Supplement to the "M13: Bioequivalence for Immediate-Release Solid Oral Dosage Forms" Concept Paper

M13C

Dated 13 December 2024

Endorsed by the Management Committee on 27 January 2025

Summary

This supplement provides greater detail on the development of the Tier 3 topics outlined in the M13: Bioequivalence for Immediate-Release Solid Oral Dosage Forms Concept Paper, endorsed by the ICH Management Committee on 10 July 2020.

Background

The M13 guideline includes 3 tiers, i.e., Tier 1 (or M13A) focusing on the bioequivalence (BE) study design and general data analysis considerations, Tier 2 (or M13B) focusing on BE for additional strengths including biowaiver considerations, and Tier 3 (or M13C) focusing on data analysis and BE assessment for highly variable drugs, drugs with narrow therapeutic index, and complex BE study design and data analysis.

The M13 Concept Paper (endorsed in July 2020) indicates that the development of the M13B topic will commence once the topics included in M13A complete ICH *Step 1* (consensus building), and the development of the M13C topic will commence once the topics included in M13B complete ICH *Step 1*. In December 2022, the M13A guideline was endorsed by the ICH Assembly at *Step 2b.* A supplement for M13B was added to the M13 Concept Paper in March 2023 to provide more information on the scope, timeframe, and expertise required to complete M13B. The supplement concept paper for M13B also stated that an additional supplement will be added for M13C topics once the M13A topics reach *Step 4* or the M13B topic reaches *Step 1*, whichever is sooner.

In July 2024, the M13A final guideline was adopted by the ICH and reached *Step 4*. Currently, M13B is targeted to complete *Step 1* in January 2025.

This supplement is added to the M13 Concept Paper to provide more information on the scope, timeframe, and expertise required to complete M13C.

Scope

Tier 3 (M13C guideline) will include:

- BE study design and data analysis for:
  1) Highly variable drugs
  2) Narrow therapeutic index drugs
- Complex BE study design and data analysis
  - Adaptive design
  - Other examples (e.g., handling missing samples)

Expertise

The M13C Expert Working Group (EWG) should include regulators and industry representatives, consistent with existing ICH procedures, being experts in pharmacokinetics and BE with knowledge of associated aspects such as biopharmaceutics, clinical pharmacology, and biostatistics. Current M13B experts may be substituted to ensure the appropriate expertise. Subject matter experts outside the M13C EWG will be consulted, as needed. Ad hoc experts may be appointed based on the need, for example, *ad hoc* biostats experts were appointed to support the dissolution similarity assessment topic for M13B.

Timing

Work on Tier 3 (M13C) is targeted to begin in January 2025 while the M13B *Step 1* document is signed off by Topic Leads. The proposed timing for completion of M13C is as follows:

- Consensus on Technical Document for M13C (*Step 2a/2b*) June 2027*
- Adoption of ICH Harmonised Guideline M13C (*Step 4*) February 2029

* Work on M13B will take precedence after consultation is complete.