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Implementation and Effectiveness of Six Sigma by Using Dmaic Approach in Pharmaceutical Industry

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----------ABSTRACT----------
six sigma is a *systematic* approach which follows five basic steps i.e. dmaic (define, measure, analysis, improve & control). all steps are encumbered multiple tools of problem solving, root cause identification and process improving and controlling. the problem of yield loss is also being solved through six sigma methodology. Initially the study is focused on defining the problem, following the process flow, drawing the project boundary in between the process flow to focus on real problem, identification and measurement of the variables which influence the yield. Identified factors are then analyzed to hunt potential causes. Significant improvement in the cause identified resulted in improved sigma level and equipment efficiency, finally the control is built keeping in view the failure mode effective analysis results for standardizing and sustaining the improvement for longer period of time through control charts and fool proof systems. the purpose of this deep dive is to investigate and identify the major potential causes which results in low profit and turnover due to low yield products in a pharmaceutical company. Manufacturing process is a major area of profit generation of pharmaceuticals and play a vital role in achieving the market share. continuous decline of its profit due to yield losses made itself a great challenge. it is identified that on an average there is 1.40% yield loss in every batch. therefore, it is necessary to stop the interruption in the production schedule and at the same time resolve the problem with suitable effective and long-term viable solution. however, six sigma methodologies are applied to resolve the complex level of problems and to have optimum and effective solution to continue smooth flow of production and to reduce the wastages.

KEYWORDS: *Six Sigma, DMAIC, Pharmaceuticals*

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I. INTRODUCTION

Six Sigma is an information driven complication resolving system resulting in reduced occurrence of errors. The attention is on procedure varieties and preference is given to consumer gratification. Continuous procedure betterment with lesser faults is the objective of this strategy. The point of Six Sigma is to make a procedure - 99.99996 % deformity free. This implies a six-sigma process delivering 3.4 defect per million prospects or fewer accordingly. Six Sigma methodology is used for identification, classification and relevancy of the problem for problem resolving. There are five phases in this system

Key Concepts of Six Sigma :

- At Its Center, Six Sigma Rotates Around A Couple Of Vital Ideas.
- Critical To Quality − Attributes Most Vital To The Client.
- Defect − Failing To Convey What The Client Needs.
- Process Capability − What Your Procedure Can Convey.
- Variation − What The Client Sees And Feels.
- Stable Operations − Ensuring Steady, Reliable Procedures To Expand What The Client Sees And Feels.
- Design For Six Sigma − Designing To Address Client Issues And Procedure Ability.

Six Sigma Has Developed With Time As A Systematic Approach Of Dmaic (Define, Measure, Analyze, Improve & Control) To Solve The Complex Problems. Define Step Consists Of Process Mapping, Process Boundary, Swim Flow Diagram, SIPOC, CTQ Analysis And Project Charter Measure Step Consists Of Cause

Effect Diagram, Cause Effect Matrix, Pareto Analysis, Data Collection Method, Graphical Summary, Process Capability And MSA. Analyze Step Consists Of Correlation Analysis, Hypothesis Test, One Sample T-Test, Linear Regression And Residual Plot. Improve Step Consists Of Multi Regression, Design Of Experiment, Improvement And Economic Value. Control Step Consists Of Failure Mode Effect Analysis, Poka Yoke (Foolproof System), Statistical Process Control (Control Charts), Control Plan And Standard Operation Producer. These Type Of Tools & Technique Has Been Used To Solve The Problem And Get Required Business Benefits It's Something Other Than What's Expected Than A Quality Structure Like TQM Or Iso. It's A Framework For Working Of Associations. As Geoff Tennant Delineates In His Book Six Sigma: Spc And TQM In Manufacturing And Services: "Six Sigma Is Various Things, And It Is More Straightforward To List Every One Of The Things That Six Sigma Quality Isn't. Six Sigma Can Be Seen As: A Thought; A Rationale; A Strategy; A Portrayal; A Goal; A Procedure."

