BREAKOUT SESSION L DAY 3:

Virtual BE Applications

Moderators: Amitava Mitra (Kura Oncology), Andrew Babiskin (FDA)

Scribes: Parnali Chatterjee (FDA), Erik Sjogren (Pharmetheus)

August 31, 2023
1–3 pm

BO Expectations

- Short introduction: set the scene!
- Share knowledge and science: focus on addressing common challenges
- Discuss openly gaps in knowledge and how to address them
- Discuss examples of what works or not

- Be vocal, curious, share your opinion
- Propose ways forward: elaborate decision trees, share data/experience, propose to form working groups, work on validation exercises

Publication planned following workshop : summarize current knowledge, discussions and proposals for future work

Clear succinct summary of the BO session is essential

Virtual Bioequivalence (VBE)

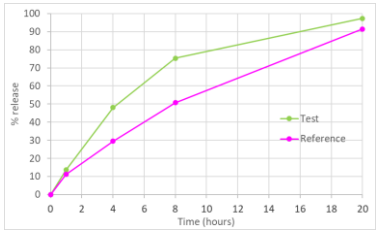
Use of physiological models to predict the outcome of a BE study comparing test and reference formulations

- Conduct “x” number of virtual trials in a model generated population in crossover manner to assess the outcome of a BE study

Applications -

- Predict outcome to support –
  - Formulation changes in late-stage clinical development
  - Generic product development
  - Specification setting
  - Manufacturing site change
  - Waiver of Fed BE study
- Minimize the number of “pilot” PK studies
- Provide more confidence in the outcome of a “pivotal” BE study

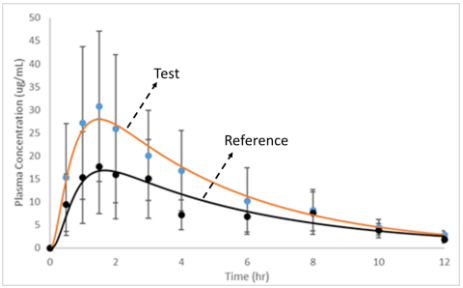
Typical Workflow for VBE



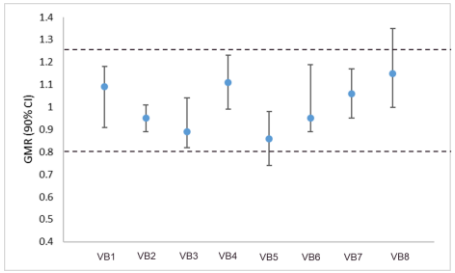
In vitro dissolution data comparing test and reference formulations

Model built & verified using available data

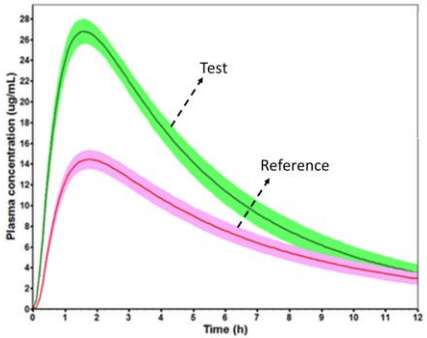
Conduct appropriate Parameter Sensitivity Analyses



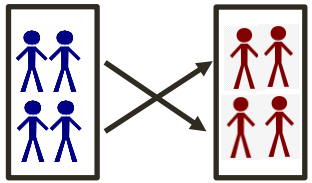
Predicted plasma PK profile and comparison with observed data



Output (GMR & 90%CI) from several VBE trials

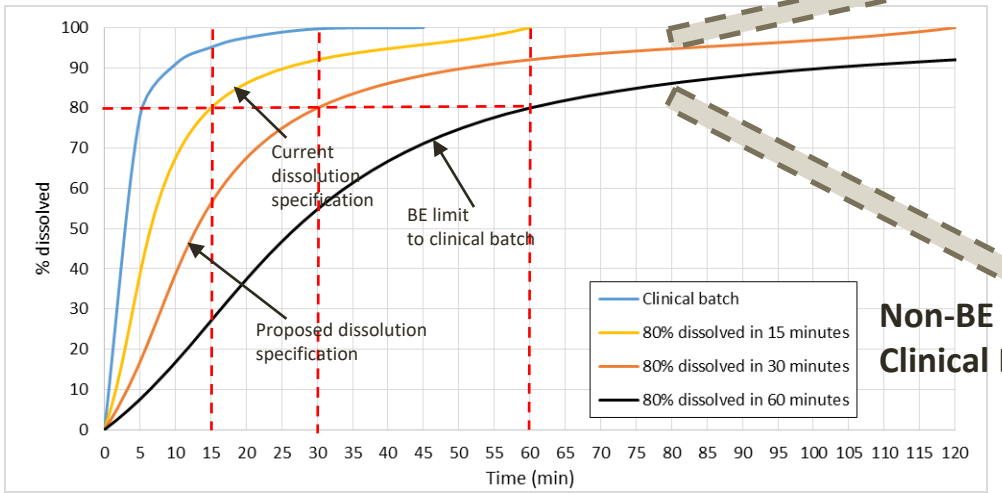


Virtual trial output comparing test and reference formulation

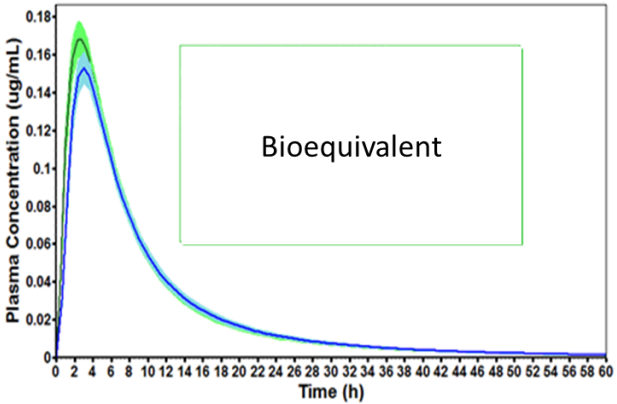


Cross-over population simulation by incorporating variability in PK parameters from previous clinical data

