An Update to CDER's Voluntary Quality Management Maturity (QMM) Program

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2024 Pharmaceutical Manufacturing and Quality Conference
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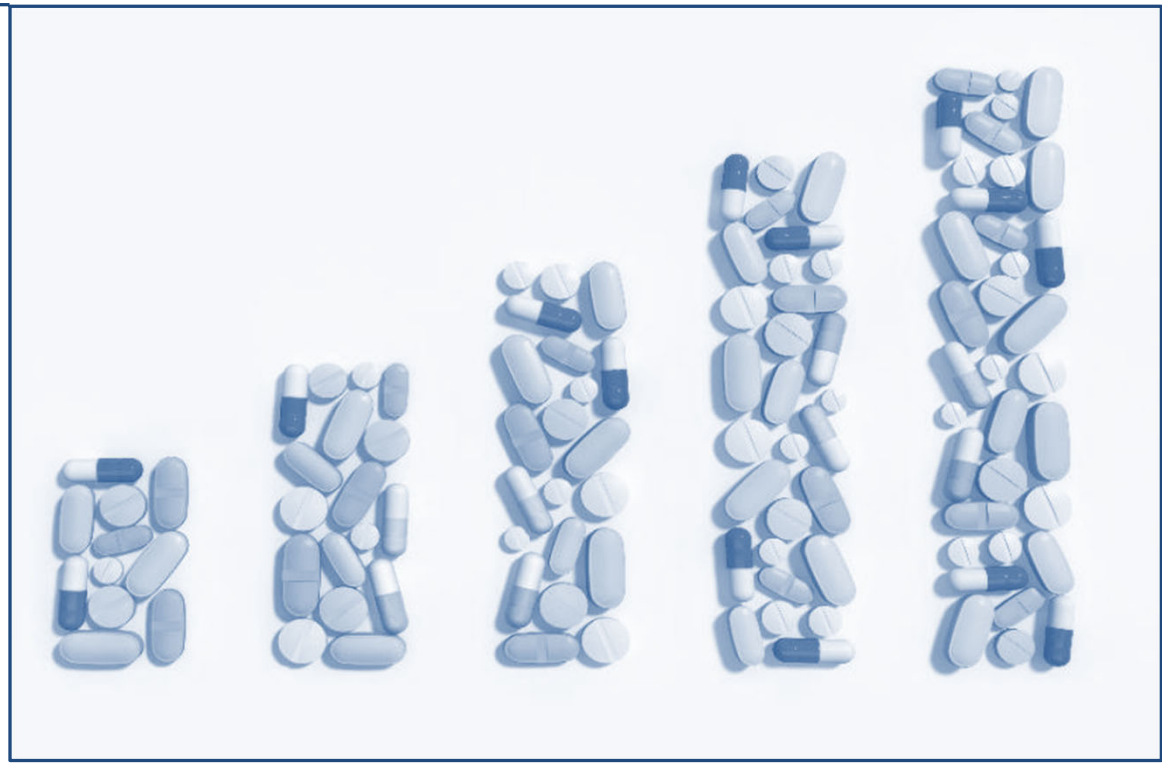

Agenda

- Introduction to Office of Quality Surveillance (OQS)
- Drug Shortages and Supply Chain Vulnerabilities
- Introduction to Quality Management Maturity (QMM)
- Update on QMM Program Development


Everyone deserves
confidence in their *next*
dose of medicine.
Pharmaceutical quality assures the
availability,
safety,
and efficacy
of *every* dose.
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INTRODUCTION TO OFFICE OF QUALITY SURVEILLANCE (OQS)

Office of Quality Surveillance (OQS)

VISION

- To be the global benchmark for pharmaceutical quality surveillance.

MISSION

- OQS turns intelligence into insights and actions to promote the availability of quality medicines for the American public.

Sleuths for Drug Quality!

