Final IWG Concept Paper
Q5A(R2) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin

Documented dated 30 November 2023

Endorsed by the Management Committee on 11 December 2023

Type of Harmonisation Action Proposed

Establishment of an Implementation Working Group (IWG) to prepare and deliver a training programme (with associated materials) in order to facilitate an aligned interpretation and a harmonized implementation of ICH Q5A(R2) in ICH and non-ICH regions. The intent of this IWG is not to provide comprehensive training on all parts of viral safety including viral clearance evaluation and characterisation and testing, but to focus on new elements included in the revision. Technical details regarding validation of Next Generation Sequencing (NGS) will not be included in this program, however elements of this technology will be included within the training programme.

Statement of the Perceived Problem:

ICH Q5A(R2) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin describes the evaluation of the viral safety of biotechnology products including viral clearance and testing. It outlines what data should be submitted in marketing application and registration packages for those products. Since the finalisation of the original Q5A Guideline in 1999, new technologies for virus detection and quantification have been developed and improved and strategies for virus clearance have evolved based on manufacturing experience and emerging scientific consensus. For this reason, the revision incorporated needed updates for ICH Q5A, including: introduction of new product types, flexibility in validation approaches, new assays and analytical methodology, and expectations for continuous manufacturing.

There is a differing level of familiarity and understanding with the technology, molecule types, and experience with the platform knowledge described in this revision. Global alignment on scientific and regulatory approaches is critical to enable the adoption of this technology and approaches and to realize the full benefits offered by revision to ICH Q5A. In addition, feedback received during the Q5A(R2) public consultation period also underscores the need for further support regarding the need for training on this revision due to the complexity and expansion of scope when compared to the previous revision. For these reasons, specific training materials are required to address the different level of understanding of key scientific and regulatory concepts amongst regulators and industry stakeholders.

Development of training materials that focus on up to four key case studies and their presentation (e.g., presentations and webinars) is essential to describe use cases for the new principles described in ICH Q5A(R2). Given the variety of approaches possible in each use case, some examples, including justification would be greatly beneficial to aid implementation and understanding.

Issues to be Resolved:

The following training materials will be created to aid in implementation:

- One or two examples of new product types,their production with examples of specific elements including but not limited to: raw and starting materials, sampling and testing locations, testing methodologies, use of a production virus, model virus selection for Q5A Case F, and evaluation of viral clearance factors
- An example that maximizes the instances in which prior knowledge, platform technology and flexibility could be applied to streamline a viral clearance validation submission. This would include but not be limited to: use of previous history of cell line and testing, modular validation

approaches for certain unit operations, testing methodologies and limited resin reuse and virus carryover studies.

- Considerations of the three pronged virus safety approach applied to a continuous manufacturing process using the Annex III process as described in ICH Q13 as a specific example. The elements of this case study would include but not be limited to: extended culture durations, sampling periodicity, and evaluation of virus clearance related to certain unit operations in "batch" mode and application of molecular methods for testing.

A description of validation of NGS will not be included, however, instances of where NGS could be used to replace conventional testing will be highlighted throughout all case studies.

Type of Expert Working Group and Resources

Given the expertise of the current EWG members and their familiarity with regulatory framework in individual regions, it is recommended that the IWG membership should generally reflect the current Q5A(R2) EWG members where possible. The IWG membership could be a slightly smaller group should a few of the current EWG members be unable to participate. A general framework of maintaining current EWG members is preferable as the case studies proposed already naturally align with existing subteams from the EWG used from drafting the guideline and efficiency of the group would be enhanced as a consequence.

Subgroups will be formed to develop the materials and training approaches through email, teleconference and in-person meetings and may mirror the groups that have worked in individual sections already. The subgroups will obtain input from the entire IWG through discussions via email and teleconferences.

The Working Group would warrant expertise from any of the following fields:

- Advanced Therapy Medicinal Products;
- Biotechnology-derived products;
- Therapeutic area-specific Safety/Efficacy: Biologists with Virology Background;
- Vaccines.

Timing

It is anticipated that the IWG will take approximately 10 months with one face-to-face meeting.

Agreement of Concept Paper by EWG	November 2023
Endorsement of Concept Paper by the ICH Management Committee	December 2023
Establishment of the ICH Q5A IWG	January 2024
IWG development of training materials and approach	February – May 2024
Face to Face Meeting to Develop Training Materials	June 2024
Finalize Training Materials	October 2024