



The Importance of Quality Throughout the Drug Supply Chain

*Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting
November 2, 2022*

Patrizia Cavazzoni, M.D.

Director

Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Supply Chain Vulnerabilities

US FDA Center for Drug Evaluation and Research

The Three Pillars

**BUILDING RESILIENT
SUPPLY CHAINS,
REVITALIZING AMERICAN
MANUFACTURING, AND
FOSTERING BROAD-BASED
GROWTH**

100-Day Reviews under
Executive Order 14017

June 2021

A Report by
The White House

Including Reviews by
Department of Commerce
Department of Energy
Department of Defense
Department of Health and Human Services

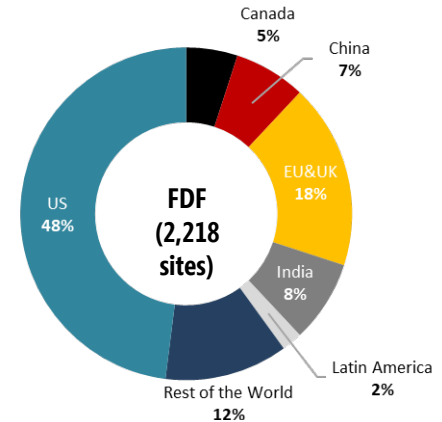
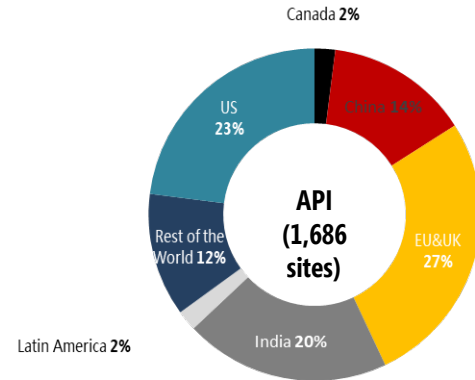


Three pillars of a secure
and robust supply chain are
**quality, diversification, and
redundancy.**

– 100-Day Report by
The White House

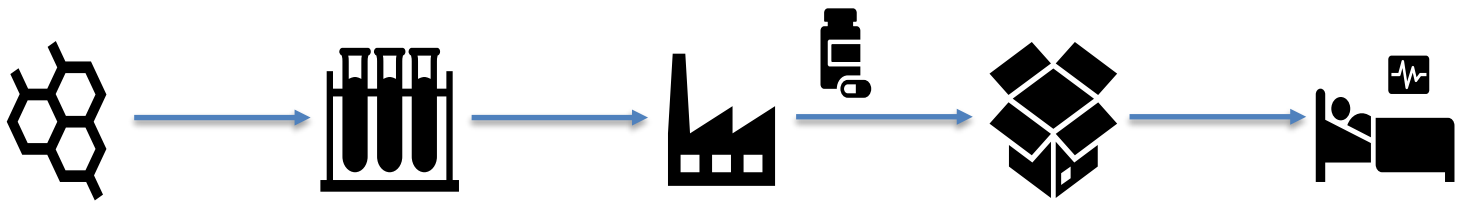
Quality: A Global Challenge

- ❑ **More than 75%** of active pharmaceutical ingredient (API) sites are outside of the US
- ❑ **More than 50%** of finished drug formulation (FDF) sites are outside of US
- ❑ Many products **launch** globally
- ❑ Regulatory strategies must be **data-driven** and **risk-based**



*FY2021 Report on the State of Pharmaceutical Quality

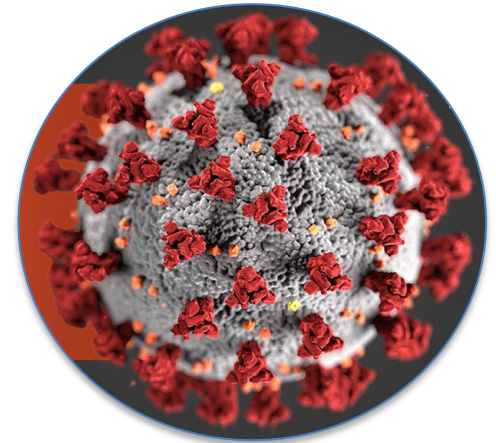
Supply Chains in the Era of COVID



| | | | |
|-----------|-----------|----------|-----------|
| | | | |
| personnel | materials | services | equipment |

Challenges from COVID

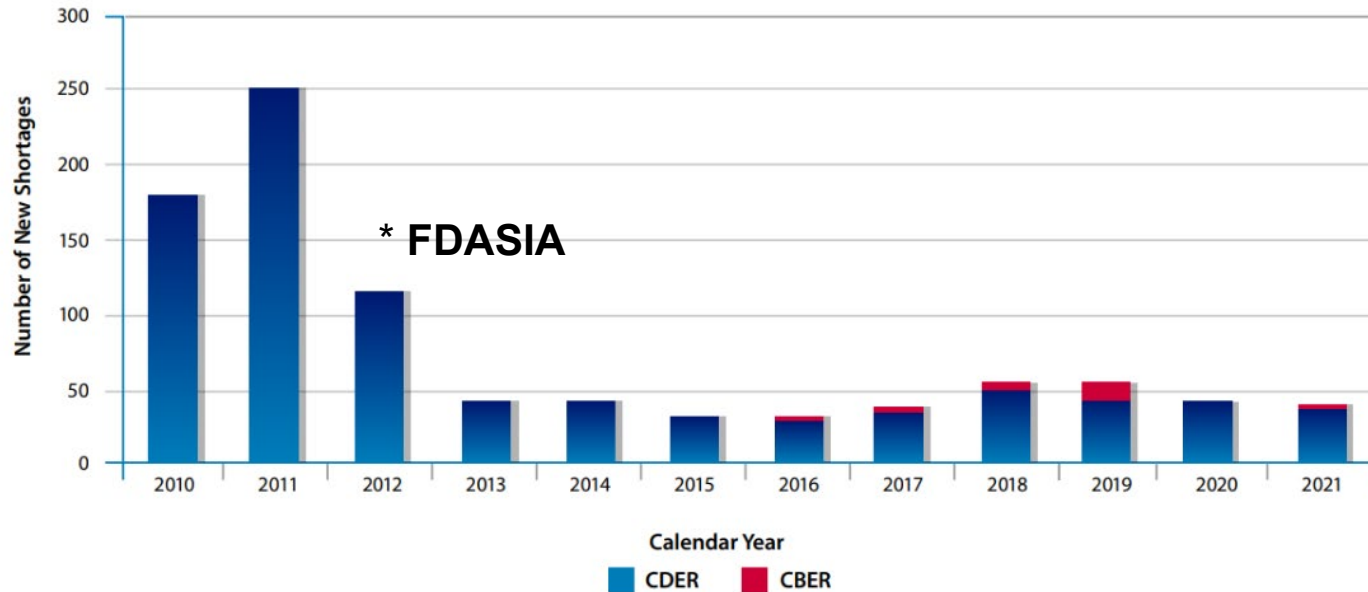
- ❑ Sudden, increased, local demand
- ❑ Competition on manufacturing lines in facilities due to limited capacity
- ❑ Supply of manufacturing components and other commodities
- ❑ Manpower and logistical challenges posed by public health safety measures



Drug Shortages

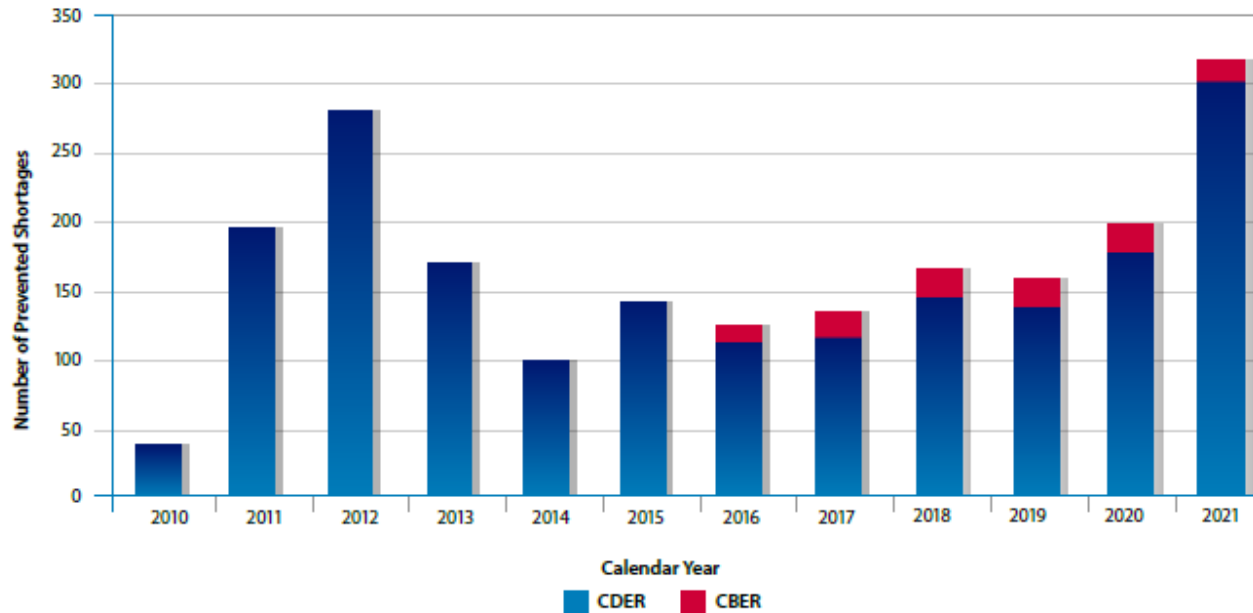
US FDA Center for Drug Evaluation and Research

