U.S. FOOD & DRUG ADMINISTRATION

# Quality Management Maturity: FDA Vision and Expectations

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# Pharmaceutical Quality

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

**Drugs are no different.**

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

**Pharmaceutical quality is**

consistently meeting standards that ensure every dose is safe and effective, free of contamination and defects.

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

# Background

- In 2004, FDA published a report on pharmaceutical quality for the 21st century that laid out the following vision:

***"a maximally efficient, agile, flexible manufacturing sector that reliably produced high-quality drug products without extensive regulatory oversight."***

- Fully realizing the 21st century pharmaceutical quality vision requires a transparent method of evaluating and communicating QMM
- When manufacturers demonstrate rigorous oversight, understanding, and control over their manufacturing processes, FDA can exercise a more flexible regulatory approach
  - Lead toward the goal of "high-quality drug products without extensive regulatory oversight"
  - Motivate continual improvement of manufacturing processes

# Steps to Quality Management Maturity

- Current Good Manufacturing Practice (CGMP) establishes a minimum standard for systems that assure proper design, monitoring, and control of manufacturing processes and facilities
- Fully realizing the 21st century pharmaceutical quality vision requires a transparent method of evaluating and communicating quality management maturity (QMM)

# More Recent Context

- Drug Shortages: Root Causes and Potential Solutions, published in October 2019, examines the underlying factors responsible for drug shortages and recommends enduring solutions.
- The report identifies three root causes for drug shortages, including:
  - **The market does not recognize and reward manufacturers for "mature quality systems" that focus on continuous improvement and early detection of supply chain issues; and**
- The report also recommends enduring solutions, including:
  - **Developing a rating system to incentivize drug manufacturers to invest in QMM for their facilities; and**

# CGMP

- As defined in 21 CFR 211 and ICH Q7
- Minimum expectations for quality
- 211.180(e) – "data can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing control procedures….."
  - (1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch
  - (2) A review of complaints, recalls, returned or salvaged drug products, and investigations conducted under §211.192 for each drug product
- ICH Q7 – product quality review
  - 2.50 Regular quality reviews of APIs should be conducted with the objective of verifying the consistency of the process

# ICH Q10 Pharmaceutical Quality System

- Augments CGMP with the concept of an effective pharmaceutical quality system (PQS)
  - Covers the entire lifecycle of a product
- Outlines activities that should be conducted to manage and continually improve the PQS
  - Process Performance and Product Quality Monitoring System (PPPQMS)
  - Corrective Action and Preventive Action (CAPA)
  - Change Management
  - Management Review
- Describes how continual improvement is facilitated by knowledge management and use of quality risk management principles

# Achieving QMM

- A quality management system (QMS) is a collection of business processes needed to consistently implement and maintain quality of product in the marketplace
- Immature quality management systems are generally reactive, collect general/non-specific metrics, and are focused on Current Good Manufacturing Practice (CGMP) compliance
- Stronger, more mature quality management systems enable ***sustainable compliance***
  - Focus on performance and continual improvement, especially outcomes and metrics that impact the patient
  - Use data-driven approaches (e.g., predictive analytics) to reduce quality issues that lead to complaints, shortages, and adverse events

