FDA/M-CERSI Physiologically Based Biopharmaceutics Modeling, PBBM Best Scientific Practices to Drive Drug Product Quality: Latest Regulatory and Industry Perspectives

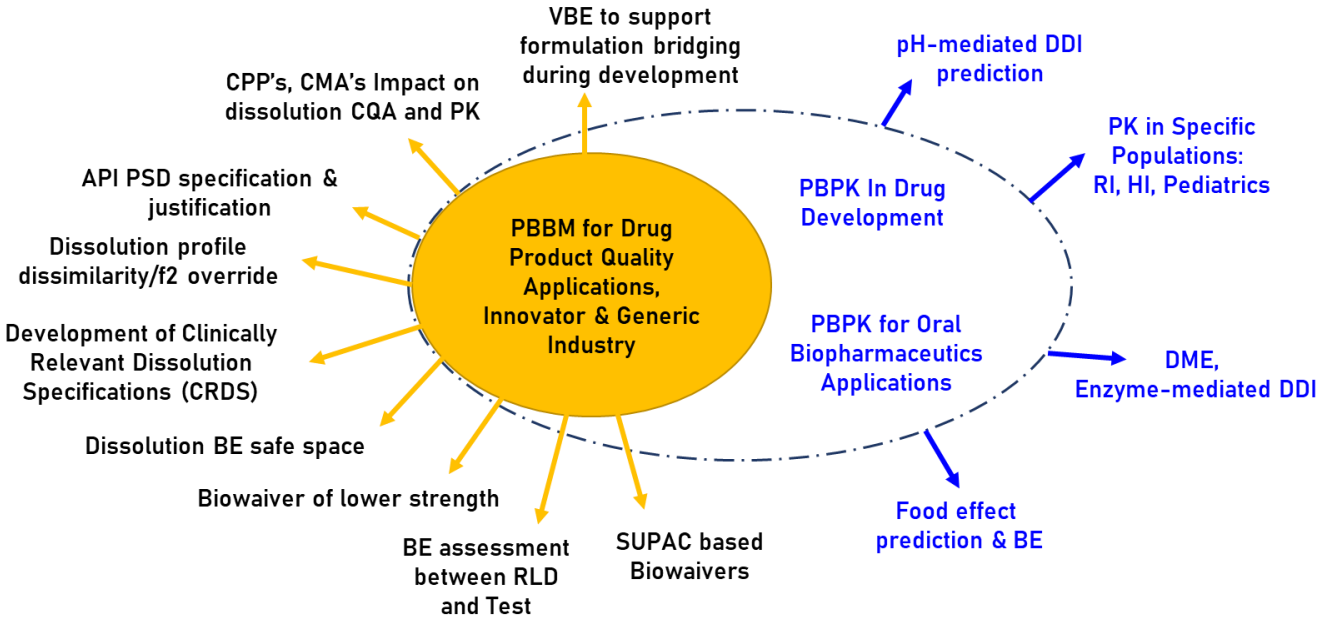
Tuesday 29 August – Thursday 31 August

University of Maryland Center of Excellence in Regulatory Science and Innovation (M-CERSI)
Location: Universities at Shady Grove (Rockville, MD)

www.pharmacy.umaryland.edu/PBBM2023

What is PBBM?

PBBM (Subset of PBPK) Examples in Oral Formulation Development



Modified from : Yuvaneshwari, K., et al., Journal of Drug Delivery Science and Technology, 2022. 69: p. 103152.
& Wu, D., et al., Pharm Res, 2023. 40(2): p. 337-357.

Physiologically based biopharmaceutics models (PBBM) are evolving tools which can be used throughout drug product development and post approval. PBBM focusses on the generation of mechanistic understanding of how drug product quality attributes interact with physiology to influence the in vivo drug performance. The application of PBBM is not only important in the development of drug products but can also be a key component for regulatory approval of clinically relevant specifications and continued quality assurance throughout the product life cycle.

