



U.S. Food and Drug Administration
Protecting and Promoting Public Health

www.fda.gov

Quality Metrics – An OPPQ Perspective

FDA/PQRI Conference on Advancing Product Quality

October 6, 2015

CDR Tara Gooen Bizjak

Senior Science Policy Advisor

Div. of Regulations, Guidance, and Standards

Office of Policy for Pharmaceutical Quality

FDA/CDER





Why Quality Metrics?

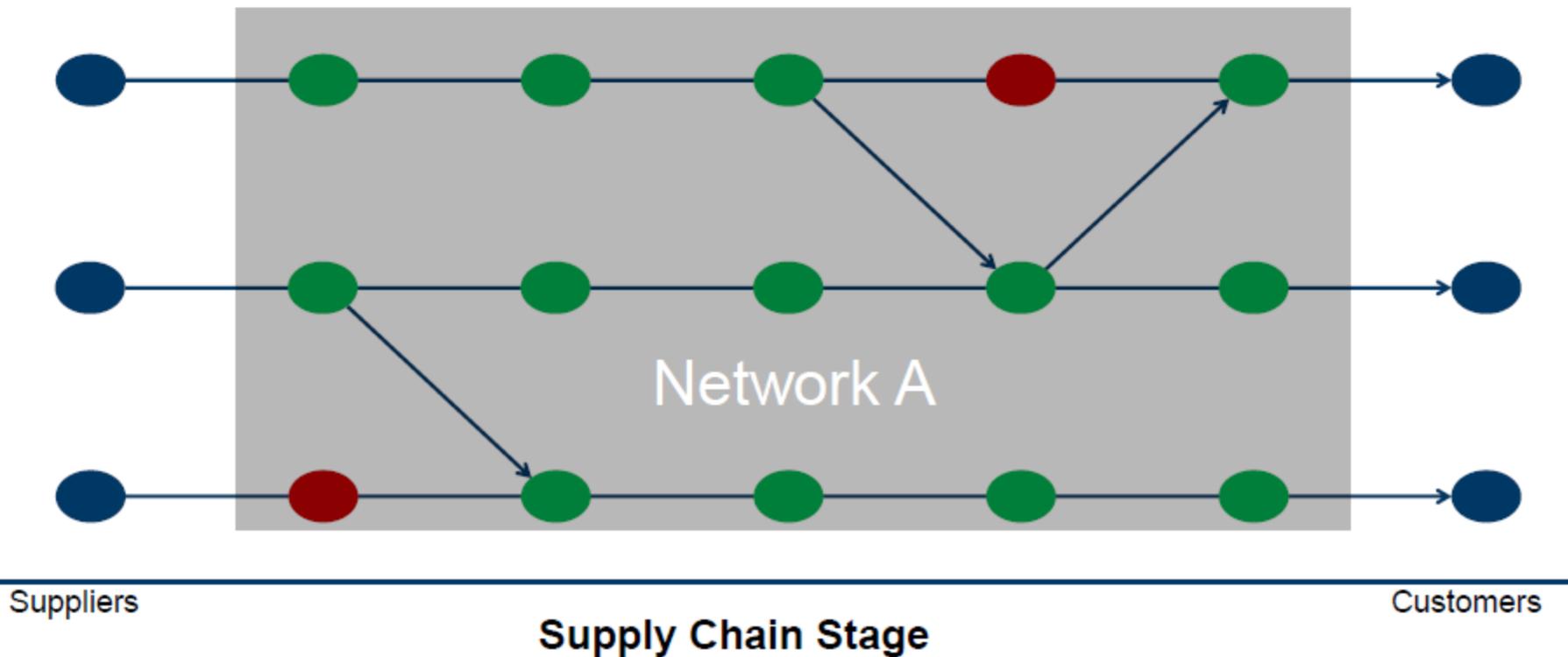
Industry

- 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)

Knowing the Supply Chain

Which Supply Chain Network Would You Chose?

