

# Quality Metrics

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# Objectives

- Pharmaceutical Quality for the 21<sup>st</sup> Century
- Why Quality Metrics (QM)?
- Initial draft of the QM Guidance
- Key Features of the QM Revised Draft Guidance
- Phased-In Approach and Benefits to Participants
- How FDA Intends to Use Metrics Data



# Pharmaceutical Quality for 21<sup>st</sup> Century Initiative

## Vision

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

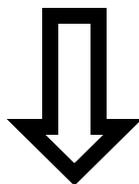
# Desired State of Manufacturing

- 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'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 reporting program  
Emerging Technology Team  
Participation in ICH Q12  
New Inspection Protocol Project





# 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
- Programs should be tailored to include those metrics that the manufacturer finds useful in performing these product- and establishment-specific evaluations

# Robust Product/Site Measurement Program



## Other Metrics Likely to be Useful

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

# Quality Metrics Programs

## Indicators of Maturity

- 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?



# Why Quality Metrics?

## 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)

# Why Quality Metrics?

## 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
- Gain insights/trends regarding the state of quality across the pharmaceutical industry



# Why Quality Metrics?



## 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



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



**FDA's Quality Metrics  
Reporting Program**



**Initial Draft  
Guidance  
July 2015**

**Federal Register  
Notice, Stakeholder  
Input**

# Initial Draft

- Request for metrics data
- Product reports
- FDA would use the data to calculate metrics:
  - Lot Acceptance rate
  - Product Quality Complaint rate
  - Invalidated Out-of-Specification (OOS) rate
  - Annual Product Review (APR) or Product Quality Review (PQR)  
On Time rate
- Public comment requested on several optional metrics
  - Senior management engagement
  - CAPA effectiveness
  - Process capability/performance

# Initial Draft – Public Docket

- Significant comments received
  - Technical comments regarding proposed metrics and definitions
  - Concerns regarding burden of data collection/formatting/submission
  - Legal concerns regarding proposed mandatory program
  - Suggestions to take a phased-in approach to allow learning by both industry and FDA

# FDA's Quality Metrics Journey: Where Are We Now?



**FDA's Quality Metrics  
Reporting Program**

**Initial Draft  
Guidance  
July 2015**

**Revised Draft  
Guidance  
November 2016  
& Technical  
Conformance  
Guide June 2016**

**Federal Register  
Notice, Stakeholder  
Input**

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# Submission of Quality Metrics Data Guidance for Industry

## ***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, Room 10661, 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 Goen 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)**

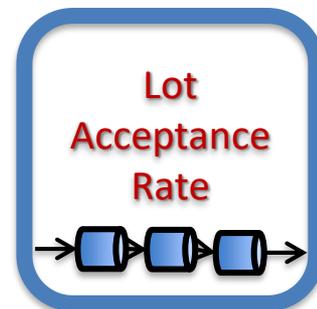
**November 2016**

Pharmaceutical Quality/CMC  
Current Good Manufacturing Practices (CGMPs)

**Revision 1**

# Revised Draft – Key Features

- Mandatory → Initial Voluntary Phase
- Product- OR site-based reporting
- Limited set of 3 metrics related to batch manufacturing, laboratory robustness, and the voice of the patient or customer (quality complaints)
- Technical edits and examples
- Incentives for participation

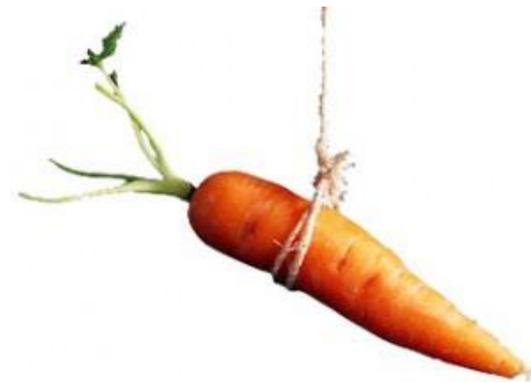


# Submission of Information is Voluntary

- During the voluntary phase of the reporting program, FDA does not intend to require the submission of this information
- FDA does not intend to take enforcement action based on errors in a quality metrics data submission made during this voluntary phase of the reporting program, provided the submission is made in good faith

# Voluntary vs. Mandatory

- 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
- Developed additional incentives for reporting



# Benefits of Participation

- Opportunities for participants to provide feedback and additional comments, as well as share knowledge from ongoing, industry-driven quality metrics programs
- FDA working informally with establishments towards early resolution of potential quality problems
- Improved inspection effectiveness (e.g., more focused inspections)
- Enhance premarket and postmarket review program (e.g., consider use of *calculated metrics* as an element of the post-approval manufacturing change reporting program)
- Reduction in inspection frequency
- Inclusion on the Quality Metrics Reporters List



