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

September 23-25, 2019

College Park, MD

BREAKOUT SESSION A DAY 3:

Discussion of several terminologies related to physiologically based pharmacokinetic modeling in support of drug product quality (e.g., physiologically based biopharmaceutics modeling)

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Session Background

The published summary of day 2 of the 2017 M-CERSI workshop on "Dissolution and Translational Modeling Strategies Enabling Patient Centric Product Development." involved different terms for physiologically based modeling depending on the application of the model (Heimbach et al. 2019).

Besides the well established term physiologically based pharmacokinetics (PBPK) the terms physiologically based biopharmaceutics model(s) or modeling (PBBM) and physiologically based pharmacokinetic(s) absorption models (PBAM) were specified.

This break out session is an opportunity for discussions on the topic of several terminologies to physiologically based modeling when used to support drug product quality and translational modeling strategies in enabling patient-centric product development .

Session Background

PBPK: Currently encompasses “all” applications of physiologically based models.

PBAM: Mechanistic absorption model, which mimic physiological conditions and incorporate dissolution information while accounting for relevant physicochemical and physiological factors leading to a prediction of systemic exposure versus time

PBBM: Focus on formulation-physiology interactions for predictions of the clinical impact of variations in formulation parameters and characteristics. Based on the same principles as PBAM but encompasses all areas of biopharmaceutics.

Definitions from Heimbach et al. 2019 with some modifications

BO Session A, Day 1, Questions

Questions

1. How are current modeling terminologies (e.g. PBPK vs. PBBM, MAM and PBAM) interrelated?

2. Do these terminologies clearly communicate a modeling focus of **formulation** and **manufacturing** dependencies for clinical performance?

3. Do these terminologies clearly represent the scope of modeling needed for their application, e.g., different routes of administration etc., in support of **formulation** and **manufacturing** changes?

4. Can we harmonize terminology or is different terms of modeling needed/motivated for different applications (such as above)?

5. What would be the advantages/disadvantages of having separate terminologies based on their major field of application (e.g., in support of CMC changes vs. clinical pharmacology issues)?

6. For definitions, do the definition tables from 2017 M-CERSI workshop need updating?

Key Points from BO Session A, Day 1, Question 1

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

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

Overall Conclusions