Historical Drug Shortages



*FDASIA – Food and Drug Administration Safety and Innovation Act
 FDA Report to Congress - Drug Shortages for Calendar Year 2021

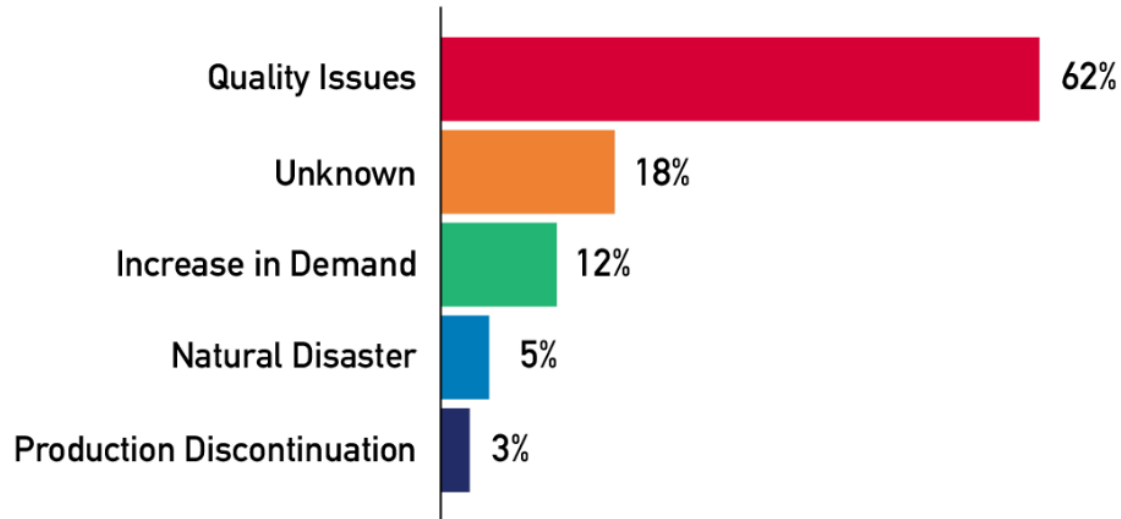
Historical Drug Shortages



FDA Report to Congress – Drug Shortages for Calendar Year 2021

Historical Reasons for Drug Shortages

Percentage of Drugs Newly in Shortage by Reason, Calendar Years 2013-2017



Most drugs in shortage were experiencing supply disruptions, specifically quality issues.

Source: Internal FDA Data

Root Causes and Potential Solutions

❑ Root Cause

The market does not recognize and reward manufacturers for “mature quality systems” that focus on continuous improvement and early detection of supply chain issues

❑ Recommendation

Developing a rating system to incentivize drug manufacturers to invest in QMM

Drug Shortages:

Root Causes and Potential Solutions

2019



FDA U.S. FOOD & DRUG
ADMINISTRATION

The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair in a ponytail is seen from behind, working at a lab bench. The background shows various pieces of laboratory equipment, including glass bottles, beakers, and pipettes, all slightly out of focus. The top half of the image is overlaid with a semi-transparent white filter.

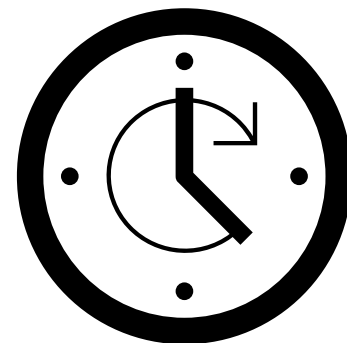
In Closing

US FDA Center for Drug Evaluation and Research

A solid red vertical bar is located on the right side of the slide, extending from the top of the blue section to the bottom.

The Future: Proactive Regulation

- ❑ CDER's Emerging Technology Program
- ❑ Framework for Regulatory Advanced Manufacturing Evaluation (FRAME) Initiative
- ❑ Holistic Supply Chain Understanding
- ❑ International Regulatory Convergence
- ❑ **QUALITY MANAGEMENT MATURITY PROGRAM**



A close-up photograph of a person's hands. The left hand holds an orange plastic pill bottle, tilted to pour three white, oval-shaped pills into the palm of the right hand. The background is softly blurred, showing a person's arm in a blue sleeve.

Patients deserve quality medicines that are available when they need them.



U.S. FOOD & DRUG
ADMINISTRATION

The Future of Pharmaceutical Quality

Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting

November 2, 2022

Michael Kopcha, Ph.D., R.Ph.

Director

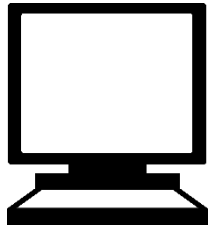
Office of Pharmaceutical Quality

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.



Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.



Drugs are no different.

A close-up photograph of a person's hands. The left hand holds an orange plastic pill bottle, tilted to pour three white, oval-shaped pills into the palm of the right hand. The background is softly blurred, showing a person's arm in a blue sleeve.

**Patients expect safe and effective
medicine with every dose they take.**

Pharmaceutical quality is
assuring *every* dose is safe and
effective, free of contamination
and defects.



**It is what gives patients confidence
in their *next* dose of medicine.**

An Array of Quality

Pharmaceutical Quality

*Gives patients confidence in their **next** dose of medicine*

| | | |
|---|----------------------------------|---|
| <p><i>Gives manufacturers confidence every batch will be acceptable to release</i></p> | <p>QUALITY MANAGEMENT</p> | <p>Performance and patient focus identifies areas of improvement and implements changes</p> |
| <p><i>Gives manufacturers confidence in every batch they release</i></p> | <p>PROCESS QUALITY</p> | <p>Manufacturing risks are controlled to provide a quality drug product</p> |
| <p><i>Gives patients confidence in every dose they take</i></p> | <p>PRODUCT QUALITY</p> | <p>Every dose is safe and effective and free of contamination and defects</p> |

CDER's Office of Pharmaceutical Quality

FDA



- Assessment
- Surveillance
- Inspection
- Research
- Policy

CDER's Site and Product Catalog

Sites:

- ❑ **7,000** human drug manufacturing sites of obligation
- ❑ **2,000** medical gas manufacturers (nearly all in U.S.)
- ❑ **600** hand sanitizer sites
- ❑ Includes **active pharmaceutical ingredient** and **finished dosage form** sites

Products:

- ❑ **170,000** finished dosage forms
- ❑ **19,000** active pharmaceutical ingredients
- ❑ **1,500** medical gases
- ❑ Includes **new drugs** and **biologics, generics, biosimilars, over-the-counter** drugs

**Based on June 2022 CDER Site & Product Catalogs and unique NDCs*



Challenge: Transparency

**BUILDING RESILIENT
SUPPLY CHAINS,
REVITALIZING AMERICAN
MANUFACTURING, AND
FOSTERING BROAD-BASED
GROWTH**

100-Day Reviews under
Executive Order 14017

June 2021

A Report by
The White House

Including Reviews by
Department of Commerce
Department of Energy
Department of Defense
Department of Health and Human Services

FDA should **lead the development of a framework to measure and provide transparency regarding a facility's quality management maturity** with engagement from industry, academia, and other stakeholders.

– 100-Day Report by
The White House



Quality Management Maturity

US FDA Center for Drug Evaluation and Research

Data for Regulatory Innovation

LAGGING INDICATORS → LEADING INDICATORS



- Quality Defect Reports
- Drug Sampling and Testing Results
 - External data
 - Application data
 - Inspection Data

- Quality Management Maturity Ratings
- Quality Metrics

Quality Management Maturity

Quality Metrics

Leadership Commitment to Quality

Business Continuity

Quality Culture

Communication and Collaboration

Sustainable Compliance

Customer Experience

Enhanced Pharmaceutical Quality System (PQS)

Advanced Analytics

Employee Ownership and Engagement

Continual Improvement

Risk Management

Manufacturing Strategy and Operations

Productivity Optimization (5S)

QMMM \neq QM

QMMM = f(QM, x, y, z...)

Foundation of Science



PDA PAPER

Quality Culture Survey Report

PRITESH PATEL¹, DENYSE BAKER¹, RICK BURDICK¹, CYLIA CHEN¹, JONATHAN HILL¹, MORGAN HILLIARD¹, and ANE SAWANT¹

¹Prishk Patel Consulting, LLC; ²PDA; ³Hengen, Inc.; ⁴Johanson & Johnson ©PDA, Inc. 2015

ABSTRACT: The Parenteral Drug Association conducted an anonymous global survey of quality culture in the pharmaceutical industry to determine whether there is a relationship between certain quality behaviors and certain quality attributes. Other studies have shown that quality culture. Other studies have shown that quality or compliance issues seen by sites and organizational certain attributes are driving good behaviors, and the de- irrespective of the geographic location of the site. Essential the current state of quality culture that survey respondent biggest gap (P -value = 0.07, F -Test). The top five local culture were (1) Management communication that quality improvement objectives and targets, (3) Clear performance included in at least half of all hands meetings, and (5) 4 mature quality attributes are related to management report central quality system sections of FCQI(1), and therefore, or in regulatory inspections. Additional research and discuss the pharmaceutical industry and regulators can adopt.