Existing Work In Pharmaceutical Companies: The Pharmaceutical Business Is The Most Controlled Organization As Compared To Another Industry. Regulated Authorities' Experts Are Vital Players In The Delivery Enhancement, Advancement And As Correspondence Connection Between The Business And Regularities, For Example, Fda. To Decrease The Number Of Deformities From Items In Pharmaceutical Enterprises, The Six Sigma Strategies Are Utilized. The Six Sigma Technique Is At First Dependent On An Information Driven, Orderly Way To Deal With Critical Thinking, With An Attention On Client Affect. Measurable Instruments Are As Often As Possible Utilized In The Process Investigation. Furthermore, Six Sigma Distinguishes A Few Key Jobs To Workers For Its Effective Execution. Six Sigma Is Turning Into An Establishment Stone Thought Among The World's Driving Enterprises Since It Has Substantiated Itself By Producing Huge Business Return. It Is Just Fitting To The End That "We Accepted, And We Are Persuaded Today That There Is An Interminable Chance To Enhance Everything" Except There Was No Other System Or Instrument Appended To That Conviction. There Is Currently, Six Sigma Characteristics, Alongside A Rationality Of Picking Up, Sharing And Ceaseless Enthusiasm That Causes Pharmaceutical Organizations To Make Strides. (Sharma, Gupta Et Al. 2011).

II. EXPECTED CONTRIBUTION/ BENEFITS

For the Evaluation and Determination of The Optimum Number of The Servers, It Is Necessary to Consider the Two Opposing Costs I.E. Yield Loss & Service for Making the Decision for Optimum the System Cost. Therefore, These Two Types of The Costs Are Incorporated in The Study as Mentioned Below;

MATERIAL COST: The Cost That Is Paid By The Interim Of Material Loss That Not Converted In Units And Shows Impact As Yield Loss.

Service Cost: Yield Loss Investigation Cost, Overtime Cost, Utilities Cost. Economic Analysis Of The Cost Will Assist The Pharmaceuticals To Line Up The Balance Between The Yield Loss & The Service Cost That Is Increase Of Operation Time / Uptime Of The Equipment And Decreasing The Servicing Cost Of Operation & Engineering Team Like Extra Time Working / Overtime.

Aim of This paper: Aim of This Study Is to Improve Product Quality, Robustness and Efficiency of Pharmaceuticals Companies That Are Struggling to Survive Due to High Regularity Compliances Using Six Sigma. This Methodology Identify Specific Problem That Are Controlled After Thorough Measurement and Analysis. As A Result, The Chance of Error Are Greatly Reduce with Improve Efficiency.

III. METHODS AND MATERIALS

OBJECTIVE

To Identify Factors Influencing Yield of Pharma Products.
To Analysis the Impact of Yield on Profit and Timely Delivery.
To Implement Six Sigma Approach to Improve the Yield & Efficiency.

Existing Method & Tools: Six Sigma Professionals' Do Not Always Follow Exactly Which Tools Establish the Set. Some of Major Statistical and Graphical Tools Commonly Used in Improvement Projects Are Listed Below. DMAIC Approach Will Be Used. A Basic Six Sigma Approach Is Used DMAIC Process Roadmap for

Improvement. Roadmap Covers the Steps Define-Measure-Analyze-Improve-Control and Is to Be Followed for The Implementation of Six Sigma Process Improvement Plans; Beside It Depends How It Can Be Executed By Individuals, Following Tool Will Used During Study, Process Mapping

Process Boundary Swim Flow	SIPOC CTQ Analysis	Project Chatter
Cause Effect Diagram	Cause Effect Matrix	
Pareto Analysis	Data Collection Method	
Graphically Summary	Process Capability	
Msa Correlation Analysis	Hypothesis Test	
One Sample T-Test	Liner Regression	
Residual Plot	Multi Regression	
Design Of Experiment	Improvement And Economic Value Failure Mode Effect Analysis (	
Poka Yoke (Foolproof System)	Statistical Process Control (Control Charts)	
Control Plan	Standard Operation Producer	

