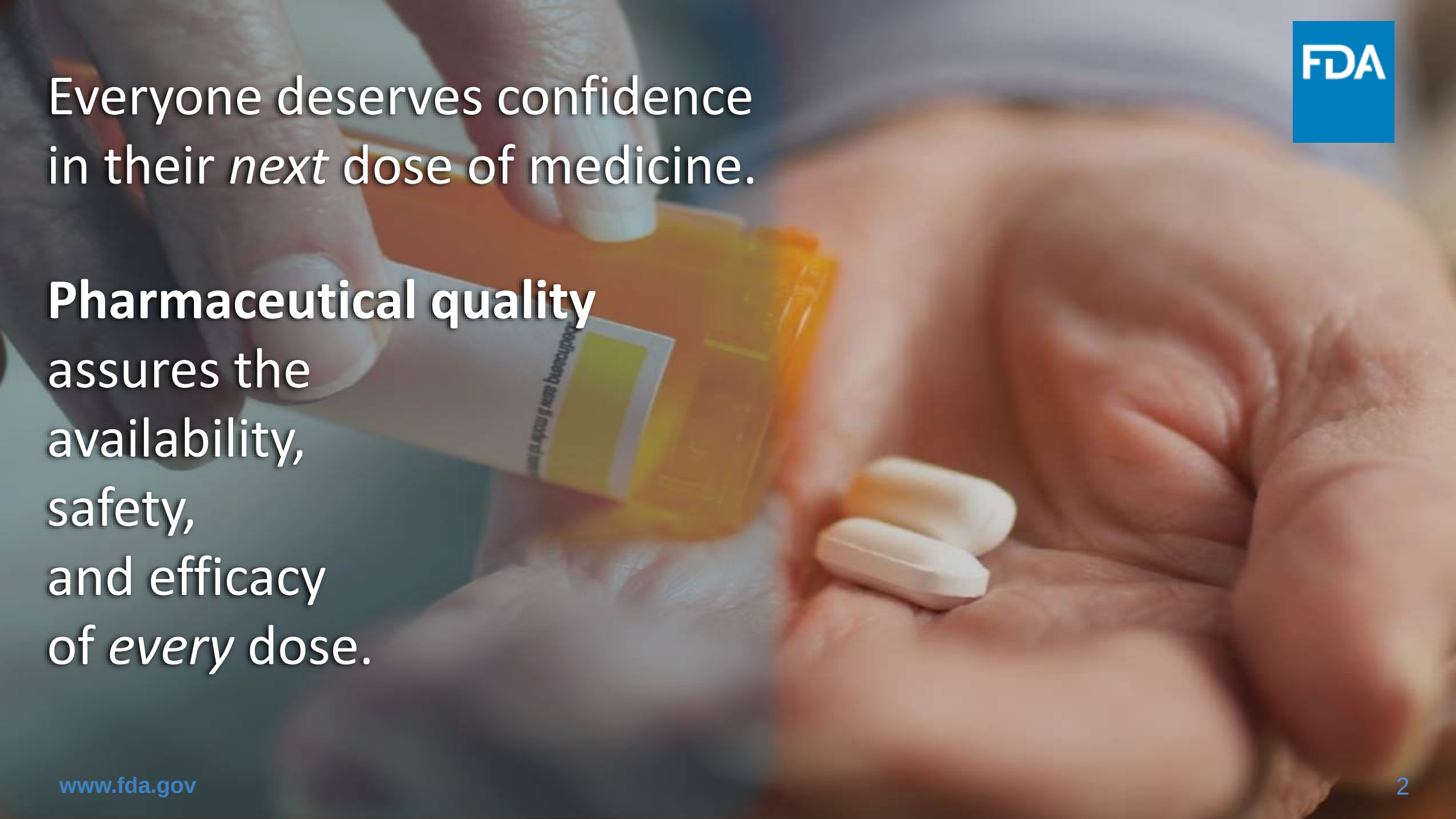
U.S. FOOD & DRUG ADMINISTRATION

Innovation:
The Future of Pharmaceutical Quality

Sau (Larry) Lee, Ph.D.
Deputy Director of Science
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Generic Drug Forum 2023
April 12-13, 2023

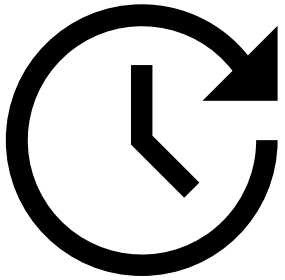


Everyone deserves confidence in their *next* dose of medicine.

