

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

Co-sponsored with AAPS and ISPE  
February 28 to March 2, 2007

### Breakout Session G: OGD's Question-based Review

Moderators:

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### Deliverables

- The breakout session will report on how QbR has changed R&D and manufacturing practices and provide feedback on the enhanced review process in the form of a list of topics for which industry would like further clarification.

### Discussion Points

1. How has the QbR made FDA's expectations clearer? Where is there a need for additional clarification?
2. How has the need to address the QbR questions changed the generic drug development process at your company?
3. How has quality by design been encouraged by the QbR process? And how does QbR promote product lifecycle management?

### Discussion Points

4. What benefits has your company observed from providing a reviewer with a QOS and pharmaceutical development report? Have reviewers demonstrated a better understanding of your scientific approach and how your specifications were developed? How has quality by design been encouraged by the QbR process? And how does QbR promote product lifecycle management?
5. What can be done to improve the QbR process?

### Shared Understanding and Agreements

- QbR has made FDA's expectations more clear - limited experience
- Guides product and process development
- Promotes communication among different functions within the company
- Points to the need for good knowledge management systems
- Will and should improve technology transfer

### Shared Understanding and Agreements

- QbR questions have changed the information gathering and data reporting of generic drug development
  - Move development activities upfront; more product and process understanding reduces risk of process scale-up
    - Technical support and technical writers added
  - Deficiency questions are science-based and are used to re-direct R&D activity for future ANDAs

### Shared Understanding and Agreements

- QbR encourages forward thinking of QbD elements and principles
  - Define the target of generic product quality profile
    - pharmaceutically equivalent to RLD
  - Understanding of properties of drug substance and product design
  - Understanding of manufacturing process
  - Development report is now more product and process design focused

### Shared Understanding and Agreements

- QbR has changed the quality assessment within OGD and has generated positive comments from the reviewers
- OGD stated that QbR is being developed for microbiology review and to a certain degree, bioequivalence review

### Remaining Challenges

- How much more information and knowledge on development activities is needed for filing?
- More clarity of FDA's expectation on QOS and P2
- Developing a risk based approach to achieve OGD's goal of up to 80% CMC supplement reduction
  - Develop metrics beyond the preliminary risk assessment strategy proposed by OGD
  - Can post-approval data be evaluated upon review or inspection and used for reg. relief?
- For some sponsors, additional development work (e.g. process) will be needed to fully address QbR prior to submission

### Recommendations

- Develop question-based review for drug substance, DMF
- Capture all the reviewer experiences
- Communicate OGD's QbR initiative and expectations
- Work with stakeholders to develop a model example for design space