Quality Metrics: A Regulatory Perspective

By

Tara Gooen Bizjak, MBSci

CDER Office of Policy for Pharmaceutical Quality

Presented By

Dr. Ademola Daramola

US FDA Office of International Programs

Indian Pharmaceutical Alliance
February 23, 2018

What are Quality Metrics?

met·rics

/ˈmetriks/

noun

noun: **metrics**; plural noun: **metricses**

1. the use or study of poetic meters; prosody.
2. [redacted]

"the report provides various metrics at the class and method level"

-met·rics

combining form

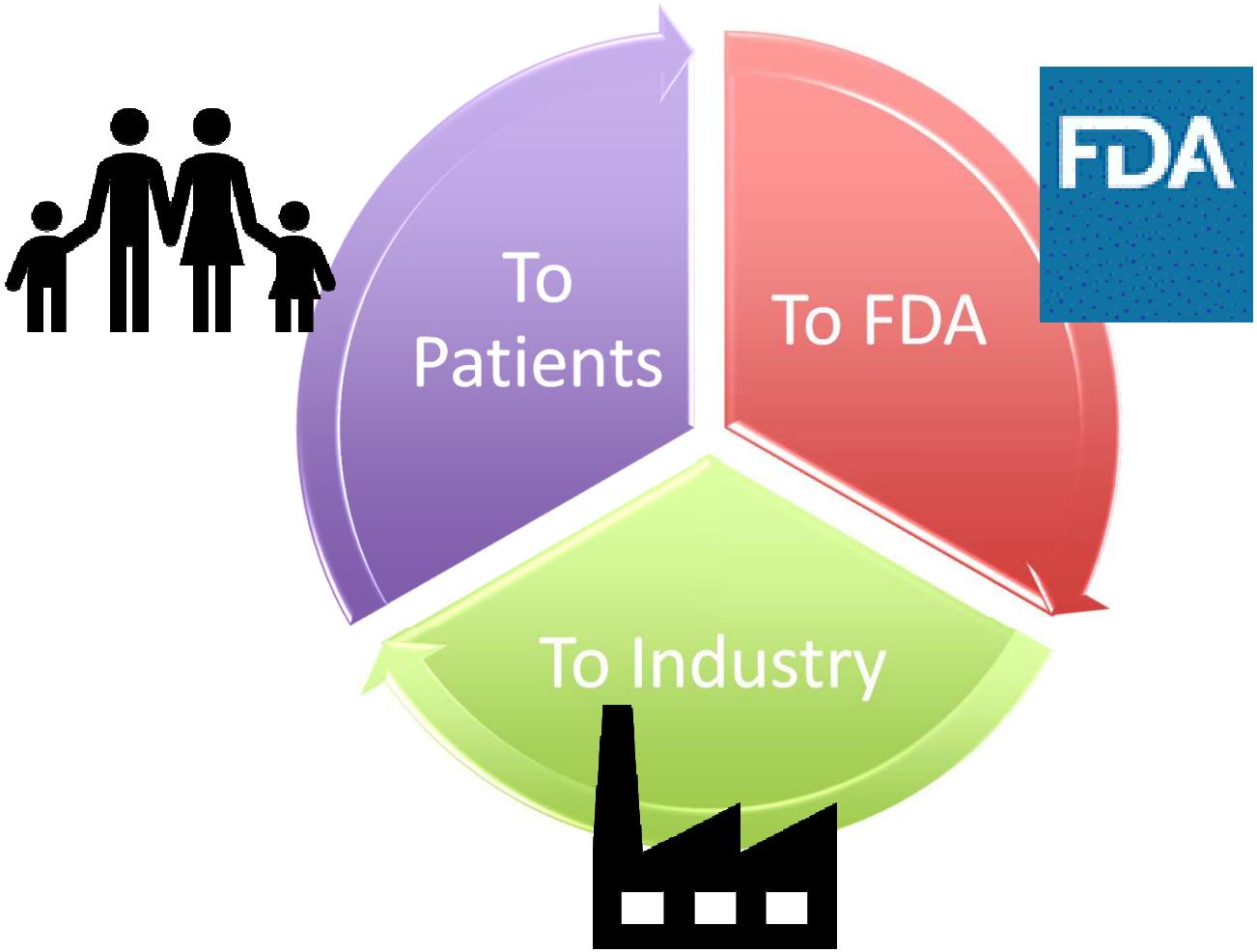
prefix: **-metrics**

[redacted]

"econometrics"

Quality metrics are used throughout the pharmaceutical industry to monitor quality control systems and processes and drive continuous improvement efforts in drug manufacturing.

