Quality Metrics and Data Driven Decisions

*PDA Pharmaceutical Quality Metrics and Quality Culture Conference*
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CDR Tara Gooen Bizjak
Senior Science Policy Advisor
Div. of Regulations, Guidance, and Standards
Office of Policy for Pharmaceutical Quality
FDA/CDER

Disclaimer

- This presentation reflects the views of the speaker and should not be construed to represent the views or policies of FDA or ICH.
Overview

• Mature quality metrics programs
• Draft guidance
• Metrics described in the guidance
• How FDA intends to use quality metrics
• Electronic portal
Why Quality Metrics?

https://spreecommerce.com/blog/data-driven-decisions

Maturity of Quality Metrics Programs

• Identifying existing problems vs. predictive analytics
• Importance of quality culture
• What are useful product- and site-specific metrics?
• How committed is senior management to overall quality?
• How committed is the entire staff to quality culture?
• Does the program improve over time?
Publication of Revised Draft Guidance

Submission of Quality Metrics Data
Guidance for Industry

U.S. FOOD & DRUG ADMINISTRATION

By: CDR Tara Gooen Bizjak
Who May Submit Quality Metrics Data Reports to FDA?

- **Product Reporter or Site Reporter**
  - Provides one report for each API or for each FDF or each covered establishment
  - For a product reporter, generally expect that the Quality Control Unit (Quality Unit) would be best positioned to provide these data

**Examples**

<table>
<thead>
<tr>
<th>Establishment 1 (mixing, granulation)</th>
<th>Establishment 2 (tablet compression)</th>
<th>Establishment 3 (packaging)</th>
</tr>
</thead>
<tbody>
<tr>
<td>data</td>
<td>data</td>
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<tr>
<td>Product Reporter submits one report to FDA</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Product A</th>
<th>For Site B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product 1 (Tablet)</td>
<td>Product 1</td>
</tr>
<tr>
<td>Product 2 (Vial)</td>
<td>Product 2</td>
</tr>
<tr>
<td>Product 3 (API)</td>
<td>Product 3</td>
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<tr>
<td>data</td>
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<td>data</td>
<td>data</td>
</tr>
<tr>
<td>Site Reporter submits one report to FDA</td>
<td></td>
</tr>
</tbody>
</table>

**Benefits of Product Reports**
- Understand the overall health and reliability of the product/process
- Oversight and control over establishments in the supply chain

**Benefits of Site Reports**
- Confidentiality concerns
- Less burdensome (per comments)
- Additional opportunity to identify a systematic quality system or facility trend

Both product reporters and site reporters would benefit from robust quality metrics programs to identify or predict areas for follow-up and/or trending.
Metrics Described in the Draft Guidance and other Metrics Likely to be Useful

Data vs. Metrics

- FDA would use the data to calculate indicator metrics

Robust Product/Site Measurement Program

- Lot Acceptance Rate
- Manufacturing process robustness
- Invalidated OOS Rate
- Laboratory operations
- Product Quality Complaint Rate
- Voice of patient/consumer
Metrics that FDA intends to Calculate

- Robustness of Commercial Manufacturing Process
- Robustness of Laboratory Operation
- Voice of the Patient/Customer

Lot Acceptance Rate
Invalidated Out-of-Specification Rate
Product Quality Complaint Rate

Metrics Likely to be Very Useful

- Lot acceptance rate
- Invalidated and validated OOS rate
- Product quality complaint rate
- Deviations without assigned root cause
- Periodic Product Review Completion
- Planned equipment/facility maintenance rate
- Quality culture
- Process performance and capability
- Senior management commitment to quality
- CAPA effectiveness (retraining, preventive actions)
- Right-First-Time
- Reliability of drug availability
- ...

FDA encourages using quality metrics beyond the draft guidance.
Importance of Quality Culture

The *behaviors* and *beliefs* characteristic of a particular social group. (Webster's dictionary)

Culture/values indicate what is important to the enterprise, thus, impacts their decision making

The importance of culture:
• The root cause of many of quality problems
• Essential for continuous improvement of the quality systems

Is Quality Culture a competitive advantage?