Pharmaceutical quality assures the availability, safety, and efficacy of *every* dose.

The Future of Pharmaceutical Quality

- Assessment Innovation
- Quality Management Maturity
- Advanced Manufacturing



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 **API** and **finished dosage form** sites

Products:

- **170,000** finished dosage form products
- **19,000** APIs
- **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*

Assessment Innovation

US FDA Center for Drug Evaluation and Research

Quick Innovation Was Necessary

- **Remote Regulatory Assessments (RRAs)**
  - 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)

GUIDANCE DOCUMENT

Conducting Remote Regulatory Assessments Questions and Answers

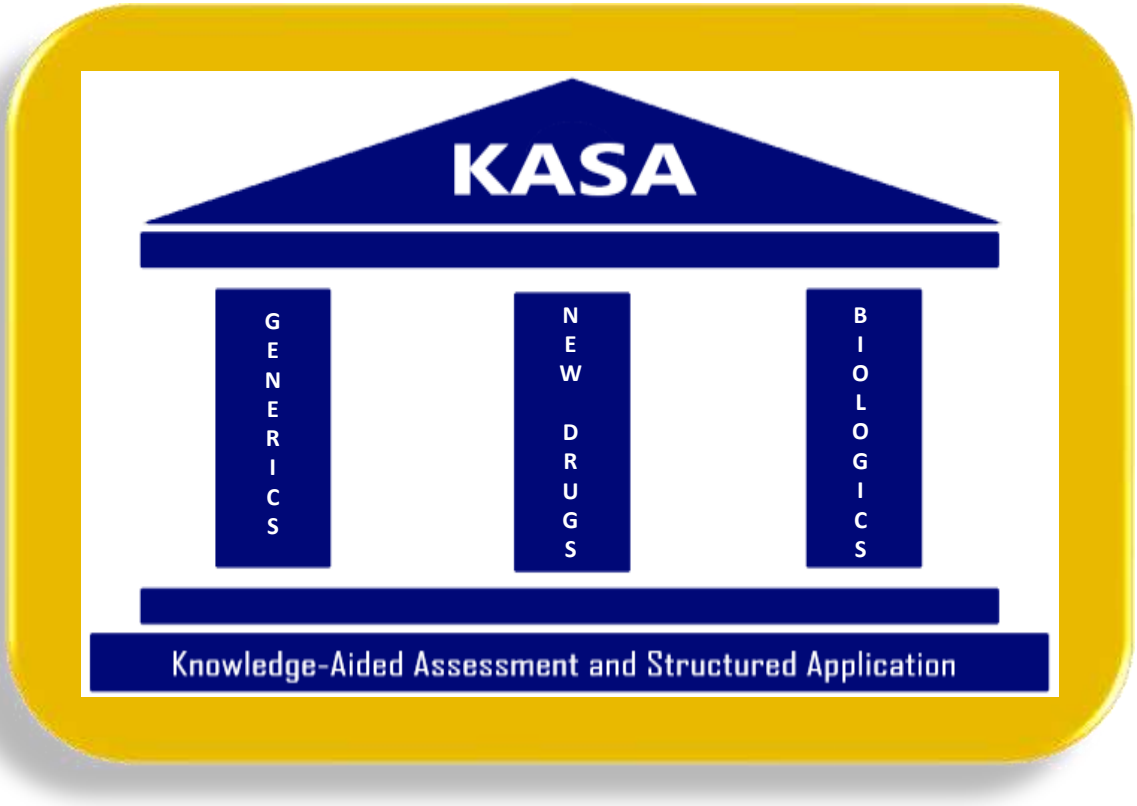
Draft Guidance for Industry

JULY 2022

Impact of Remote Regulatory Assessments

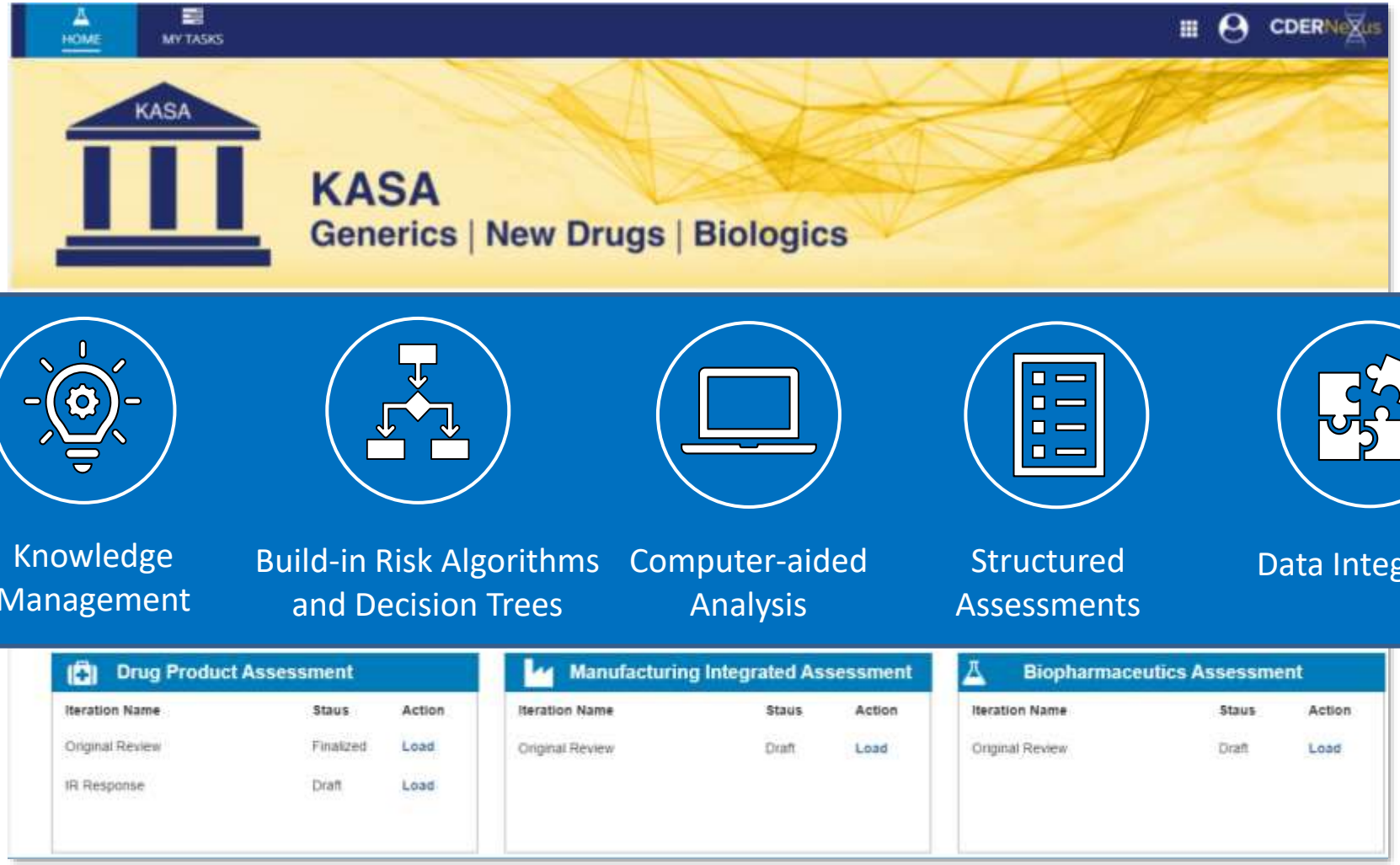
- **Conducted** 65 pre-license facility inspections
- **85 applications** acted on using remote regulatory assessments.
- **Approved:**
  - **7 biosimilars**, and making **2** determinations of interchangeability
  - **914** generic drugs, including **86** complex generics
- **Maintained on-time action >90% overall**
  - Across all submissions with goal dates

Quality Assessment Transformation: KASA



A data-based platform for structured quality assessments and applications that supports knowledge management

KASA = **K**nowledge-aided **A**ssessment and **S**tructured **A**pplication



- **KASA for generic solid oral dosage forms was live as of 2021**
- **FDA Release of KASA 4.0 for Drug Substance in ANDA, NDA and DMF**

Quality Management Maturity

US FDA Center for Drug Evaluation and Research

An Array of Quality

Pharmaceutical Quality

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

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

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)

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

Introduction

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

[OPQ] is responsible for overseeing the quality of drugs. The OPQ report on the State of Pharmaceutical Quality states that "A quality drug is consistently safe and effective, free of contamination and defects."[1]

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

1

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 Energy
Department of Defense
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

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.