Quality Metrics Programs are Important



Why are Quality Metrics important?

To Patients:

- More reliable patient access to important therapies
  - Commitment to ongoing improvement by industry leads to more robust manufacturing processes
  - Fewer recalls
  - Fewer quality-related drug shortages

Why are Quality Metrics important?

To Industry:

- Enables continual improvement of process performance and product quality
- Supports continual improvement of the pharmaceutical quality system
- Important element of oversight and controls over the manufacture of drugs to ensure quality (section 501 FD&C Act)

Existing Quality Metrics Programs

- Many manufacturing establishments currently use quality metrics as a part of the process validation lifecycle and pharmaceutical quality system (PQS) assessment
- Current good manufacturing practice (CGMP) for human drugs requires manufacturers to have an ongoing program to maintain and evaluate product and process data that relate to product quality
- Continued process verification includes a Periodic Product Review (PPR):
  - conducted at least annually
  - data collected includes relevant process trends and quality of incoming materials or components, in-process materials, and finished products
- Individual programs should be tailored to include those metrics that the manufacturer finds useful in performing these product- and establishment-specific evaluations

Indicators of Quality Metrics Program Maturity

Immature → **Mature**

- Minimal program (e.g., bare minimum information in the Annual Product Review)
- React to existing problems
- Only general, non-specific metrics

- Predictive analytics
- Thoughtful metrics selection
- Assess quality culture and overall commitment
- Senior management and general staff commitment to overall quality
- Continual improvement of product and process
- Continual improvement of the metrics program

Current Research Indicates Quality Metrics Programs are a Good Business Practice

- Collaborative research with St. Gallen University (Switzerland) and FDA
- Developing a model for Pharmaceutical Quality System (PQS) Excellence
- Outcomes from Year 1
  - Sites with *highest risk profile* were observed to have Low (Process) Stability and Low Inventory (regarding the following metrics: Rejected Batches, Customer Complaint Rate, and Service Level Delivery (On-Time in Full))
- Implications from Year 1
  - Research supports alignment of reporting of quality performance metrics with internal operational excellence programs
  - Fostering Quality Maturity will have a positive impact on the *Quality Behavior* at a firm, leading to superior Cultural Excellence and subsequently providing the *foundation of PQS Excellence*

- Report can be obtained at: http://tectem.ch/institute/opex/fda

Why are Quality Metrics important?

To FDA:

- Additional insight into the state of quality for product and facility
- More quantitative and objective measure of quality at the product, site, and system levels
- Enhance risk-based surveillance inspection scheduling model
- Improve effectiveness of inspections
- Help to identify factors leading to supply disruption

Pharmaceutical Quality for 21st Century Initiative

Vision

"A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight."

-- Dr. Woodcock (2003)

Desired State of Manufacturing

- Manufacturers have extensive knowledge about critical product and process parameters and quality attributes
- Manufacturers strive for continuous improvement
- FDA role: Initial verification, subsequent audit
- Minimal manufacturing supplements needed for postapproval changes

Selected Objectives for FDA/CDER's Office of Pharmaceutical Quality

- Encourage use of modern, more efficient manufacturing technologies
- Develop approaches to increase regulatory flexibility for postapproval changes
- Focus on robust analytics and surveillance techniques to monitor the state of manufacturing in the pharmaceutical industry.