Introduction

The U.S. Food and Drug Administration (FDA) 2012 Safety and Innovation Act has given the FDA new authority to collect data and information prior to or in lieu of on-site inspections. The FDA intends to use this new authority to collect product and/or site-specific data to calculate quality metrics. Quality metrics will be used to gauge the good manufacturing practice (GMP) status of pharmaceutical manufacturing scheduling, help identify and prevent drug shortages. Performance and quality metrics are widely used management and continuous improvement tools in the pharmaceutical industry. However, there is increasing recognition that, in addition to metrics, quality culture plays a critical and complementary role because it affects the decisions that contribute to the data that are used for calculating the metrics. A good quality culture is often described as one that puts the interests and safety of patients and consumers above all else and where people do what is right versus what is good enough.

Corresponding Author: ppate1015@gmail.com
doi: 10.37471/pdajp.2015.01078

Vol. 69, No. 5, September-October 2015

Following Janet Woodcock, Director of the US Food and Drug Administration (FDA) Center for Drug Eval-

^{*} Corresponding Author: University of St. Gallen, Dufourstrasse 40a, CH-9000, St. Gallen, Switzerland. E-mail: p.patel@prishkpc.com
doi: 10.37471/pdajp.2015.01078

Vol. 72, No. 5, September-October 2018



Volume 16
Issue 1 Steps Towards Digital Transformation in the Pharmaceutical Manufacturing Landscape
Linking Data, Analytics, Knowledge and Risk

12-15-2021

Holistic Risk-based Site Surveil: Site Quality Risk Identification an Pharmaceutical Industry*

Matteo Bemasconi
Institute of Technology Management, University of St

Thomas Friedli
Institute of Technology Management, University of St

Nuala Cahnan (editor)
Technological University Dublin, nuala.cahnan@tudub

Follow this and additional works at: <https://arrow.tud>

Part of the Pharmacy Administration, Policy and I

Recommended Citation
Bemasconi, Matteo; Friedli, Thomas; and Cahnan (ed) Pharmaceutical Industry: Level 2 Vol. 16: Iss. 1, Art Available at: <https://arrow.tudublin.ie/level2/vol16/iss1/art1>

This Regulation, Data, and the Patient is brought to you for free and open access by the Current Publications at ARROW@TU Dublin. It has been accepted for inclusion in Level 3 by an authorized administrator of ARROW@TU Dublin. For more information, please contact arrow.admin@tudublin.ie, arrow.com@tudublin.ie, or arrow@tudublin.ie.

This work is licensed under a Creative Commons Attribution-NonCommercial-Share Alike 4.0 License

© 2020

© 2020

¹ Department of Industrial Engineering and Management, Tsinghua University, Beijing 100084, China

² Center for Pharmaceutical Innovation and Engineering Research, Tsinghua University, Beijing 100084, China

³ Academy for Advanced Interdisciplinary Studies, Tsinghua University, Beijing 100084, China

501

Level 3

Article 8

Journal of Pharmaceutical Innovation
<https://doi.org/10.1007/s12241-021-01679-7>

ORIGINAL ARTICLE

Quantitative Analysis of the QMS for Pharmaceutical Manufacturing

Guozu Wang^{1,2}, Weibing Wang¹, Qing Zhang^{1,3}

Accepted: 18 July 2021
© The Author(s) 2021

Abstract
Purpose: To propose a statistical methodology for quantitative analysis of the quality management system (QMS) of pharmaceutical manufacturing.

Methods: (1) Based on the manufacturing data from two established active pharmaceutical ingredient (API) manufacturers in China from 2010 to 2019, the linear regression with Pearson correlation coefficient is used to find the correlations between the improved QMS operation indicators and performance indicators. (2) A stepwise multiple linear regression is used to identify the independent operation indicators with the biggest impact on a given performance indicator. (3) The Akaike Information Criterion is used to predict the performance indicators based on the operation indicators.

Results: (1) Correlation: the right-time rate correlates strongly with various changes and deviations, the customer compliance correlates with changes, deviations, and CAPAs, and the CAPA on-time completion rate correlates with deviations in quality. (2) Impact: the right-time rate and the customer compliance are mostly impacted by the total deviation rate, the deficiency rate of foreign inspections is mostly impacted by deviations in equipment and instruments, and deviations due to human error. (3) CAPA on-time completion rate is mostly impacted by deviations in facility and utilities. (4) Predictability: the right-time rate, the customer compliance, the deficiency rate of foreign inspections, and the CAPA on-time completion rate can all be predicted based on the existing data with statistical significance.

Conclusion: Deviations emerge as a key leading indicator for the performance of QMS. The proposed statistical methodology provides a basis for the data-driven quality management and regulation, where visibility and predictability are likely to progress as the data accumulate.

Keywords: QMS · Pharmaceutical manufacturing · Statistical modeling · Performance · Deviations

Introduction

Quantitative characterization of the quality management system (QMS) for pharmaceutical manufacturing has been a research subject of academia, industry, and regulator for years. A successful characterization usually requires a large

amount of real-world manufacturing quality data and a systematic statistical approach.

Major of Georgetown University and Nickerson of Washington University studied manufacturing quality risk based on the US Food and Drug Administration (FDA) site inspection data for the purpose of prioritizing GMP inspections to manufacturing sites with high-quality risks [1]. They also included site operation data of manufacturing facility, human resources, deviation management, and manufacturing performance. Data was collected by using survey questionnaires to 50 active pharmaceutical ingredient (API) and finished dosage forms (FD) manufacturing sites. The data was product-based, i.e., data was collected for each product for each site, on a monthly basis from 1999 to 2003.

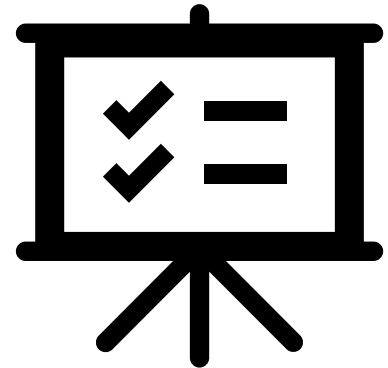
The statistical analysis using linear regression and Pearson correlation coefficient is site-based by aggregating data of all the products for each site. They found that larger sites

Published online: 12 September 2021



Today's Agenda Topics

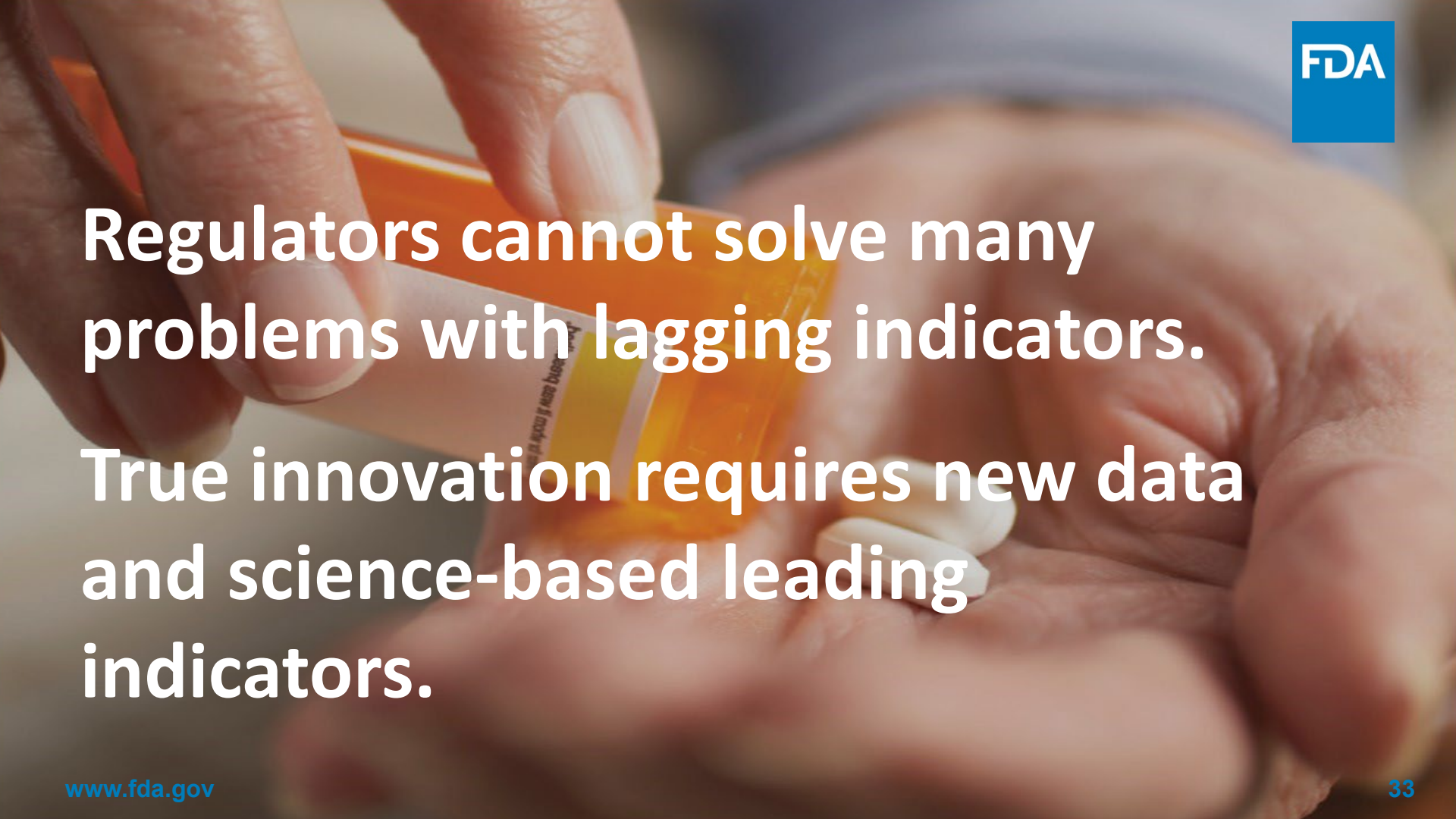
- Lessons learned from FDA's QMM program
- Stakeholder perspectives
- FDA's vision for QMM
- Potential benefits to stakeholders and FDA



The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair in a ponytail is seen from behind, working at a lab bench. The bench is cluttered with various pieces of laboratory equipment, including beakers, flasks, and bottles. In the background, there are fume hoods and more lab equipment. The entire image has a blue color overlay.

