ICH Q12
Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

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Disclaimer

• This presentation reflects the speaker’s perspective on this topic and does not necessarily represent the views of Perrigo Company.
Panel Discussion with Audience Participation

• Nick Cappuccino
  Vice President & Head of Quality
  Dr. Reddy’s Laboratories

• Dawn Culp
  Vice President, Global Regulatory Affairs Policy
  Mylan Inc.
Q12 – Vision and Goals

• Promote innovation and continual improvement
• Improve regulators’ understanding and confidence in manufacturers’ Pharmaceutical Quality Systems for management of post-approval changes
• Facilitate risk-based regulatory oversight
• Global harmonization of change management
Major Components of ICH Q12

• Regulatory Commitments
  – aka - Established Conditions
  – aka – Approved Matters

• Post Approval Change Management Protocols
  – aka – Comparability Protocols

• Assurance of a Company’s PQS
  – aka – Compliance with ICH Q10
Regulatory Commitments
[Established Conditions (USA) or Approved Matters (JP)]

Certain binding information or elements concerning the manufacture and control of a pharmaceutical product, including:

- Description of the product
- Elements of the manufacturing process
- Facilities and certain equipment,
- Specifications, and
- Other elements of the associated control strategy that assure process performance and desired quality of an approved product.
Regulatory Commitments
[Established Conditions (USA) or Approved Matters (JP)]

– Changes to Established Conditions would need to be communicated to the regulatory agency in an applicable regulatory submission (e.g., PAS, CBE30, CBE, or AR).

– Changes to non-Established Conditions could be made strictly under a company’s PQS and would not require a regulatory submission.
Potential Benefits of Established Conditions
-- Analytical Method --

ECs for an Analytical Method could be defined as the outputs of the original method validation (e.g., Linearity, Specificity, Accuracy, Precision)

Therefore, the method could be changed without regulatory submission, if the general type of the method stays the same (e.g., chromatographic, spectroscopic, electrophoretic) AND the validation results are in accordance with the agreed validation criteria.
Potential Benefits of Established Conditions
-- Process Change --

ECs for manufacturing process could be defined in general terms (e.g., blending operation) in conjunctions with process endpoints based on material attributes (e.g., blend uniformity, NIR metric, etc.)

Therefore, the process could be changed without regulatory submission, if the general type of operation stays the same AND the process endpoints (acceptance criteria) remain unchanged.
Post-Approval Change Management Protocol

- A regulatory tool that facilitates approval of CMC changes to an approved marketing application by enabling prospective planning of future change(s) including the assessment of the impact of the proposed change(s) on product quality.
A PACMP typically involves two steps:

- Submission of a protocol describing the proposed change, its rationale, risk assessment and proposed studies & acceptance criteria to assess the impact of the change(s);
  - The protocol is approved by the regulatory authorities in advance of the implementation of the proposed changes.
- Submission of the actual results/data based on the approved protocol.
Utility of a PACMP - Example

- Prepare PACMP
- Manufacture product using the change
- Submit PACMP for review
- FDA reviews while you collect stability data (~3 - 6 months)
- Upon approval of PACMP, submit final data (e.g., CBE-30)
- Launch at day 31
Blue Sky Potential for PACMPs

• A single PACMP for a group of changes for a single product
• A single PACMP for changes that would be implemented across multiple products (e.g., change in stopper across multiple products) and/or at multiple sites (change in analytical method across multiple sites)
• Utilization of PACMPs as a ‘one-step’ process
Q12 must be implemented in conjunction with other ICH guidance documents
Benefits & Risks of Q12 for the Generic Drug Industry

Benefits

• Increased focus on quality assurance
• Stimulation of innovation & continual improvement
• Streamlined post-approval change implementation
• Fewer prior-approval supplements
Benefits & Risks of Q12 for the Generic Drug Industry

Risks

• Longer review times?
• More questions from regulators?
• Increased number of review cycles?
• ECs increase in detail rather than decrease?
• Shift of supplements from CBE30 to PAS?
IGPA Representatives on Q12 EWG

- Keith Webber – Perrigo Co.
- Nick Cappuccino – Dr. Reddy’s Labs
- Graham Powell – Mylan (UK)
- Takeshi Sugiura – Towa Pharma (Japan)
In Closing

• ICH Q12 has great potential to support innovation and continual improvement in the post-approval period.
• The EWG is working cooperatively across the industry and regulatory components to achieve these goals.
• Visionary implementation of the final guideline will be critical to its success.
Discussion Stimuli

• How is Q12 different from all the other ICH guidelines?
• What are the challenges to achievement?
• How does industry and agency define/measure success?
• What are the risks? What are the benefits?
• Questions/comments from the audience.