Primarily insourced, low utilization, higher inventories

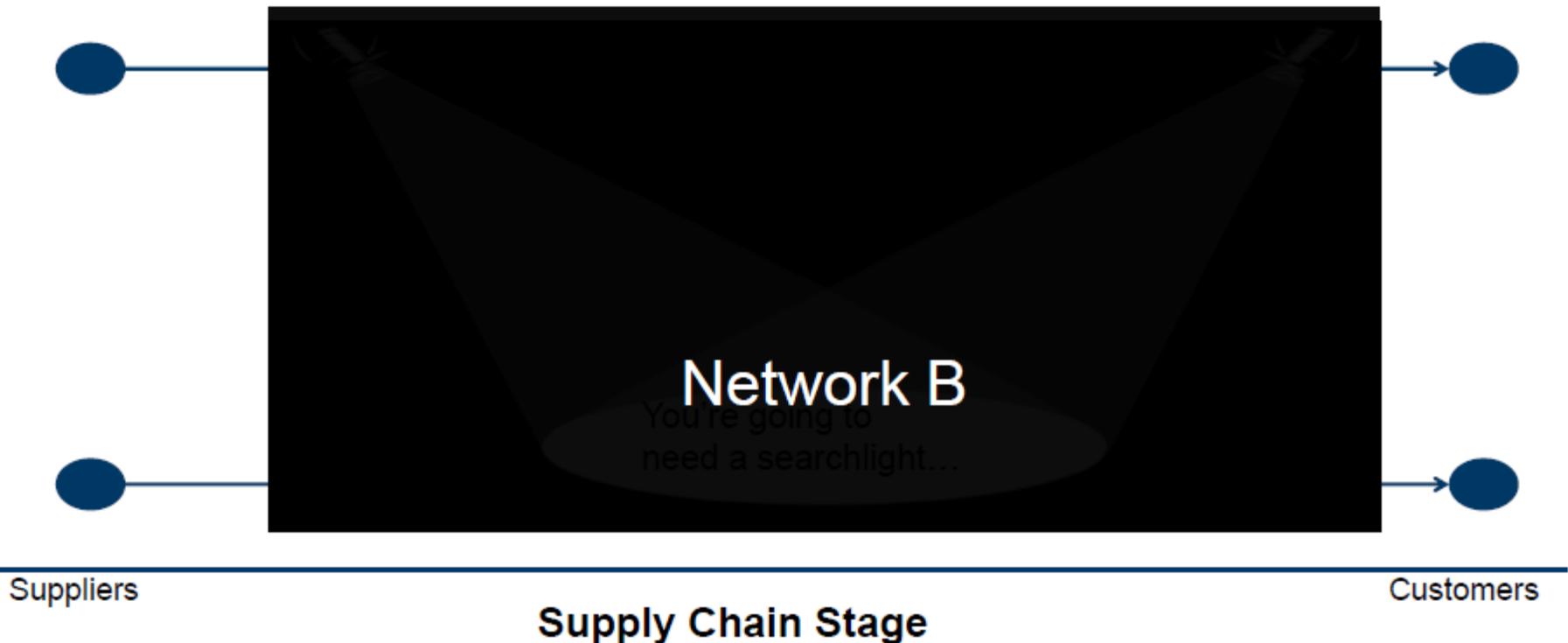




Knowing the Supply Chain

What About This One? Can You See It?

Primarily outsourced, high utilization, low inventories





Why Quality Metrics?

FDA

- Provide more 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



Why Quality Metrics?

Patients

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



U.S. Food and Drug Administration
Protecting and Promoting Public Health

www.fda.gov

Discussion on Robust Quality Metrics Programs



Foundation for Quality Metrics

- Industry quality measurement programs are not new
 - At least annual product quality reviews
 - Internal audits
 - Management reviews
 - Supplier qualification and ongoing monitoring

Maturity of QM programs

- Leading vs. lagging indicators
- Develop useful product- and site-specific metrics
- Senior management engagement
- Commitment to quality culture
- Evolution of quality metrics programs over time





Identified Challenges

- Existing metrics are defined differently at different sites
 - Even between sites operated by the same manufacturer
- Complicated supply chains
- Context matters
 - A single number does not reflect the state of quality





Request for Quality Metrics 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, 1240 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)

FDA Issues Draft Guidance



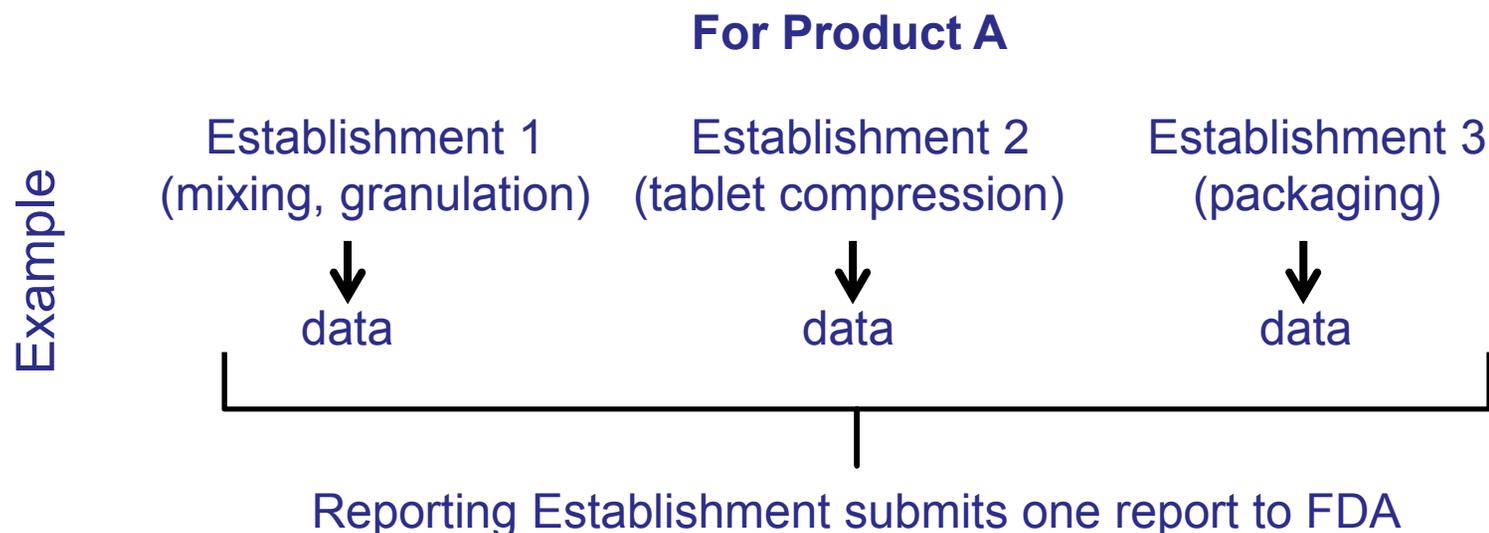
Who would report?

