FDA/M-CERSI Physiologically Based Biopharmaceutics Modeling, PBBM Best Scientific Practices to Drive Drug Product Quality: Latest Regulatory and Industry Perspectives
(*draft agenda*)
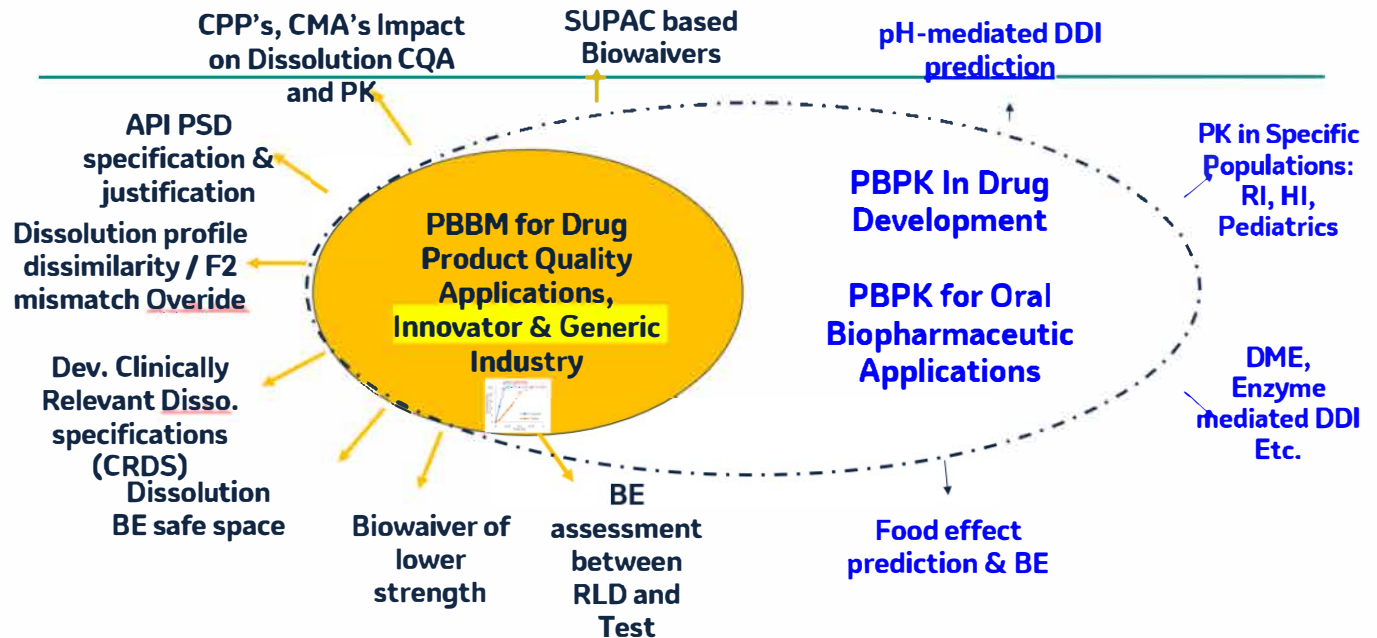**Tuesday 29 August – Thursday 31 August**
University of Maryland, Baltimore School of Pharmacy, M-CERSI
Location: Universities at Shady Grove (Rockville, MD)

www.pharmacy.umaryland.edu/PBBM2023

What is PBBM?

PBBM (Subset of PBPK) Examples in Oral Formulation Development

Modified from: Yuvaneshwari K., Kollipara, S. et al., *Journal of Drug Delivery Science and Technology*, 2022. **69**: p. 103152
Wu, Heimbach et.al, Pharm Res. 2022 Jul 15. doi: 10.1007/s11095-022-03319-6.

