Final Business Plan

ICH Q14: Analytical Procedure Development and Revision of Q2(R1) Analytical Validation
dated 14 November 2018

Endorsed by the Management Committee on 15 November 2018

1. The issue and its costs

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

  Since there is no ICH guideline on Analytical Procedure Development, applicants often report analytical validation results alone and rarely present performance evaluation with analytical development outcomes. This makes regulatory communication unproductive when non-conventional (e.g., multivariate models for process control) analytical procedures are employed. Additionally, the lack of guideline impedes opportunities for the applicant to present a scientific basis for flexible regulatory approaches (*e.g.,* Quality by Design concept) to post-approval Analytical Procedure changes.

  The current Q2(R1) "Guideline on Validation of Analytical Procedures: Text and Methodology" is not directly applicable to analytical procedures such as Near Infrared (NIR) Spectroscopy. The lack of clear guidelines can lead to submissions with inadequate validation data for these analytical procedures, resulting in recursive information requests and responses, which can delay application approval. The delays are often the case for procedures reliant on multivariate models, a category for which no ICH validation guideline exists. Such methods are commonly used in process control and real time testing of pharmaceutical products. Taking into consideration the differences between multivariate and traditional methods, the current approach outlined in Q2(R1) is not sufficient to establish suitability of multivariate analysis methods using spectroscopic or spectrometric data.

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

  Non-action leads to delayed access to medication and potential increase of costs to patients because of multiple rounds of information requests resulting in delay of approval. The current situation also deprives industry of an opportunity to present the knowledge obtained through applying the enhanced approaches to analytical procedures, and to provide a scientific basis for more robust methods and more flexible regulatory approach. Thus, currently more resources for change management are required and this will remain the case in the absence of Q2(R1) revision. In addition, new continuous manufacturing approaches being applied in the pharmaceutical industry (for both biologics and synthetic-based products) require fast, real time test methods (*e.g.,* NIR and Raman spectroscopy, and in the future mass spectrometry) to assure that the process is in a state of control all of the time. However, the current version of Q2(R1) does not provide guidance for validation of analytical methods based on multivariate data. Overall, the impetus for industry to develop robust analytical methods for such continuous processes is diminished and delays implementation of efficient processes for new drug manufacturing and quality control testing. The revisions proposed present a more comprehensive guideline to

develop and validate analytical procedures and will reduce additional burden associated with repetitive regulatory review of applications for drug approval.

2. <u>Planning</u>

- *What are the main deliverables?*

  The objective of this proposal is to provide an opportunity to present the knowledge obtained through applying enhanced approaches to validation of analytical procedures, to provide the guidance on how to apply and to indicate a policy for more flexible regulatory approaches. The proposed guideline will facilitate selecting or identifying conditions for methods and/or model updates and re-validations that ease assessment of post-approval changes by regulatory agencies and enable more efficient and sound scientific and risk-based change management. Applying the enhanced approach for analytical procedures (*i.e.*, Quality by Design) will contribute to the resource-efficient drug development and streamline post-approval CMC changes.

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

  Because activities are strongly interrelated, one Expert Working Group will be designated to establish the new Analytical Procedure Development and revise ICH Q2(R1). This dedicated Expert Working Group will potentially determine the feasibility to combine both documents in to one for simplification and clarity. An Expert Working Group composed of experts with knowledge and proficiency in the area of analytical chemistry and pharmaceutical control is needed.

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

  By Fall 2018; Final Concept Paper, The first Face to Face EWG meeting
  Spring 2019; 2nd F2F EWG meeting
  Fall 2019; 3rd F2F EWG meeting
  (Finish two drafts to be reviewed within Member/Observer parties for both).
  Spring 2020; 4th F2T EWG meeting
  (Step 2 for both)
  Spring 2021; 5th F2F EWG meeting
  (Step 4 for both)

- *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?*

  Case studies can be collected to help discussion at EWG meeting and to form the basis of training materials of the guidelines when implemented.

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 proposal can provide timely access to new drugs for patients by elimination of multiple review cycles. In addition, clear guidance in this area may encourage the use of more advanced analytical procedures and modernization of existing methods, leading to more robust quality oversight by pharmaceutical drug manufacturers.

- *What are the regulatory implications of the proposed work – is the topic feasible*

(implementable) from a regulatory standpoint?

These guidelines would have no legal issues, be in alignment with ICH Q8-12, and have no impact on the existing regional regulatory procedures.

- *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?*

  Although the new guideline Q14 will be for S4, P4 and P5 of CTD, there will be no necessity to change the CTD/eCTD sections and ICH M8 documents.

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

- *How and when will the results of the work be evaluated?*
  The benefits of these guidelines would be evaluated after the implementation.
  The impact of the new guideline could be evaluated based on the information described in the submitted document by a survey in all agencies.