Links Between QMM and ICH Q12

Ben Stevens

Director of Regulatory CMC Policy and Advocacy

GSK

PDA Parenteral Drug Association

2024 Pharmaceutical Manufacturing and Quality Conference

CONNECTING PEOPLE SCIENCE AND REGULATION®

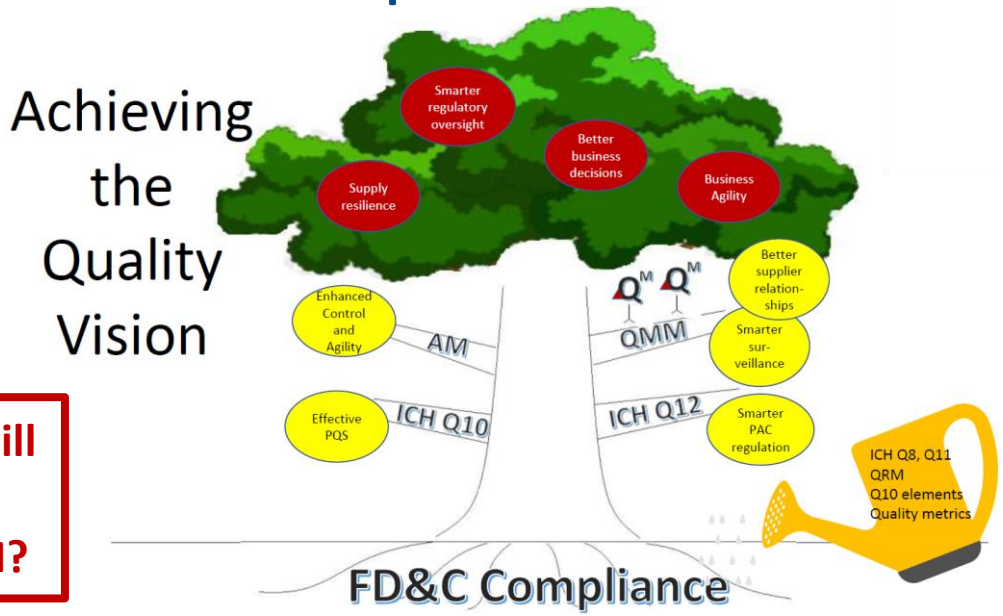
Agenda

- FDA’s connection of QMM and ICH Q12
- Developments related to PQS evaluation for Q12 submissions
- Growing focus of QMM and PQS for supply chain resilience
- Conclusions

2022 FDA SBIA QMM Workshop

"QMM, Quality Metrics, and ICH Q12: Do They Complement Each Other?

Ashley Boam, FDA Director of OPPQ



Key Question: QMM is OPTIONAL but will we get the same benefit from Q12 in REALITY if we don't participate in QMM?

https://www.fda.gov/drugs/news-events-human-drugs/quality-management-maturity-workshop-05242022

https://www.fda.gov/media/166246/download?attachment

FDA QMM AdComm 2022

- FDA backgrounder directly calls out their position on benefit of QMM for Agency and Industry implementation of Q12

https://www.fda.gov/media/162740/download

A transparent rating system could:

- Inform purchasers about the level of QMM at sites from which they purchase drugs.
- Empower manufacturers to identify ways to improve the effectiveness of their pharmaceutical quality systems, realize regulatory flexibilities described in *ICH Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management*, inform selection of contract facilities, and obtain efficiency gains (e.g., speed, throughput, supply timeliness) from investing in quality.
- Provide FDA additional insight into the state of quality for products and facilities and help to identify factors that can lead to supply disruption.

The FDA would benefit from QMM ratings by being more informed about the quality management practices at sites, allowing for better resource allocation decisions (e.g., inspection timing and frequency) and regulatory flexibility (e.g., related to post-approval changes). This is a move away from focusing solely on negative outcomes and one that would move the FDA closer to performance-based regulation. Perhaps most immediately, QMM ratings would ease the process of regulating post-approval changes. The ICH Q12 guidance provides a framework to facilitate post-approval changes in a more predictable and efficient manner, increasing transparency between industry and regulatory authorities, and supporting innovation and continual improvement. In addition to compliance with CGMP requirements, an effective PQS is necessary for firms desiring to use the tools described in ICH Q12. As noted in the FDA's draft guidance *ICH Q12: Implementation Considerations for FDA-Regulated Products*,[1] while the FDA will not require an inspection before an applicant can make use of ICH Q12 principles, the determination of PQS capability will consider, among other things, conformance with ICH Q10, especially regarding change management practices. Clearly, a robust QMM program would enable CDER to more effectively implement ICH Q12.

