Considerations and Potential Regulatory Applications for a Model Master File

Hybrid Format: In person (at The Universities at Shady Grove; Rockville, MD) and virtual workshop
May 2-3, 2024

The purpose of this workshop is to engage stakeholders among model developers, industry, and FDA in a discussion on the concept, scope, and regulatory application of a Model Master File (MMF). The goals of this workshop are to illustrate how MMFs can improve the efficiency with which evidence from modeling and simulation (M&S) can facilitate drug product development. Additionally, the workshop will explore how M&S can increase efficiency in application assessment and consistency in regulatory use and acceptance of established models.

Agenda

May 2, Day 1

8:30 AM – 8:35 AM	**Welcome and CRCG Opening Remarks**	
	James Polli, PhD	Co-Director, CRCG
	Anna Schwendeman, PhD	Co-Director, CRCG
8:35 AM – 8:45 AM	**FDA Opening Remarks**	
	Iilun Murphy, MD	Director, OGD, FDA
8:45 AM – 8:50 AM	**Workshop Overview**	
	Lanyan (Lucy) Fang, PhD	Deputy Director, DQMM, ORS, OGD, FDA
8:50 AM – 9:20 AM	**Keynote Speaker**	
	Evolution of Pharmacometrics in Drug Development and Regulation	
	Carl Peck, MD	Adjunct Prof., UCSF/Cofounder & Expert Consultant, NDA Partners/ProPharma
	Clearing the Path for Modeling and Simulation in Drug Applications	
	Robert Lionberger, PhD	Director, ORS, OGD, FDA

Session 1: Defining the MMF Framework: Model Sharing-Model Acceptance-Model Communication
(Session Lead/SME: Dr. Eleftheria Tsakalozou)

In this session, regulators and industry presenters will provide a comprehensive and detailed description of the MMF framework, discuss considerations and challenges with implementing the MMF, and highlight how the MMF can facilitate the integration of M&S approaches into drug product development and regulatory assessments.

9:20 AM – 9:25 AM	***Introduction to Session and Speakers***	
	Eleftheria Tsakalozou, PhD	Senior Pharmacologist, DQMM, ORS, OGD, FDA
9:25 AM – 9:40 AM	***The Development and Framework of MMF as a Regulatory Initiative***	
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, FDA
9:40 AM – 9:55 AM	***Drawing Parallels Between DMFs and MMFs***	
	Erin Skoda, PhD	Supervisory Chemist, DPQA XVIII, OPQA III, OPQ, FDA
9:55 AM – 10:10 AM	***Model Development Lifecycle (MDLC) and Applications in Clinical Development. Implications for MMF***	
	Timothy Nicholas, PhD	Head of Tech. & Innovation, Pharmacometrics & Systems Pharmacology, Pfizer
10:10 AM – 10:25 AM	***Model Master File Framework in Generic Product Development: Challenges, Opportunities and Case Examples***	
	Sivacharan Kollipara, MPharm	Team Lead, Biopharmaceutics, Dr. Reddy's Laboratories Ltd.
10:25 AM – 10:55 AM	***Panel Discussion***	
Moderators:	**Lanyan (Lucy) Fang, PhD**	Deputy Director, DQMM, ORS, OGD, FDA
	Ke Ren, PhD	Deputy Director, DB III, OB, OGD, FDA
Panelists:	**Stella Grosser, PhD**	Director, DB VIII, OB, OTS, FDA
	Sivacharan Kollipara, MPharm	Team Lead, Biopharmaceutics, Dr. Reddy's Laboratories Ltd.

	Timothy Nicholas, PhD	Head of Tech. & Innovation, Pharmacometrics & Systems Pharmacology, Pfizer
	Bhagwant Rege, PhD	Director, DPQA VI, OPQA I, OPQ, FDA
	Partha Roy, PhD	Director, OB, OGD, FDA
	Erin Skoda, PhD	Supervisory Chemist, DPQA XVIII, OPQA III, OPQ, FDA
	Flora Musuamba Tshinanu, PhD	Professor, University of Namur; Belgian FAMHP
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, FDA
	Hao Zhu, PhD	Director, DPM, OCP, OTS, FDA
10:55 AM – 11:05 AM	***Coffee Break***	

Session 2: MMF Applications for Oral Dosage Forms

(Session Lead: Dr. Yi-Hsien Cheng; SME: Dr. Arindom Pal)

This session will offer case studies and discussions about situations in which an MMF can support product development and regulatory submissions for oral drug products.

