Advisory Committee For Pharmaceutical Science
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General BA/BE Guidance
Orally Administered Drugs

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Guidance for Industry

BA and BE Studies for Orally Administered Drug Products — General Considerations

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

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BA and BE Studies for Orally Administered Drug Products-General Considerations

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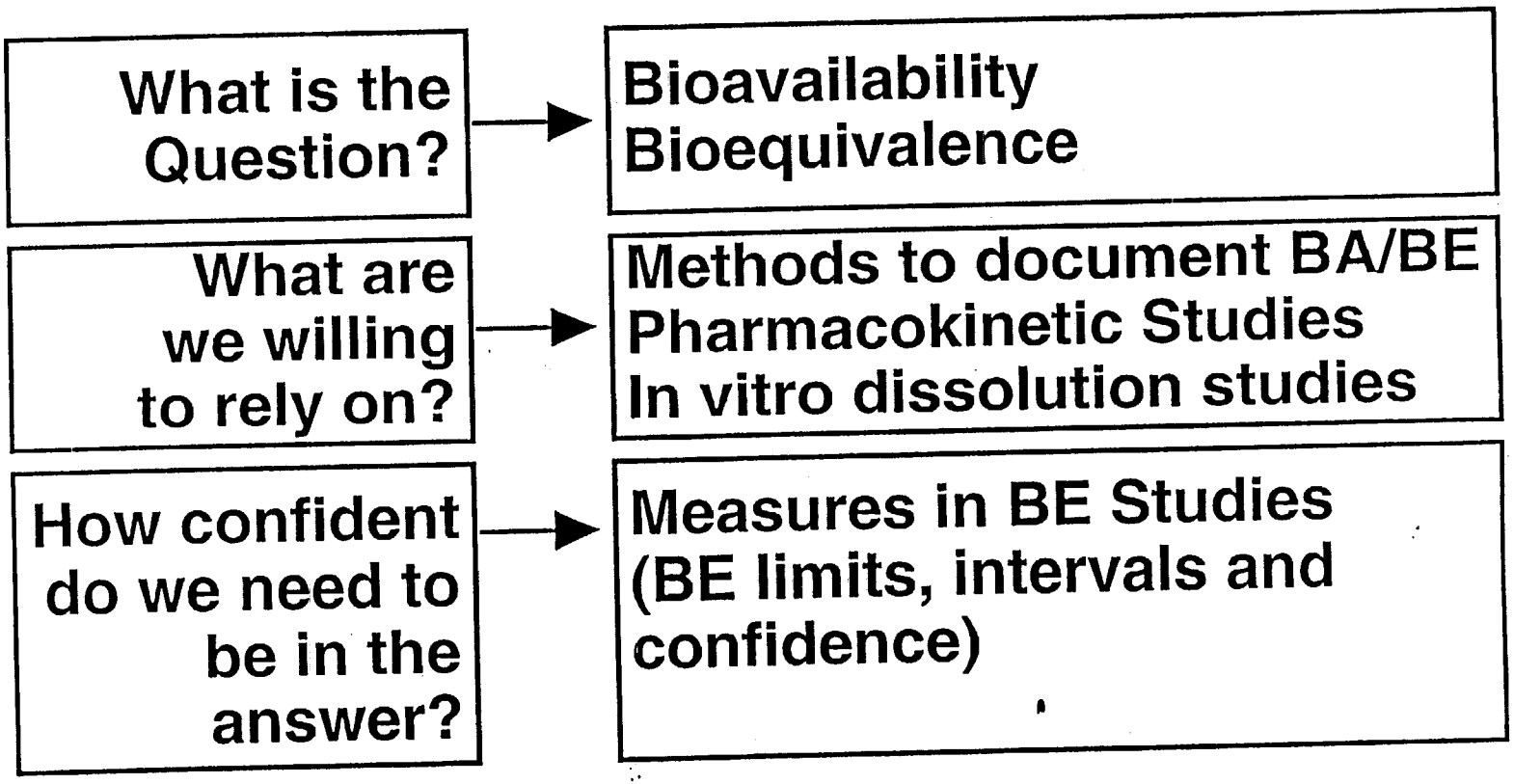
General BA/BE Guidance



General BA and BE Guidance

- Intends to provide 'how to' information for bioavailability and bioequivalence studies to meet requirements set forth in 21 CFR 320 for orally administered drug products.
- Biopharmaceutic aspects of drug product quality, i.e., release of the drug substance from the drug product into systemic circulation.
- Choice of criteria (average, individual) in bioequivalence comparisons.
- Use of early, peak and total exposure measures in bioequivalence comparisons.

Study Design
Replicate Study Design

Replicate study designs are recommended for pivotal BE studies for a two year period using PK measures with the exceptions where:

- Products contain drugs with long half life (e.g., > 96 hours).
- A steady-state design is needed.
- Excessive blood collection and/or other safety factors would arise as a result of treatment replication.

Bioequivalence Studies

Criteria for assessment

Criteria	Individual Bioequivalence	Average Bioequivalence
Study Design	Replicate Crossover 2 x 2 x 12 (subjects) Total Treatments = 48	Crossover 2 x 24 (subjects) Total Treatments = 48

- To assess the likelihood of subject x formulation interaction. Applicants can power their studies for an average criterion, the total number of treatments will be approximately the same as those needed for non-replicate studies.

General Bioavailability and Bioequivalence Guidance

- The intent is to reduce the regulatory burden while maintaining sound scientific principles consistent with public health objectives for optimally performing drug products.
- Specific examples of reduction of the regulatory burden include:
  - Biowaivers for lower strengths of MR dosage forms; (In addition to Biowaivers for lower strength IR products and ER beaded capsules)
  - Elimination of multiple dose BE studies for MR dosage forms;
  - Biowaivers for higher strength of IR dosage forms; and
  - Reduced emphasis on measuring metabolites in BE studies.