Quality Metrics - Key Performance Indicator for Pharmaceutical Industry

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***Abstract*: Quality plays an important role to achieve customer satisfaction as their valuable feedbacks add more to the quality of product. It helps in making an effective quality management plan to reach the goal of quality. In most of the pharmaceutical industries monitoring of quality systems are done by Quality metrics. During the manufacturing operations Key Performance Indicators (KPI) are represented by a systematic approach of Quality metrics. Its aim is to measure, evaluate and monitor the product and process lifecycle. It also plays a key role in selection of material suppliers and also to minimize the supply chain disruptions. The data of quality metrics can contribute in the development of an effective Pharmaceutical Quality Management which leads to higher level of safety, efficacy, delivery, and performance. Quality metrics helps in gaining the desired quality output by meeting the FDA and cGMP requirements. Therefore it is an important aspect to enhance product quality and helpful in operations and continuous improvement.**

***Keywords*: Quality, Key Performance Indicator (KPI), Quality Metrics (QM), Manufacturing Operations, Pharmaceutical Quality System (PQS)**

1. Introduction

Quality Metrics in pharmaceutical manufacturing is commonly usedto measure, evaluate, and monitor the product and process lifecycle. The data obtained from the quality metricsmay lead to higher levels of safety, efficacy, delivery, and performance.[1]Quality metrics are used throughout the drug and biological product industry to monitor processes and drive continuous improvement efforts in manufacturing.[2] A key component of this work is related to the evolution and effectively watch over the quality performance in pharmaceutical manufacturing as well as in distribution operations. Quality is the first and foremost requirement of pharmaceutical throughout the operations in its business perimeter.[4] Pharmaceutical companies are controlled and guided by the Pharmaceutical Quality System in context of quality. The system provides oversight and assurance which are the key elements necessary for controlling the laboratory processes and the pharmaceutical manufacturing processes throughthe entire life of the products from when the products are developed to when they are sold.[5]Pharmaceutical Quality System is driven by standards of Good Manufacturing Practices (GMP), and Good Distribution Practices (GDP), with supporting concept of GXP. The deployment of quality professional and experts are more in manufacturing plant as compared to any other sectors of pharmaceutical operations.[4]It is important to note that quality metrics must be established in an effort to directly improve the product quality.[6]

2. Key Features of Quality Metrics

- In pharmaceuticals, they are used to validate the manufacturing process.
- Continuous improvement and updation of pharmaceuticals can be achieved by it.
- Quality attributes process parameters can be determined and assessed in the pharmaceutical manufacturing.
- Manufacturers can easily process data, evaluate drugs quality and maintain products with the help of quality metrics.[5]

3. Background on FDA's Quality Metrics Program

3.1**Year 2004,** FDA presented the report "Pharmaceutical CGMPs for the 21st Century – a Risk-Based Approach",narrating FDA's intent to implement a modern, risk-based pharmaceutical quality assessment system.

3.2**Year 2012,** with the transit of the Food and Drug Administration Safety and Innovation Act, FDA was authorised to collect records and information of pharmaceutical manufacturing from regulated industry as part of FDA's risk-based oversight.

3.3**Year 2013,**as part of an effort to understand the underlying causes of product shortage (78 FR 9928), FDA requested public input on the use of quality metrics data to evaluate the product manufacturing quality.

3.4**Year 2014,** FDA gained additional perception when the Brookings Institute get together with FDA to summon an expert workshop titled, "Measuring Pharmaceutical Quality through Risked-Based Assessmentand Manufacturing Metrics", which offered an opportunity for pharmaceutical manufacturers, purchasers, regulators, and other stakeholders to discuss the goals, objectives, and challenges for a pharmaceutical quality metrics program.

3.5**In July 2015,** FDA presented the draft guidance stating"Request for Quality Metrics" (80 FR 44973), in which a proposed mandatory program for product-based reporting of quality metrics was described.

3.6**In November 2016**,FDA brings out a revised draft guidance entitled "Submission of Quality Metrics Data"(81 FR 85226).This guidance expressed an initial voluntary phase of the QM Reporting Program, in which participants have to report the data either by product or establishment, with the help of FDA submission portal.

