SIX SIGMA AND PHARMACEUTICAL INDUSTRY

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Abstract

The Concept of Six Sigma begins with a process model and its implementation is called Business Process Management (BPM) and the process of Six Sigma began at Motorola in the 1980's. Six Sigma is the letter σ in the Greek alphabet used to denote Standard deviation, a statistical measurement of variation. Standard deviation can be thought of as a comparison between expected results or outcomes in a group of operations versus those that fail. Bill Smith of Motorola Coined the term Six Sigma and is also called the father of Six Sigma; The Quality leader responsible for the term Total Quality Management is Feigen Baum; robustness in quality management was pioneered by Dr Taguchi; quality leader who did extensive work in Japanese industry is Dr Deming who paved the way for Quality Management Concept; Walter She wart is also one of the contributors in Six Sigma, he is sometimes referred to as father of Statistical Control he introduced the concept of control charts in 1924. In 1920s, contributions by Walter Shewhart, who showed the relation of process corrections based on three sigma deviations from the mean and introduced the control chart and distinction of special versus common cause variation. With Six Sigma Standard deviation we arrive at 3.4 defects per million opportunities or 99.9997 percent this would mean that at six sigma, an airline would only loose three pieces of luggage for every one million passengers that it handles. The Three primary elements of Six Sigma are Customers, Processes & Employees. The Italian Sociologist Vilfredo Alfredo Pareto demonstrated the 80/20 rule which signifies that 80 percent of your outcomes come from 20 percent of your inputs. Pareto 's rule is widely used in Six Sigma principles.

Six Sigma is implemented in phases (DMAIC)-Define, Measure, Analyze, Improve and Control

Keyword: - DMAIC, KPI, Defects, Standard Deviation, Bill Smith

I. Introduction

In this article the application of Six Sigma in pharmaceutical industry is briefly given, the brief objective is that to reduce the defects in the production process of medicine making and thereby improve the savings of the organization concerned and process improvement. The article gives the use of Minitab a statistical software to do analysis on data which can be collected from the organization as well as the use of KPI's formulas (Key Performance Indicators) which can increase the level of efficiency at which the organization operates.

1.2 Objectives of Applying Six Sigma: ·

- ➢ Reducing defects ·
- ➢ Controlling variation and improving predictability
- ➢ Reducing costs – without "unintended consequences"
- ➢ Improving end-to-end process management and measurement
- ➢ To increase customer satisfaction
- ➢ To enhance competitiveness
- ➢ To change organizational culture·
- ➢ To make advancements toward formal quality award application
- ➢ To develop organizational competencies
- ➢ To improve organizational performance

1.3 Six Sigma and the Pharmaceutical Industry

Drug discovery and development is very expensive. Of the thousands of compounds investigated for use in humans, very few are ever approved. Drugs very often fail during the development stage and thus do not return any revenue for the company. Including the costs of failures, developing a new drug to market is estimated to cost US $1.5 Billion and continues to grow (Gassmann et al. 2008). The time from drug discovery to approval can take up to 15 years. Because of the huge cost of bringing a drug to market, companies apply for a patent for their drugs giving exclusivity rights typically in the range of 20 years. This patent protection is expected to enable the owner of the patent to recover the costs of research and development through high profit margins. However, when a patent on a protected drug expires, a generic drug is usually already developed and prepared for immediate sale by a competitor. The pharmaceutical industry has traditionally not been too concerned with being efficient perhaps due to the large profit margins. In recent years the industry has been focused on expanding R&D capabilities via an open innovation strategy as a means to capture as much innovation as possible to drive new opportunities. . As many companies' patents begin to expire, as drug research pipelines weaken, fewer companies are seeing products move from the clinical to the marketing stage. Thus, pharmaceutical companies have to look inward, to strengthen processes and quality by design to become more efficient. Pharmaceutical companies need to find ways of reducing late-stage failures, safety withdrawals and recalls and at the same time find ways to intensify their efforts to remain market leaders after patents expire if they are to compete with the cheaper generic drugs. Pharmaceutical manufacturing techniques have not kept up with the advances in technology that most other industries have gone through in the last decade. The industry must now try to find ways of improvement while meeting product, customer, regulatory and efficiency demands. This has led to the need that most pharmaceutical companies have which is trying to reduce operational costs without affecting compliance. Their work includes looking at ways to increase the effectiveness of both their operational Six Sigma strategy applied to the pharmaceutical industry - how customer benefit and manufacturing processes by improving efficiency, optimizing resources, reducing waste and rejects and controlling inventory. The pharmaceutical industry is large and dynamic; however, as described above, it is not immune to the need for change. Proven management strategy from other industries perhaps offers the best solution but it will require committed leadership if is to be successfully implemented. Six Sigma has been used by some of the world's most successful companies leading to savings of billions of dollars, striking increases in speed and capacity and achieving better customer relationships. Six Sigma is a flexible system used to achieve, sustain and maximize business success. The focus of Six Sigma is to enhance customer satisfaction and reduce costs by using facts and statistical analysis to minimize the non-desirable variation in the business processes.

