Final Business Plan

Model-Informed Drug Development General Principles Guideline

Dated 27 October 2022
Endorsed by the Management Committee on 10 November 2022

1. The issue and its costs

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

  Many regulatory authorities expect to receive, and currently accept model- based analyses as part of dossier submissions. However, the lack of common documentation standards, model assessment expectations and understanding of terminology hinders assessment of quality of the data used, the robustness of the analysis, vis-à-vis the modelling impact and credibility with respect to its intended applications. As a result, the level of integration of MIDD into regulatory decision making can vary between regulatory authorities, from application to application, and within authorities for the same or similar submissions.

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

  The lack of harmonisation results in the underutilization of MIDD approaches in drug development and regulatory decision making. This has led to missed opportunities to fully leverage the learning from available data to both optimise design and enhance the interpretation of subsequent confirmatory studies. Furthermore, robust modelling and simulation, can expedite drug development and make it more efficient; in addition, appropriate applications and interpretations of MIDD are needed to further ensure the health and safety of patients.

2. Planning

- *What are the main deliverables?*

  A new overarching ICH MIDD General Principles Guideline that will broadly cover the general principles and good practices for use of MIDD. The Guideline will establish a common understanding on principle and role of MIDD across quantitative scientists and decision makers, both within and between regulatory authorities and industry. Additionally, the guideline will harmonize expectations regarding documentation standards, model assessment, data used in analysis, etc.

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

  The composition of the MIDD Expert Working Group (EWG) is expected to be diverse and should include representatives with expertise in the areas of general clinical pharmacology and pharmacometrics, and colleagues with particular expertise which spans the MIDD scope. For example, EWG colleagues with the experience of the implementation, planning, conduct, documentation, submission and regulatory review of Population Pharmacokinetics, Physiological

Based Pharmacokinetics, exposure response, Model Based Meta-Analysis, disease progress modelling and Quantitative Systems Pharmacology applications would be appropriate. Similarly experience of developing and implementing associated standards and good practices, associated regional regulatory guidelines as well as experience of informing non-experts with respect to these approaches would be valuable.

Financial resources to attend face-to-face meeting are also required.

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

  It is anticipated that this guideline will take approximately 3 years for completion.

- *What will be the key milestones?*

  The informal WG will have a kick-off meeting in September 2022 and have a face-to-face meeting in November 2022. It is anticipated that a *Step 2b* Guideline will be completed by 2Q/3Q of 2024 and that *Step 4* will be reached by 4Q of 2025, with implementation to follow in 2026.

- *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. 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?*

  MIDD can help to conserve resources for industry, aid regulators in containing human exposure and enhancing regulatory review. Given MIDD increases efficiency it can potentially reduce time for approval and availability of new medicines globally as well informing their better use. Therefore, aligning with the ICH mission to achieve greater harmonisation worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.

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

  The ICH MIDD Discussion Group (2021-2022) discussed this topic and the published "Considerations with respect to future MIDD related guidelines document" provides the background on the alignment across members on the need and feasibility for this as the next MIDD related guideline to be developed. ICH M15 will outline principles for model-informed drug development in full respect of regional regulations and legal frameworks.

- *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?*

It is premature to anticipate the need for a consult with CTD/eCTD at this stage. We will revisit as part of the aligned approach to documenting MIDD application in regulatory submissions.

4. Post-hoc evaluation

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

A post hoc evaluation plan will be proposed after development of the guideline.