In Closing

US FDA Center for Drug Evaluation and Research

A close-up photograph of a person's hands. The left hand holds an orange plastic pill bottle, tilted to pour several white, oval-shaped pills into the palm of the right hand. The background is softly blurred, showing a person's arm in a blue sleeve.

Regulators cannot solve many problems with lagging indicators. True innovation requires new data and science-based leading indicators.



U.S. FOOD & DRUG
ADMINISTRATION

QMM Lessons Learned

Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting

November 2, 2022

Jennifer Maguire, Ph.D.

Director

Office of Quality Surveillance

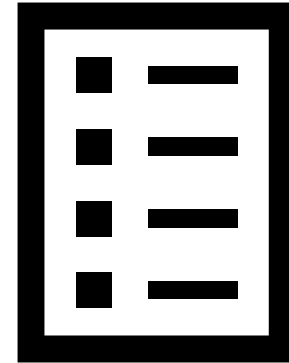
Office of Pharmaceutical Quality

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

AGENDA

- ❑ Understanding Quality Management Maturity (QMM)
- ❑ FDA's Pilot Programs and related activities – Lessons Learned
- ❑ Economic Analysis – Key Findings



Understanding Quality Management Maturity (QMM)

US FDA Center for Drug Evaluation and Research

Why Develop a QMM Program?

The [Report on Drug Shortages: Root Causes and Potential Solutions](#) (2019) identified one potential root cause of drug shortages was that *the market does not recognize and reward manufacturers for “mature quality systems” that focus on continuous improvement and early detection of supply chain issues.*

An enduring solution proposed was to *develop a rating system to incentivize drug manufacturers to **voluntarily** invest in Quality Management Maturity (QMM).*

Understanding QMM

Drug manufacturers achieve higher levels of quality management maturity (QMM) when they successfully integrate business and manufacturing operations with quality practices and technological advancements.



FDA's QMM Pilot Programs and Related Activities – Lessons Learned

US FDA Center for Drug Evaluation and Research

QMM Pilot Programs (2021-2022)

☐ **Two pilots:**

- Finished Dosage Form Pilot Program – 7 domestic sites
- Active Pharmaceutical Ingredient Pilot Program – 8 foreign sites

☐ **Assessments should enable:**

- Establishing best practices and identifying continuous improvement opportunities
- Protocols and associated scoring that maximize inter-rater reliability and provide a quantitative overall rating
- Cross-sectional comparison against industry peers

☐ **Assessed multiple practice areas:**

- Leadership and Governance
- Stakeholder Engagement and Satisfaction
- Quality Culture
- Continual Improvement
- Workforce Engagement
- Sustainability

FDA's Role

FDA participated in the pilot as spectators to observe and learn. Lessons learned from the pilots will be used to help FDA:

- ✓ Identify mature quality management practices
- ✓ Develop assessment framework
- ✓ Develop scoring system
- ✓ Perform assessments
- ✓ Provide QMM assessment scores
- ✓ Provide reports to participants

QMM Assessment Protocol – Key Learnings

Preparation

- Orient participants, set expectations, schedule appropriate staff
- Provide examples of documentation used to substantiate QMM score

Protocols

- Streamline topic areas and number of questions
- Consider sector-specific questions
- Separate questions for corporate vs. site staff

Discussion

- Speak with management and staff separately

Time Management

- Strict time limit per question was not effective strategy



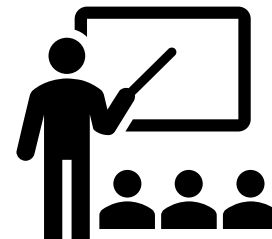
Developing a Rubric to Score QMM Assessments

- ❑ The QMM pilot program contractors independently developed rubrics used to define criteria for how scores were assigned.
- ❑ Scores were generated for each practice area in addition to a final aggregated score reflecting all practice areas.
- ❑ Development of the rubric is dependent on the practice areas that will be evaluated and verification of participant responses through suitably identified supporting information.

Pilot Scoring Approach – Key Learnings

- ❑ **Objective criteria to discern between levels are critical**
 - Multiple assessors may be needed to minimize bias
 - Need objective approach for managing conflicting scores to reduce bias

- ❑ **Streamline scoring rubric to allow less room for interpretation and improve scoring precision**
 - Maximize inter-rater reliability
 - Maximize consistency in scoring



Assessor Behaviors – Key Learnings

Training

- Distinguish above-the-bar behaviors from CGMP* compliance
- Interview skills – avoid leading questions, put staff at ease
- Remain neutral – do not impose opinions
- Understand the audience
- Repeat questions when necessary
- Allow enough time for staff to respond
- Stay on topic

*CGMP – Current Good Manufacturing Practice



Examples of Participant Feedback

Pilot participant feedback shows positive sentiment for the program

The assessment results will be used for the improvement of processes and programs and for communication within the corporate organization.

In the same way that QMM data is useful in assessing a potential API supplier, the data could be useful in assessing a contract lab or other contract facility.*

We could envisage using the QMM score to reduce the frequency, content, and time spent on vendor audits.

We will look at various behaviors/actions listed in each maturity level and strive to move to the next level.

*API – Active Pharmaceutical Ingredient

Economic Analysis

OPQ funded research with the University of Maryland through the FDA's Centers of Excellence in Regulatory Science and Innovation (CERSI) program.

- ❑ **Goal:** Identify effects of a quality rating system on drug product market structure including dis/incentives for manufacturers to strengthen their processes.

- ❑ **Findings:**
 - Market is characterized by an asymmetric information problem.
 - Absent a standardized methodology to assess differences in manufacturing quality, the market is unable to differentiate drug products based on manufacturing quality.
 - Despite a market characterized by price inelasticity, the analysis suggests that quality ratings should incent manufacturers to invest in quality.

Impact of QMM on Supply Networks

FDA applied a systems thinking approach to study possible direct and indirect effects of a QMM program on the end-to-end supply network.

- Engaged with offices including ORA, OQS, OPMA, DSS, and OMQ.
- Analyzed priorities and relationships between stakeholders.

Lessons Learned:

- Increased FDA's awareness of external factors that may affect stakeholders in the supply chain.
- It may be important to consider sector-specific incentives.

In Summary

- ❑ Lessons learned from the QMM Pilot Programs will help guide development and operational decisions in conjunction with findings from research initiatives and continued engagement with industry partners and other stakeholders.
- ❑ Sentiment about the QMM program has been overall positive!



U.S. FOOD & DRUG
ADMINISTRATION

Stakeholder Perspectives

Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting

November 2, 2022

Adam Fisher, Ph.D.

Director, Science Staff—Immediate Office

Office of Pharmaceutical Quality

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

Road to a QMM Program

2020

Duke | MARGOLIS CENTER
for Health Policy

Understanding How the Public Perceives and Values Pharmaceutical Quality
Private Workshop Summary
Washington, DC | February 6, 2020

“Stakeholders largely agreed that there is a need to develop and implement quality... scores within the industry.”

Concepts responsible for overseeing the quality of a drug are the responsibility of state or pharmaceutical quality states that “A quality drug is consistently safe and effective, free of contamination and defects.”

Throughout the day, stakeholders used the term “pharmaceutical quality” to refer to two distinct concepts. First, they used it to describe the quality of the manufacturing process, and its ability to produce a reliable supply of drugs that is resilient against supply disruptions and shortages. Second, stakeholders used the term to describe a product that is free of contamination and defects that might affect its safety or effectiveness. These different uses of the term “pharmaceutical quality” highlight one of the key takeaways of the workshop: there is a need for a better shared understanding of what pharmaceutical quality means, how it affects stakeholders, and how it can be measured.

The Private Workshop

The workshop consisted of two breakout groups representing patient and provider perspectives as well as buyer and payer perspectives. The groups explored stakeholder understandings of pharmaceutical quality and the ways that quality impacts decision making. In the final portion of the day, the breakout groups joined together to share lessons learned and discuss ways forward.

Key areas for future action included assessing perceptions of pharmaceutical quality; continuing communications about quality with patients and providers; facilitating transparency between manufacturers, regulators, and purchasers; and developing quality ratings and scores.

Breakout Group A: Patients and Provider Perspectives

Breakout Group A first considered how patients and providers define pharmaceutical quality, differentiate between pharmaceutical quality issues and drug side effects, and perceive FDA’s role in regulating pharmaceutical quality. The group then considered the decisions healthcare providers make surrounding pharmaceutical quality and how those decisions impact patient care, as well as how patient preferences around quality influence medical decision making. Group A consisted of fifteen providers, patient advocates, professional society representatives, and pharmacists, as well as additional FDA

2021

BUILDING RESILIENT
SUPPLY CHAINS,
REVITALIZING AMERICAN
MANUFACTURING, AND
FOSTERING BROAD-BASED
GROWTH

“FDA should lead the development of a framework to measure... a facility’s quality management maturity with engagement from industry, academia, and other stakeholders.”

