ICH Q12 - Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

Training Material

Module 7 – Additional approaches

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Additional approaches

- In addition to the tools explained in previous modules, following additional approaches are included in ICH Q12
  - **Chapter 8 - Structured approaches to frequent CMC changes**: Provides guidance for a structured approach for frequent post-approval changes using analytical methods as an example
  - **Chapter 9 – Stability data approaches to support the evaluation of CMC changes:** Provides strategies for confirmatory stability studies enabling more timely implementation of the change
- Manufacturers of authorised products can use these additional approaches to facilitate implementation of change.

Chapter 8

Chapter 8 – Structured approaches to frequent CMC changes

- This chapter of ICH Q12 describes a structured approach for frequent CMC changes
- This is an alternative approach that does not require necessarily:
  - a PACMP or
  - ECs
- These approaches may be applied when the following conditions exist:
  - The company has an effective and compliant (see Chapter 6) PQS change management process which incorporates a risk management system
  - The change is within the scope of structured approach and criteria can be met
- The steps to be followed and data to be generated are defined in the structured approach

Chapter 8 – Structured approaches to frequent CMC changes (2)

- The strategy is exemplified with a description of an approach for analytical procedure changes in Annex II
- Similar structured approaches could be developed and applied for other frequent CMC changes such as scale, packaging, etc.
- If the approach is followed and all criteria are met, the change can be made with immediate or other post-implementation notification, as appropriate, to the relevant regulatory authorities

Chapter 8 – Structured approaches to frequent CMC changes (3)

- It is recommended that MAHs contact regional authorities for advice before implementing a change according to this procedure, as this approach might not be available in all regions and in all situations

- Structured approaches for frequent CMC changes are typically applicable to lower-risk changes, since they do not require prior approval by a regulatory agency

