Qualification of the Cold Chain System in Drug Logistic

Author: Yailyn Otero Torres
Advisor: Rafael A. Nieves-Castro, PharmD.
Manufacturing Engineer Department

Abstract

Distributions Centers for pharmaceutical products have experienced significant changes in recent years in terms of the cold chain, adapting to new social, economic, and technological structures. The main objective of this process is to maintain a constant cold temperature of refrigerated pharmaceutical products, which requires maintaining a refrigeration specification of 2°C to 8°C. This article aims to use DMAIC tools to help us ensure that deliveries from more distant routes to different customers consistently meet the required temperatures from their departure from the distribution center to delivery to the customer.

Key Terms — *Cold Chain System, Distribution Centers, DMAIC Method, Pharmaceutical Products*.

Problem Statement

The distribution center in Caguas plays a crucial role in supplying medications, vaccines, and pharmaceutical products to clinics, hospitals, and pharmacies throughout Puerto Rico. Maintaining the quality and stability of pharmaceutical products is essential to ensure their effectiveness in prescribed treatments. One critical specification in this process is keeping the cold chain, which requires a constant temperature between 2°C and 8°C from preparation to delivery to the customer. This requirement is necessary to preserve the stability of the product and guarantee the effectiveness of the medicine, ensuring patient safety, minimizing financial losses, and establishing documentary evidence that provides a high level of security during the distribution process. The center servers distant areas such as Aguada, Sabana Grande, and Rincon, and failure to comply with these specifications can put the integrity of the pharmaceutical product at risk.

Methodology

The execution of the Cold Chain Qualification in the logistics of pharmaceutical products was carried out using the DMAIC methodology. This methodology is part of the Six Sigma tools that contribute to the best performance and success of the projects. The abbreviation of DMAIC reflects the five fundamental phases of the methodology: define, measure, analyze, improve, and control.
In Table 1, we can learn a brief definition of the five phases of the DMAIC methodology.

Table 1: DMAIC Methodology		Timeline
DEFINE	Define the process and establish goal	November 2023
MEASURE	Measure to determine process needs	December 2023
ANALYZE	Analyze the data to find the best design	January 2024
IMPROVE	This stage indicates the actions necessary to improve the process, i.e., an improvement plan.	February 2024
CONTROL	After the improvement has been made, measurements should continue to ensure that the improvement has permanently helped solve the problem.	March 2024

Figure 1: DMAIC Methodology

Results and Discussion

DEFINE PHASE

In this section, a chapter of the project was developed to detail the status of the objectives, scope, challenges, schedule, interested parties, and key aspects that facilitate the monitoring and control of the project improvement process. This ensures that each strategy and objective is aligned with the company's expectations at meets regulatory requirements, thus ensuring product quality and stability. Refer to Figure 2 Project Chapter.

Figure 2. Project Charter	
Project Statement	The distribution center in Caguas plays a crucial role in supplying medications, vaccines, and pharmaceutical products to clinics, hospitals, and pharmacies throughout Puerto Rico. Maintaining the quality and stability of pharmaceutical products is essential to ensure their effectiveness in prescribed treatments. One critical specification in this process is maintaining the cold chain, which requires a constant temperature between 2°C and 8°C from preparation to delivery to the customer. This requirement is necessary to preserve the stability of the product and guarantee the effectiveness of the medicine, ensuring patient safety, minimizing financial losses, and establishing documentary evidence that provides a high level of security during the distribution process. The center servers distant areas such as Aguada, Sabana Grande, and Rincon, and failure to comply with these specifications can put the integrity of the pharmaceutical product at risk
Business Case	The main objective is to use a DMAIC tool that helps us ensure that deliveries consistently comply with the established parameters, maintaining the temperature range of 2°C to 8°C from the distribution process
Project Goal	The goal is to guarantee that the distribution route system for pharmaceutical products within the distribution center in Caguas meets the specific temperature range of 2°C to 8°C for refrigeration on the most distant routes(Aguada, Sabana Grande and Rincon).
Team Member	**Coordinator**
	Quality Representative.
	Project Manager

MEASURE PHASE

In the measurement phases, the impact of the refrigerated product distribution system on the farthest routes, such as Aguada, Sabana Grande, and Ricon, will be evaluated concerning customer delivery, aiming to determine if it stays within the specified temperature range of 2°C to 8°C throughout the distribution process.