Department of Health and Human Services
Department of Health and Human Services



THE WHITE HOUSE
WASHINGTON

2022

The National Academies of
SCIENCES • ENGINEERING • MEDICINE


CONSENSUS STUDY REPORT



“Establishing a quality rating system... is a long-term initiative that will have to be developed in collaboration with business partners and with stakeholders.”

MEDICAL PRODUCT
SUPPLY CHAINS

Engagements on the Road to QMM



“CDER will continue to engage stakeholders during and after the development of the QMM rating program.”

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
An Office of Pharmaceutical Quality (OPQ) White Paper

Quality Management Maturity: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals

Abstract

CDER is taking another step towards realizing the vision for pharmaceutical quality in the 21st century: a maximally efficient, agile, flexible manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight. Research conducted by trade associations, academics, and regulators has demonstrated that Quality Management Maturity is essential to achieving this vision. To increase transparency and incentivize investment in pharmaceutical manufacturing, OPQ is developing a framework to objectively rate the Quality Management Maturity of pharmaceutical manufacturing sites.

- ❑ **Stakeholder Meetings**
 - E.g., Duke-Margolis (Feb 3, 2020)
- ❑ **QMM Stakeholder Workshop**
 - May 24-25, 2022
- ❑ **Pharmaceutical Science and Clinical Pharmacology Advisory Committee**
 - Today

Engagements on the Road to QMM

“CDER will continue to engage stakeholders during and after the development of the QMM rating program.”

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
[An Office of Pharmaceutical Quality \(OPQ\) White Paper](#)

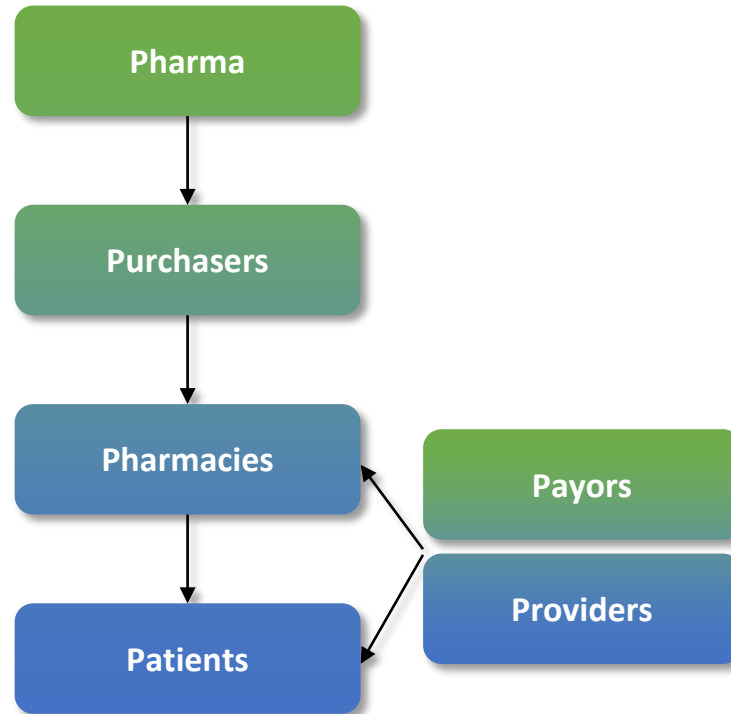
Quality Management Maturity: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals

Abstract

CDER is taking another step towards realizing the vision for pharmaceutical quality in the 21st century: a maximally efficient, agile, flexible manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight. Research conducted by trade associations, academics, and regulators has demonstrated that Quality Management Maturity is essential to achieving this vision. To increase transparency and incentivize investment in pharmaceutical manufacturing, OPQ is developing a framework to objectively rate the Quality Management Maturity of pharmaceutical manufacturing sites.

- Key Challenges Identified with Stakeholders
- Key Elements of a Program Identified with Stakeholders
- Feedback from Workshop Stakeholders

“6 Ps” Impacted by QMM Ratings



Key Challenges Identified with Stakeholders

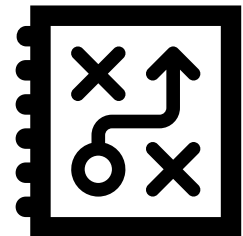
US FDA Center for Drug Evaluation and Research

Key Challenges to Achieving QMM



Clearly defining the scope and meaning of QMM ratings

- Stakeholders use “pharmaceutical quality” in different ways (e.g., product, process, facility, supply chain)
- Ratings will reflect the QMM at a manufacturing site and not the quality of the product or process
- High QMM ratings will not be a “guarantee” for a site’s products

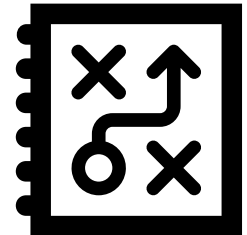
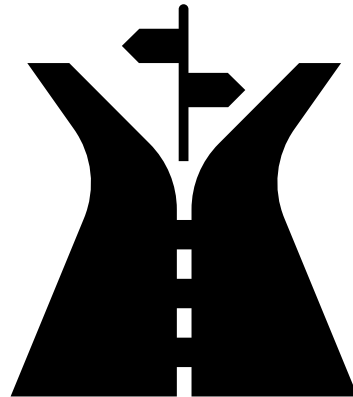


Key Challenges to Achieving QMM



Convincing purchasers to consider QMM in decision-making

- Perception that QMM exists if the drug has been approved by FDA
- Describe the value of using QMM in purchasing decisions

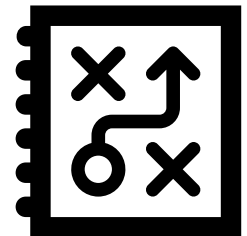


Key Challenges to Achieving QMM

Separating QMM assessments from CGMP* inspections

- Transparency, engagement, and collaboration are critical
- QMM assessments will be a CDER surveillance function

**CGMP – Current Good Manufacturing Practice*

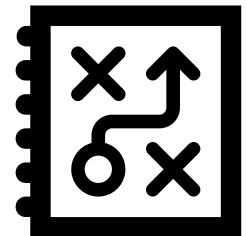
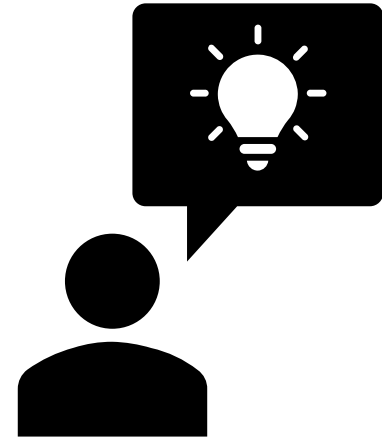


Key Challenges to Achieving QMM



Relying on purchasers to understand their supply chains

- Purchasers must know the specific facilities manufacturing the drugs or components they purchase (esp. APIs*)
- FDA may not be able to disclose specific information about the drug product supply chain
- Most purchasers already require supply chain site information as part of their decision-making process



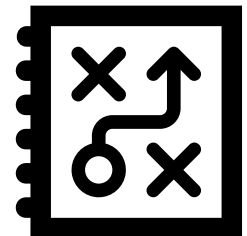
*APIs – Active Pharmaceutical Ingredients

Key Challenges to Achieving QMM



Relying on the market to reward facilities with higher QMM

- ❑ QMM ratings should incentivize continual improvement
- ❑ But not over-consolidate the market and/or markedly raise purchasing costs
- ❑ Research may be needed to avoid unintended consequences, such as market over-consolidation

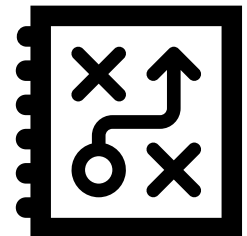
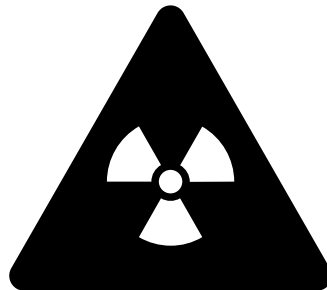


Key Challenges to Achieving QMM



Addressing potential risks of QMM in decision-making

- ❑ Healthcare professional responsibility/liability
 - Ratings based on manufacturing sites not products
- ❑ Use of QMM ratings in marketing



Key Elements of a Program Identified with Stakeholders

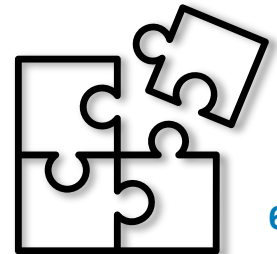
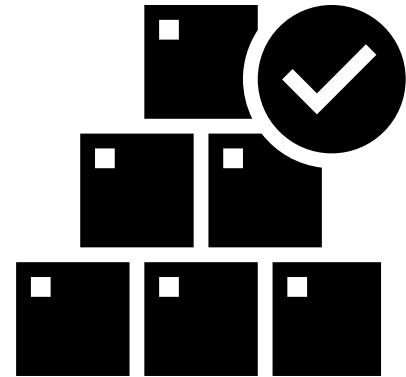
US FDA Center for Drug Evaluation and Research