OQS leverages pharmaceutical intelligence on manufacturers and the products they make, knowledge of CGMP regulations/guidance, and analytics to help the Office of Pharmaceutical Quality (OPQ) assure drug quality and availability:

- Surveil quality throughout the product lifecycle
- Understand and model pharmaceutical supply chains
- Advance the science of quality surveillance
- Promote industry adoption of mature quality management practices

CDER's Site and Product Catalogs

Sites (Includes active pharmaceutical ingredient and finished dosage form):

- **6,500** human drug manufacturing sites of obligation
- **1,800** medical gas manufacturers

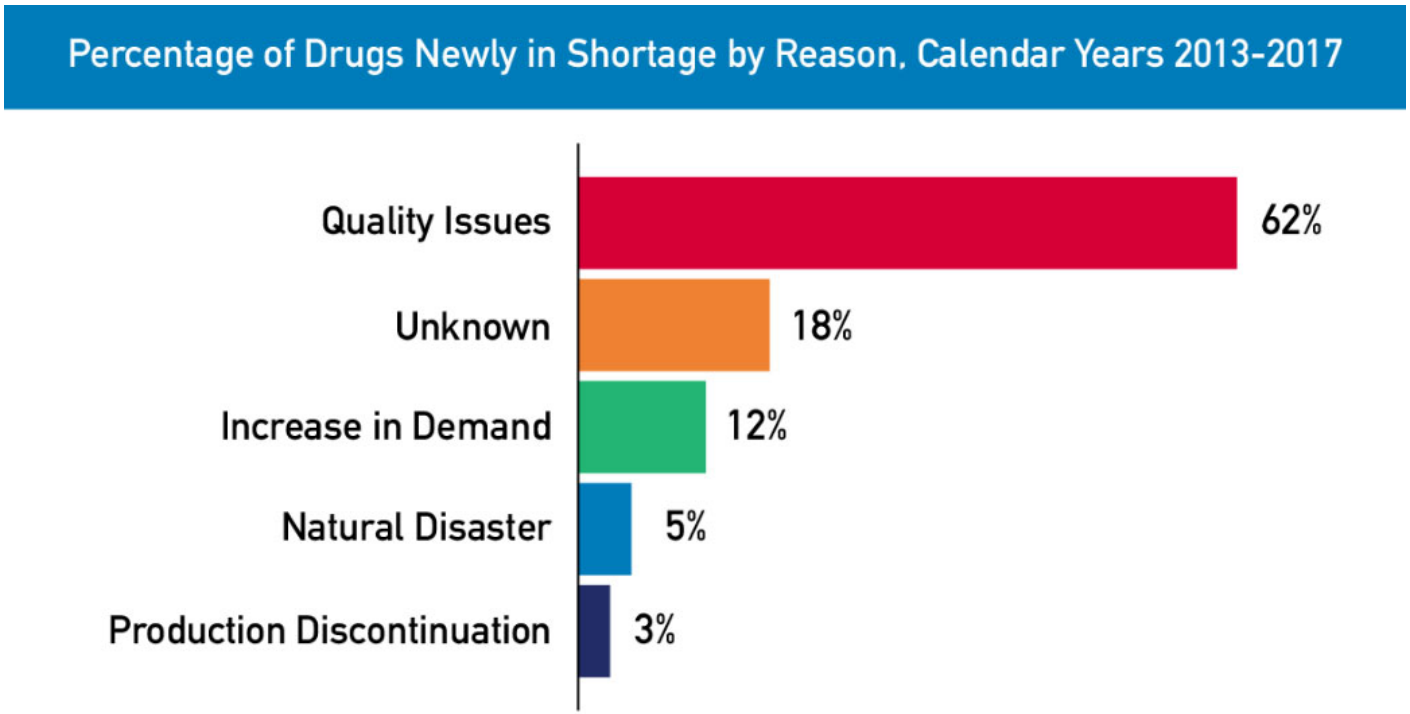
Products (Includes new drugs and biologics, generics, biosimilars, over-the-counter drugs)**:**

