Final Business Plan

Targeted Revisions of the ICH Stability Guideline Series
(Guidelines ICH Q1A-F, ICH Q5C)
25 October 2022
Endorsed by the Management Committee on 15 November 2022

1. The issue and its costs

- *What problem/issue is the proposal expected to tackle?*

There are four key problems that the proposal is expected to address:

1. The current stability guidelines are written as individual chapters, which leads to interpretation of the chapters on an individual basis with uncertainty around how they should work together. This leads to variability in application and interpretation.
2. Certain topics within the guideline are routinely interpreted differently by users and regulators. The perceived ambiguity leads to diverging expectations.
3. The stability chapters do not reflect modern analytical technologies and tools. Incorporation of guidance and associated training activities that address the use of stability modelling and risk management could enable earlier patient access to high quality medicines.
4. The current guideline does not address stability considerations for advanced and emerging product types[1].

- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with "non-action"?*

There is general alignment that the science of stability has advanced significantly since the last revision to ICH Q1 in 2003. Further, it is recognised that the interpretation of the current ICH Q1/Q5C series is variable. It is also recognised that the guidelines as written do not provide adequate guidance for advanced product types. Finally, the guideline is not fully aligned with more current ICH regulatory guidelines and risk management principles (ICH Q8-Q12). Failure to address these issues will result in continued divergence in regulatory requirements, unnecessary delays of product to patient, and the potential for unnecessarily short product shelf-life, wasted product and redundant testing.

2. Planning

- *What are the main deliverables?*

The envisioned result is a combined guideline, ICH Q1, with integrated annexes and/or appendices that address specific topics beyond the core stability recommendations and product type[1] specific recommendations, as required. It is also essential to revisit and update existing training material and create training material for new topics.

[1] Product type refers to all aspects of the drug product, including drug substance, intermediates, and devices.

- *What resources (financial and human) would be required?*

  One Expert Working Group (EWG) will be designated to establish a core stability guideline for the stability evaluation of pharmaceuticals, incorporating core content of ICH Q1A-F and Q5C under ICH Q1. The EWG should include regulators and industry representatives with background and expertise in either (or both) the technical and regulatory aspects of pharmaceutical stability. Representatives should comprise expertise in Chemistry, Manufacturing and Controls (CMC), Good Manufacturing Practices (GMP), API/drug substance, drug product, small and large molecules, statistics, and predictive modelling. The EWG should also include experts in Cell and Gene Therapy/ATMP product types to help add this topic in the revised guidance.

  What is the time frame of the project?

  The revision is anticipated to take 3 years to complete, with a target delivery by end of 2025.

- *What will be the key milestones?*

  The proposed milestones are below:
  Q4 calendar year 2022 - Final Concept Paper, Business Plan
  Q4 calendar year 2024 – Complete *Step 1*
  Q4 calendar year 2025 – Complete *Step 4* and training materials

- *What special actions to advance the topic through ICH, e.g., stakeholder engagement or training, can be anticipated either in the development of the guideline or for its implementation?*

  The following special actions may help advance development of the guideline:
  - Workshops/engagement with technical experts for incorporating guidance on new analytical tools, modelling, and stability risk assessment.
  - Workshops/engagement with technical experts on addressing special consideration for advanced or emerging product types.

  The following special actions may aid implementation of the revised guideline:
  - Development of training materials related to the guideline updates with a focus on new content.
  - Development of case studies.

3. <u>The impacts of the project</u>

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*

  Revision of ICH Stability Guideline Series Q1A-F and Q5C is recommended to a) streamline by combining into a single guideline focused on core stability principles; b) promote harmonised interpretation by addressing potential gaps and areas of ambiguity; and c) address additional technical issues, including relevant stability strategies and innovative tools that strengthen the application of risk management; and d) consider inclusion of new topics, such as stability considerations for advanced therapies. The anticipated benefits include:

- Increased harmonisation of interpretation and application (reduce diverging interpretations of guideline) and increased alignment with other ICH guidelines.
- Provision of guidance for use of tools to support application of shelf-life/retest for rapidly developed programs/breakthrough therapies (improve access of important medicines to patients and decrease waste).
- Adoption of knowledge-based and platform-based strategies into the guideline could lead to reduction in redundant stability studies, improving efficiency and decreasing waste and cost.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*

  The topic is implementable from a regulatory standpoint. New content to the guideline will reflect topics that are well-understood and will aim to align with other current regulatory guidelines.

- *Will the guideline have implications for the submission of content in the CTD/eCTD? If so, how will the working group address submission of content in the dossier? Will a consult be requested with the ICH M8 working group?*

  Any CTD content related to the ICH Q1 update should be incorporated into the relevant existing CTD/eCTD quality modules and therefore this guideline update is not expected to impact CTD/eCTD submission content.

4. Post-hoc evaluation

- *How and when will the results of the work be evaluated?*

  At the conclusion of each stage, we will determine whether deliverables and their timelines were met by comparison against our concept paper and business plan. After training is complete, if practical, a survey may be distributed to regulators to measure its effectiveness.