

FDA's Pharmaceutical Quality Initiatives -
Implementation of a Modern Risk-based Approach

Co-sponsored with AAPS and ISPE
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Breakout Session A: Implementation of Quality by Design (QbD) CMC Pilot Program

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Deliverable

The Best Practices for implementation of QbD from the participants will be assimilated. The overall objective is to reach alignment of the FDA and industry regarding the submission and review of QbD-based applications (with focus on opportunities outside the CMC pilot).

Discussion Point #1

What types of information should you include when submitting an application using a QbD approach? What is the value of sharing this information?

Shared Understanding and Agreements (Question 1)

- Knowledge rich submission
- Compelling story (QbD approach)
- Rationale for risk-based approach with product profile
- Drug substance, input materials should be fully characterized
- Both non critical and critical parameters should be discussed. The decision process for definition of critical versus non critical should also be included

Shared Understanding and Agreements (question 1)

- Need to agree early upon definitions
- Summary and focused information more important than quantity
- Control strategy should be described. This is then implemented and monitored by quality systems
- Summary of risk assessment for process, product and facility

Shared Understanding and Agreements (question 1)

- Quality link to Safety and Efficacy is essential
- Information regarding edge of failures could be useful
- Some difference of opinion in sharing both what worked and what did not work
- DoEs help in understanding and predicting process and product performance

Shared Understanding and Agreements (question 1)

- A science based cGMP based Internal change control program is critical

Discussion Point #2

How, and where, should QbD information be presented in the submission? How will a QbD submission be different from a traditional submission?

Shared Understanding and Agreements (Question 2)

- Both FDA and industry did not express any strong preference or any particular concern
- It can be managed within CTD-Q
- Include information where it is logical and easy for reviewer to locate
- Provide links where appropriate
- Most participants stated P2 as a key document

Discussion Point #3

What are the challenges/concerns and opportunities in a) the preparation of a QbD-based submission, and b) the implementation of QbD?

Shared Understanding and Agreements (Question 3)

- Many expressed that there should be a balance of information between what is available at site versus what is included in NDA
- There was some concern expressed about probability of getting more questions leading to delay of approval

Shared Understanding and Agreements (Question 3)

- There is opportunity for including QbD type information for approved products for which it was not shared in original application
- Including a comprehensive QbD in submission is a challenge. It may be difficult for a reviewer to find information, if not presented in a logical manner
- QbD requires sponsors to think systematically

Shared Understanding and Agreements (Question 3)

- For some companies a business case for QbD may be difficult to establish
- Some participants were not certain whether Regulatory flexibility will truly result from a QbD approach

Discussion Point #4

What do you think of the review process and practices in the CMC Pilot?

Shared Understanding and Agreements (Question 4)

- There was enhanced communication between FDA and industry
- There were increased number of questions under the CMC pilot program but these were resolved quickly

Shared Understanding and Agreements (Question 4)

- Both industry and FDA learned from the process
- Most participants did not see an issue in sharing information with FDA
- Multidisciplinary approach for review was extremely helpful. Chemists, senior management, microbiologist, compliance and inspectorate; all were proactively engaged

Discussion Point #5

CMC Pilot is a mechanism to facilitate the implementation of QbD. What other mechanisms/avenues can be used by the agency to facilitate the implementation of QbD?

Shared Understanding and Agreements (Question 5)

- Some participants recommended discussion of QbD opportunity during EOP2 or later in development

Shared Understanding and Agreements (Question 5)

- Engage scientific organizations such as ISPE for developing technical guidances
- More workshops and case studies discussion

Remaining Challenges

- Resources for FDA
- Harmonization among Boards of Health
- Training and expertise of all level of staff in manufacturing plants
- Training and expertise of FDA staff
- Transfer of knowledge between R&D and Plants
- Transfer of knowledge between review division and field

Recommendations

- Industry and FDA to share experience from CMC pilot program
- FDA to publish 'common themes' for QbD related issues
- Collaborate with ISPE and others to develop technical guidances
- Regulatory agreement should be formalized
- Participants in CMC pilot program recommended extending interaction beyond approval