- **200,000** finished dosage forms
- **20,000** active pharmaceutical ingredients
- **800** medical gases

**Based on January 2024 CDER Site & Product Catalogs and unique NDCs*

SHORTAGES AND SUPPLY CHAIN VULNERABILITIES

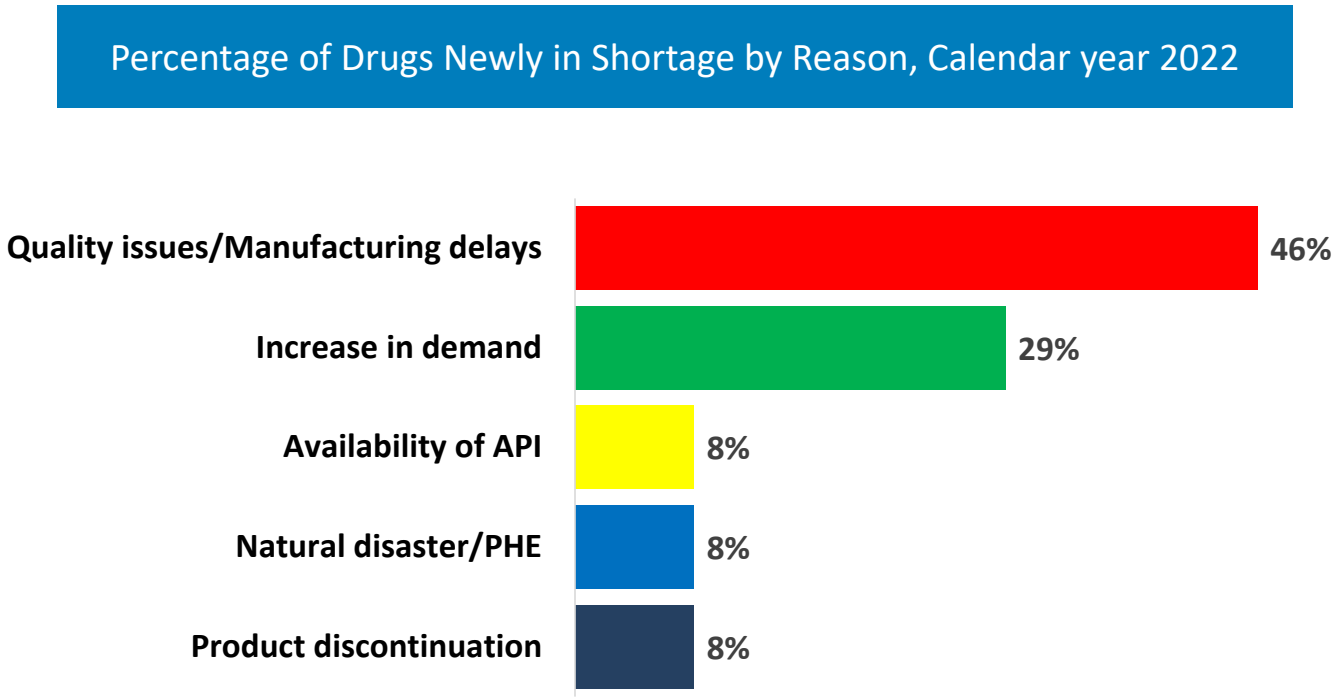
Reasons for New Shortages - Historical



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

Source: Internal FDA Data

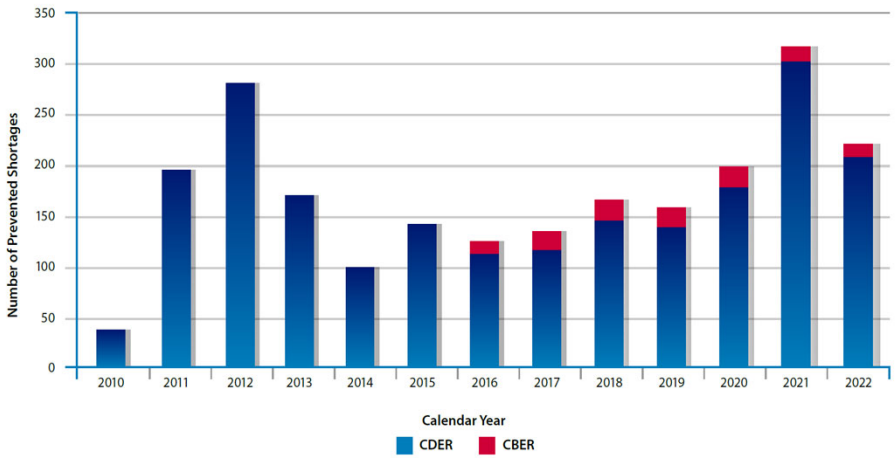
Reasons for New Shortages - CY 2022



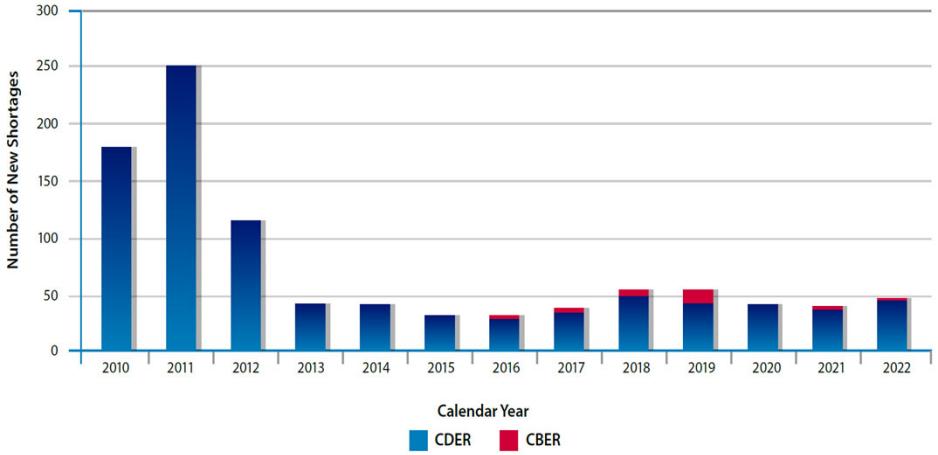
Note: Percentages do not equal 100% due to rounding.

Prevented Shortages and New Shortages

- Through ongoing industry engagement, the number of **prevented** drug shortages has grown, while the number of **new** drug shortages remains stable.
- Depending on precipitating and mitigating events, drug shortages may endure for months to years (e.g., plant remediations, agency approvals).
- If this work begins earlier, there is a greater likelihood to prevent or mitigate a shortage.



Total Prevented U.S. Drug Shortages Per Year



Total New U.S. Drug Shortages Per Year

Source: Annual Report on Drug Shortages for Calendar Year 2022

Challenges to Drug Product Availability

Supply chain factors that can result in shortages:

- Manufacturing Reliability
- API and Key Component Availability
- Aging Manufacturing Facilities
- Natural Disasters and Public Health Emergencies
- Economic Issues
- Geopolitical Issues
- Global Production Capacity Shortfall
- Lack of Incentives to Produce Excess Supply (over market demand)

Drug Shortages – One potential solution

- 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*

- Enduring Solution: *Incentivize drug manufacturers to invest in 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 to optimize product quality, enhance supply chain reliability, and drive continual improvement.