11:05 AM – 11:10 AM	***Introduction to Session and Speakers***	
	Yi-Hsien Cheng, PhD	Pharmaceutical Scientist, DQMM, ORS, OGD, FDA
11:10 AM – 11:25 AM	***Regulatory Perspective of Model Master Files Utilities for Oral Drug Products***	
	Fang Wu, PhD	Senior Pharmacologist, DQMM, ORS, OGD, FDA
11:25 AM – 11:40 AM	***What is Additionally Recommended in MMF: Product Specific Component of the Model***	
	Yunming Xu, MS, PharmD	Biopharmaceutics Reviewer, DPQA VI, OPQA I, OPQ, FDA
11:40 AM – 11:55 AM	***Practical Considerations for Developing and Employing Model Master Files***	
	Nikunjkumar Patel, PhD	Senior Director of PBPK Consultancy, Certara Inc
11:55 AM – 12:10 PM	***Model Master File for Oral Dosage Forms: Important Considerations and Potential Applications***	
	Viera Lukacova, PhD	Chief Scientist, Simulations Plus, Inc.
12:10 PM – 12:20 PM	***PBBM/PBPK Model Considerations (Part 1): PBBM Global Workshop Summary***	
	Greg Rullo, MS	Executive Director CMC Regulatory Innovation, Astra Zeneca
12:20 PM – 12:30 PM	***PBBM/PBPK Model Considerations (Part 2): PBBM Template and Context of Use***	
	Tycho Heimbach, PhD, FAAPS	Senior Principal Scientist/Director, Merck Research Laboratories
12:30 PM – 1:15 PM	***Lunch Break***	
1:15 PM – 1:45 PM	***Panel Discussion***	
Moderators:	**Tycho Heimbach, PhD, FAAPS**	Senior Principal Scientist/Director, Merck Research Laboratories
	Rebecca Moody, PhD	Pharmaceutical Scientist, IO, OPQA II, OPQ, FDA
Panelists:	**Tausif Ahmed, PhD**	Vice President & Head, Biopharmaceutics and Bioequivalence, Global Clinical Management (GCM), Dr. Reddy's Laboratories Ltd., Hyderabad, India
	Essam Kerwash, MD, PhD	Senior Clinical Pharmacology Assessor, MHRA
	Viera Lukacova, PhD	Chief Scientist, Simulations Plus, Inc.
	Nikunjkumar Patel, PhD	Senior Director of PBPK Consultancy, Certara Inc
	Greg Rullo, MS	Executive Director CMC Regulatory Innovation, Astra Zeneca
	Fang Wu, PhD	Senior Pharmacologist and Scientific Lead, DQMM, ORS, OGD, FDA
	Yunming Xu, MS, PharmD	Biopharmaceutics Reviewer, DPQA VI, OPQA I, OPQ, FDA
1:45 PM – 1:55 PM	***Coffee Break***	

Session 3: MMF Applications for Long-Acting Injectable Drug Products

(Session Lead: Dr. Yuqing Gong; SME: Dr. Robert Hopefl)

This session will offer case studies and discussions about situations in which an MMF can support product development and regulatory submissions for long-acting injectable drug products.