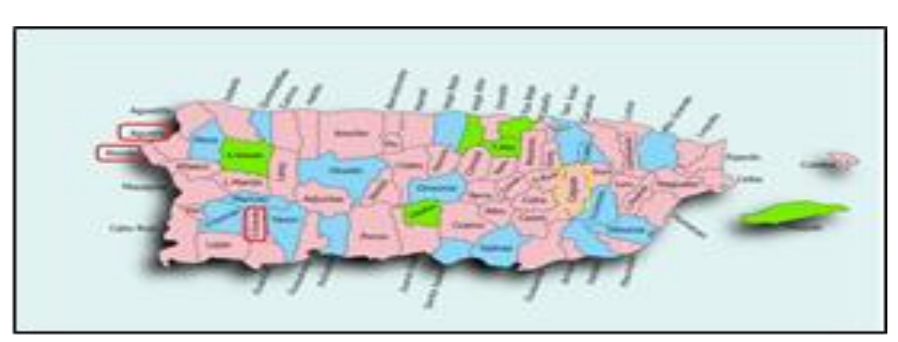

Figure 3: Map of Puerto Rico with the Farthest Routes.

Caguas to the Destination		
Routes	Approximate Distance	Approximate Time
Sabana Grande	81 miles	2 hours
Rincon	102 miles	3 hours
Aguada	115 miles	3.5 hours

Table 2: Distant of the Routes

Number Route	Routes	Approximate Time	Number Route	Routes	Approximate Time
1	Aguada-Rincón	2.5 hours	31	Morovis	1 hour
2	Moca- Añasco	2 hours	32	Corozal	50 minutes
3	Mayagüez A	1.55 hours	33	Barranquitas A1	1 hours
4	Mayagüez B		34	Naranjito-Toa Alta	51 minutes
5	San Sebastián	1.50 hours	35	Toa Alta-Toa Baja	51 minutes
6	San Sebastián-Moca	1.57 hours	36	Dorado-Toa Baja	40 minutes
7	Moca	2.03 hours	37	Toa Baja 1	40 minutes
8	Aguadilla A	2.01 hours	38	Carolina A2	40 minutes
9	Aguadilla B	2.01 hours	39	Bayamón-Catano	28 minutes
10	Cabo Rojo-Hormigueros	1.54 hours	40	Bayamón B	32 minutes
11	Hormigueros-San German	1.45 hours	41	Bayamón A	32 minutes
12	Guánica-Lajas	1.29 hours	42	Guaynabo-Bayamón	25 minutes
13	Adjuntas-Jayuya	1.25 hours	43	Area Metro C	30 minutes
14	Utuado-Lares A1		44	Area Metro A	30 minutes
15	Isabela	1.42 hours	45	Guaynabo- Puerto Nuevo	22 minutes
16	Lares	1.34 hours	46	Santurce	23 minutes
17	Camuy-Quebradillas	1.19 hours	47	Guaynabo A2	22 minutes
18	Hatillo	1.16 hours	48	Guaynabo Pueblo	22 minutes
19	San German-Sabana Grande	1.39 hours	49	Santurce	
20	Yauco-Guayanilla	1hr 22 min	50	Hato Rey-Rio Piedras	25 minutes
21	Ponce A1	1.05 hours	51	Hospital Metro	30 minutes
22	Ponce A2	1.05 hours	52	Trujillo Alto	28 minutes

