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 1:

Best Strategies for Determining Solubility, Supersaturation and Critical Supersaturation

Moderators: Vidula Kolhatkar (FDA); James Butler (GSK)

Scribes: Jennifer Dressman (Goethe U); Lynne Taylor (Purdue University)

Session Background

Reliable, reproducible data to characterize drug solubility in the GI tract is invaluable for use in PBPK modelling. How do we ensure best practice?

When there is the potential for supersaturated drug concentrations, determination of “solubility” is even more complex due to dependence upon dynamics. How do we ensure best practice and avoid pitfalls in these scenarios?

Questions being considered in this break-out session

What are the most relevant solubilities for PBPK?

What are the issues when measuring solubility?

- *General issues (stability, controlling pH, duration of experiment etc.)*
- *Media-specific issues (compendial media, biorelevant media, HIF)*
- *Outline the best practices for measuring solubility*

When is it necessary to assess supersaturation and which are the best practices for measuring supersaturation?

How can precipitation be best characterized with a view to modeling and simulation?

What are the pros and cons of the various experimental set-ups that are designed to measure supersaturation and precipitation (bilayer, two-stage, transfer, BioGit, ASD, TIM etc)

When can we rely on solubility data vs solution concentration time profile (e.g. a dissolution profile) to develop a model?

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

What are the most relevant solubilities for PBPK?

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

What are the issues when measuring solubility?

- General issues (stability, controlling pH, duration of experiment etc.)

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

What are the issues when measuring solubility?

- Media-specific issues (compendial media, biorelevant media, HIF)

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

What are the issues when measuring solubility?

- Outline the best practices for measuring solubility

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

When is it necessary to assess supersaturation and which are the best practices for measuring supersaturation?

Key Points from BO Session A, Day 1, Question 4

How can precipitation be best characterized with a view to modeling and simulation?

Key Points from BO Session A, Day 1, Question 5

What are the pros and cons of the various experimental set-ups that are designed to measure supersaturation and precipitation (bilayer, two-stage, transfer, BioGit, ASD, TIM etc)

Key Points from BO Session A, Day 1, Question 6

When can we rely on solubility data vs solution concentration time profile (e.g. a dissolution profile) to develop a model?

Overall Conclusions