IV. METHODOLOGY

Data Will Be Collected from Pharma Company Using Check Sheets, Data Collection Sheet. Log Sheets. Six Sigma Methodology Have A Controlling Toolbox That's Is Full of Various Charts, Methods, Diagrams, Tables for Conducting Six Sigma (Continuous Improvement) Study. During Study Must Select Right for Right Job as Per Your Data for Successful Results. At Its Core, Six Sigma Contains Comprehensive Statistical Tools and Statistical Analysis to Enable Quality Gains. Mainly Focus on Primary Statistical Tools Along with Some Project Management Tools and Their Effective Use In A Six Sigma Project. Statistical Tools Are Used for Statistical Analysis and Used During All the Research Phases - Define, Measure, Analyze, Improve, And Control (Dmaic).

Analysis: Six Sigma Methodology Have A Controlling Toolbox That's Is Full of Various Charts, Methods, Diagrams, Tables for Conducting Six Sigma (Continuous Improvement) Study. Six Sigma Contains Comprehensive Statistical Tools and Statistical Analysis to Enable the Gains

Tools/ Software: Mintab Is A Software Product That Helps You to Analyze the Data. This Is Designed Basically for the Six Sigma Professionals. Minitab Is A Tool Which You Need to Analyze Data and Drive Meaningful Solutions to Your Toughest and Business Problems. Minitab Have Convenient Features That Stream Line Your Workflow, Detail Set of Statistics for Exploring Your Data and Graph for Share Your Story. Minitab Have Comprehensive Method of Analysis Like Basics Statics, Regression of Anova, Quality Tools, Design of Experiment, Control Charts, Measurement System Analysis and Reliability. Minitab Have Smart Data Import That Easily Identify the Mismatch, Properly Identify the Missing Data and Make No Impact of Colum Length During Importing Data from Excel To Mintab. Along with This It Also Has Good Option of Automatic Graph Updating and Make Ready for Smart Presentation.

V. DATA COLLECTION AND ANALYSIS

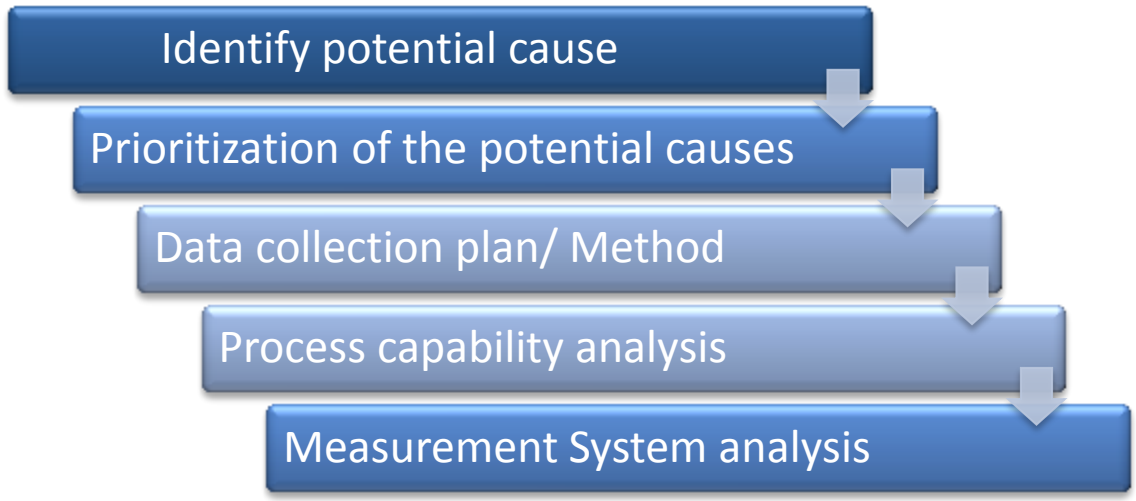
Data Collection Step Is Consisting Of Two Steps Data Collection Plan And Data Collection Sheet.