1:55 PM – 2:00 PM	***Introduction to Session and Speakers***	
	Yuqing Gong, PhD	Pharmacologist, DQMM, ORS, OGD, FDA
2:00 PM – 2:15 PM	***Regulatory Utility of MMF for Development of LAI Drug Products***	
	Andrew Babiskin, PhD	Team Lead, DQMM, ORS, OGD, FDA

2:15 PM – 2:30 PM	***Bridging CQAs and Systemic Exposure of LAIs by Multiphysics Simulation***	
	Tonglei Li, PhD	Professor and Allen Chao Endowed Chair, Industrial and Molecular Pharmaceutics Department, Purdue University
2:30 PM – 2:45 PM	***Model-Based Bioequivalence Methods Serving as MMF for LAI Drug Products***	
	Andrew Hooker, PhD	Prof. of Pharmacometrics, Dept. of Pharmacy, Uppsala University, Sweden
2:45 PM – 3:00 PM	***Model Master File in the Context of LAI***	
	Daniela Silva, PhD	Scientist II, Simulations Plus, Inc
3:00 PM – 3:30 PM	***Panel Discussion***	
Moderator:	**Yuqing Gong, PhD**	Pharmacologist, DQMM, ORS, OGD, FDA
	Pratik Saha, PhD	Director, Biopharmaceutics, Drug Product Development, GlaxoSmithKline
Panelists:	**Khondoker Alam, PhD**	Senior Pharmacologist, DQMM, ORS, OGD, FDA
	Andrew Babiskin, PhD	Team Lead, DQMM, ORS, OGD, FDA
	Murray Ducharme, PharmD, FCCP	President and CEO, Learn and Confirm Inc, Montreal, Canada; Professor Associé, Faculté de Pharmacie, University of Montreal, Canada
	Andrew Hooker, PhD	Prof. of Pharmacometrics, Dept. of Pharmacy, Uppsala University, Sweden
	Tonglei Li, PhD	Professor and Allen Chao Endowed Chair, Industrial and Molecular Pharmaceutics Department, Purdue University
	Rebecca Moody, PhD	Pharmaceutical Scientist, IO, OPQA II, OPQ, FDA
	Daniela Silva, PhD	Scientist II, Simulations Plus, Inc
3:30 PM – 3:35 PM	**Closing Remarks for Virtual Attendees**	
	Lei K Zhang, PhD	Deputy Director, ORS, OGD, FDA
3:30 PM – 3:40 PM	***Coffee Break***	

Session 4: Small Group Discussions (in-person only)
(Moderator: Dr. Lanyan (Lucy) Fang)

3:40 PM – 3:50 PM	***Model Master File: Considerations on Development and Regulatory Role***	
	Eleftheria Tsakalozou, PhD	Senior Pharmacologist, DQMM, ORS, OGD, FDA

3:50 PM – 5:30 PM ***Discussion Topics***

- What are key considerations when developing an MMF in terms of its content and format?
- What are the potential benefits/incentives for stakeholders to develop and use a MMF for oral dosage forms and long acting injectables in the generics space?
- What are the considerations and overall input on two potential MMF case examples?

5:30 PM – 5:35 PM	**Closing Remarks for Day 1**	
	Lei K Zhang, PhD	Deputy Director, ORS, OGD, FDA

May 3, Day 2

8:30 AM – 8:40 AM	**Opening Remarks for Day 2**	
	Shiew Mei Huang, PhD	Deputy Director, OCP, OTS, FDA
8:40 AM – 8:45 AM	**Workshop Day 2 Overview**	
	Eleftheria Tsakalozou, PhD	Senior Pharmacologist, DQMM, ORS, OGD, FDA

Session 1: Pathways for Regulatory Acceptance of Dynamic Tools in the New Drug Space (Session Lead/SME: Dr. Jiang Liu)

This session will illustrate the pathways for regulatory acceptance of dynamic tools for new drug development. The session also includes a panel that will engage in discussing best practices for increasing the efficiency/reusability of models.

