FROM PILOTS TO GLOBAL ALIGNMENT: THE BENEFITS AND FUTURE OF QUALITY MANAGEMENT MATURITY (QMM)

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ABSTRACT

The Quality Management Maturity (QMM) initiative by the U.S. Food and Drug Administration (FDA) is configured to encourage pharmaceutical manufacturers progress beyond fulfilling regulatory requirements, concentrate on sustained quality advancement. This concept became prominent after the FDA's drug shortage report in 2019, which pointed out that numerous supply interruptions were a result of inadequate quality management. To investigate methods for evaluating quality maturity, the FDA executed a pilot program from 2020 to 2022. The pilot program assisted in determining effective assessment techniques and highlighted the key aspects that embody a robust quality culture, including leadership engagement, continuity of operations, technical skills, and participation from employees. Using insights gained from the pilot, the FDA introduced the prototype assessment protocol in 2024. This new more organized method ensures uniform evaluation across manufacturing facilities and is undergoing further enhancements in 2025.The QMM framework is in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q10 and Q12, which allows for increased regulatory flexibility. The program provides significant advantages, such as improved reliability in the supply chain, enhanced patient access to medications, and acknowledgment for firms with sophisticated quality systems. This study primarily intends to explore the QMM pilot initiatives and the assessment protocol evaluation program prototype, emphasizing their role in global alignment and their benefits.

Keywords: Quality Management Maturity (QMM), Pilot programs, Center for Drug Evaluation and Research (CDER), Protocol evaluation program.

INTRODUCTION

The Federal Drug Shortage Task Force, which involves multiple agencies, released findings titled Drug Shortages: Root Causes and Potential Solutions in 2019. The report determined sixty-two percent of medications faced shortages from 2013 to 2017 were associated with manufacturing or quality control problems. The Drug Shortage Task Force found that a key factor behind deficit in medicinal products is the industries inability in recognize or incentivize production companies that have established quality management systems, which enhance early identification of quality issues and promote proactive improvements in business practices. The Center for Drug Evaluation and Research (CDER) collaborated with outside contractors to implement two pilot initiatives focused on evaluating the QMM of drug production facilities between October 2020 to March 2022. [1]

To address persistent drug shortages, the Drug Shortages Task Force outlined three long-term strategies, one of which involves creating a rating system to encourage pharmaceutical companies to pursue QMM. QMM reflects a high level of operational excellence, where companies consistently apply dependable and well-structured processes to meet quality goals and foster ongoing improvement. In response, the FDA has assembled a cross-functional team spanning multiple centers to guide the development of this QMM rating initiative. As the CDER advances the program, stakeholders have begun pinpointing critical obstacles that must be addressed to ensure its success. A well-designed QMM rating system that tackles these challenges and incorporates essential components stands to benefit both the FDA and all parties involved in the pharmaceutical supply chain.[2]

On November 2, 2022, a group of experts from the Pharmaceutical Science and Clinical Pharmacology Advisory Committee (PSCP) came together talk about how CDER's QMM program could affect the pharmaceutical industry especially when it comes to drug shortages and keeping the supply chain strong. After thoughtful discussion, the committee gave its full support to moving the program forward. In response, CDER promised to keep the conversation going by involving industry voices and gathering public feedback to help shape the program. After the advisory committee meeting, CDER connected with various internal and external stakeholders.[3]

The QMM of a pharmaceutical manufacturing facility is most effectively assessed by a group of evaluators using a standardized method. These teams may consist of FDA personnel, independent contractors, or a mix of both. The preliminary assessment protocol could incorporate a set of inquiries designed to gather responses that contribute to evaluating the maturity of a facility. These teams examine the facility's quality culture and practices. At the end of every evaluation, participants will obtain a report that emphasizes aspects the organization might want to focus on for ongoing enhancement.[1]

In United States, Current Good Manufacturing Practice (CGMP) standards outline criteria for legally marketing medicinal products alongside adherence to CGMP standards, a robust Pharmaceutical Quality System (PQS) is essential for companies that wish to utilize the tools outlined in ICH Q12. The ICH Q10 PQS guidance enhances CGMP by introducing the idea of a comprehensive pharmaceutical quality system throughout the product lifecycle. QMM requires, among other things, the thorough implementation of the principles of ICH Q10 to facilitate ongoing improvement.[2]

QMM PILOT PROGRAMS

CDER performed two pilot initiatives to evaluate the QMM of pharmaceutical manufacturing facilities between October 2020 and march 2022. Seven domestic manufacturers of finished dosage forms (FDF) for the U.S. market were assessed for maturity in first pilot phase. Eight foreign manufacturers of Active Pharmaceutical Ingredients (APIs) were assessed for second pilot phase. Each initiative led under distinct contractor and gave useful findings for CDER to build a protocol to evaluate manufacturing sites.[4]

