Quality Metrics and KPIs in pharmaceutical industry

PDA Israel
Quality Metrics and KPIs
Free webinar, 20th March 2022

Sasha Nezlin
UroGen Pharma Ltd.

http://www.pdaisrael.co.il/Annual22/index.html

Presenter

- Sasha Nezlin, VP Quality, UroGen Pharma
- Member of the Executive Committee of the Israel Chapter of PDA
- Extensive experience in Quality Systems, Quality Operations, Analytical R&D, Quality Control, Supplier Quality, regulatory audits, etc. – from start-ups to multinationals.
- Some past positions:

  VP Quality Intec Pharma

  Head of Quality, Omrix Biopharmaceuticals (J&J)

  QC Manager, Teva Pharmaceuticals (Kfar Saba)

Why quality metrics?

W. Edward Deming stated:

"*Data are not taken for museum purposes; they are taken as a basis for doing something. If nothing is to be done with the data, then there is no use in collecting any. The ultimate purpose of taking data is to provide a basis for action or a recommendation for action…*"

It may sound clear and simple, but it is not so easy to design and maintain a metrics system in a way that serves its purpose well.

Good execution requires careful consideration of the definition of a KPI / metric, the data sources, and evaluation of results.

This also includes the need to monitor processes which are under control, but may deviate, in which case the data would allow us to react immediately.

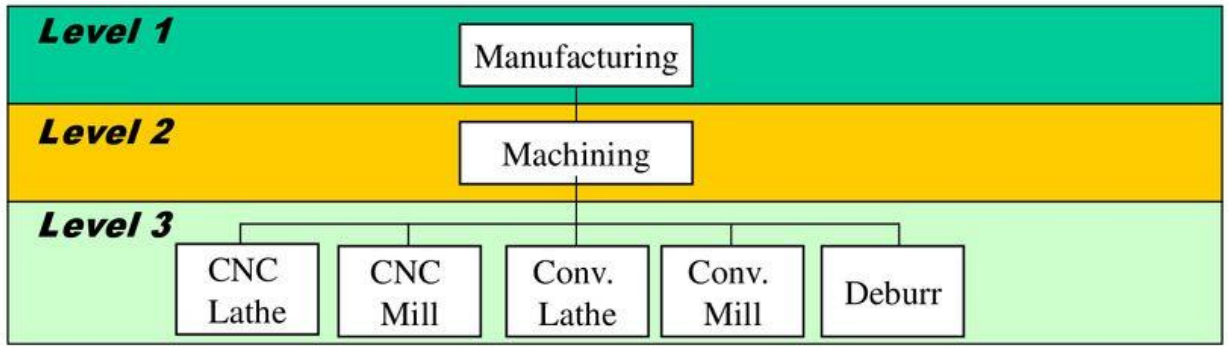
Why quality metrics?

Why quality metrics?

Aero – space industry

Procurement Quality Assurance

Example-Quality Metrics Tree



Using Manufacturing/Machining as the Level One and Level Two Processes, the identified Level Three Process Metrics could include the following:

1. Percentage of processes for which capability is established
2. Elapsed time vs. hands on time
3. Amount of hands on time (in hours) devoted to non-value added steps in:
   - Inspection, Rework, Duplicate approvals
4. Cost of non-value added steps (hands on time x costing rate)
5. Number of defects or errors in output (per hour/day/week/per unit/page/form)
6. Number of on-time deliveries (per schedule, contract, or promise date)
7. Cost of quality (cost of prevention activities + cost of detection/correction activities)
8. Machine Capability Studies

