Final Business Plan
M13: Bioequivalence for Immediate-Release Solid Oral Dosage Forms
Dated 19 June 2020
Endorsed by the Management Committee on 10 July 2020

1. The issue and its costs

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

  Current regional or multi-regional guidelines or guidances have different views and criteria regarding design of bioequivalence (BE) studies and data analysis. This lack of harmonisation can result in product developers having to follow different approaches in different regions and conducting additional BE studies, hampering a streamlined global drug development. These issues create unnecessary burden on product developers and result in potentially limiting or delaying access to affordable drugs to patients.

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

  Unharmonised BE study design and standards can lead to requiring additional BE studies if product developers pursue a regulatory marketing authorisation in more than one jurisdiction. This results in increased drug development costs overall, delayed access to patients and unnecessary additional exposure of healthy volunteers to medicinal products.

2. Planning

- *What are the main deliverables?*

  Topics will be grouped into three tiers with the main deliverable as a series of harmonised M13 guideline documents on BE study design, data analysis of BE studies, biowaiver for additional strengths, advanced BE study design considerations, and data analysis and BE assessment for highly variable drugs and drugs with a narrow therapeutic index. The guidelines developed would provide consistent and harmonised approaches for addressing these issues.

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

  Formation of an Expert Working Group (EWG). The EWG should include experts in the field of pharmacokinetics (PK), PK study design, BE, biopharmaceutics, clinical pharmacology, in vitro dissolution, and biostatistics. Additional experts may be consulted or invited ad hoc to provide input on BE study design, assessments, data analysis and interpretation, as needed. Financial resources to attend face-to-face meetings are also required. It is envisaged that an EWG member needs 18 - 24 days/year to work on the development of this series of guidelines.

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

  The expected timeframe for completion of the first guideline of the series including the Tier 1 topics is three years. To complete all three guidelines in the series as outlined in the concept paper will take a longer time (about five to seven years). A more detailed proposal on the development of Tier 2 and Tier 3 topics will be generated by the M13 EWG after completion of Tier 1 topics. The work plan will be discussed with the ICH Management Committee for endorsement.

- *What will be the key milestones?*

  Below is an estimated timeline including key milestones:

  First Guideline in the Series (M13A)

o Approval of the Concept Paper Outline	November 2019
o Establishment of the informal Working Group	February 2020
o Finalisation of the Concept Paper and Business Plan	June 2020
o Approval of Final Concept Paper & Business Plan	July 2020
o Consensus on Technical Document (Step 2a /2b)	June 2022
o Adoption of ICH Harmonised Guideline (Step 4)	November 2023

Estimated starting time for second guideline in the series or annex	July 2022
Estimated starting time for third guideline in the series or annex	July 2024

- *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?*

  It is premature to anticipate the need for any special actions to advance the topic through ICH at this stage. The EWG will revisit the need for any special actions as we make progress.

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?*

  Harmonisation of BE study design and standards would benefit both innovator and generic product developers as the same approach could be followed in multiple jurisdictions, potentially reducing duplicative work. Patients would also benefit as harmonisation would help regulatory agencies in the timely authorisation and availability of quality, safe and effective drugs based upon harmonised acceptance criteria. Furthermore, harmonisation could improve global access to drugs.

- *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 PK/BE data will need to agree globally on accepting the harmonised approaches for study design and data analysis. The topics included in the

series of M13 guidelines are considered implementable from a regulatory standpoint. This series of M13 guidelines will supersede multi-regional, national and regional guidelines, and mutual use of the data in different countries/regions based on the harmonised guideline will become possible. Given the broad range of topics addressed in most current BE guidelines, it is expected that some aspects of the multi-regional, national and regional guidelines will remain in effect until such time as all guidelines in the series of M13 guidelines are complete.

- *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?*

  There is a possible implication for the submission of content in the CTD/eCTD. The working group will consider this point in detail during the development of the guideline and request a consult with ICH M8 working group, if applicable.

4. Post-hoc evaluation

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

  The results of the work will be evaluated by surveying the product developers to determine whether the harmonisation reduces inconsistency and/or helps cost saving. This will occur up to 5 years after the implementation of the guideline.