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

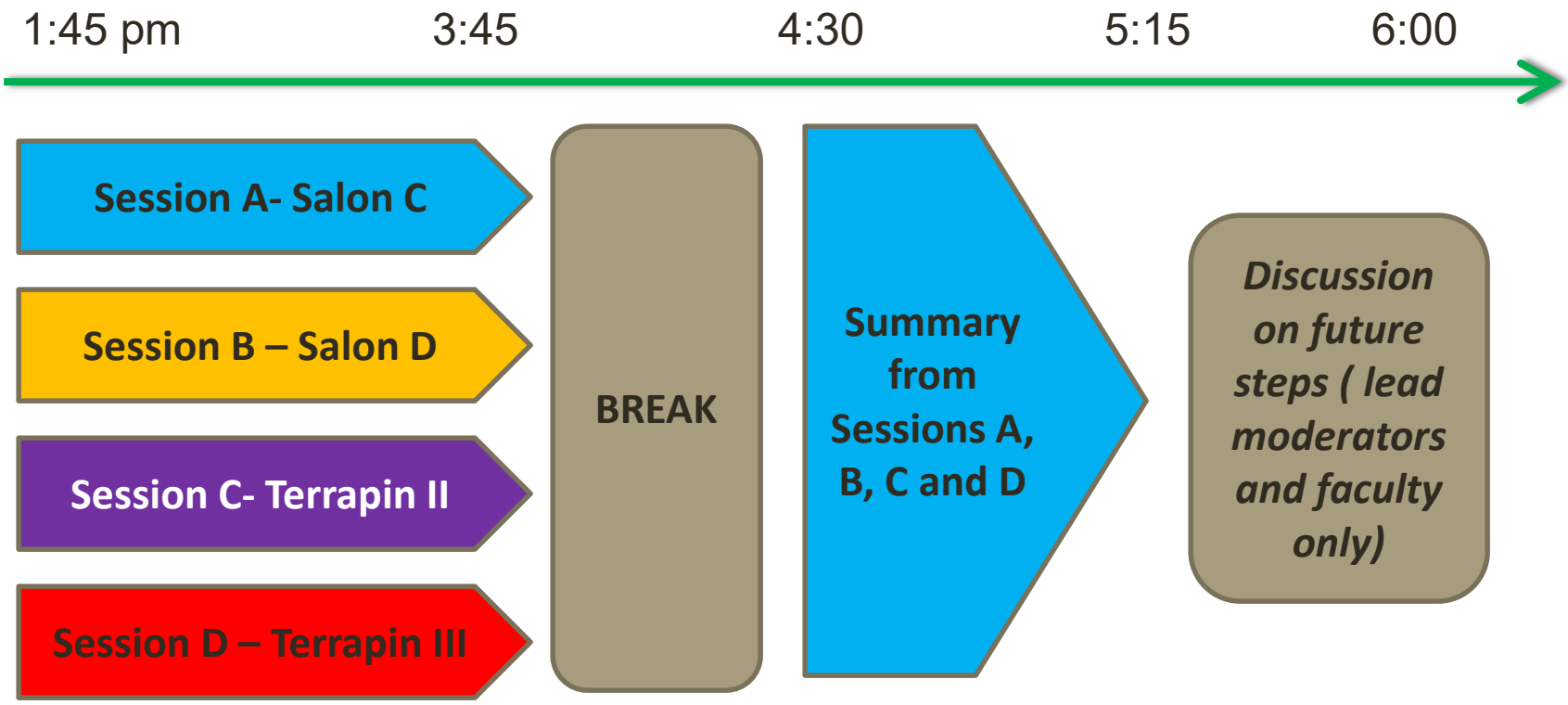
September 23-25, 2019

College Park, MD

Day 1 Breakout introduction

In vitro biopredictive methods

D1 BO Organization



- 2-hour BO sessions running in parallel
- Please respect your session assignment (you can see the colors on your badge)
- Series of questions for each BO topic for discussion (order of importance)

Expectations

- Short introduction by moderator : set the scene !
- Share knowledge and science : we are all scientists these three days
- Discuss the 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, propose to 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

D1 Theme : in vitro biopredictive tools

Breakout Session A - Salon C
Best strategies for determining solubility, supersaturation and critical supersaturation.

Breakout Session B - Salon D
Best strategies for the development of biopredictive (clinically relevant) dissolution methods, a key element for successful modeling and simulation.

Breakout Session C - Terrapin II
Gastrointestinal systems parameters (mucus, volume, motility): Where are the pitfalls and how can we overcome them?

Breakout Session D - Terrapin III
Permeability along the gastrointestinal tract. Translation from biopharmaceutical measurement to a model parameter?

Workshop expectations

Day 1 : Discussion of modelling parameters

Drug substance: solubility
How to obtain a meaningful solubility measurements *in vitro* ?
What solubility drives dissolution *in vitro* and *in vivo* ?

Drug substance: precipitation
How well does *in vitro* precipitation translate to in vivo precipitation. Is the measurement clinically relevant ?

Drug substance: permeability
Regional differences, impact of excipients and food on permeability, how to measure and predict human jejunal Peff and predict regional differences.
Should we use top down PK data, can we use preclinical info ?

Workshop expectations

Day 1 : Discussion of modelling parameters

Drug product : dissolution and its integration in PBPK tools
What terms should be used to describe dissolution methods (clinically relevant, biopredictive, biorelevant, QC…)
How should we select an appropriate dissolution method?
Can we predict dissolution or should we measure it ?
What is a mechanistic model vs. a mathematical one ?

System parameters : **Volume, transit and hydrodynamics**
Learnings from *in vivo* exploration ?
Are our dissolution models too simple ?
Are our stomach transit models too simple ?
Where to go from now ?

In preparation for Day 3 BO sessions:

Please take some minutes to complete the following survey to share your understanding/evaluation of the area of PBBM modelling submissions

https://www.surveymonkey.co.uk/r/W2K55MV

Completely anonymous
Results will be shared and discussed on Day 3

Thanks !