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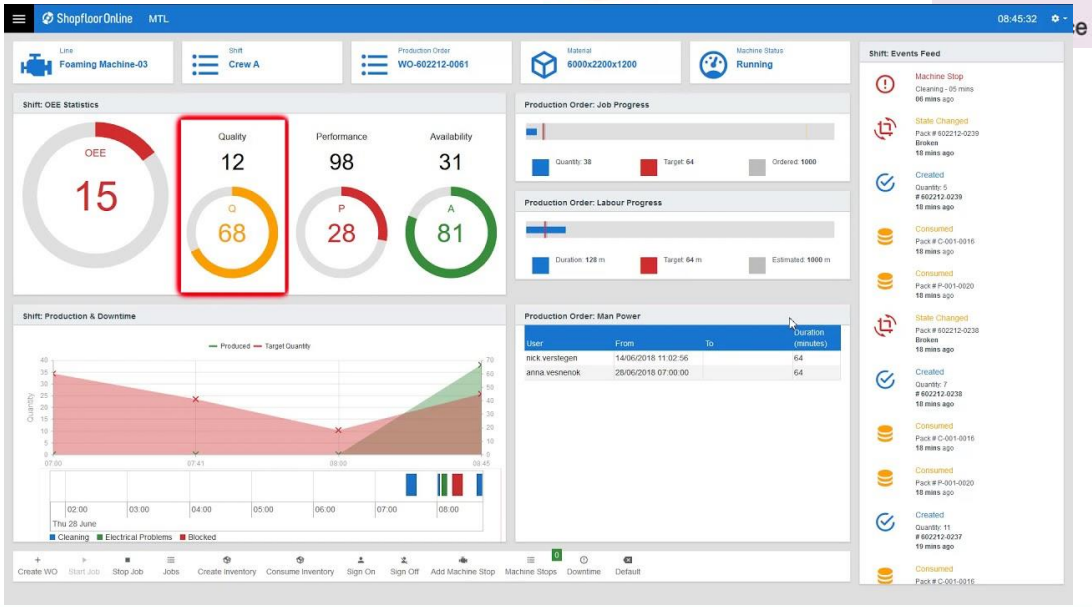
Why quality metrics?



Semiconductors industry
Automotive industry
Financial
Manufacturing
Maintenance / Engineering
Human Resources
Supply Chain
Sales / Marketing

Quality Metrics → pharmaceutical industry

Quality Metrics have been used in pharmaceutical industry for years – e.g. to measure operational performance.

But quality can be measured on different levels and for many processes. Done in the right way, Quality Metrics can enable companies to reach a high quality performance. They will benefit from a continuous improvement in both ***operational performance*** and ***GMP compliance***. And both are important for the ***continuity of business*** and ***product supply***.

Quality Metrics Definitions

Metric: a measure against a standard (standards of measurement by which efficiency, performance, progress, or quality of a plan, process, or product can be assessed).

Indicator: provides indication of performance (qualitative or quantitative), e.g., to evaluate success of an organization or activity.

KPI: key performance indicator; target critical areas of performance (not all indicators are key)

They should help to develop, collate and analyze information that provides current performance feedback, anticipates future needs and enables actions. For this, data must be accurate, timely appropriate, correctly analyzed and meaningful.

What's the Difference: KPI vs Metrics

Metrics and KPIs are often confused, but the clear difference is KPIs are the key measures that will have the most impact in moving your organization forward. They clearly articulate and provide insight into what your organization needs to measure and achieve to reach your long-term objectives.

Metrics also track and provide data on your organization's standard processes but **are not the** most important metrics your organization needs to measure, monitor, and perform against to make progress against your strategic plan.

It's easy to use the two terms interchangeably, but ➔

- Key Performance Indicators help define your strategy and clear focus.
- Metrics are your "business as usual" measures that still add value to your organization but aren't the critical measure you need to achieve.
- Every KPI is a metric, but not every metric is a KPI.

Points to be considered in Metrics and KPIs Development:

- Quantitative vs. qualitative data.
- Data is required to be SMART (Specific, Measurable, Accepted, Realistic, Time Bound). Data "*for information*" can be useful to establish a baseline.
- Measure product specific/operational quality performance, the performance of the overall Quality System and Quality Culture.
- Only a few selected KPIs for senior management, more for management on the ground.