# Quality Management Maturity

Planning

Quality Management System

Performance Management/Continual Improvement

Quality Metrics

Quality Culture

Manufacturing Strategy and Operations

Supply Chain Management

Predictive Analytics

Customer Experience

Management Review/Responsibility

Workforce Management

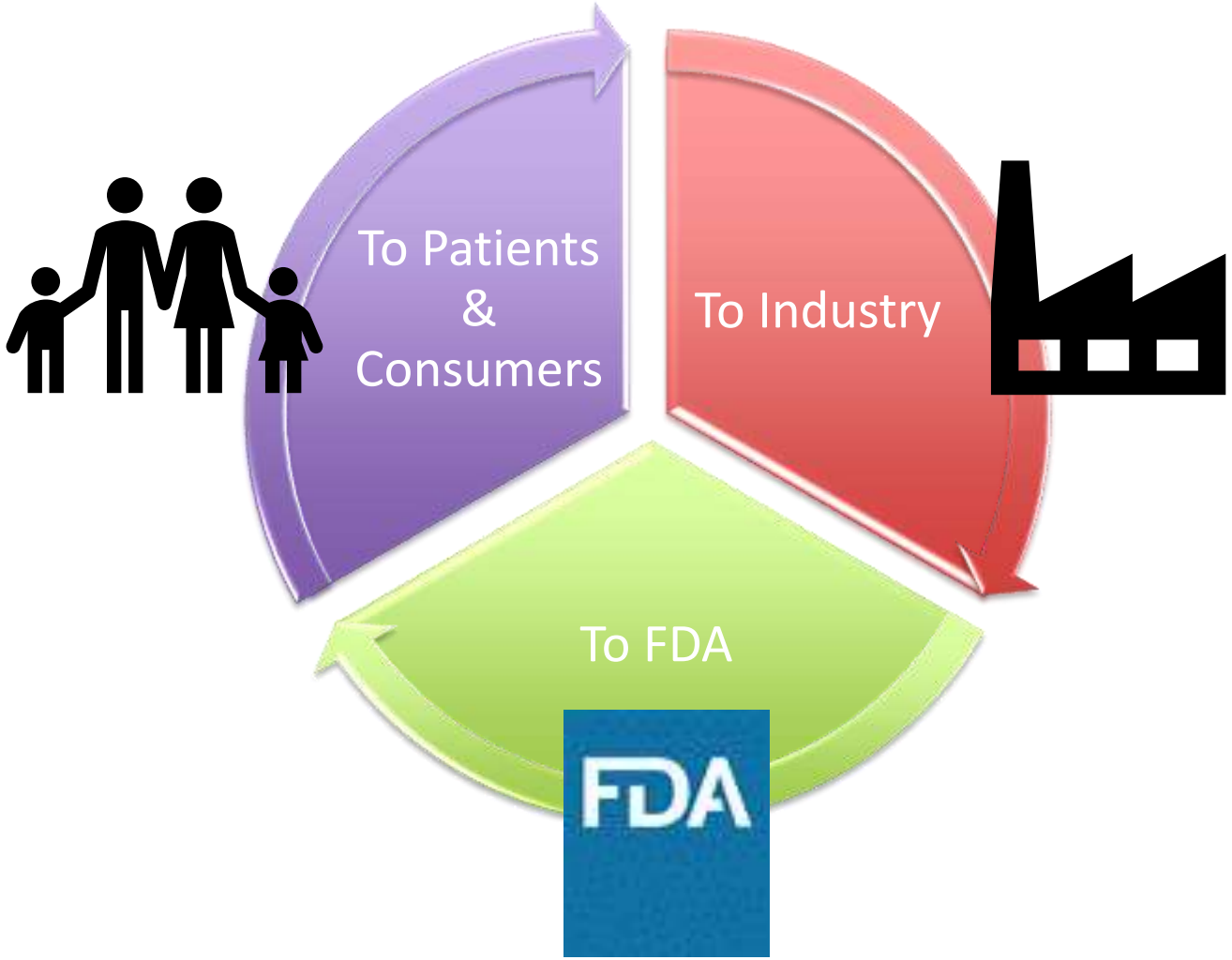
Risk Management

Safety, Environment and Regulatory Compliance

# What does QMM Look Like?

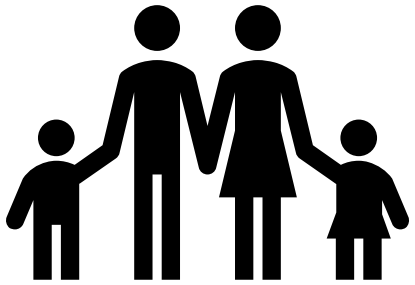
- Manufacturers and those with oversight and controls over manufacturing take ownership for quality:
  - Management sets the tone of commitment to quality
  - Invest in people
  - Organizational objectives drive quality
  - Quality systems shape culture
  - Focus on innovation and continual improvement
  - Move to performance-based quality management
  - Robust metrics program with a focus on analytics
  - Include risk management plans and forecasting to ensure reliability of supply

# QMM is Important



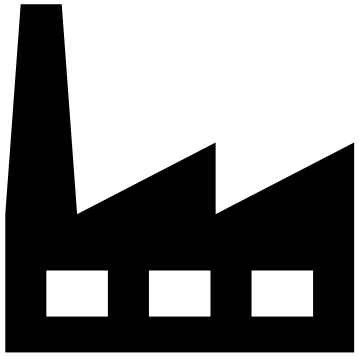
# Why is QMM Important *to Patients and Consumers*?

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



# Why is QMM Important *to Industry*?

- Important element of oversight and controls over the manufacture of drugs to ensure quality (section 501 FD&C Act)
- Fewer recalls and improved corporate image
- Enables continual improvement of
  - process performance
  - product quality
  - pharmaceutical quality system
- Leads to quality system efficiencies, cost savings and regulatory flexibility



# Why is QMM Important *to FDA*?

- Additional quantitative and objective insight into the state of quality for products and facilities
- Enhance risk-based allocation of surveillance tools
- Improve effectiveness of inspections
- Help to identify factors leading to supply disruption

# CDER's Vision for QMM

- CDER has identified the need for a system to measure and rate a drug manufacturing facility's QMM, and the ability to deliver high-quality drug products reliably and without disruption
  - Incentivize improved quality management systems by rewarding facilities that achieve a high degree of QMM
  - Provide transparency into the market for purchasers
  - Reduce the likelihood of quality problems that can lead to drug shortages by improving robustness of quality management systems

# QMM and Quality Metrics

- Quality metrics are a key aspect of a mature QMS (using data-driven approaches to reduce quality issues)
- Any assessment conducted to assess a facility's QMM would necessarily be an evaluation at a point in time
- Quality metrics data would be important to provide information about the quality of the facility and manufacturing process performance on an ongoing basis and in between on-site assessments

# Building a QMM Program

- 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
- Voluntary program
- Seek and incorporate stakeholder input

# Next Steps

- Quality Benchmarking Study with Dun and Bradstreet
  - Comprehensive study of pharmaceutical quality management practices
  - Collaboration to produce a knowledge base that characterizes the state of quality management practices
- Integrate QMM questions into the NIPP PAI and SIS protocols
- Engage with industry and academia
  - Inform the development of a rating system to measure QMM

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