## Want to know more?

For more details about the revised draft guidance including examples, please see:

CDER Small Business and Industry Assistance (CDER SBIA) Webinar - Revised Draft Guidance for Industry: Submission of Quality Metrics Data

<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm530313.htm>

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



# Vision Remains the Same

- Focus the use of resources on areas of highest risk to public health
  - Establish a signal detection program as one factor in identifying establishments and products that may pose significant risk to consumers
  - Identify situations in which there may be a risk for drug supply disruption
  - Improve the effectiveness of establishment inspections
  - Improve FDA's evaluation of drug manufacturing and control operations



# Quality Metrics in the Short Term

- 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
  - Enhance pre-market and post-market review program
  - Reduction in inspection frequency based on reporting
- Improve and mature the program based on feedback and analytics
  - Publish summary of initial reports
- Ensure program supports, not deters, emerging technology

# Quality Metrics in the Short Term

- Continuing discussions with external groups
  - Measuring and assessing quality culture
  - Ongoing improvement in definitions and examples
  - Continuing discussions with a range of industry groups/representatives
    - Non-application products
    - Contract manufacturers
    - Active ingredient manufacturers
  - Evaluate additional sources of data to study quality metrics



# Quality Metrics in the 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 premarket and postmarket review program (e.g., post-marketing change reporting program)
  - Potential reduction in inspection frequency based on *data*
- Continue to encourage emerging technology
- Other incentives?

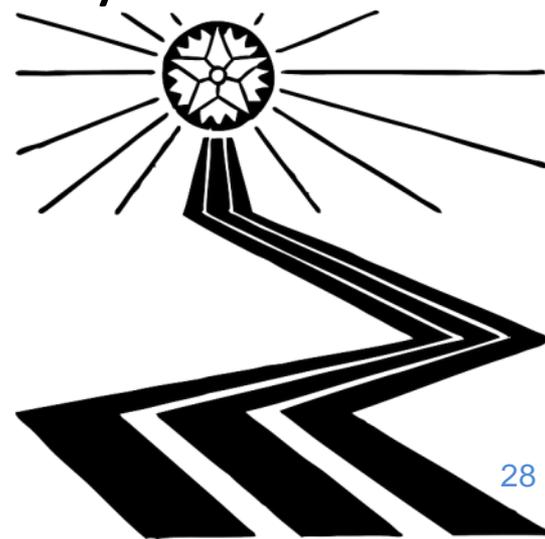


# Quality Metrics in the Long Term

- Voluntary reporting alone may not be sufficient to accomplish FDA's goals for the program
- Greater net benefit for FDA and industry likely to result from a fully operational program
  - Incorporate initial learnings
  - Fuller participation
- Continuing to plan for notice and comment rulemaking

# Summary

- Quality Metrics play an important role in the desired state of pharmaceutical quality and regulation – minimal but effective regulatory oversight that results in quality drugs available for patients
- Development of the FDA program is a journey that has reached an important next step
- In collaboration with participating industry stakeholders, we will incorporate learnings from this initial phase of the program to more fully realize the potential of quality metrics



# “Get More Innovative by Rethinking the Way You Think”



Innovating how we innovate

Analyzing how we analyze

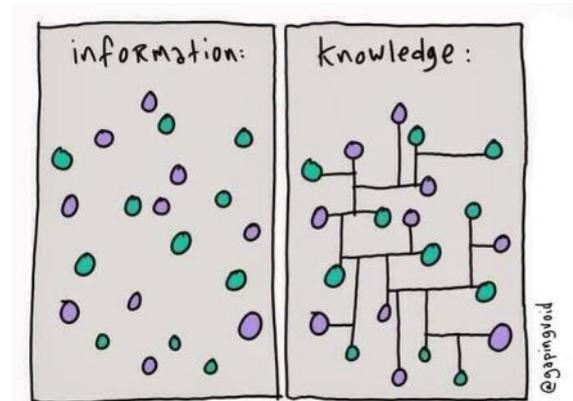
Improving how we improve



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



<https://andrewpetrosniak.files.wordpress.com/2012/12/gutfeeling.png?w=300>



<http://alfredlua.com/wp-content/uploads/2016/11/Info-vs-Knowledge.jpg>

For more information or to contact OPQ:

[Quality Metrics for Drug Manufacturing](#)

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm526869.htm>

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THANK  
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