What could go wrong?

- Too many metrics, complex and time-consuming.
- Driving wrong behaviors and actions can lead to unintended consequences in order to achieve metrics target.
- Actions without understanding the context surrounding the results.
- Not all have same value - determine the crucial few!
- Metrics alone will not deliver. Metrics not meeting targets should lead to actions.

FDA publishes request for comments on Quality Metrics

https://www.federalregister.gov/documents/2022/03/09/2022-04972/food-and-drug-administration-quality-metrics-reporting-program-establishment-of-a-public-docket

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Notice

Food and Drug Administration Quality Metrics Reporting Program; Establishment of a Public Docket; Request for Comments

A Notice by the Food and Drug Administration on 03/09/2022

This document has a comment period that ends in 80 days. (06/07/2022)

SUBMIT A FORMAL COMMENT

Read the 1 public comment

PUBLISHED DOCUMENT

AGENCY:

Food and Drug Administration, HHS.

ACTION:

Notice; establishment of a public docket; request for comments.

SUMMARY:

The Food and Drug Administration (FDA or Agency) is announcing the establishment of a docket to solicit comments on changes to FDA's previously proposed quality metrics reporting program (QM Reporting Program). This notice describes considerations for refining the QM Reporting Program based on lessons learned from two pilot programs with industry that were announced in the **Federal Register** in June 2018, a Site Visit Program and a Quality Metrics Feedback Program, as well as stakeholder feedback on FDA's 2016 revised draft guidance for industry entitled "Submission of Quality Metrics Data." FDA is interested in responses to the questions listed in section III of this document, in addition to any general comments on the proposed direction for the program. This notice is not intended to communicate our regulatory expectations for

DOCUMENT DETAILS

Printed version: PDF

Publication Date: 03/09/2022

Agencies: Food and Drug Administration

Dates: Submit either electronic or written comments by June 7, 2022.

Comments Close: 06/07/2022

Document Type: Notice

Document Citation: 87 FR 13295

Page: 13295-13299 (5 pages)

Agency/Docket Number: Docket No. FDA-2022-N-0075

Document Number: 2022-04972

Why it is important to let FDA know what you think!

Regulations.gov
Your Voice in Federal Decision Making

SUPPORT

Docket / Document (FDA-2022-N-0075-0001) / Comment

PUBLIC SUBMISSION

Comment from Raman Mehta

Posted by the **Food and Drug Administration** on Mar 11, 2022

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Comment ID
FDA-2022-N-0075-0002

Tracking Number
l0j-qybp-s3p5

Comment Details | Submitter Info

Document Subtype
Electronic Regulation from Form

Received Date
Mar 9, 2022

Comment

The process mentioned in the guidance is probably the complex monitoring protocols. for example IOOSR /LAR etc. Means their calculation is very complex, stage wise, product wise, block wise, site wise. it bring complexity to the system and ultimately this guidance got no attention due to this.

Rather than this agency must focus on developing and open source platform, where the manufacturer upload the data the the statistics are automatically generated. So much user friendly that would be and every manufacturer would adopt it quickly.

The agency must avoid, manual processes that generates errors and make employee life miserable.

Intensive guidelines are making human life difficult and leading to stress and suicide events in industry. Because human brain can handle limited processes.

Develop software for industry.

FDA Docket on Quality Metrics

Stakeholders have indicated that different industry sectors may prefer different quality metrics.

To provide flexibility to manufacturers, FDA would focus less on standardization of quality metrics and definitions. Instead, FDA would identify **practice areas** that are critical to ensure **sustainable product quality and availability** and would permit manufacturers to select a metric(s) from each practice area that are meaningful and enable establishments to identify **continual improvement** opportunities. *The metric definitions would not specify how establishments calculate particular metrics*. Rather, the reporting establishment would select the most appropriate metric(s) from each practice area and inform FDA how it was calculated.

