

The Present and Future of Pharmaceutical Quality

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

Director

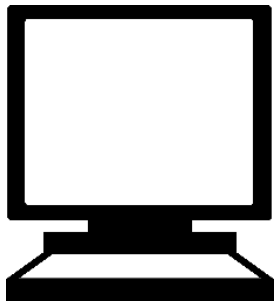
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Generic Drug Forum 2022

April 26, 2022

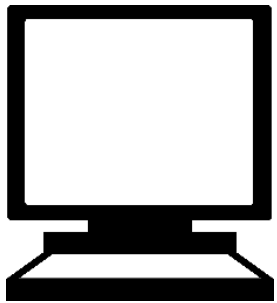
Pharmaceutical Quality

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.



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.

A close-up photograph showing a hand holding an orange pill bottle and pouring several white, oval-shaped pills into the palm of another hand. The background is softly blurred, focusing attention on the action of dispensing medication.

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

The Present and Future of Pharmaceutical Quality

FDA

- **Facility Assessment**
- **Quality Management Maturity**
- **Advanced Manufacturing**



The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair tied back is seen from behind, working at a lab bench. The bench is cluttered with various pieces of laboratory equipment, including glass bottles, beakers, and pipettes. In the background, there are more lab benches and equipment, creating a sense of a busy research environment. The overall color palette is dominated by light blues and greys, with a darker blue overlay at the bottom.

Facility Assessment

US FDA Center for Drug Evaluation and Research

CDER Facility Assessments

- Maintaining **same quality standards** using risk-based assessment
- Using **alternative tools to inspections**
- **Conducting necessary inspections** consistent with FDA's Resiliency Roadmap



Innovation Was Necessary



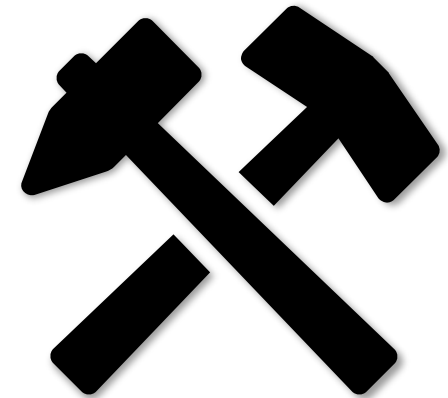
- **Alternative tools to inspections**
 - Information in lieu of inspection - FD&C 704(a)(4)
 - Mutual Recognition Agreement (EU and UK)
 - Info from regulators via confidentiality agreements
 - Remote Interactive Evaluations (RIEs)



Impact of Alternative Tools

Using Alternative Tools

- Supported the approval of **over 750** ANDAs & **over 8,000** application supplements
- Reduced pre-approval inspections by **over 50%** & enabled **over 250** quality assessments




Conducted **over 40** pre-approval inspections & **over 20** mission-critical inspections

State of Inspections

- On Feb. 7, FDA resumed **US domestic surveillance inspections** given the decline in COVID-19 cases
- FDA continues **foreign and domestic mission-critical inspections**
 - Still leveraging alternative tools
- Planning for additional **foreign surveillance inspections** is ongoing



“FDA remains committed to the health and safety of its investigators and will continue providing the protection needed to safely inspect facilities”

The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair tied back is seen from behind, looking towards a laboratory bench. The bench is cluttered with various pieces of scientific equipment, including glass bottles, beakers, and pipettes. The lighting is bright and even, typical of a laboratory setting. The overall color palette is dominated by light blues and greys, with a darker blue overlay at the bottom where the text is placed.

Quality Management Maturity

US FDA Center for Drug Evaluation and Research

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)

