

FDA's Pharmaceutical Quality Initiatives – Implementation of a  
Modern Risk-based Approach  
Co-sponsored with AAPS, ISPE, & FDA  
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### Breakout Session : Post-Marketing Regulatory Process

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### Issues Discussed

- Routine submission and review of post-approval changes is a burden on industry and FDA resources
- Requirements of an internal quality system to review and approve changes
- Recommendation for revision to current process
- Effect on Annual reports
- Impact on inspection process
- Design space concepts for legacy products

### Objective

- To gather information and identify opportunities in streamlining the current post-marketing regulatory process in order to make better use of resources by both FDA and industry

### Shared Understanding and Agreements

- Current post-approval regulatory process needs revision based on risk assessment
- Suggest elimination of all CBE supplements
- Reduce options to two categories: PAS and Annual Reports

### Shared Understanding and Agreements

- Both critical and non-critical changes can be managed through a firms quality system
- Multi-site companies should have a single robust global change management system
- Should include multi-disciplinary review
- Should be supported by knowledge management system

### Shared Understanding and Agreements

- Do not want to develop a list of changes which should or should not be submitted to FDA
- Only changes with a potential negative impact on safety to patient should be submitted for prior approval
  - Unsure how to determine this
  - Different for each product/category

### Shared Understanding and Agreements

- Annual reports should be limited to a summary or index of changes
- Supporting data should be maintained by the manufacturer
- Elements or Summary of the Annual Product review may also be useful and incorporated

### Shared Understanding and Agreements

- Change to current post-approval system should not negatively impact the inspection process
- Inspection remains a review of the overall quality system and is not a comprehensive product review
- Revision to system should not shift burden from Center to the Field
- There must be coordination (understanding) between Field and Center

### Shared Understanding and Agreements

- Design space “concepts” can be incorporated into legacy products
  - Can leverage existing or historical data into product knowledge
  - Perform risk assessment
  - Update filings defining “design space” into more modern terms
- Future changes then handled through firms quality system

### Remaining Challenges

- Need for urgency to develop short term improvement to current process
  - Revision to regulations/legislation is lengthy process
- Need to identify process for risk analysis for “Critical” vs. “Non-critical” changes

### Recommendations

- Strategies to implement agreed-upon issues
  - Eliminate all CBE supplements (CBE0 and CBE30)
  - Reduce options to two categories: PAS and Annual Reports
  - Only changes that have the potential for adverse consequences to the patient (i.e. affect safety) should require prior approval from FDA – all others should be reported in the Annual Report

### Recommendations

- Strategies to implement agreed-upon issues
  - Revise guidelines on requirements for Annual reports
  - Develop understanding between Field and Center for Roles/Responsibilities in new paradigm
  - Develop “ICH Q11” for Management of Global Post-Approval Changes

## Recommendations

- Proposals to resolve remaining challenges
  - Develop guidance document on “new” post-approval regulatory process
  - Revise regulations/legislation at a later date
  - Work with industry to define “potential negative impact on safety to patient”