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
7:30-8:30 am	**Registration**	
	Session Moderators: Paul Seo, FDA Sumit Arora, Janssen	
8:30-8:40 am	**Welcome & Workshop Objective**	**Speaker:** Bhagwant Rege, FDA
8:40-9:10 am	**PBBM Impact & Future perspective**	**Keynote Speaker:** Jennifer Dressman, Fraunhofer Institute for Translational Medicine and Pharmacology ITMP
9:10-9:40 am	**Regulators Discussion of case study 1**	**Speaker:** Shereeni Veerasingham, HC
9:40-10:10 am	**Regulators Discussion of case study 2**	**Speaker:** Evangelos Kotzagiorgis, EMA
10:10-10:30 am	**Break**	
10:30-11:00 am	**Regulators Discussion of case study 3**	**Speaker:** Shinichi Kijima, PMDA
11:00-11:45 am	**Round table discussion on case studies** *(45 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 Evangelos Kotzagiorgis, EMA Shereeni Veerasingham, HC Shinichi Kijima, PMDA **Moderators:** Paul Seo, FDA Sumit Arora, Janssen
11:45 am-12:15 pm	PBBM case study *30 min*	**Speaker:** Mario Cano Vega, Amgen
12:15-1:00 pm	**Lunch**	

Tuesday 29 August WORKSHOP AGENDA: Afternoon Session

Time	Event	Speaker
1:00 -1:15 pm	Introduction to Breakout Sessions A-E: **Day 1: Considerations for in vitro data inputs to PBBM** **Speaker**: Sandra Suarez Sharp, Simulations Plus	
1:15-1:45 pm	**Hot topic A: Solubility:** *From in vitro best practices to in vivo relevance*	**Speaker**: Deanna Mudie, Lonza
1:45-3:45 pm	**Breakout Session A:** *Best practices for solubility as input to PBBM*	**Moderator 1:** Evangelos Kotzagiorgis, EMA **Moderator 2:** Claire Mackie, **Scribe 1:** Tessa Carducci, Merck **Scribe 2:** Mario Cano Vega, Amgen
1:15-1:45 pm	**Hot topic B:** *Development of biopredictive dissolution methods*	**Speaker**: Raimar Loebenberg, University of Alberta
1:45-3:45 pm	**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
1:15-1:45 pm	**Hot topic C:** *Methods for integrating dissolution in PBBM*	**Speaker**: Xavier Pepin, Simulations Plus
1:45-3:45 pm	**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:** Sundeep Dhareshwar, Novartis **Scribe 2:** Shruthi Vaidhyanathan, BMS
1:15-1:45 pm	**Hot topic D:** *Precipitation: From in vitro best practices to in vivo relevance*	**Speaker**: Christian Wagner, Merck group
1:45-3:45 pm	**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
1:15-1:45 pm	**Hot topic E:** *Permeability: From in vitro best practices to in vivo relevance*	**Speaker**: Hans Lennernäs, Uppsala University
1:45-3:45 pm	**Breakout Session E:** *Best practices for integration of permeability in PBBM*	**Moderator 1:** Christer Tannergren, AZ **Moderator 2:** Rodrigo Christofoletti, U of FL **Scribe 1:** Xiaojun Ren, Novartis **Scribe 2:** Eleftheria Tsakalozou, FDA
3:45-4:40 pm	**Break for participants***	
3:45-4:40 pm	*Moderators & Scribes prepare Breakout session output	
4:40-5:30 pm	**Feedback from BO sessions A, B, C, D and E**	**Speakers:** All moderators and scribes from 5 BO sessions (10 min per session)
5:30-6:00 pm	**All faculty and OC members meet to debrief/next steps**	
6:00 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
	Moderators: Kimberly Raines, FDA Tycho Heimbach, Merck & Co	
8:30-8:40 am	Welcome Day 2	**Speakers:** Tycho Heimbach, Merck & Co. Kimberly Raines, FDA
8:40-9:10 am	**Regulatory Discussion/ Case Study 5** *Focus: Data Inputs and Collection*	**Speaker**: Mary Malamatari, MHRA
9:10-9:40 am	**Regulatory Discussion/ Case Study 4** *Focus: Base Model Development*	**Speaker:** Luiza Borges, ANVISA
9:40-10:00 am	**Break**	
10:00-10:30 am	**Regulatory Discussion/ Case Study 6** *Focus: Model Validation and Application*	**Speaker:** Rebecca Moody, FDA
10:30-11:15 am	Roundtable Discussions on Day 2 case studies *(45 min)* **Focus areas** *Model Validation, PK and data inputs, IV and oral data, preclinical data scaling. Independent clinical data use, non-BE*	**Regulators:** Rebecca Moody, FDA Luiza Borges, ANVISA Mary Malamatari, MHRA Evangelos Kotzagiorgis, EMA Shereeni Veerasingham, HC Shinichi Kijima, PMDA Paul Seo, FDA **Moderators:** Tycho Heimbach, Merck & Co Claire Mackie, Janssen
11:15-11:45 am	PBBM case study	**Speaker:** Tycho Heimbach, Merck & Co.
11:45 am-12:30 pm	**Lunch**	
1:00-1:15 pm	Introduction to Breakout Sessions F-I: ***Day 2: PBBM Base Models, Model Validation and Application Steps***	**Speaker**: Liang Zhao, FDA
1:15-1:45 pm	**Hot topic F:** *Considerations for model development: data inputs, disposition and absorption parameters, dealing with sparse data.*	**Speakers**: Tycho Heimbach, Merck & Co. David Turner, Certara Kimberly Raines, FDA *10 min each*
1:45-3:30 pm	**Breakout session F**	**Moderator 1:** Lanyan (Lucy) Fang, FDA **Moderator 2:** Cordula Stillhart, Roche **Scribe 1:** Philip Bransford, Vertex **Scribe 2:** Xiaojun Ren, Novartis
1:15-1:45 pm	**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 Luiza Borges, ANVISA *15 min each*