An Array of Quality



Pharmaceutical Quality

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

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

The Promise of QMM

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



THE WHITE HOUSE
WASHINGTON

QMMM \neq QM

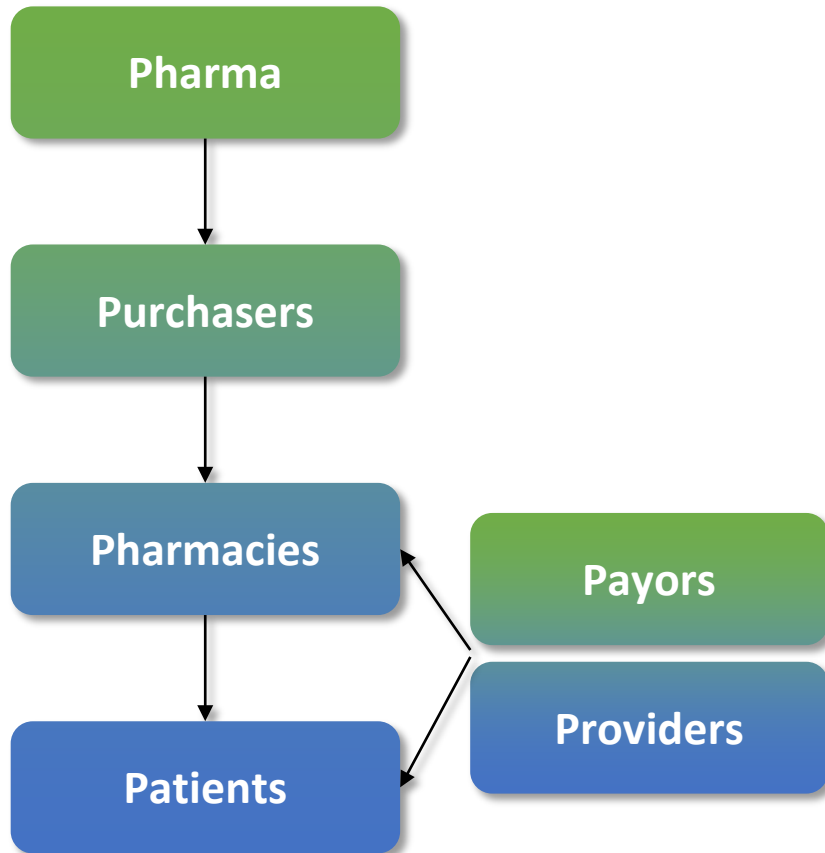
QMMM = f(QM, x, y, z...)

Road to Achieving QMM

- **QMM white paper** released April 5
 - Importance of QMM
 - Key challenges and elements for successful QMM implementation
- **QMM stakeholder workshops** to be held May 24-25
- **QMM Advisory Committee** meeting to follow at a later date



“6 Ps” Impacted by QMM Ratings



Stakeholder	Benefits
Pharmaceutical Manufacturers	<ul style="list-style-type: none"> ✓ Positive and proactive performance acknowledged ✓ “Good actors” rewarded
Purchasers ³	<ul style="list-style-type: none"> ✓ Improved supply chain transparency for decision-making ✓ Quality ratings backed by FDA insight and non-public data
Pharmacies	<ul style="list-style-type: none"> ✓ Improved supply chain transparency ✓ Less risk of failing to meet demand and medication error
Payors	<ul style="list-style-type: none"> ✓ Improved supply chain transparency for decision-making ✓ Less need to respond to drug shortage
Providers	<ul style="list-style-type: none"> ✓ Less risk of drug shortage impacting their patients ✓ More confidence in the supply of drugs they prescribe
Patients	<ul style="list-style-type: none"> ✓ Less risk of drug shortage impacting their care ✓ More confidence in drug availability

The background of the slide is a blurred photograph of a laboratory. In the foreground, a person with dark hair tied back is seen from behind, looking at a piece of equipment. The background shows various laboratory glassware, including bottles and flasks, on a counter. The overall scene is brightly lit and has a clean, professional appearance.

Advanced Manufacturing

US FDA Center for Drug Evaluation and Research

What is Advanced Manufacturing?

- Novel **manufacturing methods** to improve process robustness and efficiency
- Novel **dosage forms** or delivery systems to improve drug delivery and targeting
- Novel **analytical tools** to improve product characterization, quality testing, process monitoring and/or control

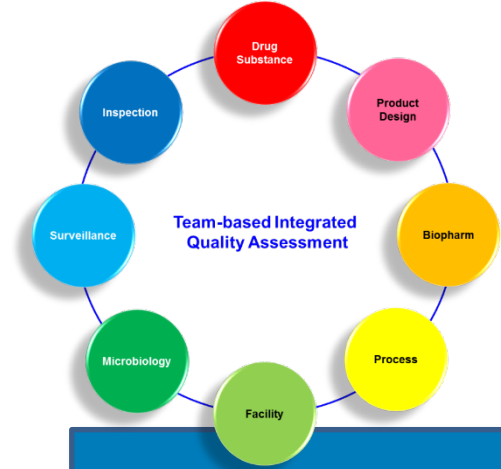
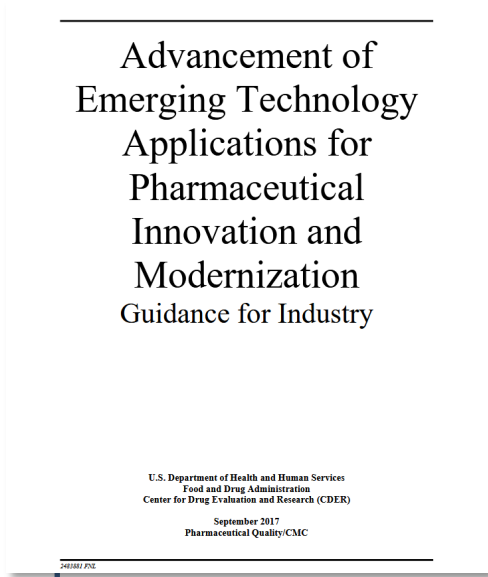


Advanced Manufacturing Benefits

Advanced manufacturing can improve manufacturing and ensure quality medicine is available.

