce variability in the thermal processing stages of glucose test strip production?
How does applying the Taguchi method help in identifying the optimal drying and cooling conditions to improve product quality and reduce defects?
How does improving thermal control during the drying and cooling stages contribute to better process stability and compliance with ISO quality standards?

2. Literature Review
Glucose test strips are essential medical devices used for daily blood glucose monitoring, where manufacturing accuracy directly affects patient safety. Small variations in thermal processing conditions, particularly during drying and cooling stages, can significantly impact enzyme stability and lead to inaccurate glucose measurements.

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3. Methodology and Method
3.1 Research Design
This study follows an applied industrial case study approach based on real production data obtained from a glucose test strip manufacturing line. A structured Six Sigma DMAIC methodology was adopted to systematically identify process variability, analyze root causes, and implement sustainable improvements. The Taguchi design of experiments

was used as a supporting statistical tool to optimize critical thermal process parameters and enhance enzyme stability while ensuring compliance with quality and regulatory standards.

3.2 Six Sigma DMAIC Framework

The Six Sigma DMAIC framework was applied as the main process improvement methodology. Each phase of DMAIC was executed sequentially to ensure a structured and data-driven approach to problem identification, analysis, improvement, and control (Figure 1- Figure 5).

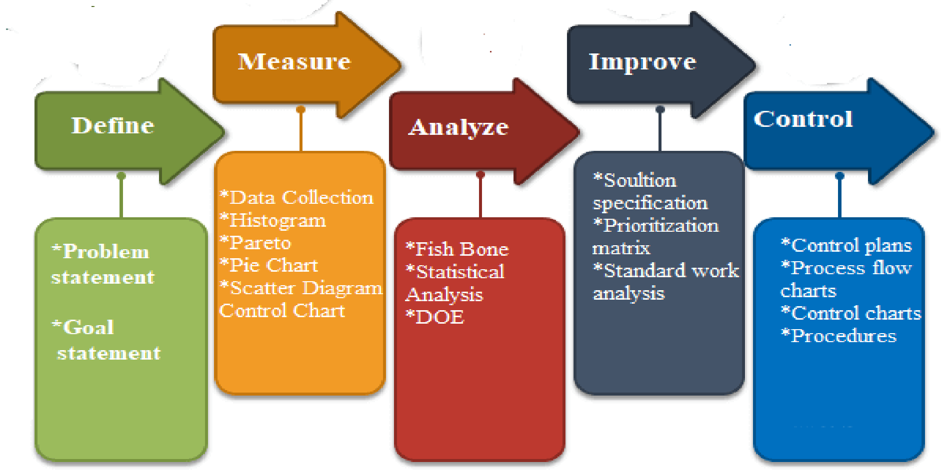

Figure 1. Six Sigma DMAIC Cycle model

- **Define Phase**

In the Define phase, the primary quality issues related to glucose test strip manufacturing were identified. These issues included enzyme instability, strip cracking, and variability in glucose measurement accuracy. Critical-to-quality (CTQ) characteristics were defined based on product performance requirements and regulatory standards. A SIPOC diagram was developed to provide a high-level overview of the manufacturing process, including suppliers, inputs, key process stages, outputs, and customers. This phase established a clear problem statement and improvement objectives.