For every 5,000 employees, moving from the bottom to the top quintile would save a company $67 million annually

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JP Zonnenberg, November 2016
Lot Acceptance Rate: Saleable and IPP Lots

Process Steps

In-Process Unit Operations

In-Process and Packaging Lots

Saleable Lots

Tableting

Fill/Finish

Encapsulation

...Packaging

FDA guidance for industry Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production (October 2006)
Invalidated Out-of-Specification Result Rate

- IOOS Rate corresponds with three data points
  - Ratio of invalidated OOS and total OOS provides context of OOS investigations attributed to the laboratory
  - Total number of tests provides context of the lab capacity for industry-wide comparison
  - Subtracting invalidated OOS from total OOS and comparing with lot acceptance rate provides a secondary measurement of manufacturing performance

How FDA Intends to Use Quality Metrics
How does FDA intend to use quality metrics?

Develop objective measures

- Quality of a drug product
- Quality of a site
- Effectiveness of systems associated with the manufacture of pharmaceutical products

Context Matters – Individual data points and metrics described in the guidance, either individually or in combination, do not definitely quantitate the quality of the establishment or its products

How does FDA intend to use quality metrics data in the voluntary phase of the reporting program?

- If a large body of data is not received, the ways in which FDA can use the information may be limited
  - May not be representative of industry
  - Self-selection bias
- Therefore, we initially expect to use the information to specifically focus on:
  - Working with establishments towards early resolution of potential quality problems
  - Helping to prepare for and direct our inspections
  - As an element of the post-approval manufacturing change reporting program
Electronic Portal

QUALITY METRICS
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

For information and technical specifications document contact (CHER) Tara Gooen 
Office of Communications, Outreach and Development at 1- 
240-852-8010 or 240-852-8019.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Regulatory Affairs
Office of Communication, Outreach and Development

FDA Issues Version 1.0
Receiving Data via the Electronic Portal

- Defined reporting period (e.g., single calendar year)
- Expect to open the electronic portal to receive reports in early 2018
- Technical Conformance Guide

“Get More Innovative by Rethinking the Way You Think”

A robust quality metrics program requires continual improvement.

Pharmaceutical Quality for the 21st Century and Quality Metrics: Looking Short Term

- Continue to encourage emerging technology
- Test and improve the electronic portal submission process
- Incentives for establishments going “above and beyond”
  - Additional opportunities for feedback from participating establishments
  - Quality Metric Reporters List
  - Considering how the calculated metrics can be used as an element of the post-approval manufacturing change reporting program
  - Reduction in inspection frequency based on reporting
- Improve the program based on feedback and analytics

Pharmaceutical Quality for the 21st Century and Quality Metrics: Looking Long Term

- Predictive analytics
  - Correlation with FDA data (e.g., inspection outcomes, recalls, FARs)
  - Drug supply disruption
- Continue to recognize participating establishments
  - Quality Metric Reporters List
  - Enhance pre-marketing and postmarketing review program (e.g., post-marketing change reporting program)
  - Potential reduction in inspection frequency based on data
- Continue to encourage emerging technology
- Notice and comment rulemaking
  - Large body of data
Acknowledgements

• Alex Viehmann, OS
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For more information or to contact OPQ:

Quality Metrics for Drug Manufacturing

CDER-OPQ-Inquiries@fda.hhs.gov

One Quality Voice

Extra slides
What would be reported?

- Reporting establishments would report data; these data should already be available per CGMP
- For the subject product:
  - Lots started, intended for distribution: saleable and in-process/packaging
  - Lots released, intended for distribution: saleable and in-process/packaging
  - Lots rejected, intended for distribution: saleable and in-process/packaging
  - Total out-of-specification results (lot release tests and long-term stability results)
  - Invalidated out-of-specification results (lot release tests and long-term stability results)
  - Total number of lot release tests and long-term stability tests performed
  - The number of product quality complaints received for the product.
  - The total number of dosage units distributed for the product.