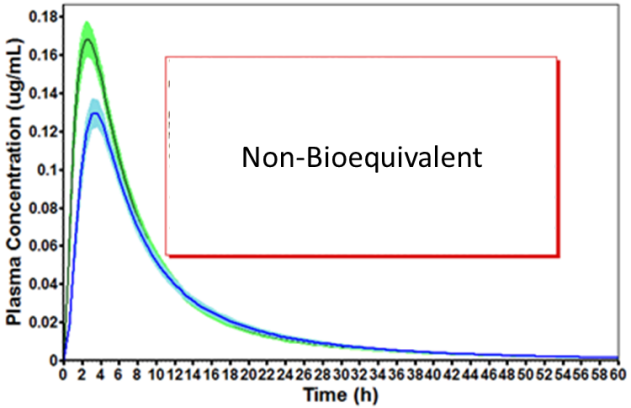
Safe Space Generation using VBE



BE to Clinical Batch



Non-BE to Clinical Batch



Clinical Pharmacology & Therapeutics, 105: 307-309 (2019)
AAPS Journal, 21: 29 (2019)

Key Points from BO Session L, Day 3, Question 1

What are the criteria for selecting populations for VBE simulations (in terms of, sample size number of trials simulated, sex, demographics, disease state)?

Key Points from BO Session L, Day 3, Question 2

Should non-BE batch be a requirement for VBE verification? What are the challenges? What are other potential options for model verification?

Key Points from BO Session L, Day 3, Question 3

What are the experiences and challenges in applications of VBE in Post-approval changes?
E.g. excipient changes for BCS 3 drug products BE

Key Points from BO Session L, Day 3, Question 4

What are your experiences with regulatory acceptance of VBE based specification justifications (e.g. dissolution, API PSD)? What are feedback(s) on the model?

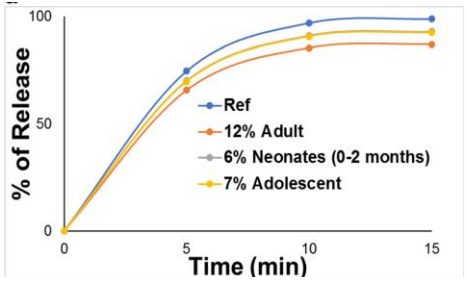
The AAPS Journal (2020) 22:107
DOI: 10.1208/s12248-020-00493-6

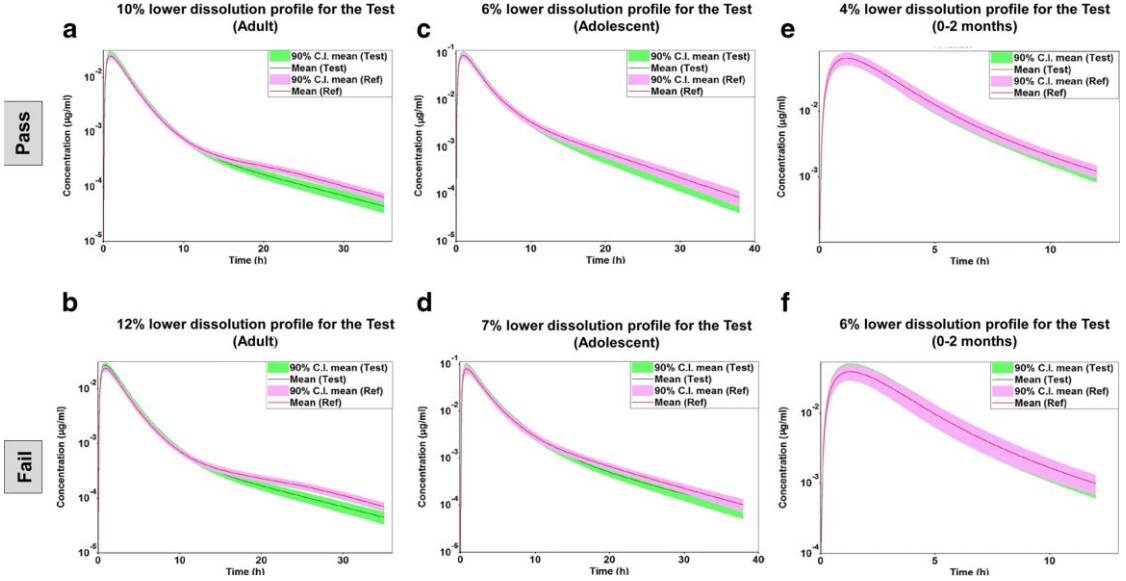
Check for updates

Research Article

Using a Physiologically Based Pharmacokinetic Absorption Model to Establish Dissolution Bioequivalence Safe Space for Oseltamivir in Adult and Pediatric Populations

Lei Miao,[1] Youssef M. Mousa,[1] Liang Zhao,[1] Kimberly Raines,[2] Paul Seo,[2] and Fang Wu[1,3]





Key Points from BO Session L, Day 3, Question 5

What are the experiences, successes, considerations and challenges in applying VBE to pediatric population?