- Owners or operators of establishments that are engaged in the manufacture, preparation, propagation, compounding, or processing of a drug, specifically:
 - Finished dosage form (FDF) of a covered drug product, or
 - API used in the manufacture of a covered drug product.
- “Covered drug product”
 - 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.
 - a marketed unapproved drug product.
 - active pharmaceutical ingredients (API) used in the manufacture of a covered FDF.



Who would report?

- “Reporting Establishment”
 - Provides one report for each API or for each FDF
 - One establishment should already possess or have access to all of the data needed to submit such reports
 - Generally expect that the Quality Control Unit (Quality Unit) will be best positioned to provide these data





What would be reported?

- Reporting establishments would report data; these data should already be available per CGMPs
 - Number of lots attempted
 - Number of specification-related rejected lots
 - Number of attempt lots pending disposition >30 days
 - Number of OOS results
 - Number of lot release and stability tests
 - Number of OOS results invalidated due to lab error
 - Number of product quality complaints for the product
 - Number of lots attempted which are released for distribution or for the next stage of manufacturing
 - Whether the associated APRs or PQRs were completed within 30 days of annual due date for the product
 - The number of APRs or PQRs required for the product



Data vs. Metrics

- 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

How does FDA intend to use quality metrics?

MR. PERFECT

By Roger Hargreaves



- Develop objective measures for:
 - Quality of a drug product
 - Quality of a site
 - Effectiveness of systems associated with the manufacture of pharmaceutical products
- Analysis of quality metrics – context matters
 - Appropriate comparators may vary
 - Compare same metric, same product, same establishment over time?
 - Compare same metric, different products, same establishment?
 - Compare same metric, establishments performing same unit operation?
 - Compare same metric, products in the same class (e.g., large molecule injectables)?
 - Other?



How does FDA intend to use quality metrics?

- Goals for use of quality metrics
 - Identify risk-based factors that could impact inspection frequency
 - Improve detection of manufacturing conditions that may lead to a shortage
- Use in conjunction with other sources of information about product and site quality
 - Inspection results
 - Recalls
 - Field Alert Reports/Biological Product Deviation Reports



Looking Toward the Future

Increasing Operational Flexibility

- Continue to encourage emerging technology
- Exploring ways to reward firms that exceed minimum expectations
- Consider whether metrics may provided a basis to assist in determining the appropriate reporting category for post-approval manufacturing changes



Summary

- Quality Metrics play an important role in the desired state of pharmaceutical quality and regulation
 - Induce the right behavior and responsibility for industry
 - 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 provided a basis to assist in determining the appropriate reporting category for post-approval manufacturing changes



Final Thoughts

- ◆ A robust quality metrics program requires continual improvement
 - Ideal metrics are specific to the product, site, and supply chain
 - Ideal metrics are not limited to the metrics in this draft guidance
- ◆ The implementation of programs like quality metrics moves us closer to realizing the vision of the Pharmaceutical Quality for the 21st Century Initiative



Acknowledgements

- ◆ Ashley Boam, OPPQ
- ◆ Russ Wesdyk, OS
- ◆ Brian Hasselbalch, OPPQ
- ◆ FDA internal Working Group on quality metrics



More Information/Contacting OPQ

- ◆ Reach us at: CDER-OPQ-Inquiries@fda.hhs.gov
- ◆ For more information on this guidance, please see the CDER SBIA webinar at <http://www.fda.gov/Drugs/DevelopmentApprovalProcesses/SmallBusinessAssistance/ucm456059.htm>
- ◆ Please provide your comments on the guidance to the docket:
 - www.regulations.gov docket #FDA-2015-D-2537

One Quality Voice