⇩

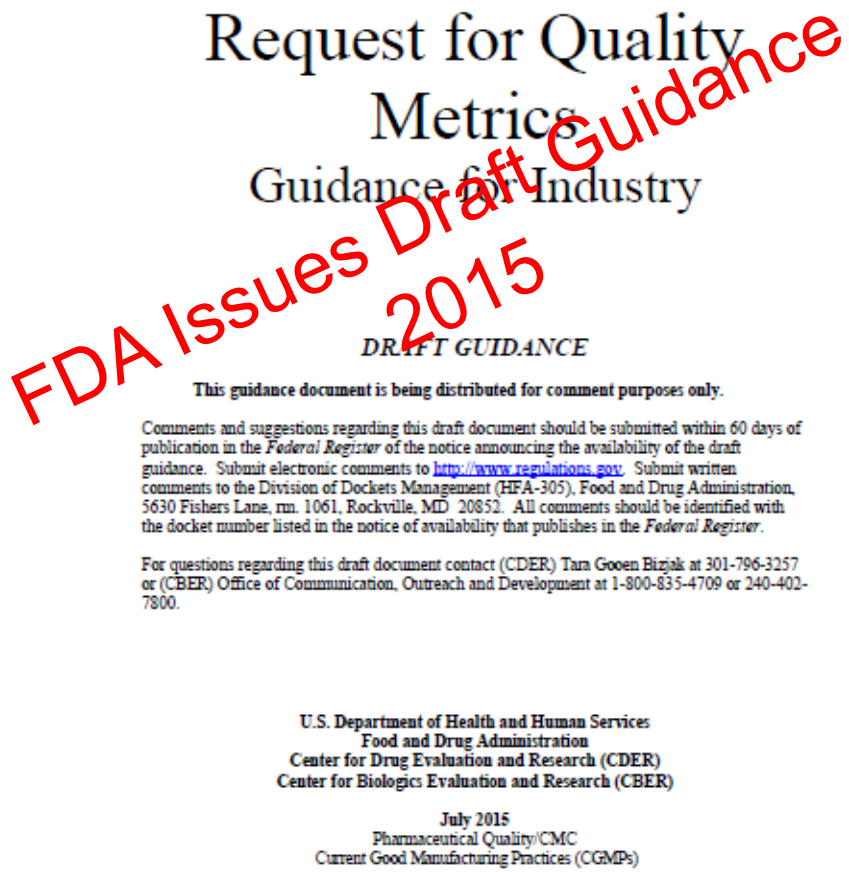
Quality Metrics program

Emerging Technology Team

Participation in ICH Q12

New Inspection Protocol Project

FDA's Quality Metrics Journey: Where Have We Been?



Request for Quality Metrics

Guidance for Industry

FDA Issues Draft Guidance 2015

DRAFT GUIDANCE

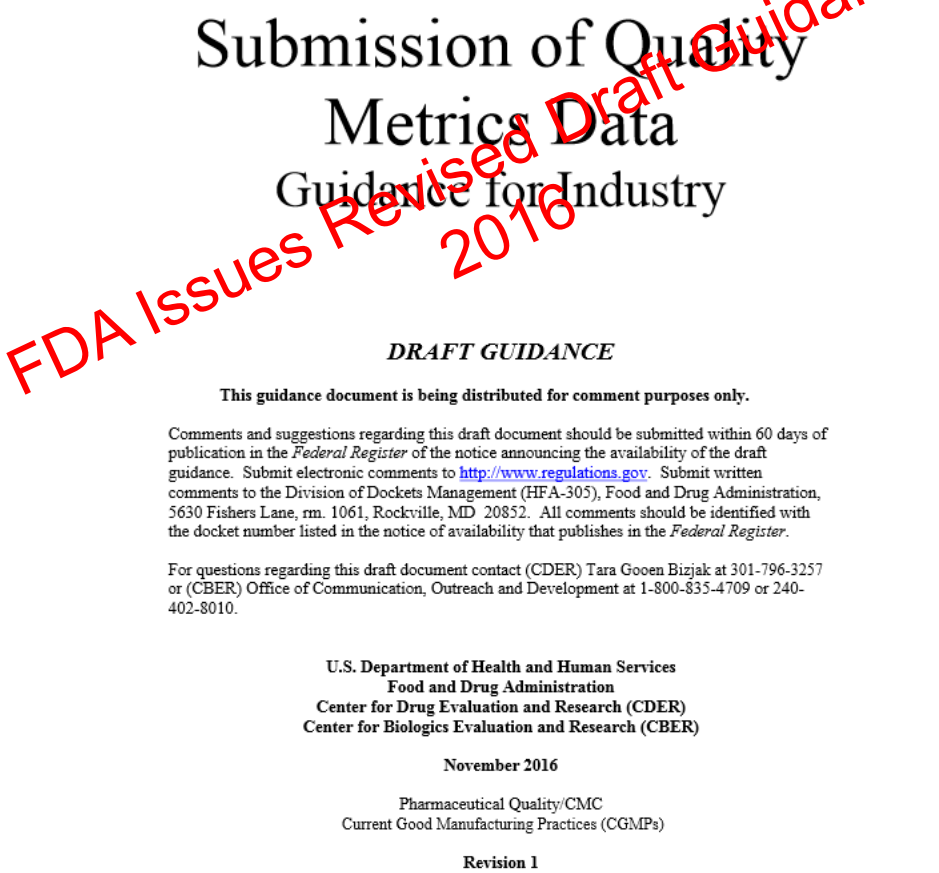
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Tara Gooen Bizjak at 301-796-3257 or (CBER) Office of Communication, Outreach and Development at 1-800-835-4709 or 240-402-7800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

July 2015
Pharmaceutical Quality/CMC
Current Good Manufacturing Practices (CGMPs)



Submission of Quality Metrics Data

Guidance for Industry

FDA Issues Revised Draft Guidance 2016

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Tara Gooen Bizjak at 301-796-3257 or (CBER) Office of Communication, Outreach and Development at 1-800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

