Best Practices for Utilizing Modeling Approaches to Support Generic Product Development

Virtual Public Workshop
October 27th and 28th
2022

Agenda

Quantitative methods and modeling approaches have been increasingly utilized by the generic drug industry and regulatory agencies, including the Food and Drug Administration (FDA), to support generic product development and regulatory assessments. These quantitative methods and modeling involve mechanistic modeling such as physiologically based pharmacokinetic (PBPK) modeling and computational fluid dynamics (CFD) modeling, quantitative clinical pharmacology tool sets such as population pharmacokinetics (PPK) approaches, and advanced data analytics methodologies. Quantitative methods, modeling, and simulation approaches are being utilized to support alternative bioequivalence (BE) approaches and to minimize the burden of (or even alleviate the need for) in vivo BE studies.

The purpose of this workshop is to discuss how to modernize approaches for efficiently demonstrating BE, to establish their role in modern paradigms of generic drug development, and to explore and develop best practices for the use of modeling and simulation approaches in regulatory submissions and approval. This workshop will engage experts from regulatory agencies, the generic drug industry, consultants, academia, and others in the field of modeling and simulation to discuss the opportunities and best practices for incorporating modeling and simulation approaches into generic drug development programs and regulatory submissions. The workshop will also identify commonalities in methodologies/workflows or in silico models supporting alternative BE approaches and clarify how a model master file may be leveraged to advance drug product development, facilitate regulatory assessment, and streamline drug product approval.

FDA and the CRCG—which is a collaboration between the University of Maryland School of Pharmacy and the University of Michigan College of Pharmacy—are dedicated to advancing programs that stimulate scientific dialogue, disseminate current insights about complex generics, and generate new knowledge in support of FDA's mission by promoting and protecting the public health through increased access to safe and effective generic medicines.

GENERAL TOPICS THAT WILL BE THE FOCUS OF THE WORKSHOP:

- Use of model integrated evidence to support demonstrations of BE in a regulatory context
- Use of the same or similar model or modeling strategy across multiple submissions related to complex drug products
- Mechanistic modeling approaches supporting BE assessments for oral drug products
- Applications of quantitative comparative approaches to support the development of complex generic drug products
- Case examples supporting the recently introduced concept of "model master files"