3.7**In June 2018,** Federal Register notice issued in 2018, FDA declared the availability of two pilot programs, a Quality Metrics Site Visit Program (83 FR 30751)and a Quality Metrics Feedback Program (83 FR 30748) for product and process quality improvement.

3.8**In March 2022,** FDA established a docket to solicit comments on changes to FDA's previously proposed Quality Metrics Reporting Program. This notice describes considerations for purifying the Quality Metrics Reporting Program based on lessons learned from two pilot programs with industry that were announced in the Federal Register in June 2018.[1]

4. FDA's approach in bringing the light over Quality-Key Performance Indicators

- The need to adhere to quality specifications is being overviewed and controlled by regulatory agencies day by day. Therefore it becomes crucial for pharmaceutical enterprise to explore Quality-Key Performance Indicatorsto measure and maintain the quality health of the organization.[4]
- These metrics provides usefulness to FDA;
    - it helps in developinginspection policies, complianceand practices, such as risk-based inspection which are scheduled for drug manufacturers,
    - it helps in improving the agency's ability to predict, and therefore, possibly lower future drug shortages,
    - it helps inencouraging the pharmaceutical industry to implement innovative quality management systems for pharmaceutical manufacturing.[2]
- USFDA aspires to use these quality metrics as an instrument to identify risk-based factors that could incline or decline the inspection frequency and that could potentially be predictive of drug supply disruption.Key performance indicators (KPIs) are an essential means in the process as they measure the manufacturing and distribution alike to have reliable information on current and desired standards.
- KPIs are used to identify where performance of quality management is good and meeting desired standards and where the performance is lacking and requires improvement.[4]

5. Key Performance Indicators/Process Parameters to be measured

Measurement is the first step that leads to control and eventually towards the improvement of the process. If one can' understand something, it can't be understood and if it can't be understood then it can't be controlled and if it can't be controlled then it can't be improved. Quality management is a broad and difficult subject with much being written by academics and quality leaders of industries. Juran's lectures to Japanese industrial executives in 1954 are considered one of the most significant contributions to modern quality management.[6]

6. Quality Metrics and there implementation among Industries

Contributors explored a range of considerations regarding the implementation and accumulation of metrics data, including potential mechanisms for collection, frequency of reporting, and level of reporting requirements for organizations, sites, and individual products. For the purpose of discussion, the agency proposed that all metrics data be reported annually by product sponsors.This reporting would be conducted at an organizational level; however each organization would collect and report data for each product and manufacturing site.

7. Pharmaceutical Manufacturing

- **Role of Purchasers in Incentivizing Quality Improvement;**Pharmaceutical purchasers, such as group purchasing organization (GPOs), pharmaceutical distributors, and health systems, can act as a critical function in motivating and improving the qualityof pharmaceutical manufacturers.Users use varying degrees of quality data to make contracting decisions, to make use of information from warning letters, inspectional observations (i.e., form 483), and other publicly available data sources. Currently, buyers have limited information on the quality level of pharmaceutical products.

- **Public Availability of Metrics Data;** FDA representatives noted that the agency does not intend to share metrics data publicly in part due to confidentiality considerations, though it is considering the possibility of reporting aggregated, de-identified metrics data back to manufacturers, which would then be free to use that information as part of their marketing strategy.[8]