INTRODUCTION TO QUALITY MANAGEMENT MATURITY (QMM)

Complementary Efforts

FDA

FDA C·D·R·H Center for Devices and Radiological Health

Voluntary Improvement Program

PDA Parenteral Drug Association

Quality Culture Initiative

APQ Advancing Pharmaceutical Quality

ISPE Quality Management Maturity Program

Advancing Pharmaceutical Quality Program

University of St.Gallen

Operational Excellence Research

dun & bradstreet

Quality Benchmarking Study

Pathway for Patient Health

Adaptability and Agility Maturity Model

QMM Program Goals

1. Foster a strong quality culture mindset

2. Recognize establishments that have advanced quality management practices and acknowledge establishments that strive to continually improve quality management practices

3. Identify areas where quality management practices can be enhanced and provide suggestions for growth opportunities

4. Minimize risk to product availability to assure reliable market supply

Addressing misconceptions… the truth is…

QMM assessments are not used to evaluate compliance with CGMP

QMM assesses manufacturing establishments, not product quality

Maturity is independent of establishment size or age, and types or numbers of products produced

QMM assessments are distinct from the collection of quality metrics

QMM is NOT an additional burden or requirement

UPDATE ON QMM PROGRAM DEVELOPMENT

Recent Milestones and Publications

Two QMM Pilots
completed in 2022

CDER White Paper #1
April 2022

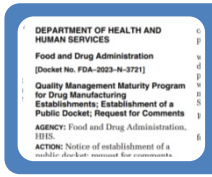
Small Business and Industry Assistance (SBIA) Workshop
May 24-25, 2022

Article on benchmarking quality practices with D&B
October 2022

FDA Advisory Committee
November 2, 2022

Article on lessons from pilot programs
January 2023

CDER White Paper #2
August 2023



FRN announcing docket of public/stakeholder feedback
September 2023

FRN soliciting volunteers for the program
January 2024

Volunteers selected for the 2024 program
April 2024

FDA Advisory Committee

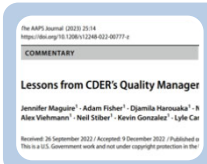
November 2, 2022

Stakeholder Engagement Efforts

On November 2nd, 2022, the Pharmaceutical Science and Clinical Pharmacology Advisory Committee voted unanimously (9-0) in support of the development of CDER's QMM Program.

CDER committed to engaging with stakeholders and soliciting public input to develop the QMM Program.

Following the advisory committee, CDER engaged with multiple internal and external stakeholders.


COMMENTARY

Lessons from CDER's Quality Manager

[Article on lessons from pilot programs](#)
January 2023

QMM Pilot Programs

Pilot 1

Domestic FDF Manufacturers

7 establishments

Pilot 2

Overseas API manufacturers

8 establishments

Lessons Learned

- Assessment process
- Scoring approach
- Assessor behaviors
- Perceptions of the assessment questions
- Reports
- Ratings


DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-N-3721]

Quality Management Maturity Program for Drug Manufacturing Establishments; Establishment of a Public Docket; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of establishment of a

[FRN announcing docket of public/stakeholder feedback](#)

September 2023

Overview of Public Docket

On September 15th, 2023, a [Federal Register Notice](#) was published to establish a 90-day [Public Docket](#) to solicit comments on the QMM Program.

The docket posed **8 questions** to the public to help guide QMM Program development.

The docket closed on **December 14th, 2023.**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September 2023

Summary of Docket Responses

Q1. 23 responses received from:	Q2. Advantages of QMM Program to sector (e.g., industry, purchasers):	Q3: Advantages of QMM Program to participating establishment:
• Drug Manufacturers • Drug Purchasers • Drug Distributors • Trade Associations • Non-profit Organizations • Individuals	• Improve quality maturity across the industry • Increased transparency resulting in improved product quality • Benchmarking maturity • Sustainable supply chain	• Use outcomes to support continuous improvement efforts • Supplement continuous improvement efforts with suppliers