Day 1: October 27, 2022

8:15 AM – 8:25 AM	**Welcome and Opening Remarks**	
	James Polli, PhD	Co-Director, CRCG
	Anna Schwendeman, PhD	Co-Director, CRCG
8:25 AM – 8:35 AM	**Opening Remarks**	
	Robert Lionberger, PhD	Director, ORS, OGD, CDER, FDA
8:35 AM – 8:40 AM	**Workshop Day 1 Overview**	
	Eleftheria Tsakalozou, PhD	Sr. Pharmacologist, DQMM, ORS, OGD, CDER, FDA
Symposium I:	***Modeling Best Practices for Generic Drug Development***	
Session 1:	**Experience Learned and Perspectives on Using Model Integrated Evidence (MIE) in the Regulatory Context**	
8:40 AM – 8:55 AM	***MIE for BE Evaluation to Support Generic Drug Development and Regulatory Approval***	
	Lanyan (Lucy) Fang, PhD	Deputy Director, DQMM, ORS, OGD, CDER, FDA
8:55 AM – 9:10 AM	***An Update of the Model-Informed Drug Development (MIDD) Program to Support New Drug Development***	
	Youwei Bi, PhD	Team Lead, DPM, OCP, OTS, CDER, FDA
9:10 AM – 9:25 AM	***EMA Experience on Model-Based BE for Generics***	
	Michiel van den Heuvel, MSc	Pharmacokinetics Assessor, Medicines Evaluation Board
9:25 AM – 10:25 AM	***Live Panel Discussion***	
Moderators:	**Liang Zhao, PhD**	Director, DQMM, ORS, OGD, CDER, FDA
	Eleftheria Tsakalozou, PhD	Sr. Pharmacologist, DQMM, ORS, OGD, CDER, FDA
Panelists:	**Tausif Ahmed, PhD**	VP & Head, Biopharmaceutics & Bioequivalence, Global Clinical Management, Dr. Reddy's Laboratories
	Pradeep Bhadauria, MPharm	President & Global CSO, Cipla
	Youwei Bi, PhD	Team Lead, DPM, OCP, OTS, CDER, FDA
	Lanyan (Lucy) Fang, PhD	Deputy Director, DQMM, ORS, OGD, CDER, FDA
	Robert Lionberger, PhD	Director, ORS, OGD, CDER, FDA
	Amin Rostami, PhD	Prof. of Systems Pharmacology & Director of CAPKR, Univ. of Manchester
	Yu Chung Tsang, PhD	CSO, Biopharmaceutics & Biostatistics, Global Regulatory Affairs, Apotex
	Michiel van den Heuvel, MSc	Pharmacokinetics Assessor, Medicines Evaluation Board
10:25 AM – 10:40 AM	***Coffee Break***	
Session 2:	**Use of the Same Model or Modeling Strategy Across Multiple Submissions: Focus on Complex Drug Products**	
10:40 AM – 11:00 AM	***Regulatory Perspective on Modeling Strategies Across Multiple Submissions***	
	Andrew Babiskin, PhD	Team Lead, DQMM, ORS, OGD, CDER, FDA
	Miyoung Yoon, PhD	Team Lead, DQMM, ORS, OGD, CDER, FDA
11:00 AM – 11:20 AM	***Utilizing Mechanistic Dermal Absorption Models to Assess Virtual BE***	
	James F. Clarke, PhD	Sr. Research Scientist, Simcyp Division, Certara
11:20 AM – 11:40 AM	***Utilizing M&S Approaches to Support Regulatory Submission for Orally Inhaled Drug Products: Case Examples***	
	Marc Kelly, BSc	Sr. Manager Materials Science, Global Inhalation R&D, Teva
11:40 AM – 12:00 PM	***Ophthalmic Drug Products: Leveraging M&S Approaches to Perform Inter-Species Predictions and Support Drug Product Development and Approval***	
	Maxime Le Merdy, PharmD	Sr. Scientist, Simulations Plus
12:00 PM – 12:20 PM	***MIE for BE Assessment of Long-Acting Injectable Products: In Silico Continuation to Steady State***	
	Murray Ducharme, PharmD	President & CEO, Learn and Confirm Inc./Prof. Associé, Univ. of Montreal
12:20 PM – 1:20 PM	***Lunch Break***	
1:20 PM – 2:20 PM	***Live Panel Discussion***	
Moderators:	**Ross Walenga, PhD**	Chemical Engineer, DQMM, ORS, OGD, CDER, FDA
	Partha Roy, PhD	Director, OB, OGD, CDER, FDA
Panelists:	**Andrew Babiskin, PhD**	Team Lead, DQMM, ORS, OGD, CDER, FDA
	Sid Bhoopathy, PhD	Sr. VP & Head, Pharmaron US Lab Services and CGT
	Jan De Backer, PhD	CEO, FLUIDDA INC.
	Murray Ducharme, PharmD	President & CEO, Learn and Confirm Inc./Prof. Associé, Univ. of Montreal
	James F. Clarke, PhD	Sr. Research Scientist, Simcyp Division, Certara
	Marc Kelly, BSc	Sr. Manager Materials Science, Global Inhalation R&D, Teva
	Maxime Le Merdy, PharmD	Sr. Scientist, Simulations Plus
	Miyoung Yoon, PhD	Team Lead, DQMM, ORS, OGD, CDER, FDA