➔ Annexes

Annex II: Structured approach to analytical procedure changes

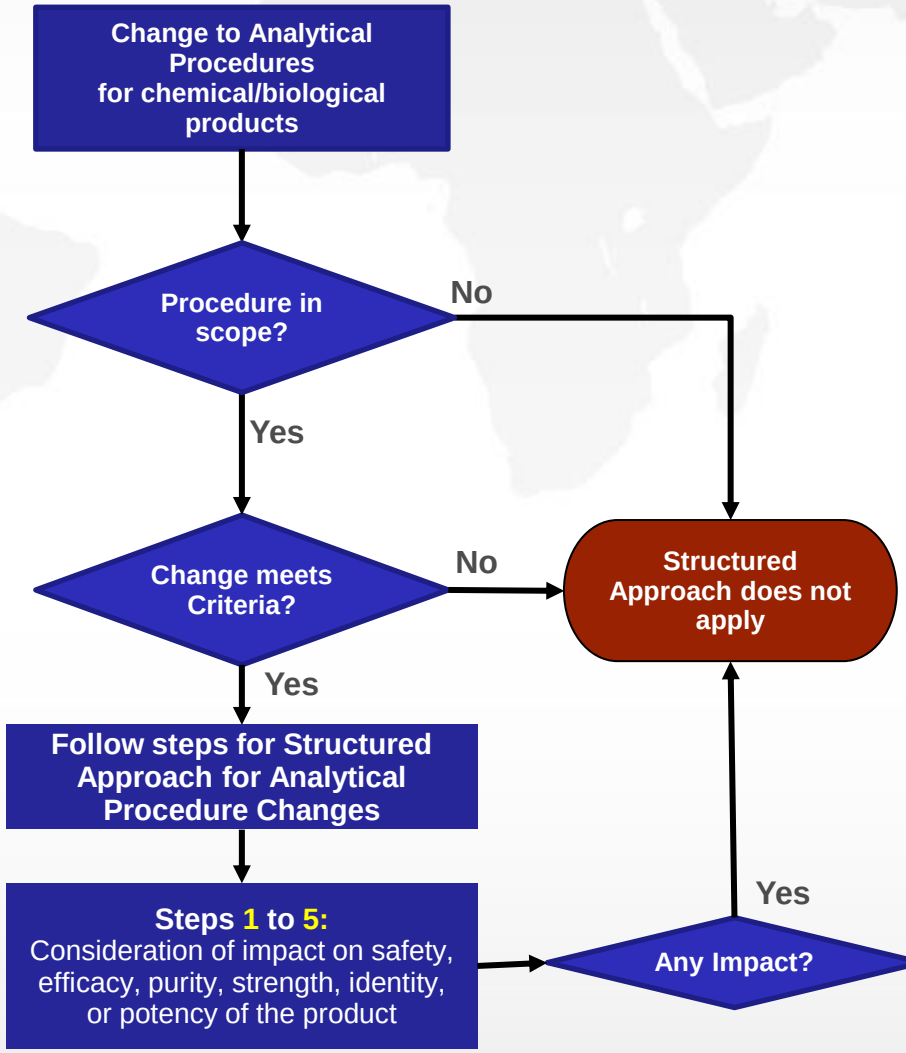
ICH Q12 Module 7

Structured approach to analytical procedure changes

- The application of “structured approach to analytical procedures changes” will benefit in smooth implementation of similar test procedures
- Conditions and exclusion criteria are specified and the approach can be used if it meets all the prescribed criteria
- With a favourable outcome of regulatory impact assessment, analytical procedure changes can be implemented the soonest

ICH Q12 Module 7

Structured approach to analytical procedure changes



Scope - Exclusion Criteria:

- PQS change management process is not effective or compliant
- Procedures where the acceptance criteria do not adequately reflect the complex information provided by the method.
- Change(s) to a test method based on a biological/immunological/ immunochemical principle or a method using a biological reagent.
- Changes to models and multivariate methods
- Changes to analytical procedures described in pharmacopoeial monographs.

Criteria (for analytical procedure changes):

- Same physicochemical basis and high-level description
- Same acceptance criteria of the validation protocol.
- Equivalent or better method based on validation results
- Comparable test results.
- No change in acceptance criteria
- No need for toxicological or clinical data.

Structured approach – General considerations

- Similar structured approaches could be developed and applied for other frequent CMC changes
- For example:
  - Change of batch size/scale
  - Extension of shelf life
  - Minor changes in manufacturing process

This is not an exhaustive list

Chapter 9

Chapter 9 – Stability data approaches to support The evaluation of CMC changes

- Chapter 9 provides additional science- and risk-based approaches that can be used to develop strategies for confirmatory stability studies supporting post-approval changes to enable more timely filing, approval, and implementation of the changes

- Such approaches could be included in a PACMP

Stability data approaches – New application vs Post approval

- The objective of formal stability studies recommended in ICH Q1A(R2) is to establish a useful shelf-life and storage conditions for a new, yet-to-be-marketed drug substance/drug product

- The purpose of post approval stability studies is to confirm a previously approved shelf-life and storage conditions for the product after implementing the CMC change

- The scope and design of such studies can use the knowledge and experience acquired since authorization

Stability data approaches – design of studies

- Apply risk assessment and previous data to identify the quality attributes.
- Use of appropriate tools to **evaluate the impact**:
  - Studies on representative material
  - Pre- and post-change comparability studies on representative material
  - Statistical evaluation
  - Predictive degradation and other models
  - Utilisation of prior knowledge and the scientific literature
- Use of confirmatory stability studies post-change
- Where applicable, include a commitment to initiate or complete ongoing, long-term stability testing post-change

Additional approaches – Summary

- Chapters 8 and 9 provide additional approaches to facilitate changes
- The structured approach for frequent CMC changes (Chapter 8) does not require any regulatory submission before using the approach for certain changes
  - Analytical procedure changes are exemplified
- Science- and risk-based approaches to confirming shelf-life are described in chapter 9 and could be used in a PACMP, for example