Final Business Plan
M12: Drug Interaction Studies
Dated 18 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?*

Drug-drug interactions (DDIs) may occur when patients are taking more than one drug. Given that it is impractical to evaluate every DDI in clinical trials during product development, systematic, risk-based approaches are used to assess DDIs. Although regulatory agencies use risk-based strategies, there are discrepancies in the approaches used among agencies. Based on the specific regional approach, regulatory agencies may require different DDI studies be conducted, leading to inconsistent expectations and recommendations. The impact of these inconsistencies includes additional studies, and different clinical interpretations across regulatory agencies.

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

Lack of harmonization contributes to the existing burden on the pharmaceutical industry to meet varying expectations from regulatory agencies during product development. Consequently, continued regional heterogeneity may increase drug development cost and delay patient access to new therapeutic products.

2. Planning

- *What are the main deliverables?*

Harmonized guidelines on in vitro and clinical DDI study requirements, design considerations, and interpretation of the findings.

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

Formation of an Expert Working Group (EWG). The EWG should include experts in the field of clinical pharmacology who are experienced in in vitro and clinical DDI assessments and interpretation. Financial resources to attend face-to-face meeting are also required

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

Three to four years.

- *What will be the key milestones?*

The informal WG will have a kick-off meeting in July 2019 and have a face-to-face meeting in November 2019. It is anticipated that a *Step 2b* Guideline will be completed by 4Q of 2021 and that *Step 4* will be reached by 2Q of 2023, with implementation to follow in 2023.

- *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?*
  Its premature to anticipate the need for any special actions to advance the topic through ICH at this stage. We will revisit the need for any special actions as we make progress.

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?*

  A harmonized guideline will lead to a consistent approach in designing, conducting, and interpreting DDI studies during the development of a therapeutic product. A consistent approach will reduce uncertainty for pharmaceutical industry to meet the requirement of multiple regulatory agencies and lead to more efficient utilization of resources. Eventually, this will help reduce the cost and bring treatments faster to the global market for patients who need the therapies.

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

  This guideline may replace regional guidelines. Harmonization on how to evaluate DDI potential of drugs is feasible because there is extensive knowledge on mechanisms of DDIs, such as alterations in drug metabolism and drug transport, and experience with DDI assessments.

4. Post-hoc evaluation

- *How and when will the results of the work be evaluated?*
  Survey the pharmaceutical industry to determine whether the harmonization reduces inconsistency and/or helps cost saving. This will occur up to 5 years after the implementation of the guideline.