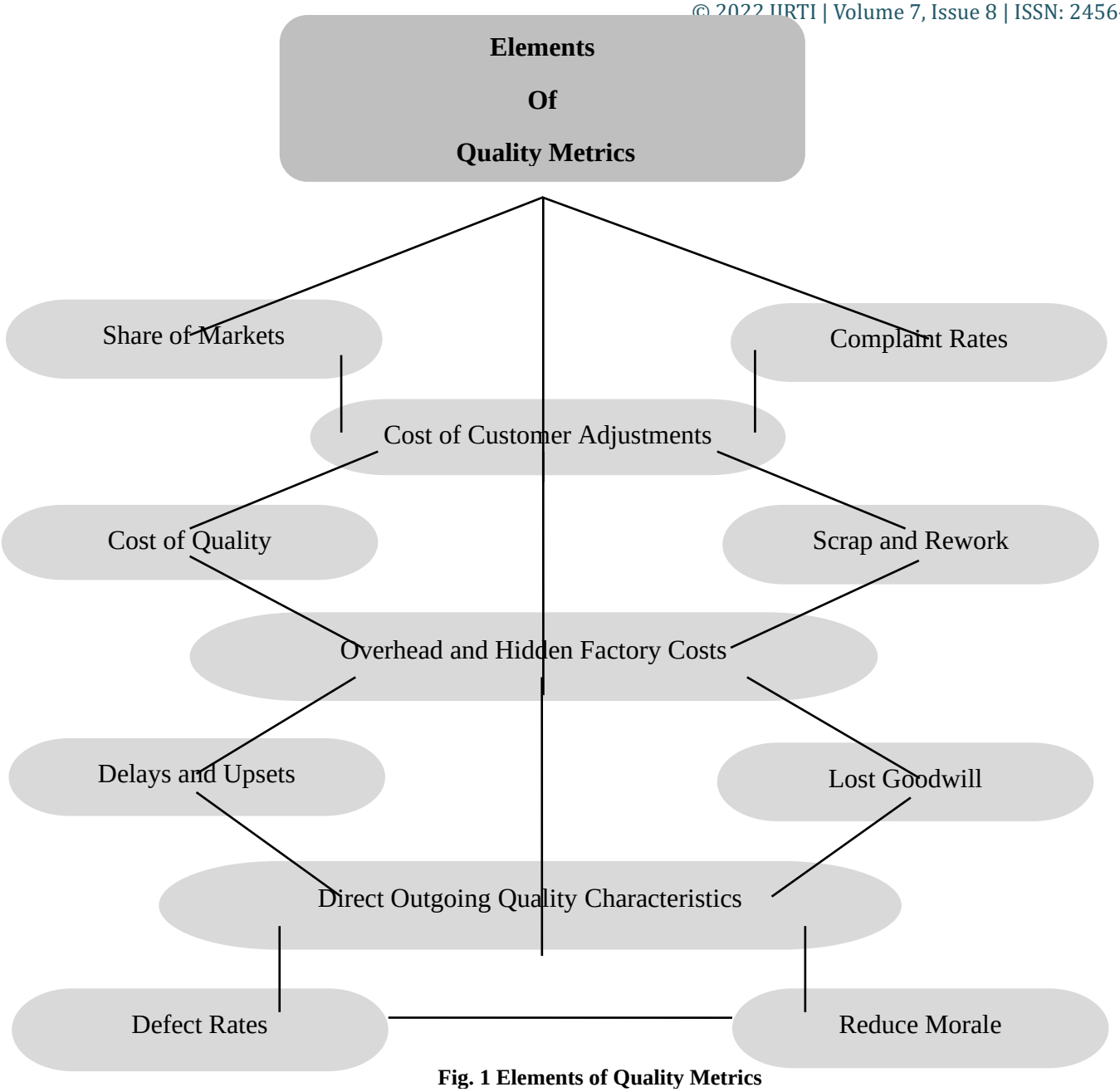

Fig. 1 Elements of Quality Metrics

These are some of the main quality attributes in any process which has direct impact on the product quality therefore they shall be measured carefully.[6]

8. Benefits of Quality Metrics[6]

1. **Quality and Patient Safety-** It involveseffective functioning of quality system and commitment to quality by manufacturer.

2. **Site Performance and Compliance –** This metrics reflect overall site system performance with respect to product quality and compliance.

3. **Accountability –** This metrics indicate how well an operation and project is performing.

4. **Alignment –** This helps toalign the entire team on a common set of strategic objective.

5. **Attention-** It corrects metrics objective incorporated into management review which provides a defined set ofexpectations of senior management.

6. **Behaviour –** It sets the right metrics that drives the right behaviour of the employees.

7. **Expectations -** This metrics allows an entire organization a common focused understanding of what outcomes are more valued by the leaders or leadership.

8. **Feedback –** This metrics provide long and short term feedbacks on the effectiveness of projects and activities.

9. **Objectivity -**This metrics form a basis of fact based organization.

10. **Motivation –** This metrics provide long and short term measurement of progress and keeps employees motivated to improve the process and quality.

11. **Visibility -**A common set of metrics used throughout an organization to create transparency and enhanced visibility.