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Summary of Docket Responses

Q4 How establishments will use information from the QMM assessments:	Q5 Potential unintended consequences or concerns about QMM Program:	Q6 QMM report should contain:
• Use as a marketing tool • Support contract negotiations • For authentication of a supplier's quality management system	• Assessor bias • Maintaining confidentiality • Loss of market share or clients due to lower maturity scores • Distinguishing between QMM assessments and CGMP inspections • Some sectors may be at a disadvantage compared to others • Need for additional resources and time may lead to misallocation of resources	• Relevant KPIs • Context for scores • Balanced feedback • Benchmark for each maturity level • Recognition of Participation (e.g., Certificate)


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September 2023

Summary of Docket Responses

Q7 Should the outcomes of the QMM assessment be made public:

- If shared, assessment outcomes or scores should be at least partially redacted
- Assessment outcomes and scores can only be shared by the establishment at their discretion
- Public scores may help identify facilities that may be less prone to drug shortages

Q8 Other feedback:

- Provide specific details about incentives
- Do not conflate goals, expectations, or topics under existing regulatory framework with QMM
- Implement QMM in conjunction with other global regulatory agencies
- Utilize existing tools to assess maturity
- Encourage full implementation of ICH Q9(R1), Q10, and ISO 9001

FRN soliciting volunteers for the program

January 2024

2024 QMM Prototype Assessment Protocol Evaluation Program – Federal Register Notice

Discusses **Practice Areas**, **Assessment Protocol** and **Rubric** to evaluate how effectively establishments monitor and manage quality and quality management systems.

Discusses selection of **up to 9 volunteer establishments.**

Federal Register Notice closed **March 25, 2024**.

CDER will use learnings to refine assessment tools, output, and business processes

QMM Practice Areas

Pre-Assessment Questionnaire

Quality Risk Management Example

P1: Explain your establishment's definition of 'risk' and 'risk management.'

Things to consider:

- Does your establishment's definition of risk include detectability? Why or why not?
- What models, if any, does your establishment use to evaluate and manage risk (e.g., ICH Q9(R1))?

Assessment Protocol

Quality Risk Management

Q1: Describe how your establishment uses risk management to inform decision making.

Ratable criteria:

- How is risk taken into consideration?
- Whether subjectivity considered or addressed?
- Are QRM methodologies or tools used?

Rubric

Quality Risk Management Example

- How is risk taken into consideration?

Level 0	Level 1	Level 2	Level 3	Level 4
Risk is not considered in the decision-making process.	Risk is not consistently considered in the decision-making process.	A systematic process for managing risk is established for the commercial stage of the product life cycle. The identified hazards and their associated risks are considered in the decision-making process. Level of formality is commensurate with the level of risk.	A systematic process for managing risk is established for all stages of the product life cycle. Risks are reviewed at a meaningful frequency. Impact to patient is considered.	Risk-based decision making is optimized based on emerging and changing circumstances.

Minimizing Subjectivity in Scoring

Assessments will be performed in teams

- Three people
- Mix of FDA staff and contractors
- Minimize assessor bias

Use of standardized tools (protocol and rubric)

- Protocol aligned to ISO standards, guidances, publications
- Assessors rate establishments using defined rubric

Development of scoring logic and algorithm

- Responses substantiated for full credit
- Inter-rater variability monitored and resolved

Potential QMM Incentives being evaluated

ENGAGEMENT IN SAFE SPACE

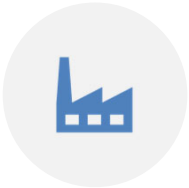
BENCHMARKING PERFORMANCE

SHARED LEARNING WITH PARTICIPANTS

QMM CERTIFICATE

REGULATORY FLEXIBILITY

INSPECTION FREQUENCY AND SCOPE



SECTOR SPECIFIC INCENTIVES

QMM is Valuable to All

- Patients and Consumers.
- Manufacturers
- Purchasers and Payers
- Healthcare Professionals
- Pharmacies
- FDA

Questions?

Contact us at CDER-QMM@fda.hhs.gov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