To further advance the science of PBBM and define best practices, real PBBM case studies for oral drug products submitted as part of global marketing applications were discussed by FDA, EMA, Health Canada, ANVISA, MHRA, and PMDA. The purpose of this workshop is to discuss the best scientific practices for developing the PBBM models for orally administered, systemically active drug products and how these models can be leveraged for streamlining pharmaceutical drug product development, and supporting manufacturing changes and controls. This workshop will engage experts from regulatory agencies, innovator and generic drug industry, consultants, academia and commercial software providers and others in the field of modeling and simulation to discuss the opportunities and best practices for incorporating drug product quality attributes within PBBM models to support development programs and regulatory submissions. The workshop will aim to identify bottlenecks/gaps which hinder the development and efficient utilization of PBBM models to support drug product quality.

Tuesday 29 August WORKSHOP AGENDA: Morning Session

Morning sessions: Regulators Discussion of Established PBBM Case Studies
Afternoon Hot Topics/Breakout Sessions: Considerations for In Vitro Data Inputs to PBBM

Time	Event	Speaker
8:00-9:30 am	**Registration & Light Breakfast**	
	Moderators: Paul Seo, FDA Sumit Arora, Janssen *The morning session will be held in Room 1400 Ballroom*	
9:00-9:15 am	Welcome & Workshop Objective	**Speaker:** Bhagwant Rege, FDA
9:15-9:45 am	**PBBM Impact & Future perspective**	**Keynote Speaker:** Jennifer Dressman, Fraunhofer Institute for Translational Medicine and Pharmacology ITMP
9:45-10:00 am	**Discussion of Case Study 1**	**Speaker:** Shereeni Veerasingham, HC
10:00-10:15 am	**Discussion of Case Study 2**	**Speakers:** Anders Lindahl, Swedish MPA Flora Musuamba Tshinanu, Belgium FAMHP
10:15-10:30 am	**Break (beverages provided-15 min)**	
10:30-10:45 am	**Discussion of Case Study 3**	**Speaker:** Rebecca Moody, FDA
10:45-11:00 am	**Discussion of Case Study 9**	**Speaker:** Øyvind Holte, Norwegian Medicines Agency
11:00 am-12:00 pm	Round table discussion on case studies ***(60 min)***. **Focus areas**: best strategies to integrate in vitro data (solubility, permeability, dissolution, and precipitation) in PBBM	**Regulators:** Rebecca Moody, FDA Luiza Borges, ANVISA Mary Malamatari, MHRA Øyvind Holte, Norwegian Medicines Agency Shereeni Veerasingham, HC Shinichi Kijima, PMDA **Moderators:** Paul Seo, FDA Sumit Arora, Janssen
12:00-1:00 pm	**Lunch (provided-60 min)**	