Because of the continuing COVID-19 pandemic, all initiative's evaluations took place online. In the FDF pilot, the evaluation occurred in two phases. In the initial phase, participating establishments were given a self-assessment protocol containing 24 questions. The participants evaluated their own establishments for each question according to a rubric that outlined five

levels of maturity. The second phase of the assessment involved a guided discussion that concentrated on practice areas requiring more clarification. These discussions allowed examiners were able to communicate in person with organization personnel during these conversations and query for more details and assisting documentation. Six focus areas were addressed in the FDF pilot, as depicted in Figure 1.

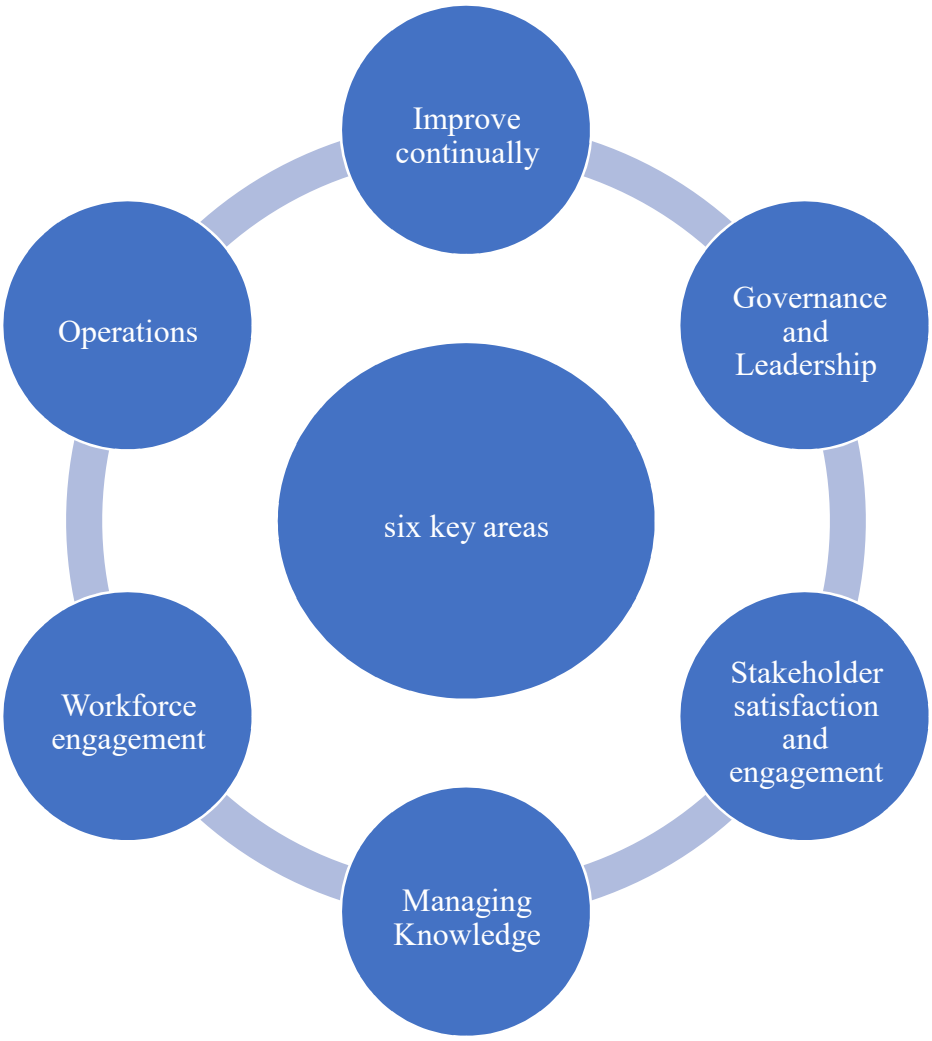

Figure 1: Six key areas were addressed during the FDF pilot.

In comparison, the API pilot phase skipped a preliminary self-evaluation. Instead, evaluators interactions with personnel organizations those involved, and consisted of sixty-six questions. Organizations involved were allowed to upload relevant documents into a portal created by the contractor. Four focus areas were addressed in the API pilot, as depicted in Figure 2.

The implementation of two pilot programs provided the FDA with valuable insights regarding the QMM assessment process, the scoring method, the conduct of assessors, and their views on the assessment questions, reports, and ratings. Early participation and well-prepared materials played a key role in helping manufacturing sites understand the QMM assessment process and make sure the appropriate personnel and records were on accessible. Self-

evaluations and unambiguous samples of documentation were valuable additions that supported maturity level judgments and guided conversations.