9. Layout to be kept in mind while developing the metrics[6]

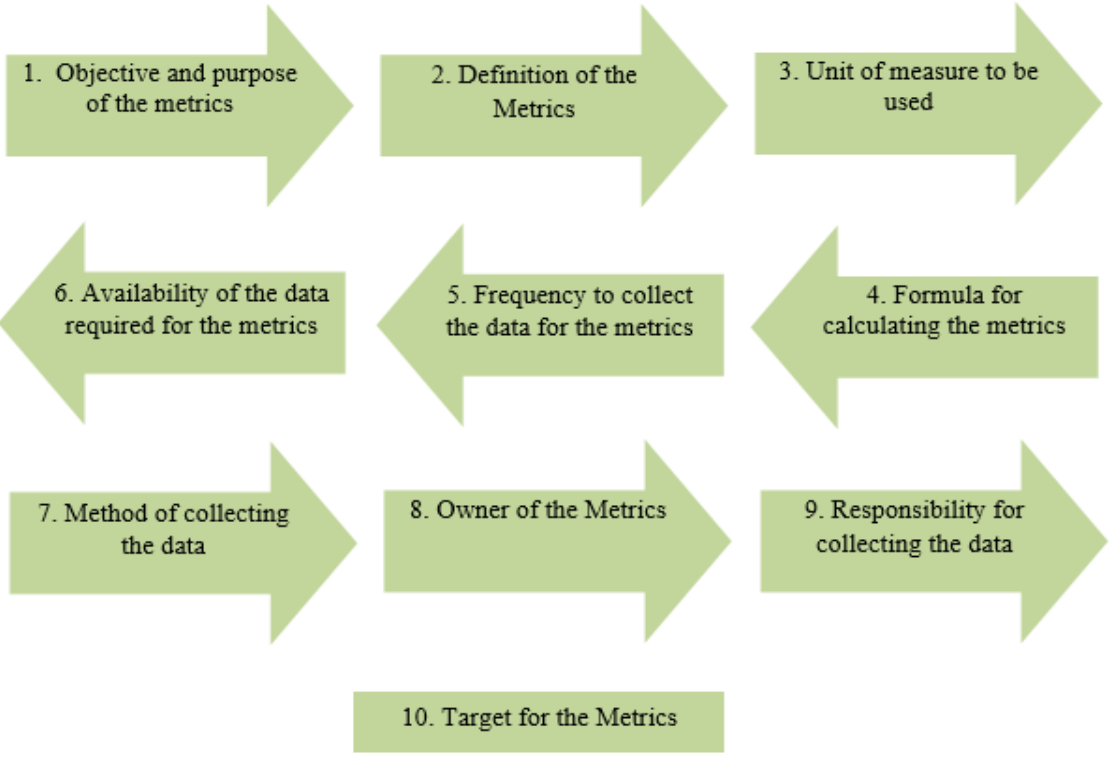

Fig. 2 Layout for Metrics

Key Performance Indicators[7]