As mentioned with drug discovery, there are frequently failures during the developmental stages of a products lifecycle and only approximately 20% of the drugs in developmental stages are likely to survive the research steps that include the Pre-clinical and Phases I-III of the strict regulatory process (Charalambous and Gittins 2005).

The following key strategies are suggested to launch a Six Sigma effort within the pharmaceutical industry: · Begin to change the traditional ways of conducting clinical trials by campaigning for the implementation of needed integration initiatives through the use of Six Sigma with a commitment from top-down leadership. ·

Focus on the integration of technology and workflow improvement in meeting challenges and extend new ventures not possible using conventional isolated implementation of technology or homegrown process improvement methodologies. ·

Provide tested research approaches for the quantitative evaluation of clinical development and process improvement strategies, the integration of which highly correlates with strong financial performance.

In 2001, the top deficiencies incurred during FDA audits in clinical trials, include the following: ·

- ➢ Non-compliance with protocol, e.g.; inclusion /exclusion criteria not met mistakes on randomization, etc.
- ➢ failure to report non-concomitant medications
- ➢ failure to maintain drug accountability
- ➢ failure to obtain proper informed consent
- ➢ failure to maintain adequate data in the CRF

In Six Sigma first the project charter is prepared by the Master Black Belt where the Problems and their causes in manufacturing and the savings we forecast after doing this improvement project are mentioned; in pharma companies where lot of data is generated, we can use this data by entering it into the statistical software Minitab to find the fastest combination of chemicals which yield good results to the patients and isolate those chemicals which don't attribute to the growth.

Process Improvement can be done in pharma companies by drawing the process map and SIPOC; from which we can find the gaps in the production process, delays etc. and improvise on that.

Pareto chart analysis can be used to find out the major contributors of defects in manufacturing in the pharmaceutical company; pareto chart option is available in Minitab and with the data of a particular year we can do the analysis for that year.

We can use control charts in Minitab to find out the special causes of variation in the pharma manufacturing process and try to reduce them as far as possible. Special cause of variation can be due to an untrained person working in the shop floor or due to ear and tear of machine or measuring instrument. Common cause of variation is inherent in the process and cannot be completely eliminated.

Implementing six sigma in pharma companies requires training of their staff, involvement of the top management on six sigma plus data collection from each critical department; it can be from manufacturing up to marketing and sales. There are also various hypothesis tests which can be done to find out in which geography the sale of the product is more and which factors contribute to the sales.

The seven elements of six sigma scorecard are given below

- ➢ Leadership and profitability (LNP)
- ➢ Management and Improvement (MAI)
- ➢ Employees and innovation (EAI)
- ➢ Purchasing and Supplier management (PSM)
- ➢ Operational Execution (OPE)
- ➢ Sales and Distribution (SND)
- ➢ Service and growth (SAG)

Category	Objective	Areas of Measurement Metric
Leadership and Profitability (LNP)	Lead Company to wellness and Profitability	Communicati onInspiration Planning Accuracy Community Perception Employee Perception Employee Recognition Compensation Asset utilization Return on investmentDebt to Equity Ratio Profitability Shareholder 's ValueGrowth
Management and Improvement (MAI)	Drive Dramatic Improvemen t	Goal Setting Rate of Improvement Planning for Improvement

Category	Objective	Areas of Measurement Metric
Employees and Innovation (EAI)	Involve Employees Intellectually	Innovative Recommendations peremployee Investment per employeeNumber of patents or publications per employee
Purchasing and Supplier Management (PSM)	Reduce cost of goodsor services	Material AcceptanceTotal spent/sale Supplier Defect rates(Sigma) Cost of Goods/Services Sold
Operational Execution	Achieve Performance Excellence	Operational Cycle TimeProcess Defect Rate (Sigma) Customer Defects, TotalDefects
Sales and Distribution (SND)	Manager Customer relations and Generate revenue	Number of Inquiries, NewBusiness Dollars/Total Sales Profit margin ($)/Sales
Service and growth (SAG)	Gain Competitive advantage and grow	Customer satisfaction Customer retention Repeat business ($)/TotalSales New Product or servicespatents or trademark

1.4 Generic Key Performance Indicator formulas Given Below which can be used by any organization

Are measurements defined to show the state of the strategic goals or targets the organization has set for itself.

What is Metrics: Combination of two or more measures used to compare s/w processes, projects and products. Set of Metrics derived from data collected from past projects at the organization level. These baselines are used as a basis to arrive at project specific quality goals for KPI's.

Effort Variation

This metric is the difference between Estimated and Actual effort as compared against the Estimated Effort.