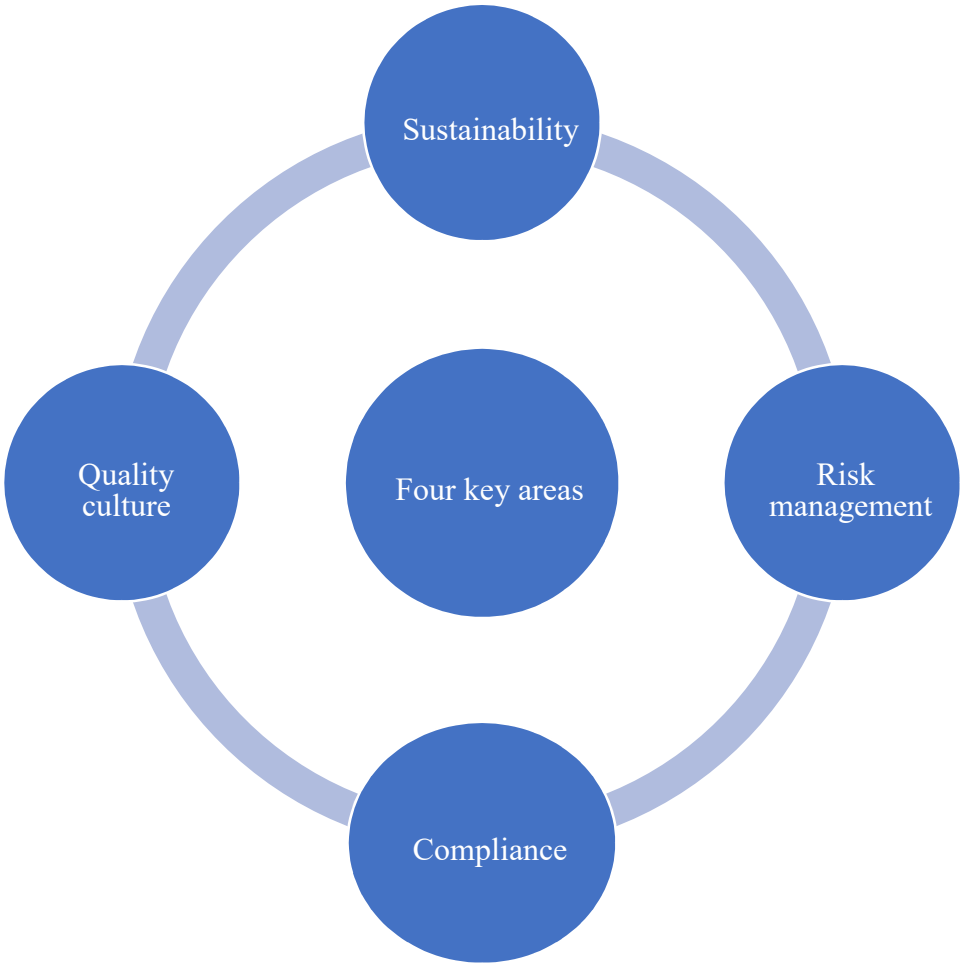

Figure 2: Four key areas were addressed during the API pilot.

To determine maturity levels, assessors used a scoring system that ranked organizations on a scale from level one to five in order to impartially evaluate an establishment's QMM. Scoring approach for assessment are displayed in Figure 3.

Figure 3: Scoring approach for assessment.

It is more likely that the ratings appropriately reflect the level of development of each distinct practice area would rise with a streamlined rubric. Using a uniform scoring system will enable organizations to compare themselves to similar organizations and monitor their development across different periods.

Based on the white paper QMM: Essential for Stable U.S. Supply Chains of Quality Pharmaceuticals, this feedback led to some of the important factors and components of a QMM

program. Overall opinions about the QMM program have been favorable. The 2022 CDER QMM Workshop, for example, polled over 400 stakeholders, and 99% of them agreed that buyers of APIs or medicinal products should "consider the QMM of the facility responsible for their production." By conducting two QMM pilots, the FDA gained knowledge about how to create and carry out a future QMM assessment standard. [5] [6]

QMM PROTOTYPE ASSESSMENT PROTOCOL EVALUATION PROGRAM

To assess how well organizations monitor and manage quality and quality systems, the QMM Assessment Tool is created by CDER. The QMM program seeks to incentivize pharmaceutical companies to adopt quality management procedures that beyond the criteria of Current Good Manufacturing Practice (CGMP). Figure 4 shows the program's goals.