Through the collective feedback gathered from pilot participants, FDA has identified the following four general practice areas as appropriate at this time for the QM Reporting Program:

(1) Manufacturing Process Performance,

(2) PQS Effectiveness,

(3) Laboratory Performance,

(4) Supply Chain Robustness.

FDA Docket on Quality Metrics

Examples of quality metrics associated with each practice include the following:

1. Manufacturing Process Performance

• Process Capability/Performance Indices (Cpk/Ppk): a ***measure that compares the output of a process to the specification limits*** and can be calculated as a proportion (e.g., total number of attributes with Ppk greater than 1.33 divided by total number of attributes where Ppk is used). It is important to consider standard deviation measurements using a reasonable sample size.

• LAR: (Lot Acceptance Rate) a measure of the ***proportion of lots that were accepted in a given time period***. Examples of inputs that can be used to calculate LAR include lots completed, lots dispositioned, lots attempted, lots rejected, lots released, lots approved, abandoned lots, and parallel/backup lots.

• Right-First-Time Rate: a measure of the ***proportion of lots manufactured without the occurrence of a non-conformance***. Examples of inputs that can be used to calculate a right-first-time rate include number of deviations, lots dispositioned, lots attempted, number of non-conformances, and lots approved in the first pass.

• Lot Release Cycle Time: a measure of the ***amount of time it takes for the lot disposition process***. Lot release cycle time can be calculated with an appropriate unit of measurement such as number of hours or days.

FDA Docket on Quality Metrics

2. PQS Effectiveness

• CAPA Effectiveness: a measure of the ***proportion of CAPA plan implemented and deemed effective*** (i.e., effectiveness verifications closed as effective). Examples of inputs that can be used to calculate CAPA effectiveness include number of CAPAs initiated, CAPAs closed on time, CAPAs closed as "effective," overdue CAPAs, and CAPAs resulting in retraining.

• Repeat Deviation Rate: a measure of the ***proportion of recurring deviation*** measures.

Examples of inputs that can be used to calculate repeat deviation rate include total number of deviations and number of deviations with the same assignable root cause.

• Change Control Effectiveness: a measure of **timeliness and effectiveness of implemented changes** to GMP facilities, systems, equipment, or processes. Examples of inputs that can be used to calculate this metric include on-time closure of the change, total number of late effectiveness checks, total number of changes initiated, number of changes that are initiated reactively versus proactively, and total number of changes deemed effective.

• Overall Equipment Effectiveness: a measure of operating productivity, ***utilizing planned production time***. Overall equipment effectiveness can be calculated using inputs related to availability (e.g., planned production time, operating time), performance (e.g., production capacity), and quality (e.g., production output that does not result in acceptable product).

• Unplanned Maintenance: a measure of the ***proportion of maintenance time that was not planned or scheduled***. Examples of inputs that can be used to calculate this metric include total maintenance hours and planned maintenance hours.

FDA Docket on Quality Metrics

3. Laboratory Performance

• Adherence to Lead Time: a measure of the ***proportion of tests in the laboratory that are completed on time according to schedule requirements***. Adherence to lead time can be calculated, for example, by tracking initiation and testing turnover time in release and stability tests (i.e., the number of days between the start date and completion date for quality control (QC)); tracking data review and documentation; tracking final result reporting prior to batch disposition; or comparing QC testing completion date against the target date.

• Right-First-Time Rate: a measure of the ***proportion of tests conducted without the occurrence of a deviation***. Right-first-time rate as a metric for laboratory performance can be calculated, for example, by tracking the invalid assay rate, the number of assays

invalidated due to human errors, or CGMP documentation errors during review.

• IOOSR: (Invalidated OOS Results) a measure that indicates a laboratory's ability to accurately perform tests. Examples of inputs that can be used to calculate this metric include ***total number of tests conducted and total number of out-of-specification results invalidated due to an aberration of the measurement process***.

• Calibration Timeliness: a measure of a laboratory's adherence to inspecting, calibrating, and testing equipment for its intended purposes as planned. This metric can be measured by ***tracking calibration criteria and schedules***.