Objective: The objective of this metric is to study the distribution of workloadby Stage and to reduce the deviation of the actual effort expended as against the estimated effort.

When it should be measured: It should be measured at overall project level, Stage level and Task level (Process level and Sub process level for SDLC stages)

Input/Measure	Formula	Example
Actual Effort Estimated Effort	(Actual Effort - EstimatedEffort)/ (Estimated Effort) *100	Estimated Effort (in persondays) = 5 Actual Effort (in persondays) = 7 Effort Variation% = =(7-5)/5 * 100 = 40%

Schedule Variation

This metric is the ratio of difference between the Actual End Date and Planned End Date Vs difference between Planned End Date and Planned Start Date forthe project.

Objective: The objective of this metric is to reduce the schedule variation by tracking it from beginning stage of the project through the end of the project, thereby reducing time overruns. Schedule Variation metric is mainly used as an indicator for capability to meet milestones

Input/Measure	Formula	Example
Actual EndDate Actual StartDate Planned StartDate Planned EndDate	((Actual End Date – Actual StartDate) – (Planned End Date – Planned Start Date)) / (Planned End Date – PlannedStart Date) * 100	Planned Start Date - 1-Jan-13 Planned End Date -31-Jan-13 Actual Start Date - 2-Jan-13 Actual End Date - 1-Feb-13 Duration Variation % = ((31 –31)/ 31) *100 = 0 %

Work Efficiency Index

Load Work Efficiency Index is the ratio of percentage of work completed to percentage of effort expended.

Objective: This metric is particularly important and mandatory for fixed bid/fixed duration projects, and close monitoring is required to prevent effort overruns.

When it should be measured: It should be measured at overall project level.

Input/Measure	Formula	Example
Percentage of Work completed -(Actual Effort) / (Actual Effort +Effort required to complete remaining work) * 100 Percentage of effort expended - (Actual Effort/ Estimated Effort) *100	(Percentage of Work completed / Percentage of effort expended)	Estimated Effort (in person days) = 10 Actual Effort (in persondays) = 5 Effort Required to complete remaining work (in person days) =7 %Work Completed = (5/(5+7))*100 = 41.66% %Effort Expended = (5/10)*100 = 50% Work Efficiency Index = (41.66 / 50) = 0.83

When it should be measured: It should be measured at overall project level, Stage level and Task level (Process level and Sub process level for SDLC stages). Schedule variation need to be calculated only when the stage is completed.

Input/Measure	Formula	Example
Actual End DatePlanned Start Date Planned EndDate	((Actual End date – PlannedEnd date) / (Planned End date - PlannedStart date)) * 100	Planned Start Date = 1-Jan-13 Planned End Date = 31-Jan-13 Actual Start Date = 2-Jan-13 Actual End Date = 1-Feb-13 Schedule Variation % =(1 / 31) * 100 = 3.22%

Duration Variation

This metric is the difference between Total Planned Vs Actual duration for the project

Objective: The objective of this metric is same as schedule variation metrics i.e. to reduce the duration variation by tracking it from beginning stage of the project through the end of the project, thereby reducing time overruns. Why we may need both Duration Variation and Schedule Variation is that at times the task/stage may be finished within Planned Duration (Delayed start compensated with delayed finish to the same extent as days it started late.) whereas it might have exceeded the committed deadline, which is ultimately the schedule slippage.

When it should be measured: It should be measured at overall project level, Stage level and Task level (Process level and Sub process level for SDLC stages). Duration variation need to be calculated only when the stage is completed

Risk Identification Efficiency %

This metric determines the efficiency of identifying

risk in a project. This helps in planning for the mitigation and contingency to be carried out in a project. This metric is computed as Number of Risk identified to Number of Risk occurred, expressed as percentage figure.

When it should be measured: It should be measured at overall project level.

Input/Measure	Formula	Example
Total no of Risks Identified Total no of UnanticipatedRisk Occurred	(Total no of Risks Identified /(Total no of risks identified + Total no of Unanticipated Risk Occurred))*100	Total no of Risks Identified = 6 Total no of Unanticipated RiskOccurred = 2 Risk Identification Efficiency % = (6/8)*100 = 75%

Benefits:

- This metric determines the efficiency of identifying risk in a project
- This helps in planning for the mitigation and contingency to be carried out ina project

Risk Mitigation Efficiency %

When it should be measured: It should be measured at overall project level.

Input/Measure	Formula	Example
Total no of Risks Identified for mitigation No. of Risk mitigated but occurred	((No. of Risk identified for mitigation - No. of Risk mitigated but occurred) / (No. of Risk identified for mitigation)) *100	Total no of Risks Identified for mitigation = 10 No. of Risk mitigated but occurred = 1 Risk Mitigation Efficiency % = (9/10)*100 = 90 %

II. References

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3. *Reference article from Google Search Engine on pharmaceutical industry*
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