Key Elements of a QMM Program



Quality culture must be foundational

- ❑ Culture must be led from the top
- ❑ Objectives drive quality
 - Integrated business and quality objectives

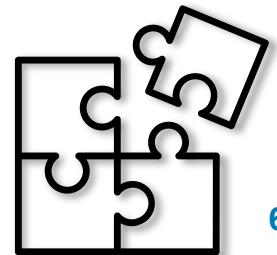


Key Elements of a QMM Program



Assessment must be objective, consistent, standardized, and validated

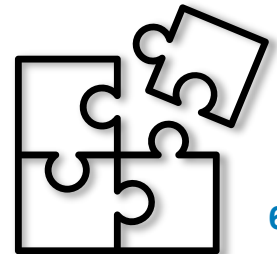
- True whether carried out by FDA or contractor
- Scope must be distinct from determining CGMP compliance



Key Elements of a QMM Program

Transparency is critical

- Understanding the intentions of the program and the impact on drug shortages and patient/consumer outcomes
- Must be clear that all drugs sold in the U.S. are of adequate quality and considered safe and effective
- A universal understanding will be needed
 - Broad communication to the public



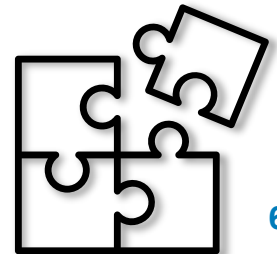
Key Elements of a QMM Program

There must be clear incentives

- Reduced inspection frequency, increased regulatory flexibility for postapproval changes (ICH* Q12), and improved supply chain insight
- There is a cost to supply disruptions and shortages
- Healthcare professionals, pharmacies, and patients may need to advocate for the use of QMM ratings



**ICH - International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use*



Feedback from Workshop Stakeholders

US FDA Center for Drug Evaluation and Research

QMM Workshop Feedback



VIRTUAL

Quality Management Maturity Workshop

MAY 24 - 25, 2022



FDA Quality Management Maturity Program 2022 Public Workshop - Part 1 - Session 1

Watch later Share

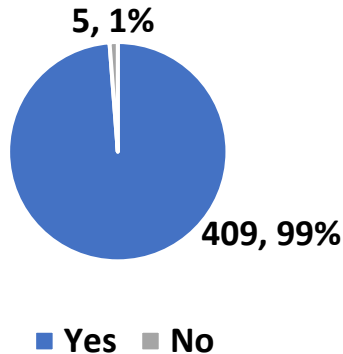
CDER SMALL BUSINESS and INDUSTRY ASSISTANCE

Watch on YouTube

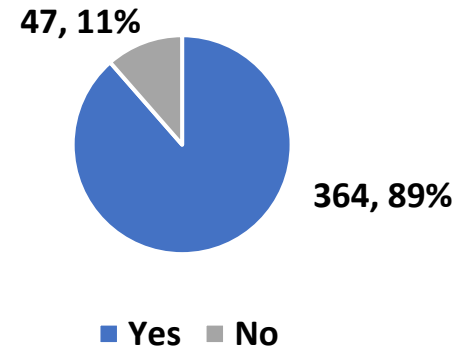
Stakeholders on a QMM Program



Should purchasers of drug products or active pharmaceutical ingredients consider the quality management maturity of the facility/manufacturer that manufactures them?



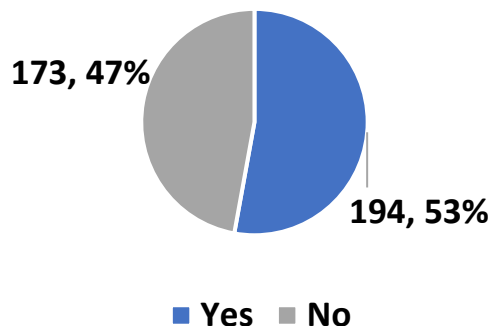
Do you believe that information on the quality management maturity of facilities making drug products or active pharmaceutical ingredients will improve decision-making in the pharmaceutical supply chain?



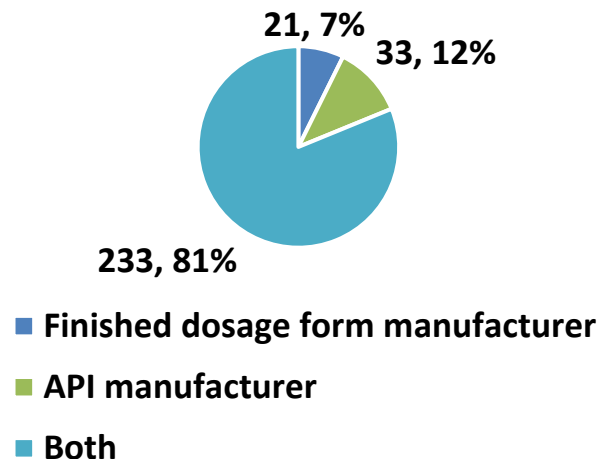
Stakeholders on Shortages



Do you believe that giving purchasers information on the quality management maturity of facilities making drug products or active pharmaceutical ingredients will reduce drug shortages in the long term?



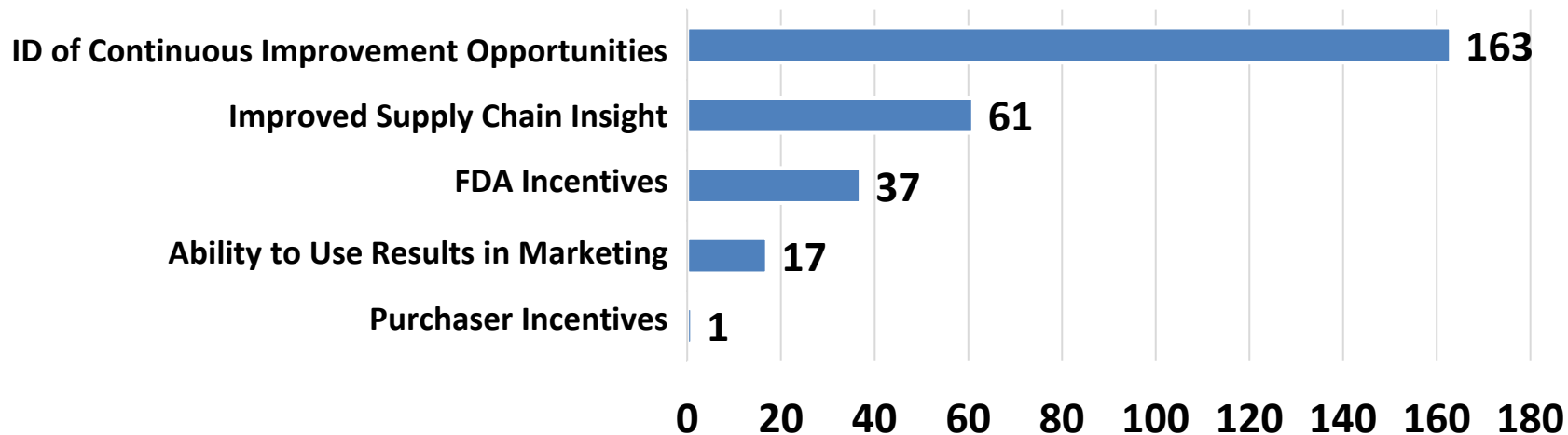
Which QMM ratings will be most valuable to prevent shortage?



Stakeholders on Incentives



What would be the biggest potential benefit for sites that participate in a QMM program?



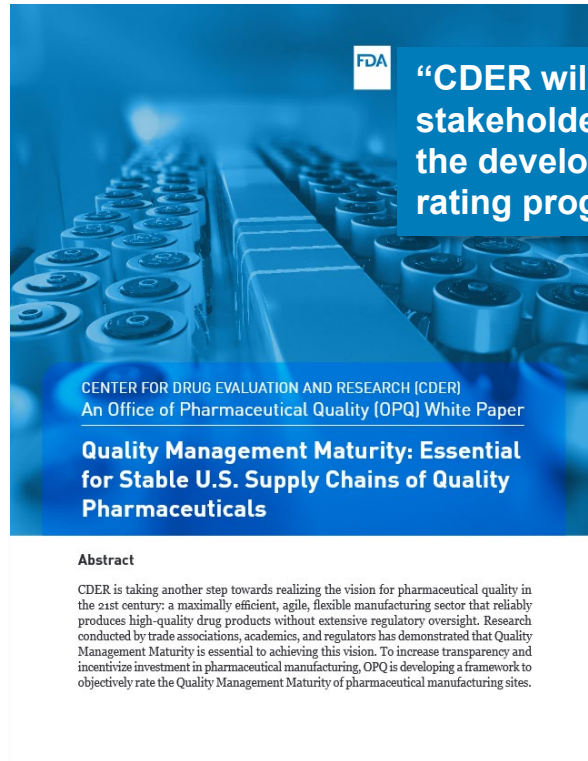
Key Concerns from Workshop

From discussions and Q&A:

- Timeline
- Incentives
- Cost burden to participate
- Unintended consequences and impact on industry
- Drug cost
- Feasibility of all firms achieving QMM
- Measuring program success
- Transparency



Engagements on the Road to QMM



“CDER will continue to engage stakeholders during and after the development of the QMM rating program.”

CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
An Office of Pharmaceutical Quality (OPQ) White Paper

Quality Management Maturity: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals

Abstract

CDER is taking another step towards realizing the vision for pharmaceutical quality in the 21st century: a maximally efficient, agile, flexible manufacturing sector that reliably produces high-quality drug products without extensive regulatory oversight. Research conducted by trade associations, academics, and regulators has demonstrated that Quality Management Maturity is essential to achieving this vision. To increase transparency and incentivize investment in pharmaceutical manufacturing, OPQ is developing a framework to objectively rate the Quality Management Maturity of pharmaceutical manufacturing sites.



U.S. FOOD & DRUG
ADMINISTRATION

FDA's Vision for Quality Maturity Management

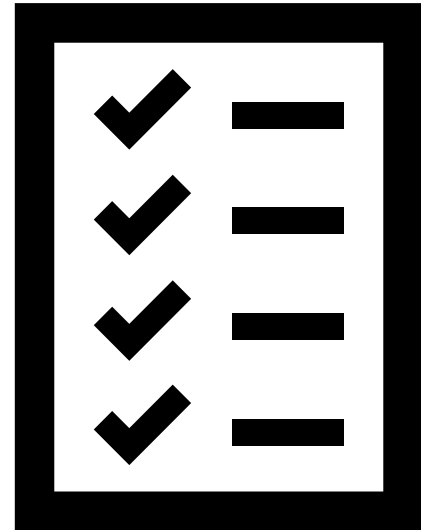
Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting
November 2, 2022

Alex Viehmann

Director, Division of Quality Intelligence II
Office of Quality Surveillance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

AGENDA

- Background: The Business Case for QMM
- Operational Considerations
- Assessment Framework

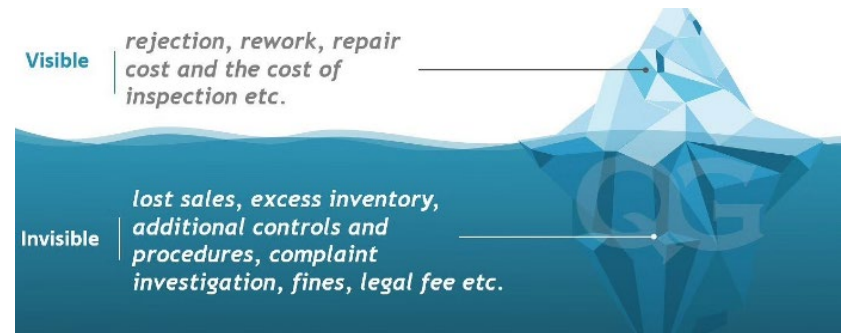


Background: The Business Case for QMM

US FDA Center for Drug Evaluation and Research

“QMM is Nothing New”

- ❑ “Quality always costs less” – W Edwards Deming
 - Good quality doesn’t have to mean higher costs
 - Achieving quality outcomes requires investment
 - Organizations whose quality practices are the most sophisticated are not necessarily the ones that spend the most
- ❑ Cost of poor quality
 - Internal and external failures
 - ❑ Loss of production, rework, scrap, loss of business
- ❑ Cost of quality
 - Inspection and prevention costs
 - ❑ Labor costs for audits, preventive/predictive maintenance, training, design improvements, implementation of advanced control mechanisms (e.g., SPC)
- ❑ High levels of QMM will lead to:
 - Higher revenues
 - Greater customer satisfaction
 - Operational efficiencies – increase in productivity

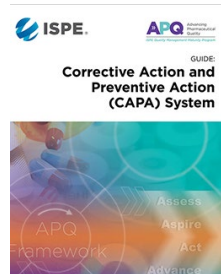


Parallel Efforts



□ Learn from efforts to date

- PDA Quality Culture Initiative
- ISPE Advancing Pharmaceutical Quality Program
- University of St. Gallen
- FDA/CDRH Case for Quality Pilot Program
- Dun & Bradstreet Quality Benchmarking Study



Business Case from other Industries



Quality ratings are successfully used in many industries:

CARFAX® revolutionized used car buying

- Widespread adoption of used car reports and quality-based estimators

Centers for Medicare and Medicaid Services (CMS) established a 5-star quality rating for nursing homes

- Prices for highest rated nursing homes rose 5-6% over lowest rated facilities

Federal agencies regulating the safety and soundness of depository institutions (banks, thrifts and credit unions) develop and apply CAMELS* ratings

- Ratings have been highly successful for federal regulators managing safety and soundness of banking sector

*CAMEL – Capital adequacy, Asset quality, Management, Earnings, Liquidity, and Sensitivity

A QMM Assessment is NOT...

The QMM assessment is not intended to be used in lieu of or as a surrogate for establishment inspections and does not evaluate compliance with CGMP*.

A QMM assessment is not a reflection of product quality. It is an evaluation of an establishment's quality practices.

**CGMP – Current Good Manufacturing Practice*

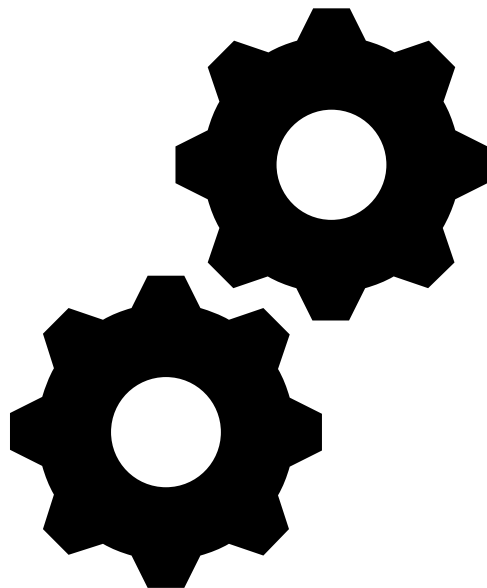
A QMM Assessment DOES...

- Identify and evaluate above-the-bar behaviors
- Identify opportunities for continual improvement
- Allow participants to become eligible for incentives
- Promote benefits from continual improvement

Operational Considerations

US FDA Center for Drug Evaluation and Research

Operationalizing a QMM Program



- Executed by FDA or contractor?
- Executed virtually or on-site?
- Reassessment period?
 - Shelf-life of assessment and related incentives
 - Conditions of factors for reassessment
- Assigning a final rating
 - Considering assessment scores plus other factors
- Communicating the QMM rating

Incentives Under Consideration

Regulatory flexibility

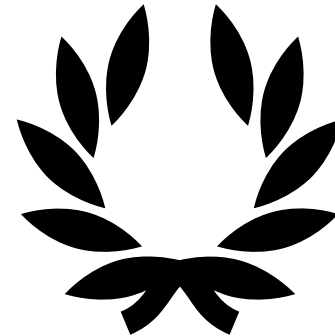
- Inform PQS* assessments to support ICH Q12 implementation
- Post-market activities (e.g., supplements)

Inspection decisions – frequency and scope

- Surveillance
- Pre-approval

Sector specific incentives

- Innovators, generics, OTCs, biologics...

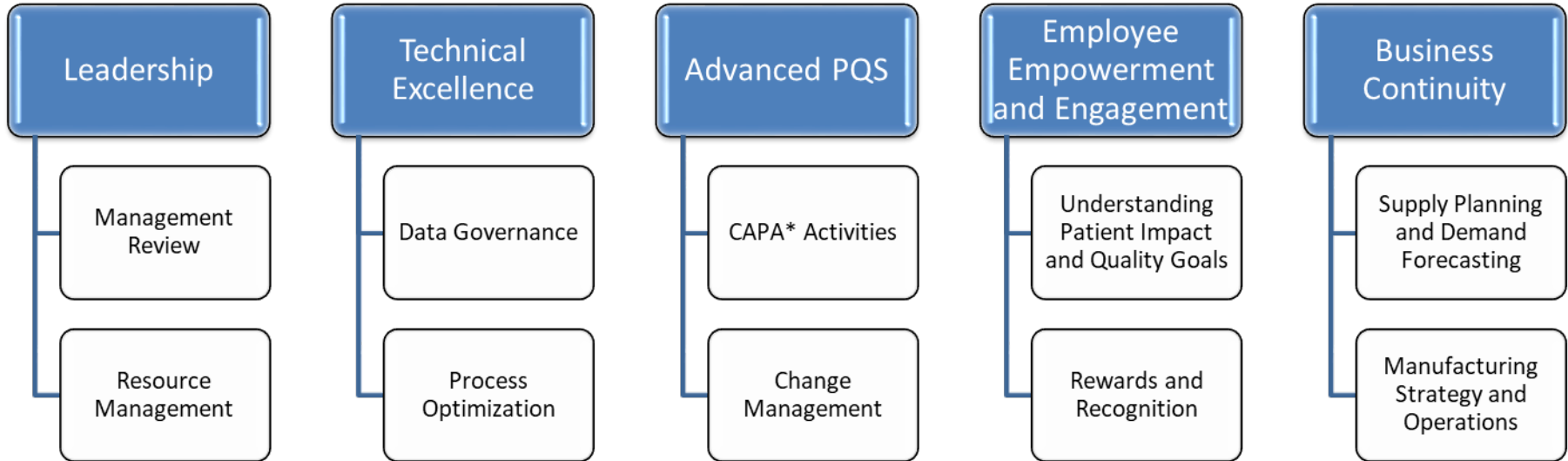


**PQS – Pharmaceutical Quality System*

Assessment Framework

US FDA Center for Drug Evaluation and Research

Example Practice Areas and Elements



*CAPA – Corrective and Preventive Action

QMM Program – Moving Forward

- Develop protocol for QMM assessments
- Develop rubric for scoring the assessments
- Operational considerations
- Final rating considerations (integration of relevant data)
- Coordinate with government partners – inform reimbursement/procurement decisions

The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair in a ponytail is seen from behind, working at a lab bench. The background shows various pieces of laboratory equipment, including glass bottles, pipettes, and other scientific instruments. The overall color palette is light and airy, with a blue overlay at the bottom.

