STATISTICAL SAMPLING PLAN ALTERNATIVES FOR SEAL STRENGTH TESTING ON PRE-SEALED TYVEK® BAGS

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Abstract

Seal strength is an important quality characteristic of sterile barrier systems used for Pharmaceutical and Medical Device Packaging operations, and subject to strict quality control industry wide. This study evaluated the feasibility of sampling plans alternatives, specific for testing of Tyvek pouches, with focus on reducing cost with minimum impact on risks. Previous studies, data analysis and results obtained showed minimum influence by variables such as suppliers, and product characteristics, , providing valuable information and the framework to support cost effective process improvements.

Background

A Sterile barrier system is the package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use [3]. Due to its criticality, many organizations may have practices that follow recognized industry standards/test methods such as the ones the American Society for Testing and Materials (ASTM) has developed throughout time, to ensure material performs at certain levels.

ASTM F88 for example, uses a defined approach to testing with purpose of measuring resistance during seal separation. This test is particularly applicable to peelable medical package seals. Different techniques were developed following the result of protocols that were designed using different material combinations, to identify the effects of variations in the use of the methods [2]. ASTM studies also demonstrated that even with differences in the end result when moving from one technique to the other, the result differs by less than 0.1 lbs/in, when comparing data using a sample size n=10 versus a sample size n=30 [2].

Information is available around the development of guidelines to establish minimum seal strength limits [4] and how to conduct testing [2]. Additionally, previous studies have shown that comparison of sample sizes n=10 versus n=30 may not show large differences in either reduction or increase in variation [2]. Based on this information, the possibility of alternative sampling plan options would be of further evaluation, given the fact that a reduction in samples may not be a factor that increases risk.

Figure 1 Product and Packaging Illustration

Problem

The project aimed to evaluate alternative sampling plans for seal strength testing, taking into consideration the historical product performance, cost, resources, risk, among other elements. The focus is to achieve the following:

1. Evaluate alternative sample plan seal strength testing with focus on reducing cost without impact on sampling risks
2. Increase efficiency in the area

Implementation of alternative sampling plans compliant to regulatory requirements, will have an impact on cost, capacity, and efficiency. Project may also be extended to any of the 80+ other facilities within Becton Dickinson company. Experiment could be applied to other products with similar performance.

Methodology

The project was developed by following the DMAIC (Define-Measure-Analyze-Improve- Control) methodology, which allows study and analysis of a problem, as well as a robust approach for the identification of possible solutions.

The first step was the collection of data, which was traced back to receipts from 82 supplier lots over a period of four (4) months. A comparison of the characteristics within the family of sterile barrier pouches was conducted and common characteristics were discarded as potential sources of variation. On the other hand, differences were further investigated to understand its contribution to the end result.

Requirements	Characteristics	Common	Different
General	Inspection Procedures	✓	
	Sampling Plan	✓	
	FMEA	✓	
Physical Requirements	Dimensions (L x W)		✓
	Material Types		✓
	Seal Width		✓
	Measuring point (6 sides)		
Functional Requirements	Testing technique	✓	✓

Table 1: Characterization of Pouches

Additionally, the differences in dimensions, material types and seal width were also discarded. Decision was made due the absence of evidence in previous studies (conducted prior to the development of ASTM F88) to establish that these characteristics were a definitive cause for a difference in the resulting value [2]. However, previous ASTM studies discovered that resulting seal strength value may vary depending on the testing technique used [2]. Therefore, testing techniques and characteristics associated to them were further evaluated.

Results and Discussion

Statistical analysis (Two (2) sample T-test) confirmed results from previous ASTM studies on the differences between testing techniques (e.g., A vs C) [2]. The test result failed to reject Null hypothesis (Ho: $\mu 1 - \mu 2 = 0$), confirming that resulting values using Technique C are greater than the ones obtained when using Technique A.

