Table 38: Core Analytical ICH Topics & Their Impact ICH Q6, Q2/14

Facilitators –

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Scope:

Current thinking has evolved significantly since ICH Q6 & Q2 were first developed. In order to adjust to the changes in science and technology ICH Q2 is being revised, ICH Q6 is proposed for revision and ICH Q14 has been adopted as a new topic for development. We are in a unique position where there is still time to influence the development and outcome of these guidances.

This roundtable is intended to discuss the impact of these changes and gather broad input on the revisions that can be shared with ICH.

Questions for Discussion:

1. What key aspects would people like to see in the revision of ICH Q6?
2. How can the revisions of Q6/ Q2/Q14 facilitate accelerated product development and lifecycle management?
3. How can Q6 be modified to apply to newer modalities?
4. Modernization: As part of a comprehensive approach what alternate justifications to define specification criteria beyond statistical analysis of manufacturing batches for clinical studies could be used?
5. ICH Q14 discusses the importance of prior knowledge, has your company been using prior knowledge in the development and lifecycle of analytical methods
    a. Have you successfully leveraged the concept of platform analytical procedures to reduce scientific and regulatory burden in a risk based manner?
6. How has change management for analytical methods evolved overtime? And how have you incorporated QRM into this process?
7. What incentives does industry need to implement Q14?
8. How do we balance science & risk based approach with the desire for specificity in some markets? (the “we are harmonised but request additional specifics and differences”)
9. Applicability/non applicability of standards for gene therapy and how are you navigating?

Discussion Notes:

January 26 and 28, February 1 and 3, *combined* –

- Discussion of ICH Q6
    - Toolbox is slightly outdated, but principles have withstood the test of time
    - Foundational concepts of 6b are strong: Don't "break it"
    - Specifications come from 4 elements: Manufacturing capability, stability, clinical experience, capability of analytical methods
    - Possibly room to expand upon management of specifications over the lifecycle considering so many products are accelerated
        - Also very relevant to biosimilar producers
    - Need to ensure that clinically relevant specification is not defined too narrowly
- General discussion
    - Could better link ICH and CTD and within ICH chapters
    - Comprehensive ICH guidance on reference standards still under discussion
    - Some impact of COVID on timelines for updates
    - There may be other ways outside of ICH chapters to cover topics that are constantly evolving (i.e. new analytical technologies), e.g. training
        - Including a topic in an ICH chapter itself often leads to the strictest interpretation, doesn't leave as much room for risk-based innovative approaches
    - Is there an opportunity to expand the concepts from Project Orbis? (ie global rapporteur)
    - Industry needs to improve our ability to tell the story. What tools are available to assist industry?
- Will update to Q6 address multi-attribute methods?
    - This has been raised as a concern, but not concrete answer
    - Important to maintain flexibility
- How can Q6 revision/Q2 and Q14 facilitate accelerated development

    - Could be easier to set reasonable acceptance criteria
    - Allows the use of critical thinking around clinical impact
- Discussion of Q14
    - Could be similar QbD for analytical development - just don't have the time
    - Industry requested Q14
    - Could lead to better understanding of method variability and better support for future method improvements
    - Opportunity to present more development data in submissions
    - Analytical methods come under more pressure when we try to leverage prior knowledge
        - Updates to both Q2 and Q14 plan to discuss platform methods
        - Companies will be incentivized to use platform methods
        - Will favor companies that are able to get to market and then backfill analytical method knowledge later to assist in method lifecycle management
    - Has anyone been successful in using platform methods?
        - Still need regulatory visibility to entire supporting dataset
        - Could run into difficulties when trying to implement at contract labs (supporting data can be proprietary to contract lab), companies can be put in a situation where they need to regenerate datasets
        - Previously solved using Quality Agreements or other agreements to protect CRL while making data available to sponsor
        - Could the guideline touch on relationship with contract labs? ICH try to avoid GMP aspects
        - Could generate data sets using "mab1, mab2, etc" - there is precedence with this with identity methods able to distinguish between molecules from various sponsors at the same CMO - regulators are still able request data as needed
        - There may be some challenges when using a CLO as they may not want to share all the data – could we develop an option to have a DMF-like submission of the supporting data for the platform

- What incentives does industry want to see
    - Lifecycle management and how to build ICH Q12 into implementation of Q14 (Q14 needs Q12 to succeed)
    - Use of prior knowledge
    - Enabling accelerated approval
    - More examples and case studies (can be included in training or annexes)

How do we balance science/risk-based approaches with desire for specificity in some markets?

- This is a pain point
- There are differences across markets in terms of what needs to be filed for methods (i.e. lack of harmonization), many region-specific requests
- Ex: different requirements of validation packages globally lead to needing to author section multiple different ways
- Is there a way in to include information on the cost and economics of divergence?
- Improve how we communicate the "why" for various approaches and the impact to patient and product
    - Can this be built into ICH Training programs and Q&A

Discussion of Q2

- Will update clarify relative potency method validation?
    - Yes, Annex 2 for individual technologies
- Including continuous method verification? Invalid rates?
    - Chapters not being written with this as a requirement
- Include more information on platform method validation

- Opportunity for public comment on Q14 coming in May