

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

September 23-25, 2019

A collaboration by FDA | CDER Office of Pharmaceutical Quality (OPQ), Small Business and Industry Assistance (SBIA), and University of Maryland CERSI

Day 1: Monday, September 23 In vitro Biopredictive Methods

Moderators: Jennifer Dressman (Goethe University), Xavier Pepin (AstraZeneca) and Poonam Delvadia (FDA)

7:30 a.m.	Registration opens	
8:30	Welcome and objectives of the workshop.	Sandra Suarez Center for Drug Evaluation and Research (CDER) FDA
8:40	The impact and future of physiological based biopharmaceutics modeling (PBBM) in support of drug product quality.	Paul Seo CDER FDA
9:10	Approaches to measure equilibrium (intrinsic) and kinetic solubility, surface pH and the impact on dissolution and membrane transport kinetics.	Lynne Taylor Purdue University
9:40	The value of biorelevant media for measuring solubility and in the development of biopredictive dissolution methods.	Jennifer Dressman Goethe University
10:10	Break	
10:25	Measurement and prediction of human permeability: current best practices, regional differences and future developments.	Erik Sjögren Pharmatheus
10:55	Biopredictive dissolution methods with a view to integration in PBPK. Challenges for low solubility IR drug products.	James Butler GlaxoSmithKlein
11:25	In vitro approaches to understanding supersaturation and precipitation of weak bases and enabling formulations.	Ed Kostewicz Goethe University
11:55	Lunch	
12:45 p.m.	The importance of fluid volume kinetics in the development of biopredictive dissolution methods.	Mirko Koziolk University of Greifswald
1:15	Introduction and expectations for breakout sessions	Xavier Pepin AstraZeneca

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<p>1:30</p>	<p>Break <i>Transition to breakout sessions</i></p>	
<p>1:45 Breakout Session A <i>Salon C</i></p>	<p>Best strategies for determining solubility, supersaturation and critical supersaturation.</p>	<p>Moderators Vidula Kolhatkar CDER FDA James Butler GSK</p> <p>Scribes Jennifer Dressman Goethe University Lynne Taylor Purdue University</p>
<p>1:45 Breakout Session B <i>Salon D</i></p>	<p>Best strategies for the development of biopredictive (clinically relevant) dissolution methods, a key element for successful modeling and simulation.</p>	<p>Moderators Bertil Abrahamsson AstraZeneca Poonam Delvadia CDER FDA</p> <p>Scribes Ed Kostewicz Goethe University Filippos Kesisoglou Merck & Co., Inc.</p>
<p>1:45 Breakout Session C <i>Terrapin II</i></p>	<p>Gastrointestinal systems parameters (mucus, volume, motility): Where are the pitfalls and how can we overcome them?</p>	<p>Moderators Mirko Koziolk University of Greifswald Xavier Pepin AstraZeneca</p> <p>Scribes Andre Dallmann Bayer AG Yang Zhao CDER FDA</p>
<p>1:45 Breakout Session D <i>Terrapin III</i></p>	<p>Permeability along the gastrointestinal tract. Translation from biopharmaceutical measurement to a model parameter?</p>	<p>Moderators Xinyuan Zhang CDER FDA Neil Parrott Roche</p> <p>Scribes Andrew Babiskin CDER FDA Erik Sjogren</p>

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		Pharmatheus
3:45	Break <i>Moderators and scribes to convene</i>	
4:30	Summary of breakout discussions	Lead Moderators
5:15	Discussion	
6:00	Adjourn	

Day 2: Tuesday, September 24 Best Practices for Model Development, Verification, and Validation

Moderators: Neil Parrott (Roche) and Sandra Suarez (CDER | FDA)

8:30	Welcome and logistics	Sandra Suarez CDER FDA
8:35	Opportunities and challenges for modeling the clinical impact (i.e. systemic exposure) of formulation and manufacturing changes.	David Good Bristol-Myers Squibb
9:05	Best practices in model development: input of solubility, supersaturation, precipitation and permeability.	Christian Wagner Merck Healthcare KGaA
9:35	Best practices for model building: parameter optimization, sensitivity analysis and how to assess the match to clinical data.	André Dallmann Bayer AG
10:05	Break	
10:20	Translating the effect of product manufacturing variants from in vitro to the clinic. Current possibilities and gaps for immediate release formulations.	James Mullin Simulations Plus
10:50	Translating the effect of product manufacturing variants from in vitro to the clinic. Current possibilities and gaps for extended release formulations.	Nikunj Kumar Patel Certara
11:20	Approaches for entering dissolution into the absorption model, reasons for selection, model assumptions, and parameter estimation strategies.	Filippos Kesisoglou Merck & Co., Inc.

