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.	**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.	**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 hydrodynamics in the development of biopredictive dissolution methods.	**Mirko Koziolek** University of Greifswald
1:15	Introduction and expectations for breakout sessions	**Xavier Pepin** AstraZeneca

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

		Pharmatheus
3:45	Break *Moderators and scribes to convene*	
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.	**Nikunjkumar 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 qualification and verification 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 *Transition to breakout sessions*	
2:05 **Breakout Session A** *Salon C*	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** *Salon D*	Strategies to handle parameter uncertainty and variability within and between subjects.	Moderators **Maziar Kakhi** CDER | FDA **Neil Parrott** Roche Scribes **David Good** BMS **Nikunjkumar Patel** Certara
2:05 **Breakout Session C** *Terrapin II*	Best practices for model development and verification and criteria for defining prediction success.	Moderators **Min Li** CDER | FDA **Xavier Pepin** AstraZeneca Scribes **Arian Emami Riedmaier** AbbVie **James Mullin**

		Simulations Plus
2:05 ***Breakout Session D*** *Terrapin III*	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 *Moderators and scribes to convene*	
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 Zhang** 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

10:05	Break	
10:20	Prediction of human pharmacokinetics utilizing in vitro chewing method and physiologically based pharmacokinetic (PBPK) analyses for abuse-deterrent hydrocodone bitartrate extended release tablets.	**Satish Sharan** CDER | FDA
10:50	Case Study: Bridging physiology-based dissolution testing to quality control testing using PBBM.	**Christophe Tistaert** Janssen
11:20	Case Study: The use of PBBM and biomarkers to provide detailed mechanistic understanding of in vivo dissolution and absorption. An industrial example.	**Xavier Pepin** AstraZeneca
11:50	Lunch	
12:40 p.m.	Case Study: A physiologically based biopharmaceutics modeling for food effects – possibilities and opportunities.	**Tycho Heimbach** Novartis
1:10	Introduction and expectation for breakout sessions	**Amitava Mitra** Sandoz
1:25	Break *Transition to breakout sessions*	
1:40 **Breakout Session A** *Salon C*	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 Scribes **Fang Wu** CDER | FDA **Tycho Heimbach** Novartis
1:40 **Breakout Session B** *Salon D*	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 Scribes

		Min Li CDER | FDA **Xavier Pepin** AstraZeneca
1:40 **Breakout Session C** *Terrapin II*	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 Mendez Lima Santos** Anvisa Scribes **Kimberly Raines** CDER | FDA **Greg Rullo** AstraZeneca **Evangelos Kotzagiorgis** (EMA)
1:40 ***Breakout Session D*** *Terrapin III*	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
3:40	*Break* *Moderators and scribes to convene*	
4:30	Summary of breakout sessions	**Lead Moderators**
5:15	Conclusions and next steps	
5:30	Discussion	
6:00	Adjourn	