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

- **Stakeholder Meetings**
  - E.g., Duke-Margolis (Feb 3, 2020)
- **QMM Stakeholder Workshop** (May 24-25, 2022)
- **QMM Advisory Committee** (Nov 2-3, 2022)

Advanced Manufacturing

US FDA Center for Drug Evaluation and Research

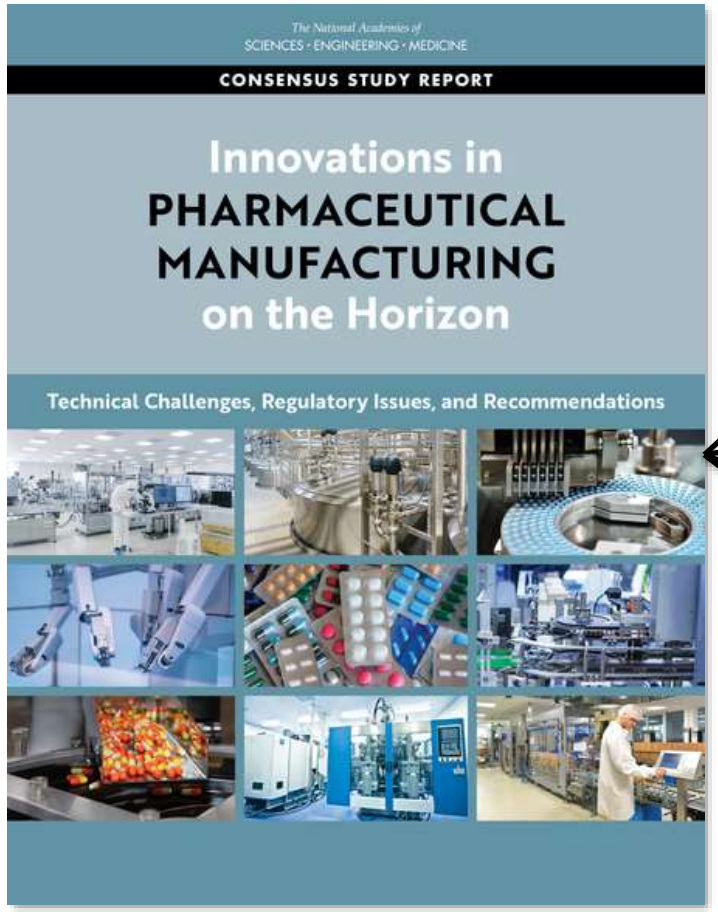
What is Advanced Manufacturing?