Session 3:	**Using Mechanistic Modeling Approaches to Support BE Assessments for Oral Products**	
2:20 PM – 2:40 PM	***Using PBPK Model to Support Risk Assessment for Oral Products, from a Regulatory Perspective***	
	Fang Wu, PhD	Sr. Pharmacologist & Scientific Lead, DQMM, ORS, OGD, CDER, FDA
2:40 PM – 3:00 PM	***PBPK Modeling to Support Risk Assessment for Oral Drug Products, Including Waiver of Fed BE Studies***	
	Rebeka Jereb, PhD	Scientist, Clinical Development, Sandoz
3:00 PM – 3:20 PM	***Oral PBPK to Support BE Evaluation for Pediatric Drugs***	
	Hannah Batchelor, PhD	Prof., Strathclyde Institute of Pharmacy and Biomedical Sciences, Univ. of Strathclyde
3:20 PM – 3:40 PM	***Approaches in Establishing BE Safe Space for Oral Solid Dosage Form***	
	Sumon Chakraborty, MPharm	Scientific Leader, Biowaiver & Biocorrelation, Apotex
3:40 PM – 3:55 PM	***Coffee Break***	
3:55 PM – 4:55 PM	***Live Panel Discussion***	
Moderators:	**Tycho Heimbach, PhD**	Biopharmaceutics Expert/Director, Biopharmaceutics & Specialty Dosage Group, Merck
	Ethan Stier, PhD	Associate Director, Lifecycle Management, OCP, OTS, CDER, FDA
Panelists:	**Hannah Batchelor, PhD**	Prof., Strathclyde Institute of Pharmacy and Biomedical Sciences, Univ. of Strathclyde
	Sumon Chakraborty, MPharm	Scientific Leader, Biowaiver & Biocorrelation, Apotex
	Rebeka Jereb, PhD	Scientist, Clinical Development, Sandoz
	Filippos Kesisoglou, PhD	Distinguished Scientist, Merck
	Myong-Jin (MJ) Kim, PharmD	Director, DTP-II, ORS, OGD, CDER, FDA
	Sivacharan Kollipara, MPharm	Team Lead, Biopharmaceutics, Dr. Reddy's Laboratories
	Fang Wu, PhD	Sr. Pharmacologist & Scientific Lead, DQMM, ORS, OGD, CDER, FDA
	Yuching Yang, PhD	Co-Lead of PBPK Program, DPM, OCP, OTS, CDER, FDA
	Lei Zhang, PhD	Deputy Director, ORS, OGD, CDER, FDA
4:55 PM – 5:05 PM	**Closing Remarks**	
	Lanyan (Lucy) Fang, PhD	Deputy Director, DQMM, ORS, OGD, CDER, FDA

Day 2: October 28, 2022

9:00 AM – 9:05 AM	**Workshop Day 2 Overview**	
	Yuqing Gong, PhD	Pharmacologist, DQMM, ORS, OGD, CDER, FDA
Symposium I/Session 4:	**Development of Quantitative Comparative Approaches to Support Complex Generic Drug Development**	
9:05 AM – 9:25 AM	***Use of Data Analytics Approaches to Support Regulatory Assessment - FDA Perspective***	
	Meng Hu, PhD	Team Lead, DQMM, ORS, OGD, CDER, FDA
9:25 AM – 9:45 AM	***Challenges in Demonstrating API Sameness for Drug Product with Complex APIs***	
	Francis-Xavier Barretto, MSc	CSO, Swati Spentose Pvt. Ltd.
9:45 AM – 10:05 AM	***Statistical Experience and Challenges in Similarity Assessment of Dissolution Profile, Particle Size Distribution, and Drug Products with Complex APIs***	
	Yi Tsong, PhD	Director, DB-VI, OB, OTS, CDER, FDA
10:05 AM – 10:25 AM	***Evaluation of Dissolution Profile Similarity for BE Assessment***	
	Youssef Mousa, PhD	Pharmacologist, DQMM, ORS, OGD, CDER, FDA
10:25 AM – 10:40 AM	***Coffee Break***	
10:40 AM – 11:40 AM	***Live Panel Discussion***	
Moderators:	**Ke Ren, PhD**	Acting Deputy Director, DB-III, OB, OGD, CDER, FDA
	Yuqing Gong, PhD	Pharmacologist, DQMM, ORS, OGD, CDER, FDA
Panelists:	**Francis-Xavier Barretto, MSc**	CSO, Swati Spentose Pvt. Ltd.
	Meng Hu, PhD	Team Lead, DQMM, ORS, OGD, CDER, FDA
	Darby Kozak, PhD	Deputy Director, DTP-I, ORS, OGD, CDER, FDA
	Youssef Mousa, PhD	Pharmacologist, DQMM, ORS, OGD, CDER, FDA
	Meiyu Shen, PhD	Team Lead, DB-VI, Office of Biostatistics, OTS, CDER, FDA
	Yi Tsong, PhD	Director, DB-VI, Office of Biostatistics, OTS, CDER, FDA

