

Final endorsed Business Plan
M10: Bioanalytical Method Validation
7 October 2016

1. The issue and its costs

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

Regional guidelines/guidances on bioanalytical method validation pertaining to chromatographic and ligand binding assay methods have been publicised to ensure the reliability of bioanalytical data regarding conditions/requirements for reference standard, validation characteristics, study sample analysis and several additional considerations such as reanalysis justification. However, there are some differences among these guidelines/guidances such as incurred sample reanalysis (for the required percentage of samples to be tested). This lack of harmonisation can lead to conducting validation experiments under several acceptance criteria, repetition of similar studies, the use of additional animals in toxicokinetic studies, which is direct contradiction to the 3R principles, and may delay of drug application.

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

The conflicting regional recommendations on the need for bioanalytical method validation and design for study sample analysis are leading to inconsistent requirements of measurements and animal use. The uncertainty around requirements is responsible for extended drug development and application timeline and general increase in the costs overall. Possible ambiguity in the scope of regional guidelines/guidances may also cause extra costs in the drug development.

2. Planning

- *What are the main deliverables?*

The main deliverable is a harmonised guideline document on bioanalytical method validation and its application to study sample analysis that will provide clarity regarding the conditions and requirements for bioanalysis in non-clinical and clinical drug development.

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

Formation of an Expert Working Group (two or three experts nominated by each Member). One expert can also be nominated by each Observer (if requested). It is desirable to include representatives with expertise in chromatography-based and ligand-binding assays.

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

The request will be submitted to the ICH Management Committee (MC) in September 2016 with expectation of the first EWG meeting face-to-face in November 2016 at Osaka.

- *What will be the key milestones?*

It is anticipated that the *Step 2 a/b* document will be completed in 2Q 2018 and that *Step 4* will be reached in 2Q 2019.

3. The impacts of the project

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

Clarifying the fundamental issues to ensure the reliability of bioanalytical data by establishing a harmonised guideline leads to assurance in the quality of drug/metabolites concentration data used in non-clinical and clinical evaluation, which will contribute to the appropriate dose finding and evaluation of safety and efficacy of the drugs to be developed. A harmonised guideline will also enable the creation of simplified, more efficient and resource sparing testing strategies. Consequently, international harmonisation of the guideline can accelerate the efficient and prompt development of safe and effective drug products with lowered cost.

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

The proposal is consistent with current laws and regulations of the ICH regions. Regulatory authorities responsible for reviewing pharmacokinetic/toxicokinetic data will need to agree globally on the recommendations for bioanalytical method validations and analysis of study samples from non-clinical and clinical studies by validated methods. This guideline will supersede regional guidelines, enabling the mutual usage of bioanalytical data set in different countries/regions based on the harmonised guideline.

4. Post-hoc evaluation

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

When certain amount of study data are accumulated for novel bioanalysis techniques or innovative molecules that exceed the principles of this guideline after the topic reaches *Step 5* in each region, the EWG may need to evaluate/update the guideline, if any.