Number Route	Routes	Approximate Time	Number Route	Routes	Approximate Time
23	Penuelas-Guayanilla	1.19 hours	53	Caguas	15 minutes
24	Arecibo-Hatillo	1.17 hours	54	Carolina-A	40 minutes
25	Arecibo	1.20 hours	55	Carolina-B	40 minutes
26	Florida-Barceloneta	1.10 hours	56	Carolina-C	40 minutes
27	Manati-Vega Baja	48 minutes	57	Guayama	49 minutes
28	Manati- Vega Baja A	59 minutes	58	Villalba-Juana Diaz	1.08 hours
29	Vega Alta-Vega Baja	43 minutes	59	Coamo-Santa Isabel	59 minutes
30	Orocovis-Morovis C	1.21 hours	60	Juana Diaz-Villalba	58 minutes

Table 3: List of the Routes

ANALYZE PHASE

During the analysis phase of the DMAIC cycle, the Ishikawa diagram, also known as the cause-and-effect or fishbone diagram, was developed to break down the possible causes of the identified problem in Figure 4 Ishikawa Diagram. This diagram allowed for the systematic organization of different categories of influences that could affect the maintenance of the specified temperature range of 2 to 8 degrees Celsius in the distribution routes farthest from refrigerated products, such as Aguada, Sabana Grande, and Rincon, which were measured in the measurement phase. By subdividing these categories into specific sub-causes, such as the distribution process, refrigeration equipment, weather conditions, product handling, and vehicle maintenance, we were able to identify a wide range of potential contributing factors to the problem.

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Figure 4: Fishbone Diagram

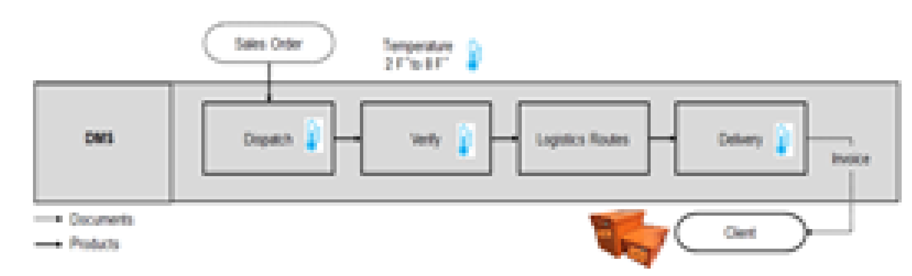

Figure 5: Distribution Process

Refrigeration Equipment

Expandable Polystyrene (EPS): The English acronym for "Expandable Polystryrene" translated into Spanish as "Poliestireno Expandido", refers to a foamed plastic material derived from polystyrene and shaped into packaging. It allows for storing materials at high/low temperatures, thereby maintaining a temperature range for a specified period.

Figure 6: **Expandable Polystyrene**

Foam Brick: Design that provides reliable protection and maintains temperature for a wide variety of products and/or packages. It has a block of frozen foam, and its packaging is similar to that of an ice pack. According to the qualification, these require meeting a precondition of 72 hours of freezing in temperatures between -25°C and – 15°C (-13°F and 5°F) before being used.

Figure 7: Foam Brick FPP64

Shipping system that maintains the temperature required by Manufacturers to transit refrigerated merchandise (36-46°F/ 2-8°C). This consists of a plastic bag assembled with an EPS container and configured with the corresponding quantity/size of foam bricks.

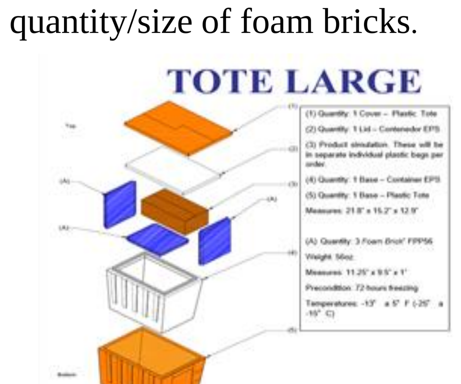

Figure 8:**Totes for Shipping**

Figure 9:Shipping System Configuration

IMPROVE PHASE

During the Improvement stage, the calibrated TRED30-16R or TRED30-7R data logger, a temperature measurement device designed specifically for refrigerated products, was incorporated into the shipping System configuration process.

