



# FDA's Vision for Quality Metrics

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# Objectives

- Pharmaceutical Quality for the 21<sup>st</sup> Century
- Why Quality Metrics?
- Product and Site-based Reporting
- What Quality Metrics?
- 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 or no manufacturing supplements needed





# Why Quality Metrics?

## Industry

- Enables continual improvement of process performance and product quality
- Supports continual improvement of the pharmaceutical quality system
- Advances operational excellence and quality practices
- Provides an important element of oversight and controls over the manufacture of drugs to ensure quality
- If applied appropriately, may improve the company's bottom line



# Why Quality Metrics?

## Patients

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

# Why Quality Metrics?



## FDA

- Quantitative and objective measure of the state 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 potential supply disruptions
  - Enhance pre-marketing and postmarketing review program



# We Have Mutual Goals

- Identify those performing above the requirements and reduce regulatory oversight
- Remove poor quality products from the marketplace
- Use quality metrics as an additional tool in the surveillance toolbox



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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## ***DRAFT GUIDANCE***

**This guidance document is being distributed for comment purposes only.**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 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 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)**

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Pharmaceutical Quality/CMC  
Current Good Manufacturing Practices (CGMPs)

**Revision 1**



# Major Changes

- Phased-in approach
  - Voluntary phase
  - Reduced footprint of quality metrics data
- Support both product and site reporting
- Technical revisions based on comments
- Incentives for firms going above and beyond
  - Quality Metrics Reporters List
  - Additional opportunities for feedback from participants
  - Factor in surveillance inspection scheduling
  - Considerations for post-approval manufacturing change reporting programs
  - FDA does not intend to initiate any enforcement actions based on quality metrics data alone



# Product and Site Reporting of Covered Drug Products by Covered Establishments



# Covered Drug Product\*

- A covered drug product is:
  - Subject to an approved application under section 505 of the FD&C Act or under section 351 of the PHS Act
  - Marketed pursuant to an OTC monograph
  - Marketed unapproved finished drug product
- This phase of the program is not focused on reporting from certain CDER and CBER regulated manufacturers

\* For the purposes of this draft guidance



# Covered Establishment

- A covered establishment is:
  - An establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a covered drug product
- Includes relevant contract establishments, such as, but not limited to:
  - Contract laboratories
  - Contract sterilizers
  - Contract packagers



# Quality Metrics Data Reports

- Product reports submitted by product reporting establishments
  - The subject of a product report is a covered drug product or an API used in a covered drug product
- OR***
- Site reports submitted by site reporting establishments
  - The subject of a site report is a single covered establishment, individually listing data associated with each covered drug product or API used in a covered drug product

# Quality Metrics that FDA Intends to Calculate

*Selection Criteria*

*Others*

# FDA's Selection Criteria for Quality Metrics Data in Draft Guidance

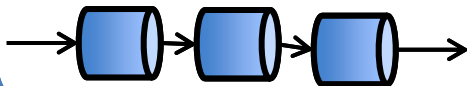


- *Objective data* to provide consistency in reporting
- Of the type contained in records *subject to inspection* under section 704 of the FD&C Act
- Valuable component in assessing the *overall effectiveness* of a Pharmaceutical Quality System
- Within *reasonable limits*, in a *reasonable manner*, while *avoiding an undue reporting burden*



# Metrics that FDA Intends to Calculate from Submitted Quality Metrics Data

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**



# Additional Quality Metrics that are Very Likely Useful

- Process capability and process performance
- **Quality culture**
- CAPA effectiveness
- Meeting Pharmaceutical Quality System timeframes
- Senior management commitment to quality
- ...



