Final Business Plan
Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin
Dated 17 November 2019
Endorsed by the Management Committee on 18 November 2019

1. The issue and its costs

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

  Since the publication of the Q5A(R1) Guideline in 1999, advances in manufacturing and improved technologies for virus detection and quantification have emerged and strategies for virus clearance have evolved based on manufacturing experience and scientific consensus. The following issues are not covered and will be addressed:

  - New classes of biotechnology products
  - Additional validation approaches for virus clearance
  - New virus assays and alternative analytical methods
  - Virus clearance validation and risk mitigation strategies for advanced manufacturing
  - Aspects of virus clearance validation that have emerged or evolved

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

  There is a general consensus that the current ICH Q5A(R1) Guideline, while useful, does not specifically address recent advances in biopharmaceutical development. Although the current global regulatory frameworks encourage the use of new technologies, the lack of an updated regulatory guideline can make implementation, regulatory approval, and lifecycle management more challenging. Specific costs from lack of action by ICH would include:

  - Potential issuance of regional guidelines/guidances with differing regulatory expectations
  - Multiple filing strategies required by companies to comply with different regulatory expectations
  - Delayed or inconsistent implementation of new technologies by industry
  - Delayed access of new therapies to patients
  - Potential burden to implement the ongoing ICH Q13 Guideline for continuous manufacturing

2. Planning

- *What are the main deliverables?*

  The main deliverable is a revised quality guideline, ICH Q5A(R2).

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

  An Expert Working Group that would include approximately 25 experts. We anticipate the need for six face-to-face meetings and multiple interim teleconferences to complete the proposed revision.

- *What is the time frame of the project?*

  The new guideline is anticipated to take three years to achieve Step 4, from November 2019 – November 2022.

- *What will be the key milestones?*

  The proposed timeline and milestones are below.

  - Final concept paper and business plan endorsed: November 2019
  - Completion of first technical document draft: November 2020
  - Completion of *Step 1, Step 2a* and *2b*: June 2021
  - Completion of *Step 3* and *4*: November 2022

- *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 are potential special actions that may be taken to advance development of the guideline:

  - Presentations of published concept paper and draft guideline at scientific conferences
  - Engagement with contract research organizations and other technical experts not directly involved in guideline authorship to solicit their input and topic expertise

  The following are potential special actions that may be taken to advance or promote implementation of the guideline:

  - Preparation of formal training materials related to the Q5A(R2) guideline and their distribution at inter-agency engagement activities and ICH-supported technical workshops

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?*

The updated guideline will allow for the following:

- Facilitation of the development and assessment of new biotechnology product types
- Flexibility in virus clearance validation approaches
- Implemention of new virus assays and alternative analytical methods (e.g., PCR, next generation sequencing) for adventitious and endogenous virus detection
- Development and assessment of virus clearance validation and testing approaches for advanced manufacturing
- Implementation of emerging and evolving aspects of virus clearance validation

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

  The proposed work is a revision to an existing Guideline. Sufficient expertise is available within the working group to perform this task.

- *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?*

  It is anticipated that any documentation related to this revision would be incorporated into existing CTD/eCTD quality modules. For this reason, the guideline would have no impact for the submission of content in the CTD/eCTD.

4. <u>Post-hoc evaluation</u>

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

  At the conclusion of each step, we will determine whether deliverables and their timelines were met by comparison against our concept paper and business plan.