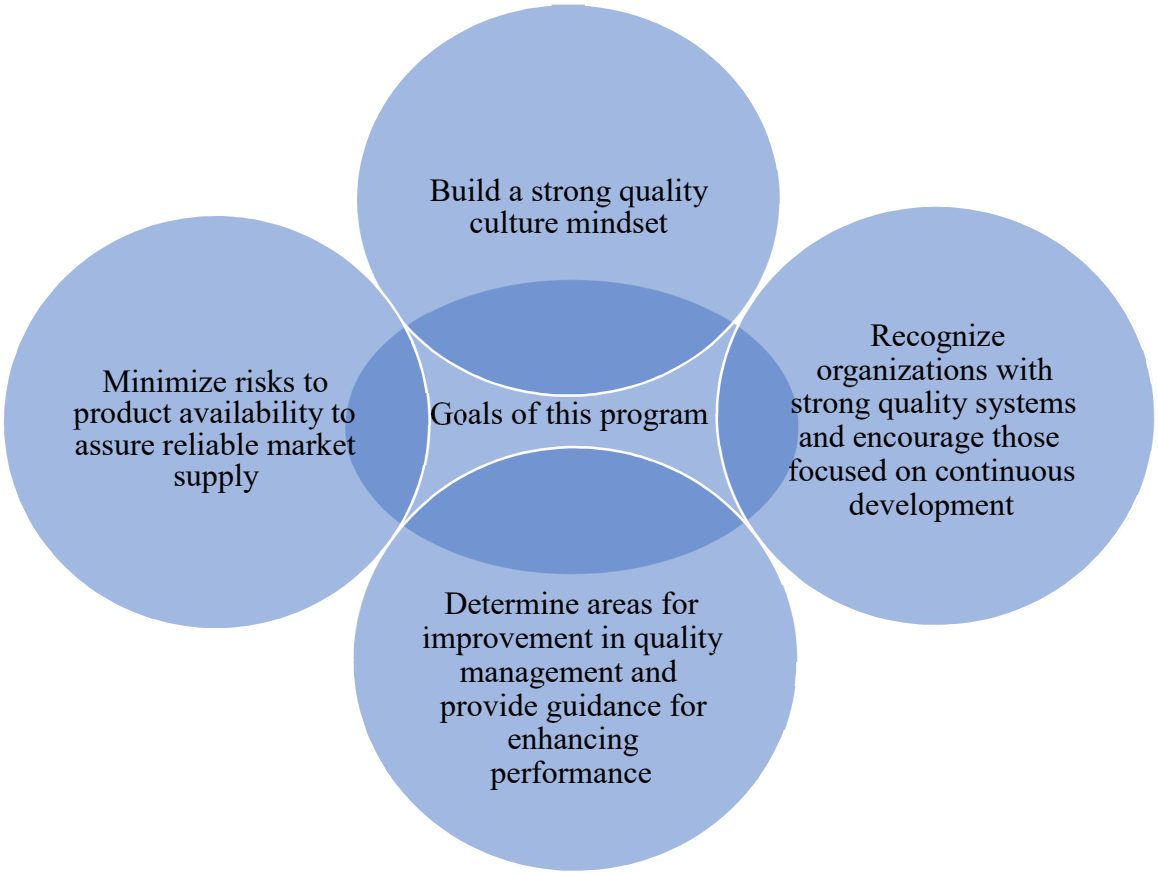

Figure 4: Goals of this program

Discussions during the onsite or hybrid assessment will be framed in part by the pre-interview questionnaire. In addition to offering insightful information about quality management policies and practices, the utilize of Initial questionnaire combined with collaborative discussions among the evaluation team and the facility enables the creation of significant improvement recommendations and a more accurate assessment of the establishment's QMM. The purpose of the assessment process is to assist organizations in strengthening their quality culture and enhancing their quality procedures.

The practice areas were determined by means of an extensive review procedure and comprised reviewing the published studies on quality management, particularly assessing aspects of pharmaceutical quality and quality culture, FDA partner feedback and stakeholder insights as well as analysis of information gathered through the two QMM pilot phase that were created and carried out by independent contractors, together with feedback of pilot participants. The practice areas for the prototype evaluation technique are displayed in Figure 5.

Figure 5: prototype assessment protocol practice areas.