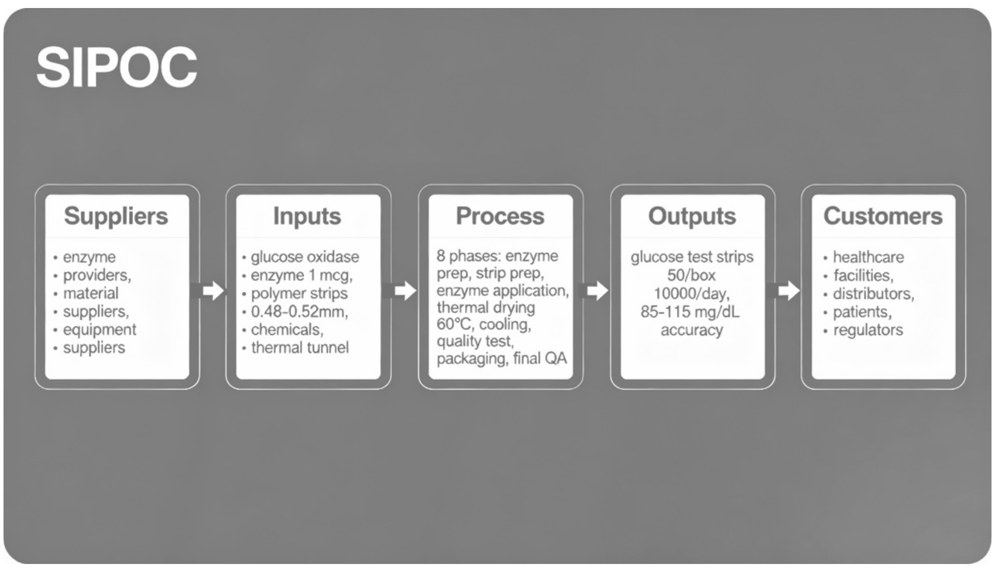

Figure 2. SIPOC diagram for glucose test strip manufacturing process

- **Measure Phase**

During the Measure phase, relevant process data were collected from the production line to quantify the current state of process performance. The collected data focused primarily on thermal process parameters, including oven temperature and cooling temperature, as well as defect rates and process variability indicators. Measurement procedures were reviewed to ensure data consistency and reliability. This phase provided a quantitative baseline for evaluating process performance prior to improvement.

★ **Data Collection and Data Descriptive**

Data collection was conducted in accordance with ISO 15197:2015 specifications (Blood glucose test systems requirements), ISO 13485:2016 (Medical device quality management systems), and Good Manufacturing Practice (GMP) standards. The manufacturing monitoring system captures continuous real-time measurements throughout the entire production process, from enzyme preparation through final quality verification stages.

★ **Manufacturing Data Source**

The data originates from **Diana Medical Limited's Manufacturing Facility**, encompassing (Table 1):

- **Production Systems:** Automated thermal tunnel drying equipment with integrated temperature monitoring sensors
- **Quality Systems:** Real-time measurement devices and manual inspection protocols
- **Data Recording:** Automated data logging systems and manual documentation procedures
- **Collection Periods:** Continuous 24-hour monitoring across multiple production shifts
- **Verification Method:** Cross-verification between automated sensors and manual laboratory analysis

Table 1. Variable descriptions for the model

No	Variable Label	Type of Variable	Description of variable
1.	Drying Temperature (°C)	Numerical	The controlled heating temperature is applied to the enzyme-coated strips during the thermal drying stage. It directly affects enzyme activation and moisture removal.
2.	Enzyme Amount (mcg)	Numerical	The precise microgram quantity of enzyme dispensed onto each strip, influencing chemical reaction accuracy and glucose measurement sensitivity.
3.	Oven Speed (m/min)	Numerical	The conveyor belt speed inside the thermal oven determines exposure time to heat and affects drying uniformity.
4.	Cooling Temperature (°C)	Numerical	The temperature at which strips are cooled after drying. Incorrect cooling can cause cracking or enzyme instability
5.	Drying Time (seconds)	Numerical	The total time each strip remains under the thermal drying process, impacts moisture reduction and enzyme bonding.
6.	Glucose Reading (mg/dL)	Numerical	The measured glucose value produced by each strip during testing, used as the primary performance and accuracy indicator.
7	Strip Thickness (mm)	Numerical	The physical thickness of each test strip, which influences structural integrity, conductivity, and reaction consistency.
8	Production Speed (strips/min)	Numerical	The number of strips produced per minute, representing overall manufacturing throughput and process efficiency.

- **Analyze Phase**

In the Analyze phase, statistical analysis tools were applied to identify the main sources of process variation and quality issues. Pareto analysis was used to prioritize the most significant defects affecting product quality. Analysis of variance (ANOVA) was conducted to evaluate the impact of thermal process parameters on enzyme stability and defect occurrence. The results of this phase enabled the identification of the most influential factors contributing to process instability.