In Closing

US FDA Center for Drug Evaluation and Research



U.S. FOOD & DRUG
ADMINISTRATION

Potential QMM Benefits to Stakeholders and FDA

Pharmaceutical Science and Clinical Pharmacology Advisory Committee Meeting

November 2, 2022

Lucinda (Cindy) Buhse, Ph.D.

Deputy Director, Operations

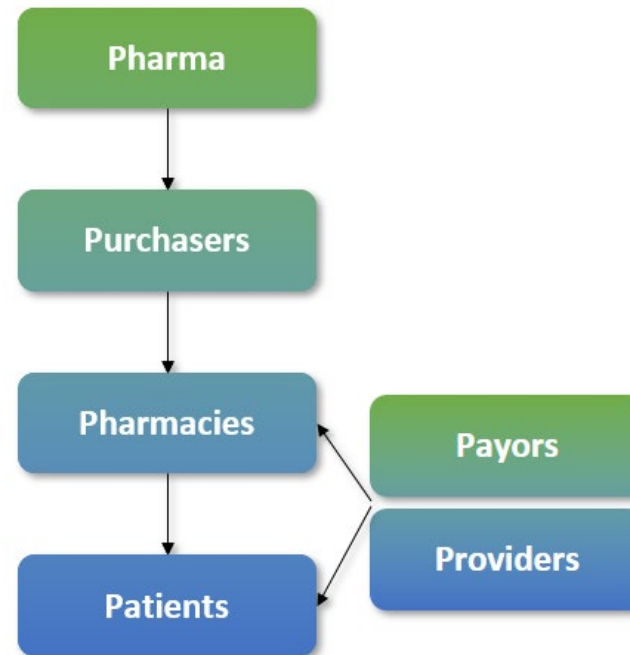
Office of the Pharmaceutical Quality

Center for Drug Evaluation and Research

U.S. Food and Drug Administration

AGENDA

- ❑ Benefits to Stakeholders:
 - Industry
 - Purchasers and Payers
 - Healthcare Professionals
 - Pharmacies
 - Patients and Consumers
- ❑ Benefits to FDA

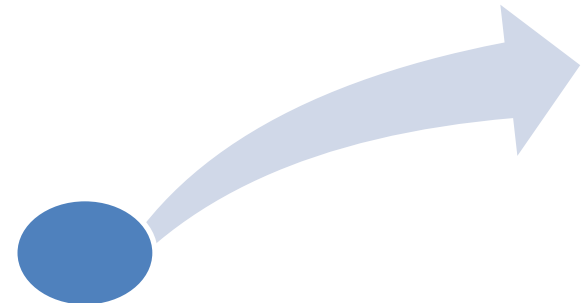


Benefits to Industry

US FDA Center for Drug Evaluation and Research

Industry

- ❑ Facilitates the use of ICH Q12 (Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management) regulatory flexibilities.
- ❑ Informs decision-making for applicants/ manufacturers in the selection of contract sites.
- ❑ Is an important element of oversight and controls over the manufacture of drugs to ensure quality (section 501 FD&C* Act).
- ❑ Enables continual improvement of
 - process performance,
 - product quality, and
 - the pharmaceutical quality system (PQS).



*FD&C – Federal Food, Drug, and Cosmetic Act

Industry

Out of Stock

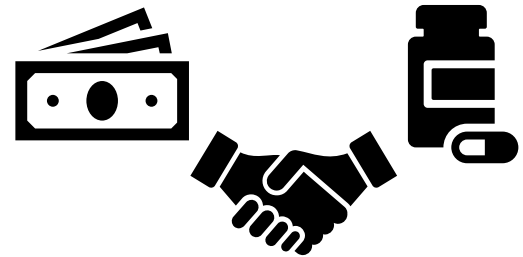


- ❑ Fewer recalls resulting in improved corporate image.
- ❑ Leader to quality system efficiencies and cost savings.
- ❑ A more robust drug supply chain and greater commitment to quality in pharmaceutical manufacturing.
- ❑ Positive and proactive performance is acknowledged.
- ❑ “Good actors” are rewarded through potential commercial and regulatory incentives.

Purchasers and Payers



- ❑ Provides greater transparency into the market overall.
- ❑ More insight into the supply chain.
- ❑ Quality ratings have insight from FDA including incorporation of non-public data.
- ❑ Less need to respond to drug shortages.



Healthcare Professionals

- Less risk of drug shortages impacting their patients.
- More confidence in the supply of drugs they prescribe and/or dispense.



Pharmacies



- ❑ Improved supply chain transparency.
- ❑ Less risk of failing to meet demand.
- ❑ Reduced risk of medication errors.



Benefits to Patients and Consumers

US FDA Center for Drug Evaluation and Research

Patients and Consumers



More reliable availability of important drug products.

- Fewer recalls.
- Fewer quality-related drug shortages.



A close-up photograph of a person's hands. The left hand holds an orange plastic pill container, tilted to pour three white, oval-shaped pills into the palm of the right hand. The background is softly blurred, showing a person's arm in a blue sleeve.

Greater confidence in their *next* dose of medicine.

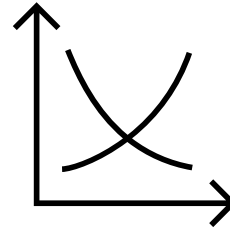
Benefits to FDA



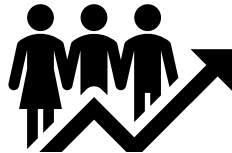
- ❑ Better informed about the quality management practices at sites.
- ❑ Better able to identify factors leading to supply disruption.
- ❑ Improved effectiveness of inspections.
- ❑ Enhanced risk-based allocation of surveillance tools.
 - Improved risk-based resource allocation for quality surveillance.
 - Better resource allocation decisions (e.g., inspection timing and frequency) and regulatory flexibility (e.g., related to postapproval changes).



Benefits to FDA



- ❑ Additional quantitative and objective insight into the state of quality for facilities.
- ❑ Advance FDA efforts toward performance-based regulation.
- ❑ Streamline the process of regulating post approval changes.
- ❑ Support FDA efforts to engage industry toward implementation of ICH Q12.

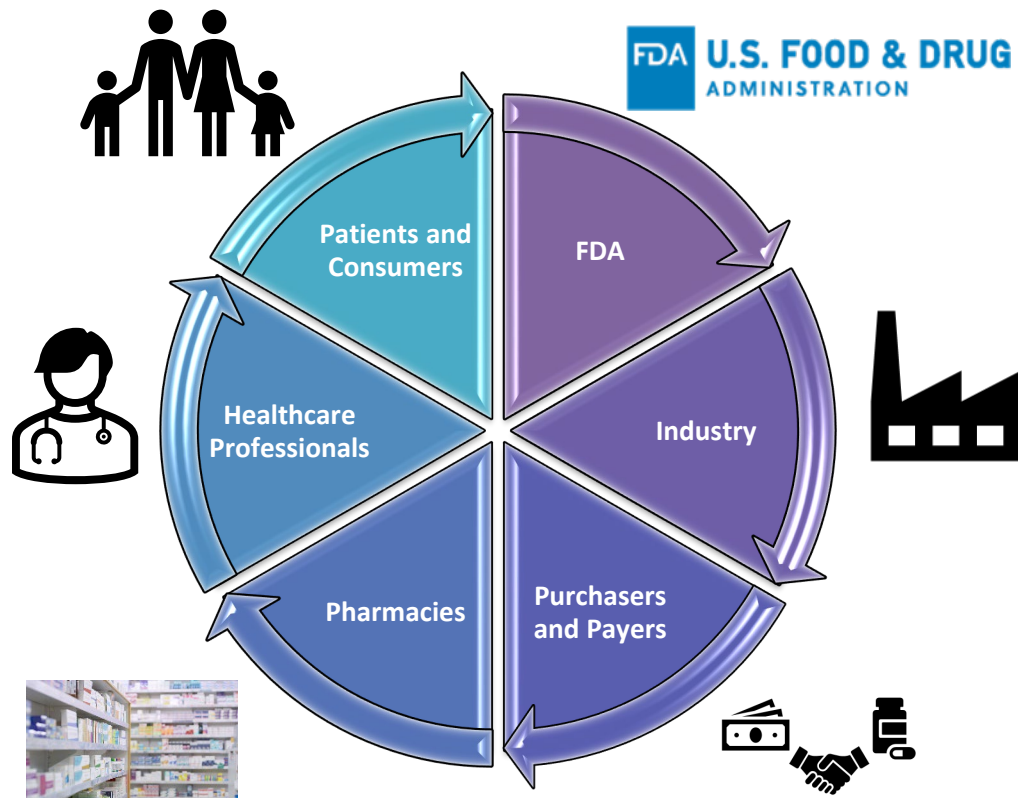


The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair in a ponytail is seen from behind, working at a lab bench. The bench is cluttered with various pieces of laboratory equipment, including beakers, bottles, and pipettes. In the background, there are fume hoods and more lab equipment. The entire image has a blue color overlay.

In Closing

US FDA Center for Drug Evaluation and Research

QMM is Important to All





U.S. FOOD & DRUG
ADMINISTRATION