Regulatory Education for Industry (REdI) and CERSI Workshop

Current State and Future Expectations of Translational Modeling Strategies to Support Drug Product Development, Manufacturing Changes and Controls

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College Park, MD

BREAKOUT SESSION D DAY 2:

Approaches to establish sameness following manufacturing/formulation changes: Advantages and disadvantages of Virtual BE

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Question 1

What are the necessary input data for a reliable virtual BE trial performed to support drug product quality, or for not conducting an in vivo study?

a. Critical quality attributes: sensitivity analysis to identify those that may impact BA

b. Good quality experimental data

Question 2

How should variability and uncertainty be captured in models used to perform virtual BE trials performed to support drug product quality or not conducting an in vivo study?

a. Inter- vs intra-subject variability incorporated in model used to perform virtual BE studies?
b. Study designs to measure intra-subject variability in the clinical setting?
c. Computational methods/algorithms to determine and incorporate intra-subject variability in models used to perform VBE studies.
d. Best approaches for evaluating and incorporating inter-occasion variability in a VBE study.
e. How to handle uncertainty (in contrast to variability)?

Question 3

Does a virtual BE study simulating patients or healthy volunteer populations provide significantly more information over a comparison of average projections?

If yes, in which scenarios?

Question 4

How should virtual BE trials conducted to support drug product quality or not conducting an in vivo study be set-up?

a. Population: healthy volunteers and/or patients
b. Crossover vs replicated design: what is the appropriate design based on the API/drug product (narrow therapeutic index, highly variable, subject-by-formulation interaction)
c. Sample size: dedicated study to determine variability? Previous data? Leverage literature?

Question 5

What are the main challenges in acceptance of virtual BE trials performed to support drug product quality, or instead of conducting an in vivo/clinical study?

a. Main challenges in utilizing virtual BE trials for regulatory decision making?
b. Pros and cons of virtual BE trials, including confidence in approach.
    - What is necessary to increase confidence and acceptance of VBE
    - High-confidence vs. low-confidence cases/applications.
    - High-risk vs low-risk cases
c. When is a virtual BE study not recommended?

Key Points from BO Session D, Day 2, Question 1

Key Points from BO Session D, Day 2, Question 2

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

Key Points from BO Session D, Day 2, Question 4

Key Points from BO Session D, Day 2, Question 5

Overall Conclusions