Tuesday 29 August WORKSHOP AGENDA: Afternoon Session

Time	Event	Speaker
1:00-1:30 pm *Room 1032*	**Hot topic A: Solubility: From in vitro best practices to in vivo relevance**	**Speaker**: Deanna Mudie, Lonza
1:30-3:00 pm *Room 1032*	**Breakout Session A: Best practices for solubility as input to PBBM**	**Moderator 1:** Evangelos Kotzagiorgis, EMA **Moderator 2:** Claire Mackie, Janssen **Scribe 1:** Tessa Carducci, Merck **Scribe 2:** Mario Cano Vega, Amgen
1:00-1:30 pm *Room 1042*	**Hot topic B: Development of biopredictive dissolution methods**	**Speaker**: Raimar Loebenberg, Univ.of Alberta
1:30-3:00 pm *Room 1042*	**Breakout Session B: Dissolution Part 1: Best practices for data generation as input to PBBM**	**Moderator 1:** Paul Seo, FDA **Moderator 2**: Nikoletta Fotaki, Univ. of Bath **Scribe 1:** Parnali Chatterjee, FDA **Scribe 2:** Ivy Song, Takeda
1:00-1:30 pm *Room 1400*	**Hot topic C: Methods for integrating dissolution in PBBM**	**Speaker**: Xavier Pepin, Simulations Plus
1:30-3:00 pm *Room 1400*	**Breakout Session C: Dissolution Part 2: Best practices for modeling dissolution as input to PBBM**	**Moderator 1:** Luiza Borges, ANVISA **Moderator 2:** Cordula Stillhart, Roche **Scribe 1:** Grace Chen, Takeda **Scribe 2:** Megerle Scherholz, BMS
1:00-1:30 pm *Room 1052*	**Hot topic D: Precipitation: From in vitro best practices to in vivo relevance**	**Speaker**: Christian Wagner, Merck group (pre-recorded)
1:30-3:00 pm *Room 1052*	**Breakout Session D: Best practices for integration of precipitation in PBBM**	**Moderator 1:** Poonam Delvadia, FDA **Moderator 2:** Mark McAlister, Pfizer **Scribe 1:** André Dallman, Bayer **Scribe 2:** Elizabeth Gray, FDA
1:00-1:30 pm *Room 2052*	**Hot topic E: Permeability: From in vitro best practices to in vivo relevance**	**Speaker**: Hans Lennernäs, Uppsala University
1:30-3:00 pm *Room 2052*	**Breakout Session E: Best practices for integration of permeability in PBBM**	**Moderator 1:** Christer Tannergren, AstraZeneca **Moderator 2:** Rodrigo Christofoletti, Univ of FL **Scribe 1:** Xiaojun Ren, Novartis **Scribe 2:** Eleftheria Tsakalozou, FDA
3:00-4:00 pm	**Break for participants* (snacks and beverages provided-60 min)**	
3:00-4:00 pm	*Moderators & Scribes prepare Breakout session output	
4:00-4:50 pm *Room 1400*	**Feedback from BO Sessions A- E**	**Speakers:** All Moderators and Scribes from five BO sessions (10 min per session)
4:50-5:20 pm *Room 1400*	**All faculty and OC members meet to debrief/next steps**	
5:20 pm	End Day 1	

Wednesday 30 August WORKSHOP AGENDA: Morning Session

PBBM Base Models, Model Validation and Application Steps
Morning Sessions: Regulators Discussion of Established PBBM Case Studies
Afternoon: Hot Topics/Breakout Sessions: Considerations for PBBM Models

Time	Event	Speaker
8:00-9:30 am	**Light Breakfast**	
	Moderators: Kimberly Raines, FDA Tycho Heimbach, Merck & Co *The morning session will be held in Room 1400 Ballroom*	
9:00-9:15 am	Welcome Day 2	**Speakers:** Tycho Heimbach, Merck & Co. Kimberly Raines, FDA
9:15-9:30 am	**PBBM case study**	**Speaker:** Tycho Heimbach, Merck & Co.
9:30-9:45 am	**Regulatory Discussion/ Case Study 5** Focus: Data Inputs and Collection	**Speaker:** Mary Malamatari, MHRA
9:50-10:10 am	**Regulatory Discussion/ Case Study 4** Focus: Base Model Development	**Speaker:** Luiza Borges, ANVISA
10:10-10:30 am	**Regulatory Discussion/ Case Study 6** Focus: Model Validation and Application	**Speaker:** Shinichi Kijima, PMDA
10:30-10:45 am	**Break (beverages provided-15 min)**	
10:45-11:45 am	Roundtable discussions on Day 2 case studies ***(60 min)*** **Focus areas** Model Validation, PK and data inputs, IV and oral data, preclinical data scaling. Independent clinical data use, non-BE, Interpolation/Extrapolation	**Regulators:** Rebecca Moody, FDA Luiza Borges, ANVISA Mary Malamatari, MHRA Flora Musuamba Tshinanu, Belgium FAMHP Shereeni Veerasingham, HC Shinichi Kijima, PMDA Paul Seo, FDA **Moderators**: Tycho Heimbach, Merck & Co Claire Mackie, Janssen
11:45 am-1:00 pm	**Lunch (provided-75 min)**	