	Liang Zhao, PhD	Director, DQMM, ORS, OGD, CDER, FDA
11:40 AM – 12:40 PM	***Lunch Break***	
Symposium II:	***Model Sharing, Acceptance, and Communication with FDA***	
12:40 PM – 1:00 PM	***Potential Types of Model Master Files***	
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, CDER, FDA
1:00 PM – 1:20 PM	***A Population PK Based Model-Integrated BE Platform***	
	Andrew Hooker, PhD	Prof. of Pharmacometrics, Dept. of Pharmacy, Uppsala Univ.
1:20 PM – 1:40 PM	***Building Mechanistic IVIVC***	
	Viera Lukacova, PhD	Chief Scientist, Simulations Plus
1:40 PM – 2:00 PM	***Improving Model Reusability via the Concept of Model Master File: What the Literature Data Tell Us***	
	Amin Rostami, PhD	Prof. of Systems Pharmacology & Director of CAPKR, Univ. of Manchester
2:00 PM – 2:15 PM	***Coffee Break***	
2:15 PM – 3:30 PM	***Live Panel Discussion***	
Moderators:	**Lanyan (Lucy) Fang, PhD**	Deputy Director, DQMM, ORS, OGD, CDER, FDA
	Mark Sale, MD	VP, IDD, Certara
Panelists:	**Stella Grosser, PhD**	Director, DB-VIII, Office of Biostatistics, OTS, CDER, FDA
	Andrew Hooker, PhD	Prof. of Pharmacometrics, Dept. of Pharmacy, Uppsala Univ.
	Rebeka Jereb, PhD	Scientist, Clinical Development, Sandoz
	Viera Lukacova, PhD	Chief Scientist, Simulations Plus
	Carl Peck, MD	Adjunct Prof., UCSF/Cofounder & Expert Consultant, NDA Partners/ProPharma
	Amin Rostami, PhD	Prof. of Systems Pharmacology & Director of CAPKR, Univ. of Manchester
	Rada Savic, PhD	Prof., School of Pharmacy and Medicine, UCSF
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, CDER, FDA
3:30 PM – 3:40 PM	**Closing Remarks**	
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, CDER, FDA

Appendix of Abbreviations

ANDA	Abbreviated New Drug Application
API	Active Pharmaceutical Ingredient
CAPKR	Centre for Applied Pharmacokinetic Research
CEO	Chief Executive Officer
CFD	Computational Fluid Dynamics
CSO	Chief Scientific Officer
CRCG	Center for Research on Complex Generics
BE	Bioequivalence
BSc	Bachelor of Science
DB	Division of Biopharmaceutics
DB-III	Division of Bioequivalence III
DB-VI	Division of Biostatistics VI
DB-VIII	Division of Biostatistics VIII
DPM	Division of Pharmacometrics
DQMM	Division of Quantitative Methods and Modeling
DTP-I	Division of Therapeutic Performance I
DTP-II	Division of Therapeutic Performance II
EMA	European Medicines Agency
FDA	United States Food and Drug Administration

IVIVC	In vitro – In Vivo Correlation
IDD	Integrated Drug Development
MD	Doctor of Medicine
MIE	Model Integrated Evidence
M&S	Modeling & Simulation
MSc	Master of Science
MPharm	Master of Sciences of Pharmacy
OB	Office of Bioequivalence
OCP	Office of Clinical Pharmacology
OGD	Office of Generic Drugs
ORS	Office of Research and Standards
OTS	Office of Translational Sciences
PBPK	Physiologically Based Pharmacokinetic
PharmD	Doctor of Pharmacy
PhD	Doctor of Philosophy
PPK	Population Pharmacokinetics
Prof.	Professor
R&D	Research and Development
Sr.	Senior
UCSF	University of California, San Francisco
Univ.	University
VP	Vice President