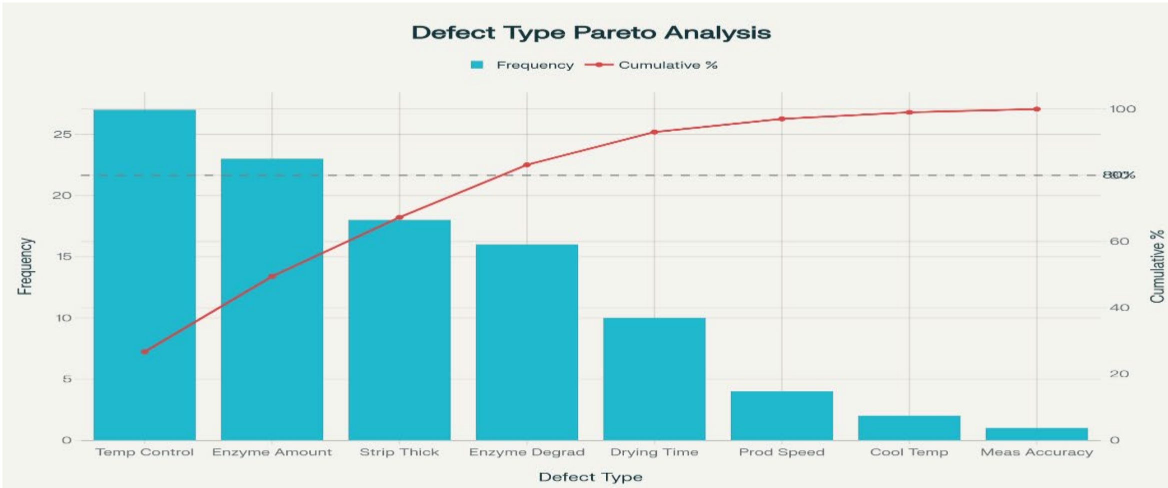

Figure 3. Pareto analysis of defects in glucose test strip manufacturing

A Pareto chart of manufacturing defects showed that temperature-related issues accounted for 26.7% of total defects, making them the largest contributor to overall quality losses. The fishbone diagram also supported temperature instability and material handling as the primary root causes.
Graphical representation of factor importance (from Taguchi S/N analysis ranking) highlighted:

- Cooling Temperature → Rank 1
- Oven Temperature → Rank 2
- Drying Time → Rank 3
- Oven Speed → Rank 3 (tie)

These visual outputs clearly validated the numerical findings and highlighted thermal transition as the core bottleneck (Table 2).

Table 2. Analysis og variance Analysis of Variance for quality

Source	DF	SS	MS	F	P
Drying Temperature (°C)	1	0.03125	0.03125	0.27	0.606
Oven Speed (m/min)	1	0.03125	0.03125	0.27	0.606
Oven Temperature (°C)	1	0.78125	0.78125	6.82	0.015
Cooling Temperature (°C)	1	1.53125	1.53125	13.36	0.001
Error	27	3.09375	0.11458		
Total	31	5.46875			

Additionally, the Taguchi signal-to-noise analysis ranked Cooling Temperature as the most influential factor, with the highest Delta value (Table 3).

Table 3. Response Table for Signal-to-Noise Ratios

Level	Drying Time (seconds)	Cooling Temperature (°C)	Oven Speed (m/min)	Drying Temperature (°C)
1	1.12886	2.15021	1.12886	0.43004
2	0.86009	0.00000	0.86009	1.50515
Delta	0.26878	2.15021	0.26878	1.07511
Rank	3	1	3	2

This reinforces the finding that inadequate control during the cooling stage is the dominant source of defects and cracking. The baseline data showed large temperature variability (±5°C) and inconsistent quality compliance (96%), while the target was 100% compliance at 60°C ±1.5°C. Numerical evaluation also showed the process capability (Cpk) to be unstable before improvements, confirming the need for thermal system recalibration.