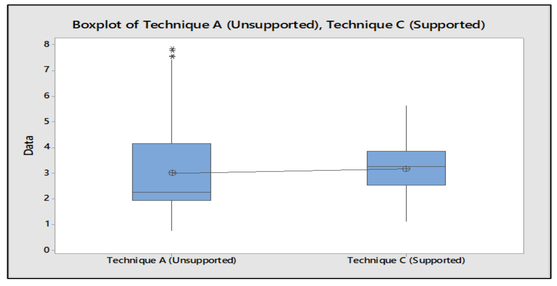

Figure 2 Two (2) sample T-test

Results and Discussion

Additional evaluation showed differences in the average for some of the measuring points (sides) in the perimeter inside both groups (Technique C – Supported) and Techniques A – Unsupported). After running an ANOVA experiment, differences were confirmed to be statistically significant.

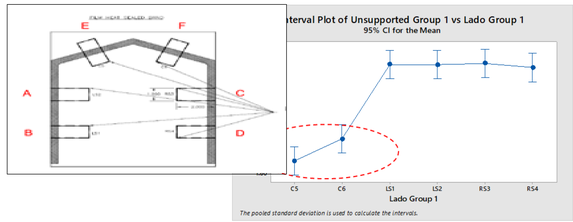

Figure 3 – ANOVA results

Although, differences in the mean value for these measuring points (sides) was considered as statistically significant, in reality the values were located at a healthy distance from the minimum specification limits (e.g., 0.75 LB/IN, 1.25 LB/IN). Capability Analysis studies were conducted, and results showed Cpk > 1.29 in all cases, suggesting results were robust enough within specification limits and located above 2.0 LB/IN.

These results led to the conclusion that any sampling capable of detecting values approaching the lower specification limits would be acceptable, if minimum risk was introduced into the process. To address the problem, different sampling alternatives were presented, considering the following:

Option #1: Allow for selection of a single measuring point from each side (e.g., A or B, C or D, E or F). This approach reduces the quantity of measuring points subject to testing by 50%. No additional risk is expected with this alternative since sampling plan (AQL = 0.65 / C=0) remained the same.

Option #2: Allow for a sampling plan of 50 units. Using OC Curves, data showed that comparison between the new sampling plan (50 samples) and the most common scenario (68 samples), increases the probability of acceptance for the supplier (Producer Risk) by 8% while Lot Tolerance Percent Defective increases by only 1% (from 3.4 to 4.4.) remaining below the 10% Lot Tolerance Percent Defective mark.

Option #3: Combination of Options #1 and #2.

Compare User Defined Plan(s)

Sample Size(n)	Acceptance Number(c)	Percent Defective	Probability Accepting	Probability Rejecting	AOQ	ATI
20	0	0.65	0.878	0.122	0.570	4297.3
30	0	0.65	0.822	0.178	0.534	6243.8
40	0	0.65	0.770	0.230	0.500	8066.9
50	0	0.65	0.722	0.278	0.468	9774.4
60	0	0.65	0.676	0.324	0.439	11373.7
68	0	0.65	0.642	0.358	0.416	12579.8
77	0	0.65	0.605	0.395	0.393	13863.3
96	0	0.65	0.535	0.465	0.347	16336.6

Figure 4 OC Curves

Conclusions

It can be stated that the objectives and main purpose of the project were achieved. Alternative sampling plans for seal strength testing were proposed, taking into consideration the product performance, cost, resources, operational efficiency, and compliance requirements.

Controls will ensure the achievement of the goal of improving efficiencies, leading to an estimated annual savings of $11.2k including materials and labor as expected (Refer to Table 2). Additionally, it will improve yield in the area and may also have an impact on capacity depending on the usage of allocated resources.

Alternatives	Option #1	Option #2	Option #3
Financials (Estimated impact on cost per year considering projected volume of receipts is ~250 lots/yr.)	$4.8k aprox ($96,000 MX)	$6.4k aprox ($128, 000 MX)	$11.2k aprox ($224, 000 MX)

Table 2: Impact on Cost/Saving

Future Work

The implementation of the project provides additional opportunities to extend actions to other products in the manufacturing plant or even in other facilities. Further experimentation can be made for evaluation of the following:

1- Implementation of sampling plans by variables using ANSI/ASQ Z1.9 [11]
2- Evaluation of material types as a factor for variability Management is looking forward to this since it can provide additional savings for higher cost products.

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Acknowledgements

This project was completed thanks to the support and effort of the IQC team at Becton Dickinson Nogales, MX. Also, thanks to the mentorship provided by Ivan M. Aviles, Ph. D, PE.

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