Q&A on Implementation of BA/BE Guideline version 2.0

1. Requirement in BE Study Report

1.1 Should the BE study requirements for registration in ASEAN Member States comply to the ASEAN Guideline for the Conduct of Bioequivalence Studies, and not country-specific requirements?

Answer: BE Studies which meet the requirements as per the ASEAN Guideline for the Conduct of Bioequivalence Studies are acceptable in all ASEAN Member States (AMS).

1.2 Could the BE study done in one AMS be accepted in all AMS without repeating the BE study and CDP?

Answer: BE studies which meet the requirements as per the ASEAN Guideline for the Conduct of Bioequivalence Studies are acceptable for review regardless of the study location. If the BE reference product is equivalent to the innovator product registered in the respective AMS (e.g. from the same drug product manufacturing site listed, in case more than 1 site), bridging CDP testing against the innovator product registered in the respective AMS is not required.

2. Comparator Products

2.1 Could a common ASEAN BE comparator product list such as Reference Listed Drug (RLD) for all AMS be established, or alternatively, a BE comparator product selection "decision tree" in the absence of a common comparator product list for specific drug molecules?

Answer: Common comparator product list is not feasible. Selection criteria already available in Section 3.1.2 of BA/BE Guideline Individual Member States is encouraged to facilitate understanding on the BA/BE Guideline to their respective industries.

2.2 Would AMS accept the BE Study & CDP report without additional CDP testing with AMS countries' RLD if the Test Product intended for registration is part of the 'Recommended Comparator product Medicines' under the WHO Prequalification Programme?

Answer: The BE study and CDP report would be accepted without additional CDP testing against the innovator product registered in the respective AMS if the BE study reference product is equivalent to the innovator product registered in the respective AMS. Under certain condition, Indonesia and the Philippines may accept the BE study which was conducted against the WHO comparator product without additional CDP testing against the innovator product registered in their jurisdiction.

3. BCS Biowaiver

Would AMS adopt the latest extension to the scope of application of the biowaiver eligibility in the WHO and US FDA guidelines to include BCS Class III compounds?

Answer: As AMS have different levels of acceptance for BCS-based biowaiver, the extension of the biowaiver to BCS Class III API-containing drug products in the ASEAN Guideline is not currently being considered.

4. Use of surfactant in Comparative Dissolution Profile (CDP)

Would AMS allow the use of surfactant (e.g. SLS) in dissolution media for poorly soluble or sparingly soluble drug products based on the justifications given? (Please refer attachment Justification Use of Surfactant)

Answer: The use of surfactant in dissolution media is acceptable, if justified, except for BCS-based biowaivers. However, for Malaysia, the use of surfactant is only allowed in quality control (QC) media.

5. Specific BE Center Inspection by each AMS Member

Would AMS accept the BE studies conducted in BE centres located in the ASEAN region without additional BE centre inspection requirement from another AMS for product registration purposes?

Answer: Currently, the BE studies should fulfil the BE centre inspection requirement in the respective AMS. Once the ASEAN Mutual Recognition Arrangement (MRA) for Bioequivalence (BE) Study Reports of Generic Medicinal Products is implemented, BE studies conducted by ASEAN listed BE centres are acceptable for review without additional BE centre inspection requirement.

6. Joint Assessment on BE Study Report & BE Centres Inspection by AMS members

Would AMS be able to provide a timeline for sharing the scope of the Joint Assessment on BE Study Report & BE Centre Inspection and its common fee structure?

Answer: There is no available mechanism particularly for joint assessment on BE study report. Currently, ASEAN JA Procedure for Pharmaceutical Products can be utilized for the purpose of the overall product evaluation by AMS.

7. Comparator Product

Can the result of a BE study be accepted for evaluation by the National Regulatory Authority (NRA) of the importing AMS if the comparator product used in the study has been approved in ICH and associated countries but is not in the list of comparator products of the importing AMS?

Answer: The BE study is acceptable if the comparator meets the eligibility criteria under section 3.1.2 of the BA/BA Guideline. Additional bridging data (e.g CDP) may be required if the comparator is not the innovator product registered with that member state.

8. BE data in the case of changing the manufacturer

Can the BE study of the product produced by manufacturer A be accepted to extrapolate the bioequivalence of the product produced by manufacturer B if:

Hypothesis 1: Product produced by manufacturer A has already been approved in the concerned AMS.

Hypothesis 2: Product produced by manufacturer A has not been registered in the concerned AMS.

If yes, what additional data need to be submitted to support this extrapolation?

Answer: Yes for both hypotheses except for the Philippines. The additional data are as per AVG, SUPAC Guidance. Additional justification is required for hypothesis 2. For the Philippines, a new BE study may be required for hypothesis 2.

9. BE data in the case of changing the API source

Do we need to specify the particle size and/or polymorphic form as essential criteria in batch analysis (as comparative tabulation) in Document 3 of MaV-3 of ASEAN Variation Guideline?

Answer: For change of API source, justification is required to show that the characteristic(s) of the API that may have an impact on bioavailability (e.g. polymorphism, particle size) between the existing and proposed API source is (are) similar. However, particle size and polyomorphism may not necessarily be included in the batch analysis.