Office of Pharmaceutical Quality: Quality Metrics, Quality Culture, and Enhancing Data-Driven Decisions

Pharmaceutical Quality Symposium

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Learning Objectives

- Discuss a select set of quality metrics which may be useful for manufacturers without a current quality metrics program
- Identify characteristics of a manufacturer's quality metrics program with strong maturity and weak maturity
- Learn about the current FDA Quality Metrics Site Visit and Feedback Programs

Quality Metrics

Many manufacturers use *Quality Metrics* to monitor quality control and continually improve product and process quality.

Drugs *should be* no different.

2013

- Drug Shortage Federal Register Notice

2014

- Brookings Meeting: "Measuring Pharmaceutical Quality through Manufacturing Metrics and Risk-Based Assessment"

2015

- Draft Guidance for Industry: Request for Quality Metrics
- CDER SBIA Webinar
- Quality Metrics Public Meeting
- ISPE Pilot Wave 1

2016

- Technical Conformance Guide: Quality Metrics
- Revised Draft Guidance for Industry: Submission of Quality Metrics Data
- CDER SBIA Webinar and Article
- ISPE Pilot Wave 2
- St. Gallen Research Initiated

2017

- St. Gallen Year 1 Report Published

2018

- Opened the Quality Metrics Site Visit Program
- Opened the Quality Metrics Feedback Program
- St. Gallen Year 2 Report Published
- Initiated Quality Metrics Site Visits

2019

- Completed 15 Quality Metrics Site Visits
- Extended Quality Metrics Feedback Program
- Initiating Quality Metrics Feedback Program
- *St. Gallen Year 3 Report (Pending)*

2020

- *Continuation of FDA Quality Metrics Feedback Program*

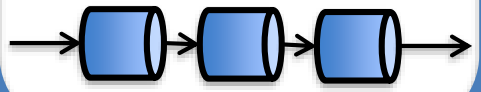
Research Indicates Businesses Benefit from Quality Metrics

- Collaborative research with St. Gallen University (Switzerland) indicates **Quality Metrics programs are a good business practice**
- The measurable Key Performance Indicators in the draft guidance are reasonable and **do make sense for a regulator**
- Cultural excellence should be incorporated into a regulatory program

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

Metrics of Interest to FDA

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

Indicators of Quality Metrics Program Maturity

Weak Maturity

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

- Evolution of metrics selection
- Promote quality culture
- Senior management commitment to quality
- Use of metrics and statistics in decision making

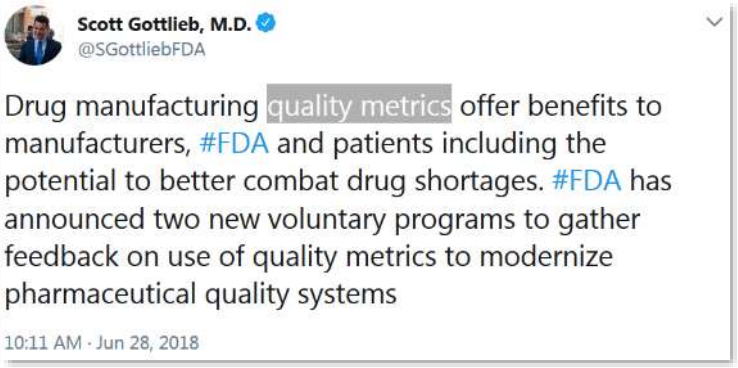
Strong Maturity

- Thoughtful metrics selection
- Predictive analytics
- Strong quality culture program
- Senior management and general staff commitment to quality
- Drive towards continual improvement of product, process, and pharmaceutical quality system

FDA Can Also Benefit from Quality Metrics

Additional insight into the state of quality for product and facility *outside of the inspection*

- 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
- Component of measuring an effective Pharmaceutical Quality System (supports the goals of ICH Q10 and Q12)



Current FDA's Quality Metrics Programs are intended to learn about existing practices