FDA is Closely Linking Inspections, Facility PQS and Q12 in NDA/BLA Review

- FDA has updated drug surveillance and pre-approval inspection compliance programs to **incorporate Q12 elements** (see Surveillance Compliance Program 7356.002 and PAI Compliance Program 7346.832)
- OPQ Q12 assessment teams include a **PQS assessor** (in addition to ECCC (Established Conditions Coordinating Committee), and AIT (Q12 Assessment Implementation Team) members to ensure consistency).
- FDA has requested **facilities implementing registered ECs to be noted in the PLCM**, creating a direct link to site PQS (i.e., for each new facility, there would likely be an assessment if that site can implement these ECs and any notification level downgrade)
- Already anecdotal industry experience of a very strong tie in between facility inspections (esp. PQS) and submitted ECs during NDA/BLA review.

Forthcoming FDA Q12 MAPP – Will New Industry Expectations Emerge?

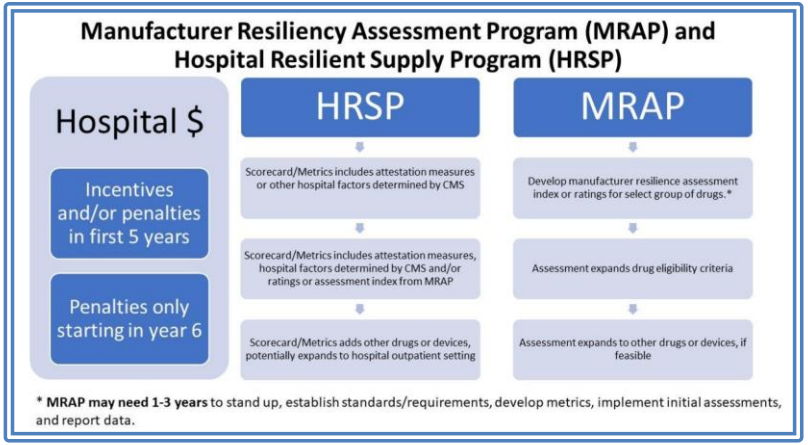
- FDA has indicated that a **CDER MAPP** (Manual of Policies and Procedures document) **is forthcoming**.
- Likely will address some of the specific elements related to surveillance and compliance in the OPQ Q12 review teams, which are a **key element of FDA's approval of ECs and class downgrade**.
- While MAPPs are intended for internal FDA procedure, recent MAPPs (e.g., MAPP 5019.1) have been used to convey requirements and have been cited in numerous information requests. **Can we expect the same here?**

QMM and Q12 in Relation to Supply Chain

U.S Department of Health and Human Services

WHITE PAPER

Policy Considerations to Prevent Drug Shortages and Mitigate Supply Chain Vulnerabilities in the United States



"HHS is working on facilitating greater transparency so the market can use information about mature quality management practices to reward resilience. FDA is developing a framework that would evaluate Quality Management Maturity (QMM) at drug manufacturing establishments. ***The QMM assessment would help gauge adoption of management practices that support a more reliable drug supply chain by reducing the occurrence of quality-related failures and improving the ability of drug manufacturers to maintain performance during supply chain disruptions, whether expected or unexpected."***

https://aspe.hhs.gov/sites/default/files/documents/3a9df8acf50e7fda2e443f025d51d038/HHS-White-Paper-Preventing-Shortages-Supply-Chain-Vulnerabilities.pdf

https://healthpolicy.duke.edu/sites/default/files/2024-01/Addressing%20Drug%20Shortages%20Through%20Quailty%20Managementv2.pdf

QMM and Q12 in Relation to Supply Chain

These positions do NOT acknowledge or address regulatory barriers as a major element of supply chain risk and stability.

- IF QMM greatly facilitates reduction in EC registration and significant downgrades in filing classes, much greater likelihood of seeing impact to supply chain.
- IF QMM does not meaningfully impact broader management of non-ECs in PQS or downgrades in notification level, much less likelihood of seeing impact to supply chain.

QMM success to mitigate supply chain issues will depend on the REAL impact on the extent to which industry can rely on Q12 tools.

Other Considerations

- Some global regulators have expressed interest in pursuing a QMM-like approach to enable better implementation of ICH Q12. **Where is this headed on a global level?**
- How does the tie in between QMM and Q12 play out against pre-existing MRAs and through other **international schemes**, such as PIC/S?
- Will the other vehicles FDA is using to support confidence in company PQS enable as much success with industry EC registration/downgrade as compared to QMM? **In theory it should, but in reality…?**
- Interplay between site-specific ECs (current FDA approach) vs. companies with robust corporate PQS? **Does a site-specific approach always make sense and does QMM participation support use of a corporate PQS basis for ECs?**

Conclusions

- FDA is clearly seeing QMM as a tool to enable broader reliance on applicant's PQS and therefore use of Q12 tools.
- While QMM is seen as a mechanism to improve supply chain resilience, the benefit here will really depend on how much it offers greater reliance on the PQS and Q12 tools.
- Impact of QMM on global Q12 use is highly uncertain – will other regulators feel obliged to follow suit or rely on FDA's scoring?
- Upcoming FDA QMM pilot will be a valuable opportunity.

Thank You!