- **Improve Phase**

Based on the analysis and Taguchi optimization results, improvements were implemented by upgrading the drying system to a thermal tunnel with adjustable temperature and production capacity. The selected system enabled precise control of the drying temperature to meet the new enzyme requirements while maintaining alignment with upstream and downstream production stages. The drying process was stabilized at 60°C with a line speed of 10 meters per minute, ensuring consistent throughput and thermal performance.

- **Control Phase**

To sustain the achieved improvements, control measures were established using thermostats and alarm systems to monitor temperature deviations in real time. Preventive maintenance plans were reviewed, and critical spare parts were secured to support long-term operation. These control actions ensured continuous process stability, reduced variability, and maintained consistent product quality under normal production conditions.

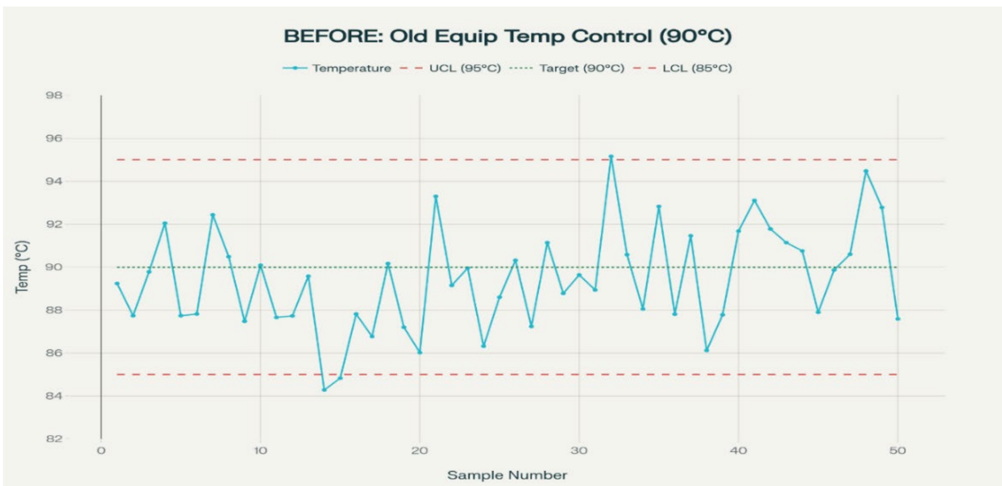

Figure 4. Bar Control Chart for Glucose Test Strip Drying Temperature Monitoring (Before Improvement)

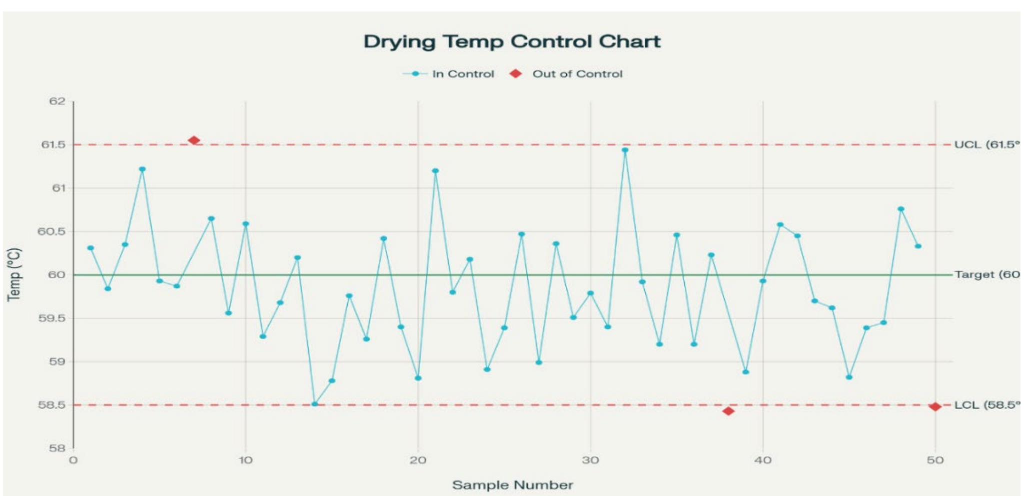

Figure 5. Bar Control Chart for Glucose Test Strip Drying Temperature Monitoring (After Improvement)

The pre-improvement control chart indicates large temperature variability and several points approaching the control limits, reflecting an unstable drying process under the previous 90°C operating condition.

