ICH Q12 Established Conditions - Concepts and Updates from Expert Working Group

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Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

- This new guideline is proposed to provide guidance on a framework to facilitate the management of post-approval Chemistry, Manufacturing and Controls (CMC) changes in a more predictable and efficient manner across the product lifecycle.

- Adoption of this new ICH Guideline will promote innovation and continual improvement, and strengthen quality assurance and reliable supply of product, including proactive planning of supply chain adjustments.

- It will allow regulators (assessors and inspectors) to better understand the firms Pharmaceutical Quality Systems (PQSs) for management of post-approval CMC changes. This new guideline is intended to complement the existing ICH Q8 to Q11 Guidelines.
How do we get there?
Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

• ICH Q12 builds on the principles outlined in ICH Q8/Q11 as well as ICH Q9 and ICH Q10

• Using the opportunities offered in ICH Q12 is optional

• Current regulation on Lifecycle activities in the ICH regions still apply
How to get there?

Proposed tools in ICH Q12

• Established Conditions
• Post Approval Change Management Protocol
  o Already know in EU and US (comparability protocols)
  o Possibility of negotiating reporting category ???
• Multiple examples
How do we get there?

• Although the CTD format has been defined across regions for a MMA, there is no harmonised understanding or approaches to define which information in a dossier that would require a post-approval regulatory action if it were to be changed.

• ICH Q12 propose that the information in a dossier that would require a post-approval regulatory action is defined as ESTABLISHED CONDITIONS.

• Current guideline definition:
  o “Established Conditions for Chemistry, Manufacturing and Controls (henceforth established conditions) are legally binding information defined in a Marketing Authorization Application. Any change to an established condition, as listed in an approved application, would initiate a regulatory post-approval change process. Any change to a non-established condition does not require regulatory interaction.”
How to identify ECs?

- ICH Q8 & Q11 recognize and illustrate that “Strategies for product development vary from company to company and from product to product. The approach to, and extent of, development can also vary and should be outlined in the submission.”
- The Applicant should consider the following when identifying ECs
- The following principles to identify what information is an established conditions
  - assessment of risk (as defined in ICH Q9) – or criticality
  - sound product development,
  - product characterization,
  - a well-justified control strategy (control strategy as defined in ICH Q10),
  - product performance, and
  - the relevant compendial requirement
Where to start in the identification of ECs?

- The guideline will provide guidance on "expected" ECs:
  - Name/structure/composition
  - Manufacturing site and testing sites
  - Specifications (DS, DP, excipients, reference material…)
  - Source material and Raw of biological origin
  - In-process tests linked to a rejection limit
  - Critical hold times (sterility/microbial assurance/product integrity)
  - Storage conditions and shelf-life
    - Process Parameters….??????
How to revise ECs?

- The strategy and methodology for controlling the quality of a product is anticipated to evolve as product and process knowledge is gained or as implementing technological advancements is considered throughout a product’s life cycle. As such, it may be necessary to revise the approved established conditions.

- The options available for a marketing authorization holder to revise an approved established condition include:
  
  o Submission of a post-approval regulatory submission describing and justifying the proposed change.
  
  o Including, in the original application, a description of the planned change and the conditions that must be met in order to allow regulatory acceptance of the change.
  
  o Submitting a PACMP, in the original application or as part of a post-approval submission, describing the change and how the change will be justified.
How to add/remove ECs?

– It is possible to change an approved established conditions to non-established conditions. Options available to change an established condition may be changed to a non-established condition if:
  o Submission of a post approval regulatory submission describing and justifying the removal of the established condition.
  o Including, in the original application, the conditions that must be met in order to allow regulatory acceptance of the removal of the established condition.
Summary of Potential Benefits by Q12

• Reduce unnecessary cost and time burdens on industry and regulators, while assuring that patients reliably have access to high quality therapies
  - Realize benefit from application of current and innovative manufacturing technologies on a timely basis

• Enable and encourage increased transparency
  - between industry and regulators
  - between MAH and (contract) manufacturers
  - between reviewers and inspectors

• Harmonization across ICH regions plus potential for application in non-ICH countries
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Thank you!