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11:50	Lunch	
12:35 p.m.	Considerations for the verification and validation of models.	Arian Emami Riedmaier AbbVie
1:05	Impact of population variability (intra and inter) and sample size for model validation and data needed to justify application of virtual bioequivalence.	Amitava Mitra Sandoz
1:35	Introduction and expectations for breakout sessions	Neil Parrott Roche
1:50	Break <i>Transition to breakout sessions</i>	
2:05 Breakout Session A <i>Salon C</i>	Challenges to predict effects of formulation changes (e.g. particle size distribution changes) on dissolution and in vivo performance using in silico models. Are the tools ready?	Moderators Sandra Suarez CDER FDA Filippos Kesisoglou Merck & Co., Inc Scribes Kimberly Raines CDER FDA James Butler GSK
2:05 Breakout Session B <i>Salon D</i>	Strategies to handle parameter uncertainty and variability within and between subjects.	Moderators Maziar Kakhi CDER FDA Neil Parrott Roche Scribes David Good BMS Nikunj Kumar Patel Certara
2:05 Breakout Session C <i>Terrapin II</i>	Best practices for model development, verification and validation, and criteria for defining prediction success.	Moderators Min Li CDER FDA Xavier Pepin AstraZeneca Scribes Arian Emami Riedmaier AbbVie James Mullin

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		Simulations Plus
2:05 Breakout Session D <i>Terrapin III</i>	Approaches to establish sameness following manufacturing/formulation changes: Advantages and disadvantages of virtual bioequivalence.	Moderators Eleftheria Tsakalozou CDER FDA Amitava Mitra Sandoz Scribes Yang Zhao CDER FDA Christian Wagner Merck Healthcare KGaA
4:05	Break <i>Moderators and scribes to convene</i>	
4:45	Summary of breakout sessions	Lead Moderators
5:30	Discussion	
6:15	Adjourn	

Day 3: Wednesday, September 25 Applications to PBBM to support Drug Product Quality

Moderators: *Amitava Mitra (Sandoz) and Andrew Babiskin (CDER | FDA)*

8:30 a.m.	Welcome and Logistics	Andrew Babiskin CDER FDA
8:35	FDA expectations in building a safe space to gain regulatory flexibility based on PBBM.	Yang Zhao CDER FDA Sandra Suarez CDER FDA
9:05	European Medicines Agency expectations in building a safe space to gain regulatory flexibility based on PBBM.	Evangelos Kotzagiorgis European Medicines Agency (EMA)
9:35	Case Study: Application of PBBM in risk assessment of effect of acid reducing agents (ARA) on pharmacokinetics and formulation development.	Neil Parrott Roche

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10:05	Break	
10:20	Prediction of human pharmacokinetics utilizing in vitro chewing method and physiologically based CDER pharmacokinetic (PBPK)	Satish Sharan CDER FDA
10:50	Case Study: Bridging physiology-based dissolution testing to quality control testing using PBBM.	Christophe Tistaert Janssen
11:20	The use of PBBM and biomarkers to provide detailed understanding of in vivo dissolution and absorption for Acabrutinib.	Xavier Pepin AstraZeneca
11:50	Lunch	
12:40 p.m.	Case Studies: Physiologically Based Biopharmaceutics Modeling For Food Effects—Possibilities and Opportunities	Tyco Heimbach Novartis
1:10	Introduction and expectation for breakout sessions	Amitava Mitra Sandoz
1:25	Break <i>Transition to breakout sessions</i>	
1:40	Discussion of several terminologies related to physiologically based pharmacokinetics modeling in support of drug product quality (e.g., physiologically based biopharmaceutics modeling).	Moderators Banu Zolnik CDER FDA Erik Sjögren Pharmatheus
Breakout Session A Salon C		Scribes Fang Wu CDER FDA Tycho Heimbach Novartis
1:40	Risk-based approach in the development and implementation of PBBM modeling to support drug product quality and clinically relevant specifications setting.	Moderators Om Anand CDER FDA Shefali Kakar Novartis
Breakout Session B Salon D		Scribes

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		Min Li CDER FDA Xavier Pepin AstraZeneca
1:40 Breakout Session C <i>Terrapin II</i>	The road towards harmonization among regulatory agencies on evidentiary standards for PBBM.	Moderators Shereeni Veerasingham Health Canada Shinichi Kijima Pharmaceuticals and Medical Devices Agency (PMDA) Baoming Ning National Institutes for Food and Drug Control (NIFDC) Gustavo Mendes Lima Santos Anvisa Kimberly Raines CDER FDA Scribes Greg Rullo AstraZeneca Haritha Mandula CDER FDA
1:40 Breakout Session D <i>Terrapin III</i>	Strategies for bridging biorelevant and quality control dissolution via PBBM.	Moderators Sandra Suarez CDER FDA Christophe Tistaert Janssen Scribes Poonam Delvadia CDER FDA Jennifer Dressman Goethe University Paul Dickinson SEDA
3:40 Break <i>Moderators and scribes to convene</i>		
4:30	Summary of breakout sessions	Lead Moderators
5:15	Conclusions and next steps	
5:30	Discussion	
6:00	Adjourn	