

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

M13B

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Summary

This supplement provides greater detail on the development of the Tier 2 topic 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 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 Tier 2 topic will commence once the topics included in Tier 1 complete ICH Step 1 (consensus building). In December 2022, the M13A guideline was approved by the ICH Assembly at Step 2B. Because the Tier 2 topic is only described in general in the M13 Concept Paper, this supplement is added to the M13 Concept Paper to provide greater information on the scope, timeframe, and expertise required to complete Tier 2. An additional supplement will be added for Tier 3 topics once the Tier 1 topics reach *Step 4* or the Tier 2 topic reaches *Step 1*, whichever is sooner.

Scope

As mentioned above, Tier 2 will discuss BE for additional strengths, including biowaiver considerations for additional strengths, and will include:

- Considerations for biowaiver of additional strengths
 - Dose proportionality in the pharmacokinetics of the comparator
 - Comparative qualitative and quantitative composition among different strengths
 - Comparative in vitro dissolution conditions
 - Assessment of similarity between dissolution profiles
- Specific topics
 - Fixed dose combination products
 - Bracketing approach

Expertise

The EWG should include regulators and industry representatives, in line with existing ICH procedures, being experts in pharmacokinetics and BE with knowledge of associated aspects

such as biopharmaceutics, in vitro dissolution, clinical pharmacology, and biostatistics. M13 experts may be substituted to assure the appropriate expertise. Subject matter experts outside the EWG may also be consulted, as needed.

Timing

The Tier 1 guideline (M13A) has reached *Step 3* and is in the process of public consultation. Consensus building on the Tier 2 guideline (M13B) started in November 2022, and the proposed timing for completion of M13B is as follows:

- Consensus on Technical Document for M13B (*Step 2a/2b*) November 2023
- Adoption of ICH Harmonised Guideline M13B (*Step 4*) November 2024