# Importance of Quality Culture

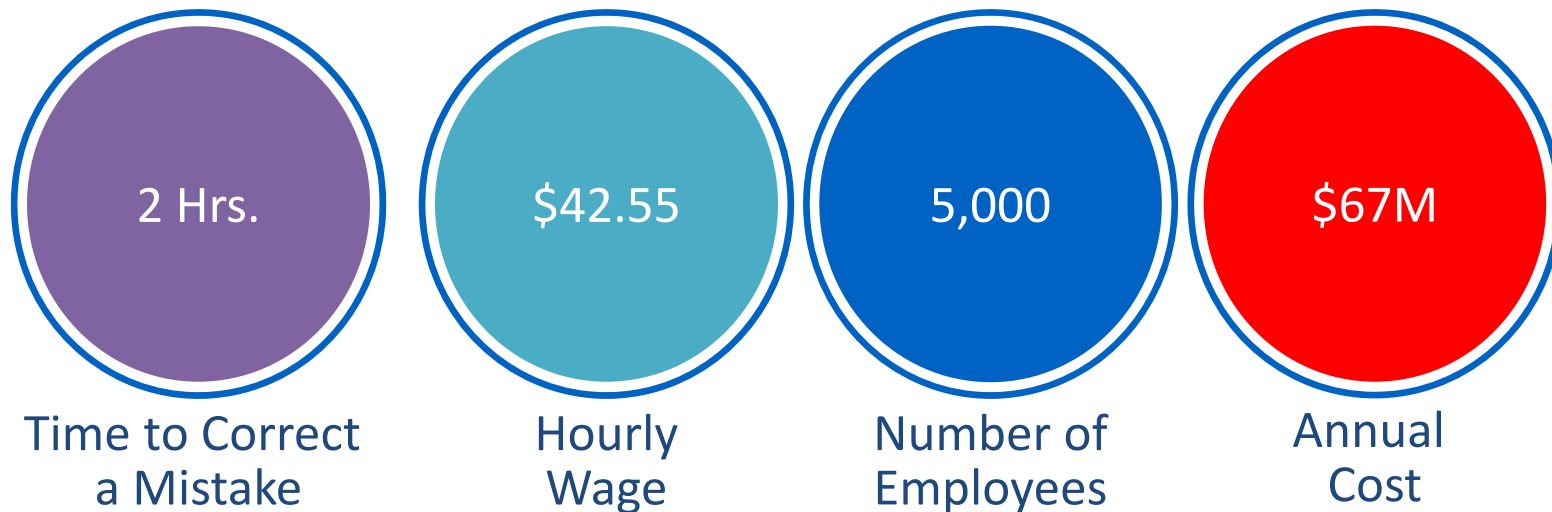
The *behaviors* and *beliefs* characteristic of a particular social group. (Webster's dictionary)

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



# Phased-In Approach and Benefits to Participants

*Voluntary Program*

*Reporters List*



## Legal Basis

- FDA may require the submission of any records or other information that FDA may inspect under section 704 of the FD&C Act, in advance or in lieu of an inspection by requesting the records or information from a person that owns or operates an establishment that is engaged in the manufacture, preparation, propagation, compounding, or processing of a drug
- Quality metrics data described in draft guidance is information of the type that FDA may inspect under section 704 of the Food, Drug, and Cosmetic Act

# 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 to this voluntary phase of the reporting program, provided the submission is made in good faith



# Disclosure

- FDA does not intend to publicly disclose information submitted to the Agency as part of the voluntary phase of the quality metrics program that is exempt from disclosure under the Freedom of Information Act as confidential commercial information, e.g., information that would reveal nonpublic commercial relationships and production volumes.





# Benefits of Participation

- Work with establishments towards early resolution of potential quality problems
- Improved inspection effectiveness
- ***Opportunities to provide feedback and additional comments***
- FDA is considering 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***



# Quality Metrics Reporters List

- Establishments that voluntarily report all or a subset of quality data
  - Product Reporters
  - Site Reporters
- Posted on <http://www.fda.gov/FDAgov/Drugs/DevelopmentApprovalProcess/Manufacturing/ucm526869.htm>
- Participation in the program demonstrates:
  - A willingness to proactively engage with the Agency
  - A commitment to increasing transparency between industry and FDA and improving quality monitoring throughout the industry

# How FDA Intends to Use Quality Metrics

*Analysis and Monitoring*



# Analysis of Quality Metrics Data

Goals for FDA's application of quality metrics:

- Develop objective measures
  - Quality of a drug product
  - Quality of a site
  - Effectiveness of systems associated with the manufacture of pharmaceutical products
- Conduct continual monitoring, assessment, and reporting on the state of quality across the inventory of drug products and facilities regulated by FDA
  - *Note: Can only be as good as the quality of available data and analytic tools*

*Voluntary reporting may  
not constitute a  
representative sample of  
the industry*



# Summary

- Quality Metrics play an important role in the desired state of pharmaceutical quality and regulation
  - Identify and reward firms going above and beyond
  - Enable better FDA surveillance of state of manufacturing and product quality
    - Enhanced site inspection scheduling
    - Potential to improve the efficiency and effectiveness of establishment inspections
  - Help to identify situations in which there may be a risk for drug supply disruption
  - Consider whether metrics may provide a basis to assist in determining the appropriate reporting category for post-approval manufacturing changes

# Questions?

For more information or to contact OPQ:

## [Quality Metrics for Drug Manufacturing](#)

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

[CDER-OPQ-Inquiries@fda.hhs.gov](mailto:CDER-OPQ-Inquiries@fda.hhs.gov)



FDA's Quality Metrics  
Reporting Program



**Voluntary Phase**