-  **Produce better quality medicine.** Facilitates six-sigma operation, no more than 3.4 defects per 1M opportunities.
-  **Re-shore drug manufacturing facilities.** Helps domestic drug manufacturers compete in a global market.
-  **Develop drugs rapidly.** Speeds the development of novel or patient-focused therapeutics.
-  **Prevent drug shortages.** Reduces today's quality-related manufacturing issues causing 62% of drug shortages.
-  **Improve emergency preparedness.** Provides more agility and flexibility to help pivot in a public health emergency.

Emerging Technology Program



Industry Develops Emerging Technology

ETP Evaluates Technology

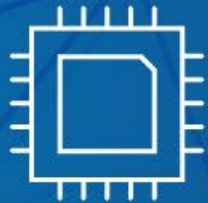
Technology Moves to Standard Quality Assessment Processes

Acceptance to ETP

Graduation



**U.S. FOOD & DRUG
ADMINISTRATION**



Framework for
Regulatory Advanced
Manufacturing Evaluation
(FRAME)

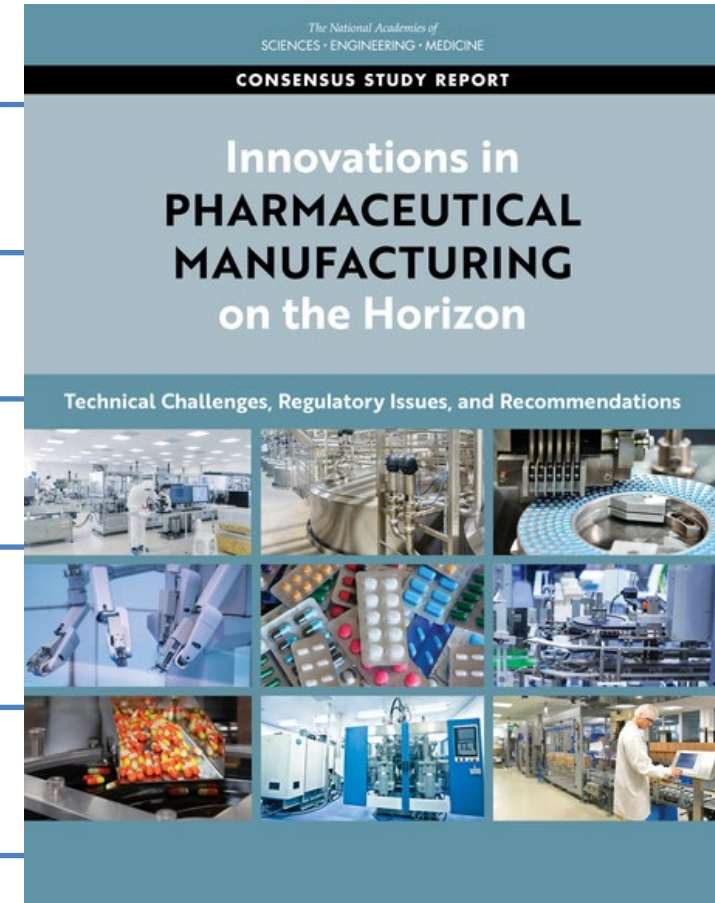
FRAME: Framework for Regulatory Advanced Manufacturing Evaluation



Establish a **regulatory framework that provides clarity and reduces uncertainty** for products manufactured with advanced technologies

The framework will need to address both **current and future manufacturing innovation.**

Scope: CDER's **submission pipeline in the next 5-10 years***.



*In NASEM's [*Innovations in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues, and Recommendations*](#)



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 white, oval-shaped pills into the palm of the right hand. The bottle has a white label with a yellow rectangular area and some partially legible text. The background is softly blurred, focusing attention on the hands and the medication.

**Patients deserve confidence in
their next dose of medicine.**

**We remain committed to giving
it to them.**



U.S. FOOD & DRUG
ADMINISTRATION