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
1:45-3:30 pm	**Breakout session G**	**Moderator 1:** Shereeni Veerasingham, HC **Moderator 2:** Nikunj Patel, Certara **Scribe 1:** David Sperry, Eli Lilly **Scribe 2:** Hansong Chen, FDA
1:15-1:45 pm	**Hot topic H:** *Considerations for model application: VBE trials vs. single representative modeling, dealing with within and between subjects variability and parameter uncertainty*	**Speakers**: Amin Rostami, University of Manchester Viera Lukacova, Simulations Plus *15 min each*
1:45-3:30 pm	**Breakout session H**	**Moderator 1:** Duxin Sun, University of Michigan **Moderator 2:** Jean-Flaubert Nguefack, Sanofi **Scribe 1:** Tessa Carducci, Merck & Co **Scribe 2:** Manuela Grimstein, FDA
1:15-1:45 pm	**Hot topic I:** *Considerations for model application: Establishing safe space and failure edges, non-BE batches and alternative IVIVR/C*	**Speakers**: Xavier Pepin, Simulations Plus Konstantinos Stamatopoulos, GSK Siri Kalyan Chirumamilla, Certara
1:45-3:30 pm	**Breakout session I**	**Moderator 1:** Haritha Mandula, FDA **Moderator 2:** Rob Ju, Abbvie **Scribe 1:** TBD **Scribe 2:** Nadia Ahmed, FDA
1:15-1:45 pm	**Hot topic J:** *Challenges and opportunities for sharing model files upon regulatory use – What can be Model Master File and how to share it?*	**Speakers**: Sumit Arora, Janssen Andrew Babiskin, FDA
1:45-3:30 pm	**Breakout session J**	**Moderator 1:** Sumit Arora, Janssen **Moderator 2:** Andrew Babiskin, FDA **Scribe 1:** Greg Rullo, AstraZeneca **Scribe 2:** Eleftheria Tsakalozou, FDA
3:30-4:30 pm	**Break** Moderators & Scribes prepare Breakout session output	
4:30-5:20 pm	**Feedback from BO sessions F, G, H, I, J**	**Speakers:** All moderators and scribes from 5 BO sessions (10 min per session)
5:20-6:00 pm	**Round Table Discussion**, Considerations for PBBM and Model Review Template	**All Attendees (draft document will be provided ahead of the meeting)**
	End Day 2	

Thursday 31 August WORKSHOP AGENDA: Morning Session

Applications of PBBM - Current State & New Horizons
Objective: Focus on sharing & maximizing current as well as future applications of PBBM