Wednesday 30 August WORKSHOP AGENDA: Afternoon Session

Time	Event	Speaker
1:00-1:30 pm *Room 1032*	**Hot topic F: Considerations for model development: data inputs, disposition, and absorption parameters, dealing with sparse data**	**Speakers (10 min each)**: Tycho Heimbach, Merck & Co. David Turner, Certara Rebecca Moody, FDA
1:30-3:00 pm *Room 1032*	**Breakout Session F**	**Moderator 1:** Lanyan (Lucy) Fang, FDA **Moderator 2:** Cordula Stillhart, Roche **Scribe 1:** Philip Bransford, Vertex **Scribe 2:** Xiaojun Ren, Novartis
1:00-1:30 pm *Room 1400*	**Hot topic G: Considerations for model validation, model acceptance/verification criteria in PBBM in view of available clinical data and model risks (impact and consequences)**	**Speaker:**: Min Li, FDA
1:30-3:00 pm *Room 1400 & 2032*	**Breakout Session G** *Discussion group will be split into two rooms*	**Moderator 1:** Shereeni Veerasingham, HC **Moderator 2:** Nikunj Patel, Certara **Scribe 1:** David Sperry, Eli Lilly **Scribe 2:** Hansong Chen, FDA
1:00-1:30 pm *Room 1042*	**Hot topic H: Considerations for model application: VBE trials vs. single representative modeling, dealing with within and between subjects variability and parameter uncertainty**	**Speakers (15 min each)**: Amin Rostami, Univ. of Manchester Viera Lukacova, Simulations Plus
1:30-3:00 pm *Room 1042*	**Breakout Session H**	**Moderator 1:** Duxin Sun, Univ. of Michigan **Moderator 2:** Jean-Flaubert Nguefack, Sanofi **Scribe 1:** Tessa Carducci, Merck & Co **Scribe 2:** Manuela Grimstein, FDA
1:00-1:30 pm *Room 1052*	**Hot topic I: Considerations for model application: Establishing safe space and failure edges, non-BE batches and alternative IVIVR/C**	**Speakers (10 min each)**: Xavier Pepin, Simulations Plus Konstantinos Stamatopoulos, GSK Siri Kalyan Chirumamilla, Certara
1:30-3:00 pm *Room 1052*	**Breakout Session I**	**Moderator 1:** Haritha Mandula, FDA **Moderator 2:** Rob Ju, Abbvie **Scribe 1:** Michael Wang, Merck & Co **Scribe 2:** Joan Zhao, FDA
3:00-3:35 pm	**Break* (snacks and beverages provided-35 min)**	
3:00-3:35 pm	*Moderators & Scribes prepare Breakout session output	
3:35-4:30 pm *Room 1400*	**Feedback from BO Sessions F- I**	**Speakers:** All Moderators and Scribes from five BO sessions (10 min per session)
4:30 pm	End Day 2	

Thursday 31 August WORKSHOP AGENDA: Morning Session

Applications of PBBM - Current State & New Horizons
Morning Sessions: Presentations on Current and Future Applications of PBBM
Afternoon: Hot Topics/Breakout Sessions: Applications of PBBM