FDA Docket on Quality Metrics

4. Supply Chain Robustness

• On-Time In-Full (OTIF): a measure of the ***extent to which shipments are delivered to their destination containing the correct quantity and according to the schedule specified in the order***. This metric can be calculated using inputs such as the number of orders shipped, number of past due orders, or number of orders shipped within tolerance.

• Fill Rate: a measure that quantifies ***orders shipped as a percentage of the total demand for a given period***. Examples of inputs that can be used to calculate this metric include total number of orders shipped, the number of orders placed, and the number of orders received.

• Disposition On-Time: a measure of the ***proportion of lots in which the disposition was carried out on time***. Examples of inputs that can be used to calculate this metric include the total number of lots dispositioned and the total number of lots dispositioned on time.

• Days of Inventory On-Hand: a measure of how a company utilizes the average inventory available. It is the ***number of days that inventory remains in stock***.

Why it is important to let FDA know what you think!

Karen Ginsbury • 1st
GMP / Quality Consultant to the pharmaceutical and allied industries

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This is your last chance to influence this docket and the focus of this program which while overall is an important direction for all industries goes WAY beyond the scope of GMPs and if finalized will become part of pharmaceutical legislation - LAW in the USA fully enforceable with 483 and wanting letter citations to follow. Will there be a grace period? How will small companies manage? How many FTES needed just to provide the info to FDA in format they demand - and why should industry do FDAs inspection work for them? Yes to #metrics which change behavior; yes to effective #QMS which #prevents bad things from happening. No to micromanagement of the QMS by regulators and non holistic time consuming exercises which the big ten already have in place having worked with FDA on the pilot program. Start-ups, small companies... how will your data be understood - OUT OF CONTEXT with out you there to explain to the inspector???? Comment submit comments to the docket - fast - or bear the consequences!

Compliance metrics

Compliance metrics are a measure of how well regulations are complied with. However, Quality metrics are should be implemented as a system of metrics with a scope and purpose beyond compliance.

The purpose of such a system includes compliance - but extends holistically to the other aspects of a healthy business, such as supply reliability, product/service quality, customer satisfaction, patient impact, and resource efficiency.

If one aspect, such as regulatory compliance, is the sole focus of a metrics system - there is a risk of negligence for the other essential contributors to a healthy business.

Summary

Metrics are good?

Metrics are bad?

Do we know what will happen next?

How do we need to prepare?

Who will be impacted? How?

References

Some suggestions for further reading on quality metrics

- "Points to Consider When Using KPIs/Metrics" Bernhard Hinsch, Sven Alexander Moritz, Ana Esteban Nunez, Timothy E. Orszula, Daniel Taylor and Alexander Nezlin, PDA J Pharm Sci Technol 2022; 76:75-87 (https://journal.pda.org/content/76/1/75.abstract)

- A Notice by the Food and Drug Administration on 03/09/2022 "Food and Drug Administration Quality Metrics Reporting Program; Establishment of a Public Docket; Request for Comments" (https://www.federalregister.gov/documents/2022/03/09/2022-04972/food-and-drug-administration-quality-metrics-reporting-program-establishment-of-a-public-docket)

- "Quality Metrics - ISPE Team Update 31-March 2016" Michael Arnold, RPh Vice Chairman-ISPE International Board of Directors https://www.ispe-casa.org/sites/default/files/Documents/REGULATORY%20COMPLIANCE%20%26%20QUALITY%20METRICS%20Quality%20Metrics%20Michael%20Arnold.pptx

- "Quality Metrics" Alicia Mozzachio, RPh, MPH Senior Advisor for International Activities Office of Policy for Pharmaceutical Quality (OPPQ) CDER FDA https://www.pda.org/docs/default-source/website-document-library/chapters/presentations/australia/quality-metrics.pdf?sfvrsn=1e188f8e_4

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Parenteral Drug Association

THANK YOU