Data Collection Plan: Three Personals Assigned for Data Collection In 10.5 Hours Shifts Because Equipment Run 6days In A Week and Following Is Data Collection Plan Has Been Developed To Identify The Real Data

Of Identified Potential Cause. In Data Collection Plan Clearly Visible That What to Measure, How To Measure, Who Will Measure, And Sample Plan Was Clearly Define
In What to Measure

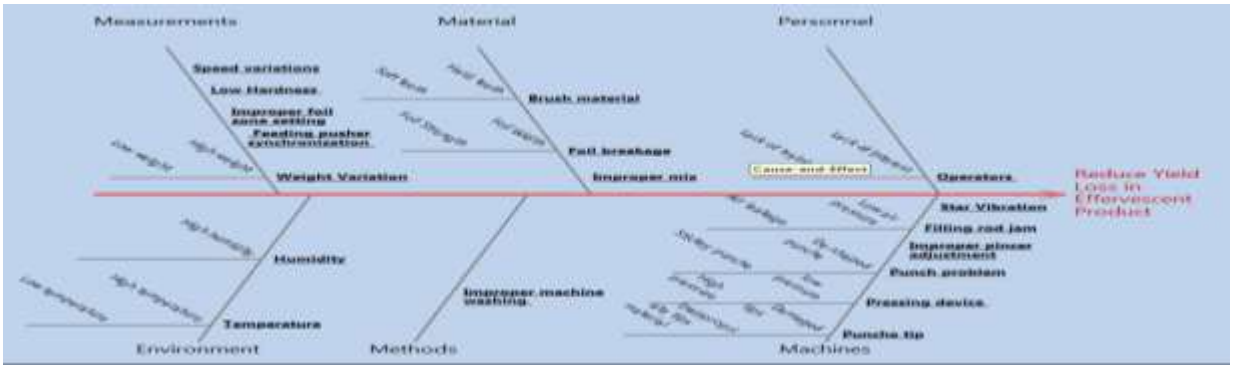
Data Analysis: Data Analysis Has Been Done Using Dmaic Process in Which Data Is Refined at Every Step and There Is Establishment of The Actual Potential Cause. In Define Step First the Flow of The Product Is Identified and In the Second Step Selection of The Project Boundary Is Done Where the Problem Is Happening. Further Sipoc Diagram Has Been Used To Understand The Supplier Of Our Product, What To Supply For The Mentioned Product, What Are The Starting And Ending Points Of The Process Associated With The Problem And The Major Steps In The Process, What Product Or Service Does The Process Deliver To The Customer, Who Are The Customers For Our Product Or Service And What Are Their Requirements For Performance.
In the Final Step the Critical to Quality Tree Explains the Criticalness Of The Problem Which May Impact on Yield. This Tree Is Developed by Taking Interviews from Machine Operators, Quality Inspectors, Line Supervisors and Officers. Whereas, Different X (Independent Variables) Are Identified By Critical To Quality (Ctq) Analysis.

In Measure Phase, The Initial Goal Is to Get As Much Information Of Process As Possible So That Both The Depth Of The Process Activities And Its Efficiency Are Fully Understood. The Identified Problems Are Measured by Following Steps;



Identification Of The Potential Cause Consists Of Fish Bone Analysis That Has Been Identified In SIPOC And CTQ Analysis And Have Been Mapped Out On Man, Machine, Material, Method, Mother Nature & Measurements. Cause & Effect Diagram (Fishbone Analysis).

Fig 4-6: Cause & Effects Diagram



Next Step Will Be Prioritizing the Potential Cause Through Cause and Effect Analysis Initially, All Causes Are Prioritized by Using Cause and Effect Matrix. After Discussion with Cross Functional Team the Causes Are Rated Accordingly. On Basis of Cause & Effect Rating Pareto Analysis Is Used to Prioritize Potential Cause Because It Is Difficult to Measure All Causes. Therefore, It Is Necessary to Identify few Vital Potential Causes So It Can Be Easily Measured and Potential Variables Will Be Identified by Pareto Analysis.