Time	Event	Speaker
7:30-9:00 am	**Light Breakfast**	
	Moderators: Bhagwant Rege, FDA Amitava Mitra, Kura Oncology Mary Malamatari MHRA *The morning session will be held in Room 1400 Ballroom*	
8:30-8:40 am	Welcome Day 3	**Speakers:** Bhagwant Rege, FDA Amitava Mitra, Kura Oncology
8:40-9:05 am	**Application of PBBM in generic product development**	**Speaker (virtual):** Sivacharan Kollipara, Dr. Reddy's Lab
9:05-9:30 am	**OGD perspective on PBBM applications for generics**	**Speaker:** Fang Wu, FDA
9:30-9:55 am	**Application of virtual BE trials to support formulation bridging**	**Speaker:** Claire Mackie, Janssen
9:55-10:25 am	**Break (beverages provided-30 min)**	
10:25-10:50 am	**Utility of the advanced oral absorption modeling for clinical pharmacology assessment**	**Speaker:** Miyoung Yoon, FDA
10:50-11:15 am	**Prediction of regional/colon absorption & MR drug product performance**	**Speaker:** Christer Tannergren, AstraZeneca
11:15 am-12:15 pm	**Application of PBBM in regulatory submissions – Clinical, NDA/MAA & post approval**	**Speakers: (10 min each)** Kimberly Raines, FDA Luiza Borges, ANVISA Mary Malamatari, MHRA Evangelos Kotzagiorgis, EMA Shereeni Veerasingham, HC Hiroyuki Tsuji, PMDA
12:15–1:00 pm	**Lunch (provided-45 min)**	

Thursday 31 August WORKSHOP AGENDA: Afternoon Session

Time	Event	Speaker
1:00-1:30 pm *Room 1032*	**Hot topic K: Introduction & case study on application of PBBM for generics**	**Speaker:** Yunming Xu, FDA
1:30-3:00 pm *Room 1032*	**Breakout Session K: PBBM in generics drug product development**	**Moderator 1:** Yi-Hsien Cheng, FDA **Moderator 2:** Rajendra Singh, Teva **Moderator 3:** Maitri Sanghavi, Certara **Scribe:** Rajesh Savkur, FDA **Scribe:** Martin Hingle, Novartis
1:00-1:30 pm *Room 1042*	**Hot topic L: Introduction & case study on virtual BE applications**	**Speaker:** Amitava Mitra, Kura Oncology
1:30-3:00 pm *Room 1042*	**Breakout session L: Virtual BE applications**	**Moderator 1:** Andrew Babiskin, FDA **Moderator 2:** Amitava Mitra, Kura Oncology **Scribe 1:** Parnali Chatterjee, FDA **Scribe 2:** Erik Sjögren, Pharmetheus
1:00-1:30 pm *Room 1400*	**Hot topic M: Introduction & case study on safe space & extrapolation**	**Speaker:** Sandra Suarez-Sharp, Simulations Plus
1:30-3:00 pm *Room 1400 & 2032*	**Breakout Session M: Safe space & extrapolation** *Discussion group will be split into two rooms*	**Moderator 1:** Kimberly Raines, FDA **Moderator 2:** Sandra Suarez-Sharp, Simulations Plus **Scribe 1:** Kevin Wei, FDA **Scribe 2:** André Dallmann, Bayer
1:00-1:30 pm *Room 1052*	**Hot topic N: Introduction & case study on MR PBBM applications**	**Speaker:** Rebecca Moody, FDA
1:30-3:00 pm *Room 1052*	**Breakout Session N: Regional absorption & MR PBBM applications**	**Moderator 1:** Anitha Govada, FDA **Moderator 2:** Christer Tannergren, AstraZeneca **Scribe 1:** Anders Lindahl, Swedish MPA **Scribe 2:** Sherin Thomas, FDA
3:00-3:35 pm	**Break* (snacks and beverages provided-35 min)**	
3:00-3:35 pm	*Moderators & Scribes prepare Breakout session output	
3:35-4:20 pm *Room 1400*	**Feedback Breakout Sessions K-N**	**Speakers:** All Moderators and Scribes from four BO sessions (~10 min per session)
4:20-4:35 pm *Room 1400*	**Concluding Remarks**	**Speaker:** Greg Rullo, AstraZeneca
End of meeting 4:35-5:20 pm	**Faculty & OC members meet to debrief/agree next steps**	