- **Feedback Program**
  - Solicits information from drug manufacturers that have implemented and are currently using quality metrics programs
  - Any data shared is for demonstration/informational purposes only

- **Site Visit Program**
  - Provides on-site learning opportunities for FDA staff involved in the development of the FDA Quality Metrics Program
  - Provides stakeholders with the opportunity to explain the advantages and challenges they've experienced with their quality metrics programs
  - Last day to submit package was December 18, 2018


FDA Announces Two Initiatives to Modernize Drug Quality Programs

Posted on July 26, 2018 by FDA Voice

By: Janet Woodcock, M.D., and Michael Kopcha, Ph.D., R.Ph.

Patients expect and deserve high-quality drugs – this means consistently safe and effective medicines free of defects and contamination. To satisfy these important expectations, the FDA strives to make sure that FDA-approved drugs are manufactured to meet quality standards to ensure that every dose is safe, effective, and capable of providing its intended benefit.

Quality metrics are used in a variety of industries to monitor the quality control systems and processes that ensure standards are met, and to identify opportunities for manufacturing improvements. For the pharmaceutical industry, the use of quality metrics offers potential benefits to patients, manufacturers, and the FDA – including the potential to better combat drug shortages.

Quality Metrics Feedback Program

- For applicants: use of existing meeting mechanisms is for convenience only; no impact on pending or planned applications
- For non-applicants: pilot established
  - Active pharmaceutical ingredient manufacturers
  - Contract manufacturers
  - Over-the-counter monograph product manufacturers
  - Marketed unapproved finished drug product manufacturers
- Submit a statement of interest and confirmation that the selection qualities are met to OPQ-OS-Qualitymetrics@fda.hhs.gov by December 30, 2019
- Format, information submitted, and duration of meetings are flexible

Quality Metrics Feedback Program

- Preference that participants are willing to share and discuss current and historical data and programs, such as:
  - Lot acceptance rate (LAR)
  - Invalidated out-of-specification (OOS) rate (IOOSR)
  - Product quality complaint rate (PQCR)
  - Process performance and capability
  - Quality culture
  - Quality system metrics
  - On-time and In-full fulfillment of orders
- Any data shared is for demonstration/informational purposes only
  - Data will not be considered part of an application, for any type of assessment, or to influence inspection planning

Quality Metrics Program – Next Steps

- Completed 15 Quality Metrics Site Visits from December 2018 to October 2019
  - Variety of individual manufacturers
  - Teams included CDER OPQ, CDER OC/OMQ, and ORA
  - Focus on quality metrics and quality culture programs

- Early learnings
  - Quality metrics and quality culture programs are a journey
    - Can take a few years to align metrics definitions at different sites and connect data systems
  - Identified continued concerns regarding data validation and how the program will address different types of manufacturers and products
- We anticipate that our specific experiences with the Site Visits and the Feedback Program (with actual data) will help to inform CDER's future direction for the Quality Metrics Program

Key Takeaways

- **Key Takeaway 1**
  Current research indicates **quality metrics and quality culture programs** are a good business practice and an important element of modern pharmaceutical manufacturing. Quality metrics and quality culture programs are **mutually beneficial** to the industry, the Agency, and patients.
- **Key Takeaway 2**
  While the following categories are not all-inclusive in order to measure the effectiveness of a quality system, they are a good place to start on a quality metrics and quality culture journey: **robustness of commercial manufacturing process**, **voice of the patient**, and **laboratory robustness.**
- **Key Takeaway**
  OPQ continues to engage stakeholders to learn more about existing metrics programs. FDA's Quality Metrics Feedback Program is open until **December 30, 2019**. We encourage interested stakeholders to contact us if they have questions.

Challenge Question

True/False

Robust quality metrics programs enable continual improvement of the product, process, and systems and are mutually beneficial to industry, the Agency, and the patient.

For more information and resources, visit:

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