Pareto Analysis : As Per 80:20 Rule Of Pareto Analysis Below Mentioned 8 Priorities Are Further Processed To Identify The Actual Cause

S No.	C&E Score
A	156
B	122
C	116
D	111
E	87
F	84
G	81
H	81

Table Shows The Top Cause 8 Cause Score As Per 80:20 Rule Of Pareto Analysis.

Analysis of Data Collection Result: Analysis Of The Collected Data Is Done Which May Be Normal Or Parametric Testing And Non-Normal Or Non-Parametric Testing. On Analysis of Above Data, It Has Been Identified That The Data Is Normal with The Following Results.

Mean	Standard Deviation	1st Quartile	3rd Quartile	Median
4929.8	9.3	4923.1	4937.8	4931.2

Capability Analysis: Process Capability Analysis of Yield Shows That the Ppk Value Is -0.73 Which Is Lower Than 1. Hence It Indicates Poor Process and It's Not Capable to Produce Targeted Yield.

Analysis Phase Is the Foundation of Statistical Analysis Of The Problem. It Statistically Evaluates the Group Of Variations To Determine The Significant Impacts On Output And Improve Process Capability.

Independent Variables	P-Value	R-Value	Result
A	0.000	-0.609	**Strong Relation**
B	0.000	-0.929	Extremely Strong
C	0.000	-0.965	Extremely Strong
D	0.440	-0.160	Weak Relationship
E	0.037	-0.382	Weak Relationship
F	0.080	0.325	Weak Relationship
G	0.000	-0.722	Strong Relationship
H	0.000	-0.722	Strong Relationship

Table Show Correlation Analysis Result In Which Out Of 8 3 Have Weak Relationship Yield Loss Problem.

Independent Variable	R-Square
A	37.0%
B	84.1%
C	91.8%
H	70.3%

Independent Variables	P-Value
A	0.000
B	0.000
C	0.000
H	0.000

Table Show Hypothesis Analysis Result In Which Out Of 8 3 Have Weak Relationship Yield Loss Problem

Design of Experiment (DOE)

Table Show Regression **Table 5.4 R-Square Values** In Which Out Of 4 3 Have Strong Relationship Yield Loss Problem

Doe: This Phase Is Driven by Optimum and Innovative Outcome, Where the Set of Possible Outcomes with Vital Solution Processed for The Implementation. However, The Major Result That Is Achieved from This Phase Is By Developing A Plan Which Creates A Difference in Current Process Output.

Three Predictors Are Filtered Out Through Multiple Linear Regression Models From Which 24 Experiments Are Designed By 3 Replicates. However, The Whole Study Identifies Two Significant Impacts Which Is B Adjustment and C Variation Which Impact Yield of An Effervescent Product. Doe Also Provided the Optimum Setting of The Parameters to Get A Maximum Yield Loss.

VI. RESULTS

From Result It Is Identified That B & C Causes Have Significant Impact.

VII. CONCLUSION

In This Study, Significant Cause Of Low Yield Was Identified. Number Of Units Were Lost Due To Yield Loss. Dmaic Methodology Is Applied To Reduce The Yield Loss. Data Of 30 Batches Is Collected And Thorough Analysis Of The Causes Has Helped Improved The Yield From 98.6% To 99.72% (Target 1% And Actual Produce 1.12%) 0.12% Additional From The Target And Process Capability Has Also Increased, Finally Standardizing And Sustaining The Improvement.

Factors	Before	After
Yield	98.6%	99.72%
Cp	0.89	3.98
Cpk	-0.72	2.20
Pp	0.90	4.29
Ppk	-0.73	2.37
Sigma Level	**3.60**	**4.20**

Economic Value of Targeted Savings and Actual Savings Are Follows. These Saving Are Calculated on Year-

Based Data. Below Result Represent A Good and Strong Process Capability After Getting Actual Predictor and Their Optimum Parameters Adjustments

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