The organization as a whole is framed by management's dedication to quality, which assure that quality remains a top priority, aligns with the business goals, and is adequately resourced. Business continuity provides operational resilience, protecting against interruptions and reducing risks within the supply chain. To increase process effectiveness and product quality, an improved pharmaceutical quality system makes use of insights gathered from a variety of products at all stages of the product lifecycle. In order to achieve operational excellence, technical excellence drives adoption of innovative production plus analytical methods suited to intended purpose while encouraging new skill growth. Ultimately, employee engagement cultivates a quality-driven culture across the organization, enabling employees to play an active role in ongoing improvement and patient safety.[1][3]

In 2024, CDER assessed nine establishments through the voluntary QMM Prototype Assessment Protocol Evaluation Program. Utilizing protocol, CDER gathered information on each establishment’s practices, behaviors, and responses to targeted questions across five practice areas. Based on the feedback and insights obtained in 2024, CDER refined its prototype QMM assessment tool for improved clarity and conciseness, and updated the evaluation rubric. In the post-assessment stage of this program, participating establishments will be urged to identify at least one improvement opportunity from the QMM report and create an improvement plan with specific goals focused on that opportunity.[4]

GLOBAL ALIGNMENT OF QMM WITH ICH Q10 AND ICH Q12

The ICH Q10 guidance introduces the concept of a comprehensive PQS across the product lifespan, which improves CGMP. ICH Q10 details the processes for managing and continuously enhancing the pharmaceutical quality system, incorporating principles of quality risk management and knowledge management. The ICH Q12 provides a framework that makes post-approval changes more efficient and predictable, thereby increasing transparency between the industry and regulatory bodies while fostering innovation and continuous improvement. Effective implementation of ICH Q12 by the CDER will be made possible by a strong QMM program.

The ICH Q10 guideline proposed that advanced quality management systems could allow pharmaceutical companies more regulatory flexibility when making changes to manufacturing after a product is approved. However, this flexibility hasn't been fully achieved. Differences in post-approval change requirements across global regulatory bodies often lead to delays and increased costs when trying to implement improvements even when supported by a robust quality system. To address these challenges, a new harmonized guideline, ICH Q12, is being developed. It focuses on technical and regulatory aspects of managing pharmaceutical products throughout their lifecycle and is expected to be finalized soon. This guideline introduces a set of mechanisms designed to encourage deeper insight into products and processes, as well as the adoption of robust pharmaceutical quality systems. It does by offering pathways for more relaxed regulatory scrutiny when it comes to specific manufacturing changes made after product approval. Once this guideline is globally adopted, it could ease the path for manufacturers aiming to upgrade their technologies and operations especially those who have struggled with the high costs and complexity of navigating diverse regulatory requirements. The FDA's QMM program offers an organized method for evaluating the maturity of quality systems, which enhances these worldwide criteria. ICH Q10's vision and ICH Q12's tools are thus supported by QMM, giving manufacturers with established systems more regulatory flexibility and streamlining post-approval modifications.[2] [7]

BENEFITS OF QMM

- Drug shortages may be lessened and supply chain resilience and robustness increased using a QMM program.
- The company's market reputation and client perceptions increased as a result.
- Using QMM in a manufacturer's supply chain could lower the chance of supply disruptions and increase transparency with suppliers.
- Costs were reduced as a result of the effective procedures, which also reduced errors, customer complaints, and recalls.
- It made it easier for the pharmaceutical industry to benchmark and share knowledge.
- It promoted a quality-driven company that prioritizes proactive, ongoing development.[8]

CONCLUSION

QMM is the level to which pharmaceutical manufacturing facilities use quality management techniques that consider patients first, promote continuous improvement, and improve supply chain dependability by strategically fusing manufacturing processes and business choices with

quality standards and emerging technologies.[4] CDER employed two contractors for these pilot projects, and they provided a set of areas to cover, including quality culture, managing risk, handling supply chain management, customer experience and managing inventories.[6] CDER developed prototype evaluation technique to assess an QMM at a facility upon findings of these two pilot initiatives. Each QMM report outlined the establishment's advantages and areas for development.[4] In addition to the explicit requirements currently found in CGMPs, advanced QMM incorporates elements like continuous improvement, improved communication prompted employees to share queries, knowledge management to improve product understanding, industrial expenditure on infrastructure, analysis of data, supply chain resilience, and managing risk activities.[7] The initiative provides significant advantages, including enhanced patient access, greater resilience in the supply chain, and acknowledgment for achieving quality excellence. The FDA's QMM program strengthens this vision by evaluating the maturity of quality systems and aligning with ICH Q10 and Q12 to facilitate regulatory flexibility and streamline post-approval modifications. In conclusion, QMM signifies an innovative move towards fostering a culture of continuous quality enhancement in the pharmaceutical industry, offering a sustainable solution to drug shortages while reinforcing their quality culture.

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