Figure 10:Shipping System Configuration

CONTROL PHASE

During the Control phase of the DMAIC cycle, a validation protocol was developed to guarantee the quality, temperature, and safety of refrigerated products throughout the distribution chain to customers. This protocol includes clear guidelines on responsibilities, storage, transportation, and handling of products, as well as specific measures to monitor and record temperature conditions in real-time and address deviations that may arise. As part of the continuous improvement of the control phase, an annual verification of the protocol must be carried out to guarantee that the products are maintained at the temperature when distributed to customers.

Conclusions

We can conclude that the Qualification of the Cold Chain System in Drug Logistics, using the DMAIC tool, has satisfactorily demonstrated compliance with the temperature parameters of 2°C to 8°C for refrigerated products. Through a rigorous planning, implementation, and monitoring process, it has been shown that products remain within the temperature ranges of 2°C to 8°C, even on the most distant routes such as Aguada, Sabana Grande, and Rincon. This shows that, regardless of the distance of the routes, the product maintains its temperature throughout the distribution chain until it reaches the customer.

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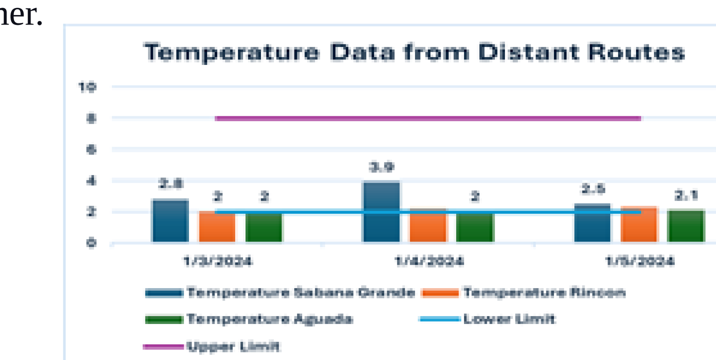

Figure 11: Temperature Data from Distant Routes

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References

[1] Blessington, M. (2015). *Sales Quota Accuracy and Forecasting*. Corpdyn.com. Available: https://corpdyn.com/wp-content/uploads/2020/01/Blessington-Quotas.pdf.

[2] Chung, D., et al. (2010). *Do Bonuses Enhance Sales Productivity? A Dynamic Structural Analysis of Bonus-Based Compensation Plans.* SSRN Electronic Journal. Available: https://doi.org/10.2139/ssrn.1491283

[3] Darmon, R. (1997). *Selecting Appropriate Sales Quota Plan Structures and Quota Setting Procedures.* Available: https://www.researchgate.net/profile/Rene-Darmon/publication/261624469_Selecting_Appropriate_Sales_Quota_Plan_Structures_and_Quota-Setting_Procedures/links/5505b0ad0cf24cee3a05058d/Selecting-Appropriate-Sales-Quota-Plan-Structures-and-Quota-Setting-Procedures.pdf.

[4] Eden, D. (1988). *Pygmalion, Goal Setting, and Expectancy: Compatible Ways to Boost Productivity.* Academy Of Management Review, 13(4), 639-652. Available: https://doi.org/10.5465/amr.1988.4307530

[5] Mason, W., et al. (2010). *Financial incentives and the "performance of crowds"*. ACM SIGKDD Explorations Newsletter, 11(2), 100-108. Available: https://doi.org/10.1145/1809400.1809422.

[6] AccuWeather. (2024). *Caguas, PR: January Weather* [Online]. Available: https://www.accuweather.com/es/pr/ caguas/00727/january-weather/272603.