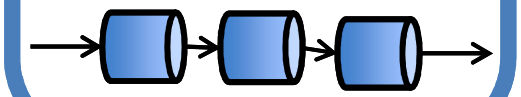
November 2016

Pharmaceutical Quality/CMC
Current Good Manufacturing Practices (CGMPs)

Revision 1

Metrics that FDA intended to Calculate per the November 2016 draft guidance revision

Robustness of Commercial Manufacturing Process



Lot Acceptance Rate

Robustness of Laboratory Operation

Invalidated Out-of-Specification Rate

Voice of the Patient/Customer

Product Quality Complaint Rate

FDA's Quality Metrics Journey: Where Are We Going?

Quality Metrics for Drug Manufacturing

SHARE | TWEET | LINKEDIN | PIN IT | EMAIL | PRINT

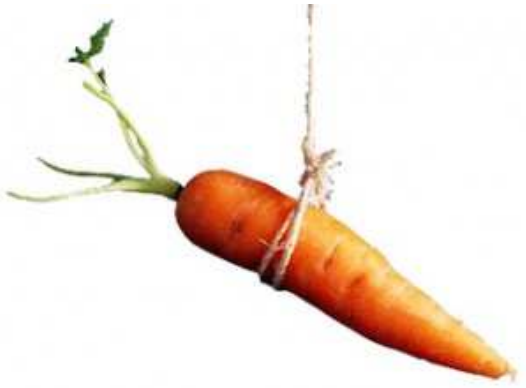
Update:

The portal is not opening in January 2018 for widespread, voluntary reporting. Stay tuned for additional updates.

https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm526869.htm

Long Term Quality Metrics Program: Voluntary vs. Mandatory Reporting

- Extent to which FDA can achieve its goals for the QM program will be largely driven by the extent of participation
  - Large body of data is needed to draw the most meaningful conclusions about the quality of a site or product
- Looking for feedback on appropriate incentives



Ideas to Continue the Quality Metrics Discussion

- Establishments could provide feedback and additional comments to FDA, as well as share knowledge from ongoing, industry-driven quality metrics programs
- Establishments to share “best practices” amongst each other to improve individual overall quality metrics programs
- FDA working informally with establishments towards early resolution of potential quality problems, as a factor in reducing inspection frequency, or perhaps as an element of the post-approval manufacturing change reporting program

Summary

- Quality metrics programs are important and beneficial to the patient, to industry, and to FDA
- Many manufacturing establishments currently use quality metrics
  - Individual programs should be tailored to include those metrics that the manufacturer finds useful in performing these product- and establishment-specific evaluations
- Current research indicates quality metrics programs are a good business practice

Knowledge is no guarantee of good behavior, but ignorance is a virtual guarantee of bad behavior.

Martha Nussbaum

Want to know more?

If you're interested in providing feedback or have a question, contact:

Tara Gooen Bizjak, MBSci

CDER Office of Policy for Pharmaceutical Quality

Tara.Gooen@fda.hhs.gov

For more information and resources, visit:

https://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm526869.htm

Background Slides

Top 10 St. Gallen Maturity Attributes

These Maturity Attributes drive Quality Behavior

1. Optimized set-up and cleaning procedures are documented as **best-practice process** and **rolled-out throughout the whole plant**.
2. A large percentage of equipment on the shop floor is currently under **statistical process control** (SPC).
3. For **root cause analysis** we have **standardized tools** to get a deeper understanding of the influencing factors (e.g. DMAIC).
4. **Goals and objectives** of the manufacturing unit are **closely linked** and consistent **with corporate objectives**. The site has a clear focus.
5. We have **joint improvement programs** with our suppliers to increase our performance.

… Continued on next slide

91% of variability of Quality Behavior can be explained by the Top 10 Quality Maturity Attributes.

Total number of maturity attributes in study: 36

Top 10 St. Gallen Maturity Attributes (continued)

These Maturity Attributes drive Quality Behavior

6. All potential **bottleneck machines are identified** and supplied with additional spare parts.
7. For product and process transfers between different units or sites **standardized procedures exist**, which ensure a fast, stable and complied knowledge transfer.
8. **Charts** showing the **current performance status** (e.g. current scrap-rates, current up-times etc.) are posted on the shop-floor and visible for everyone.
9. We regularly **survey our customer`s requirements**.
10. We rank our suppliers, therefore we conduct **supplier qualifications and audits**.

91% of variability of Quality Behavior can be explained by the Top 10 Quality Maturity Attributes.

Total number of maturity attributes in study: 36