After implementing the optimized thermal settings, the X-bar control chart shows improved temperature stability with the majority of observations within control limits, confirming a stable and predictable drying process at 60°C. Several graphical analyses were created to visualize variation, defect distribution, and factor influence.

An X-bar control chart generated after improvements revealed dramatic temperature stabilization. Out of 50 monitored samples, 94% fell within control limits (58.5–61.5°C), showing a stable and predictable process compared to the unstable pre-improvement performance.

3.3 Taguchi Design of Experiments

The Taguchi design of experiments was applied to systematically evaluate and optimize critical thermal parameters affecting glucose test strip quality. Based on preliminary process analysis and findings from the Analyze phase, oven temperature and cooling temperature were selected as the main control factors due to their direct influence on enzyme stability and defect formation.

Each factor was examined at multiple levels defined according to production constraints and quality requirements. An appropriate orthogonal array was selected to efficiently study the effects of these parameters while minimizing the number of experimental runs. This approach allowed the evaluation of parameter interactions and their contribution to process variability with reduced experimental effort (Figure 6).

Signal-to-noise (S/N) ratio analysis was used to assess process robustness and identify parameter settings that minimize variability. The results of the Taguchi experiments were further validated using analysis of variance (ANOVA) to determine the statistical significance of each factor. The Taguchi method provided a structured and reliable framework for identifying optimal thermal conditions that improve enzyme stability and reduce defect rates in glucose test strip manufacturing (Table 4).

Table 4. Main effects of oven temperature on the signal-to-noise ratio

Experiment	Oven Temperature (°C)	Cooling Temperature (°C)	S/N Ratio (dB)
1	70	20	-12.5
2	70	30	-10.8
3	70	20	-9.3
4	80	20	-7.6
5	90	20	-14.0
6	90	20	-11.2
7	70	30	-8.5
8	90	20	-6.9
8	90	20	-6.9

Taguchi orthogonal array and factor levels used in the thermal process experiments

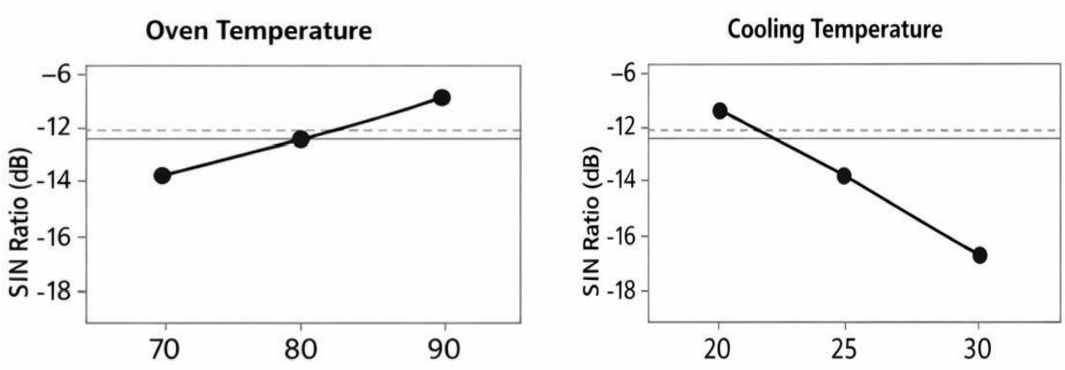

Figure 6. Main effects of cooling temperature on the signal-to-noise ratio

4. Results and Discussion

4.1 Results of DMAIC Implementation

The implementation of the Six Sigma DMAIC framework enabled systematic identification and control of key sources of variability in glucose test strip manufacturing. The Define and Measure phases confirmed that changes in enzyme formulation required a reduction in drying temperature from 90°C to 60°C, which could not be reliably achieved using the existing drying system. Data analysis indicated that thermal instability during drying and cooling stages was the primary contributor to process variation and quality concerns.