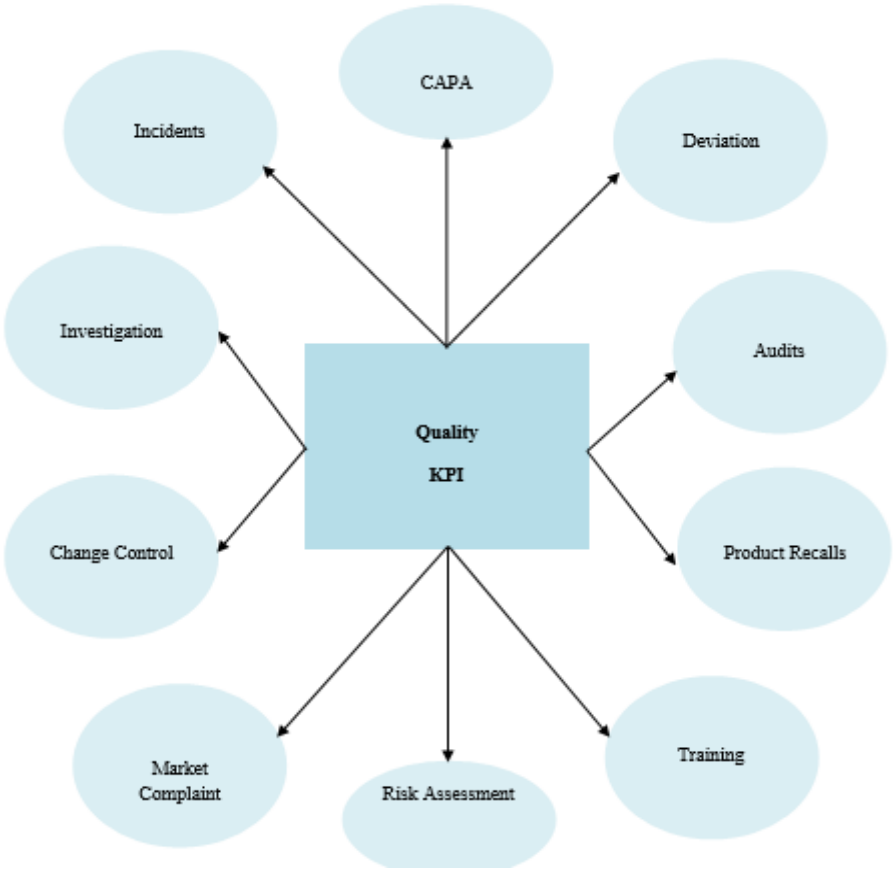

Fig. 3 Quality Key Performance Indicators

10. Case study

Report from the Pharma Congress 2016, Germany, "Quality Metrics at Aenova"

- Europe's largest Pharma Congress of its kind took place on 12th and 13th of April, 2016 in the Swissotel Dusseldorf, Germany. More than 1,000 delegates attended the ten GMP/ FDA conferences organized in these two days.[9]
- The Pharma-Technica which is associated with the Pharma Congress is the exhibition for pharmaceutical suppliers and service providers. The exhibition space was extended this year which can accommodate 90 more exhibitors who presented their innovations and news with regard to pharmaceutical technology.
- 50 lectures, almost exclusively case studies were discussed from pharmaceutical companies such as Pfizer, Novartis, Boehringer Ingelheim and many more.
- Dr. Andreas Konig, senior vice president at Aenova addressed the Pharma Congress with a keynote. Aenova is a fast-growing pharmaceutical company in the area of contract manufacturing.
- Quality Metrics are a hotly-debated topic. At the end of July 2015, the U.S. FDA presented a draft guide entitled "Request for Quality Metrics - Guidance for Industry".
- The FDA discussed which indicators will have to be submitted regularly in future by pharmaceutical and API companies to FDA. Currently, the FDA Guideline is being intensively discussed because the FDA tends to use the data as part of the planning for future inspections.
- This idea can be helpful in identifying early stage problems related to manufacturing and quality assurance.
- Companies with stable processes (keyword "CPK value") should be "rewarded" and their inspection cycle should be longer than for companies with less stable processes and more process deviations.
- Dr. Konig showed in his case study that the Key Performance Indicators (Quality Metrics) are already measured today. The following "Core KPIs" have been defined on the corporate level;
    - Deviations
    - Complaints
    - CAPA
    - Changes.
- The basis for discussing improvements is the trend of KPIs. Furthermore, to identify "Best Practice", the absolute KPI values are compared and finally the KPI values are used to formulate new objectives for "Quality Targets".
- Dr. Konig underlined that KPIs should be considered in a multidimensional way at different levels of the company and thus data can be aggregated at the different levels.
- All data are systematically collected at the site Quality Board's level and essential statements are then actualized in second step which are summarized for Aenova's Quality Board in the form of charts and metrics for decision-making.
- Deciding KPIs/Quality Metrics helps in improving the transparency and implementing necessaryenhancement measures as well as defining quality targets for continuous improvement.
- It is important to note that there may be a risk of pseudo-transparency which doesn't reflect the reality. KPIs will never ever be able to replace the knowledge of the persons involved in the process.[10]

Conclusion

The Quality Key Performance Indicator (Quality-KPI) serves as a tool to maintain quality of pharmaceutical products. Pharmaceutical industry requires an identification and tracking of KPI for quality mainly during manufacturing and distribution operations.A set of effective KPI comprising of overall strategy should be formulated for manufacturing and distribution operations. Lack of integrated manufacturing, distribution, quality and overall compliance in a single solution impacts the ability to consistently deliver quality products that is compliant with regulatory norms.A good quality metrics system supports both industries in their profitability and in GMP compliance. There will always be an open space for the continuous improvement of quality metrics by the industries to enhance quality, safety and efficacy of their pharmaceutical products.

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