- 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

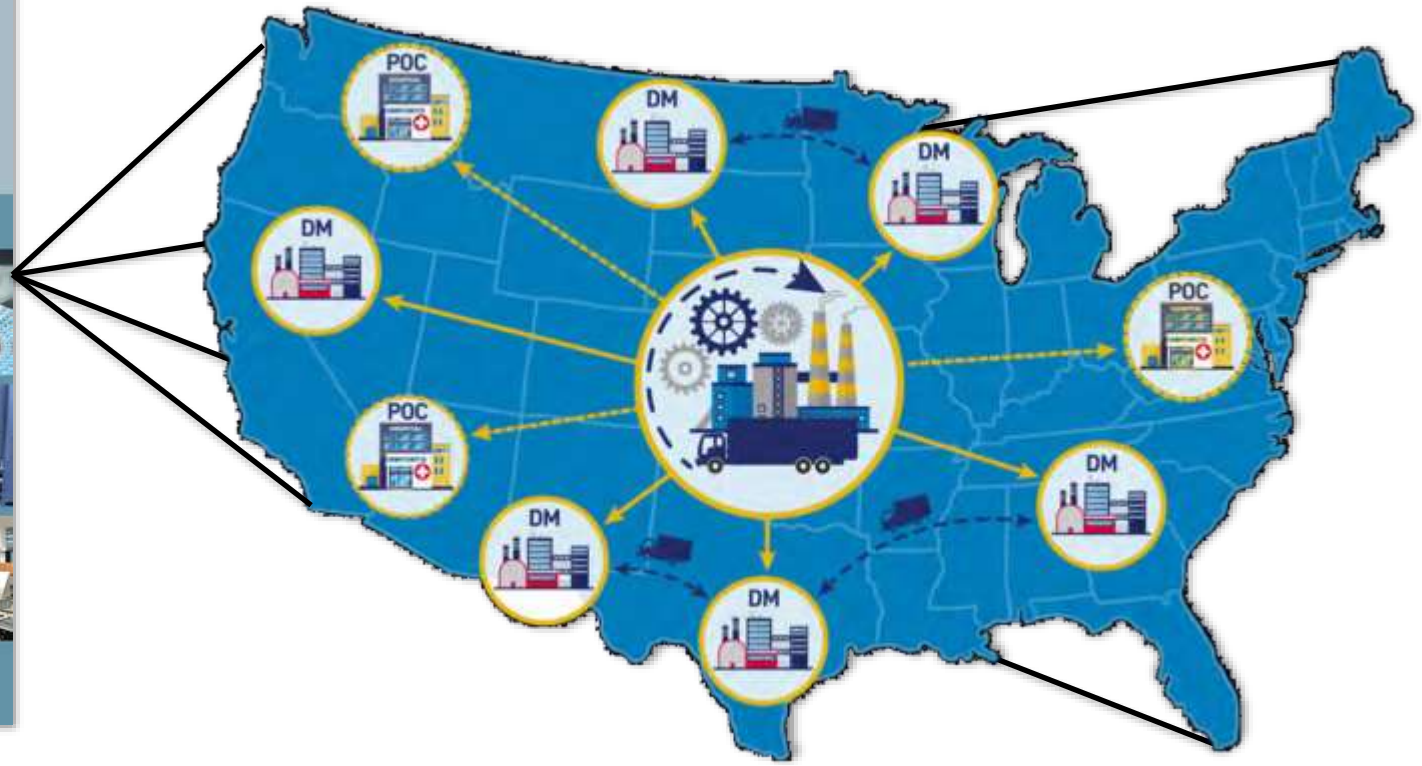
Emerging Technology Program

WHAT	An OPQ program established in late 2014 that promotes and facilitates the **adoption of innovative approaches to pharmaceutical product design and manufacturing**
WHO	A **cross-functional team** (approximately 30 members with additional ad-hoc SME members) with representation from all relevant FDA quality review and inspection programs **Offices include: OPQ, OC, ORA (*One Quality Voice*)**
HOW	The program provides an **opportunity for industry to engage and collaborate early with the FDA** to discuss, identify, and resolve technical and regulatory issues during a novel technology's development and adoptions

FRAME: Framework for Regulatory Advanced Manufacturing Evaluation



INTEGRATED, FLEXIBLE, AND DISTRIBUTED



*NASEM *Innovations in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues, and Recommendations* (2021)

FRAME Public Engagement

- ✓ **Published** CDER DM and POC Manufacturing of Drugs Discussion Paper
- ✓ **Collaborated** with PQRI to implement DM/POC Public Workshop
- ✓ **Published** CDER FRAME AI Discussion Paper in Federal Register
  - 60 days public comment period

Organizing AI public workshop in partnership with PQRI

Dispelling the Myths of AM

- **The use of AM is not mandated by FDA**
  - FDA approves drugs if they comply with standards, regulations, and laws
  - Benefits of using AM in some, but not all, instances
- **AM is not just for innovator companies**
  - Multiple developers of generics have engaged with CDER's ETP
- **Generic drug companies are not required to implement AM because an innovator company has done so**
  - Specification criteria are based on patient relevance and not on process capability
- **AM applications have not taken longer to review and approve…**

In Closing

US FDA Center for Drug Evaluation and Research

Innovation is the active ingredient in regulating pharmaceutical quality.

Let’s continue working together to ensure patient access to quality medicine.

FDA U.S. FOOD & DRUG ADMINISTRATION