Time	Event	Speaker
	Moderators: Bhagwant Rege, FDA Amitava Mitra, Kura Oncology Mary Malamatari, MHRA	
8:30-8:40 am	Welcome Day 3	**Speakers:** Bhagwant Rege FDA Amitava Mitra, Kura Oncology
8:40-9:40 am	**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 Shreeni Veerasingham, HC Shinichi Kijima, PMDA
9:40-10:10 am	**Application of Virtual BE Trials to support formulation bridging**	**Speaker:** Claire Mackie, Janssen
10:10-10:30 am	**Break**	
10:30-11:00 am	**Application of PBBM in generic product development**	**Speaker:** Sivacharan Kollipara, Dr. Reddy's Lab (virtual)
11:00-11:30 am	**OGD perspective on PBBM applications for generics**	**Speaker:** Fang Wu, FDA
11:30 am-12:00 pm	**Utility of the advanced oral absorption modeling for clinical pharmacology assessment**	**Speaker:** Miyoung Yoon, FDA
12:00-12:30 pm	**Prediction of Regional/Colon absorption & MR drug product performance – Recent learnings**	**Speaker:** Christer Tannergren, AstraZeneca
12:30–1:15 pm	**Lunch**	

Thursday 31 August WORKSHOP AGENDA: Afternoon Session

Applications of PBBM - Current State & New Horizons
Objective: Focus on sharing & maximizing current as well as future applications of PBBM

Time	Event	Speaker
	Moderators: Bhagwant Rege, FDA Amitava Mitra, Kura Oncology Mary Malamatari, MHRA	
1:15-1:30 pm	Introduction to Breakout sessions J-M **Day 3: Applications of PBBM and VBE**	**Speaker:** Mary Malamatari, MHRA
1:30-2:00 pm	Hot topic K: *Introduction & Case Study on application of PBBM for generics*	**Speaker:** Joan Zhao, FDA
2:00-3:45 pm	**Breakout session K:** *PBBM in generics drug product development*	**Moderator 1:** Yi-Hsien Cheng, FDA **Moderator 2:** TBD **Scribe 1:** Anders Lindahl, EMA (MPA Sweden) **Scribe 2:** Rajesh Savkur, FDA
1:30-2:00 pm	**Breakout session L:** *Introduction & case study on virtual BE applications*	**Speaker:** Amitava Mitra, Kura Oncology
2:00-3:45 pm	**Breakout session L:** *Virtual BE applications*	**Moderator 1:** Andrew Babiskin, FDA **Moderator 2:** Amitava Mitra, Kura Oncology **Scribe 1:** Yunming Xu, FDA **Scribe 2:** Erik Sjögren, Pharmetheus
1:30-2:00 pm	Hot topic M: *Introduction & case study on safe space & extrapolation*	**Speaker:** Sandra Suarez-Sharp, Simulations Plus
2:00-3:45 pm	**Breakout session M:** *Safe space & extrapolation*	**Moderator 1:** Kimberly Raines, FDA **Moderator 2:** Sandra Suarez-Sharp, Simulations Plus **Scribe 1:** Kevin Wei, FDA **Scribe 2:** André Dallmann, Bayer
1:30-2:00 pm	Hot topic N: *Introduction & case study on MR PBBM applications*	**Speakers:** Rebecca Moody, FDA
2:00-3:45 pm	**Breakout session N:** *Regional absorption & MR PBBM applications*	**Moderator 1:** Anitha Govada, FDA **Moderator 2:** Christer Tannergren, AstraZeneca **Scribe 1:** Mirko Koziolek, Abbvie **Scribe 2:** Sherin Thomas, FDA
3:45-4:45 pm	**Break**	
4:45–5:30 pm	Summary & Feedback Breakout Sessions K-N	**Speakers:** Breakout session Moderators & Scribes
5:30–5:45 pm	**Concluding Remarks**	**Speaker:** Greg Rullo, AstraZeneca
End of meeting 5:45-6:30 pm	**Faculty & OC members meet to debrief/agree next steps**	