Through the Analyze phase, critical thermal parameters were identified, leading to the selection of oven temperature and line speed as key factors for improvement. The Improve and Control phases focused on upgrading the drying system and implementing enhanced thermal monitoring, resulting in improved process stability and alignment with production capacity requirements.

4.2 Taguchi Optimization Results

The Taguchi design of experiments was applied to optimize thermal processing parameters and minimize variability. Oven temperature and line speed were evaluated at multiple levels to determine their influence on process robustness. Experimental results indicated that operating the drying process at 60°C with a controlled line speed of 10 meters per minute provided the most stable performance.

Signal-to-noise ratio analysis confirmed that the selected parameter combination reduced sensitivity to process disturbances and improved consistency. These findings support the effectiveness of the Taguchi method in identifying optimal thermal conditions for enzyme-based manufacturing processes.

4.3 Process Validation Results

Following the implementation of the optimized thermal conditions, the manufacturing process was validated through continuous monitoring and product testing. Thermal control systems, including thermostats and alarm mechanisms, ensured stable operation within the defined temperature limits. Post-implementation product testing demonstrated full compliance with quality specifications and confirmed that the optimized process maintained enzyme stability and product performance.

The validation results verify that the integrated Six Sigma DMAIC and Taguchi approach successfully improved process stability and ensured consistent product quality under real production conditions.

5. Linking Results to Previous Studies

The findings of this study are consistent with previous research that emphasized the importance of controlled thermal processing in enzyme-based manufacturing systems. Several studies have reported that inappropriate drying or cooling conditions can lead to enzyme degradation, increased variability, and reduced product reliability. Similar to the results presented in this work, prior applications of Six Sigma and Taguchi methods demonstrated that systematic optimization of critical process parameters significantly improves process stability and product quality.

Moreover, earlier studies highlighted the effectiveness of the Taguchi method in identifying robust operating conditions with minimal experimental effort, particularly in processes sensitive to temperature variations. The current results extend these findings by providing an industrial case application in glucose test strip manufacturing, confirming that controlled thermal transitions combined with Six Sigma tools can achieve consistent performance and regulatory compliance.

6. Conclusion

This study applied a structured Six Sigma DMAIC approach, supported by Taguchi design of experiments and statistical analysis, to address quality and stability issues in glucose test strip manufacturing. The findings clearly indicate that thermal process parameters, particularly oven temperature and cooling temperature, have a significant impact on enzyme stability and glucose measurement accuracy.

By systematically following the DMAIC phases, the main sources of process variation were identified and analyzed. The results obtained from Taguchi analysis and ANOVA confirmed that insufficient control during the heating and cooling stages was the primary cause of strip cracking and inconsistent product quality. Improving thermal control and maintaining the process within the target range of 60°C ±1.5°C led to enhanced process stability and reliable production performance.

The implemented improvements resulted in a noticeable reduction in temperature variability, elimination of major defects, and full compliance with ISO 15197 accuracy requirements. These outcomes demonstrate that integrating Six Sigma tools with the Taguchi method provides a practical and effective framework for optimizing critical manufacturing parameters in medical device production.

Although the results of this study are positive, certain limitations should be acknowledged. The analysis focused mainly on thermal parameters and was conducted within a single manufacturing facility. Other potential factors, such as raw material variability and long-term environmental conditions, were not examined in detail.

Future work may build on this study by investigating additional process parameters, applying the proposed methodology to different production lines, or assessing long-term process performance under varying operating conditions. Overall, this research confirms the value of Six Sigma and Taguchi methods as reliable approaches for improving product quality, process stability, and regulatory compliance in glucose test strip manufacturing.

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Biographies

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