8:45 AM – 8:50 AM	***Introduction to Session and Speakers***	
	Jiang Liu, PhD	Associate Director for Therapeutic Review, DPM, OCP, OTS, FDA
8:50 AM – 9:10 AM	***A Brief Introduction on the Fit-For-Purpose Program***	
	Hao Zhu, PhD	Director, DPM, OCP, OTS, FDA
9:10 AM – 9:30 AM	***Current Practice in Model Evaluation and Assessment for PBPK Model's Reusability in New Drug Development***	
	Yuching Yang, PhD	Clinical Pharmacometrics Team Lead, DPM, OCP, OTS, FDA
9:30 AM – 9:50 AM	***Potential of Repeated Usage of Population PK Model to Support BE Assessment in New Drug Development***	
	Joga Gobburu, PhD, MBA	Professor, SOP and SOM, University of Maryland Baltimore
9:50 AM – 10:20 AM	***Panel Discussion***	
Moderators:	**Jiang Liu, PhD**	Associate Director for Therapeutic Review, DPM, OCP, OTS, FDA
Panelists:	**Joga Gobburu, PhD, MBA**	Professor, SOP and SOM, University of Maryland Baltimore
	Martin Klein, PhD	Senior Mathematical Statistician, DB VIII, OB, OTS, FDA
	Cynthia J. (CJ) Musante, PhD	VP, Scientific Research, Global Head, Pharmacometrics & Systems Pharmacology, Translational Clinical Sciences, Pfizer
	Yuching Yang, PhD	Clinical Pharmacometrics Team Lead, DPM, OCP, OTS, FDA
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, FDA
	Hao Zhu, PhD	Director, DPM, OCP, OTS, FDA
10:20 AM – 10:30 AM	***Coffee Break***	

Session 2: MMF Applications for Locally Acting Drug Products

This session will offer case studies and engage in discussions about situations in which an MMF can support product developme nt and regulatory submissions for locally acting drug products including orally inhaled drug products, drug products applied on the skin, and ophthalmic drug products.

10:30 AM – 10:35 AM	***Introduction to Session and Speakers***	
	Steven Chopski, PhD	Chemical Engineer, DQMM, ORS, OGD, FDA
10:35 AM – 10:50 AM	***Regulatory Perspective on MMF Applications for OIDPs, Ophthalmic Drug Products, and Drug Products Applied on the Skin***	
	Ross Walenga, PhD	Senior Chemical Engineer, DQMM, ORS, OGD, FDA
10:50 AM– 11:05 AM	***EMA Experience with Qualification of Modelling and Simulation Methods***	
	Flora Musuamba Tshinanu, PhD	Professor, University of Namur; Belgian FAMHP

Sub-session 2a: Orally Inhaled Drug Products (OIDP) (Session Lead: Dr. Ross Walenga)

11:05 AM – 11:20 AM	***Advancing Orally Inhaled Products Through Digital Twins and In-Silico Trials: Strategies for MMF Creation***	
	Jan De Backer, MSc, PhD, MBA	CEO, FLUIDDA
11:20 AM – 11:35 AM	***Physiologically-Based Biopharmaceutical Modelling in Virtual Comparative Clinical Endpoint Studies of Orally Inhaled Drugs***	
	Markus Fridén, PhD	Senior Principal Scientist, Biopharmaceutics, Inhalation Product Development, AstraZeneca

Sub-session 2b: Drug Products Applied on the Skin
(Session Lead: Dr. Eleftheria Tsakalozou)

11:35 AM – 11:50 PM	***Modeling Methodologies Integrating Diverse Data Sets to Support the Development and Approval of Dermatological Products***	
	Abdullah Hamadeh, PhD	Research Associate, School of Pharmacy, University of Waterloo, Canada
11:50 AM – 12:05 PM	***Development and Verification of Mechanistic Dermal Absorption Models for Submission in a Model Master File***	
	James F. Clarke, PhD	Associate Principal Scientist, Simcyp Division, Certara
12:05 PM – 12:55 PM	***Lunch Break***	
12:55 PM – 1:25 PM	***Panel Discussion***	
Moderator:	**Khondoker Alam, PhD**	Senior Pharmacologist, DQMM, ORS, OGD, FDA
	Sujatha Sonti, PhD	VP, Drug Product Development, R&D, Medicine Development & Supply, GlaxoSmithKline
Panelists:	**James F. Clarke, PhD**	Associate Principal Scientist, Simcyp Division, Certara
	Jan De Backer, MSc, PhD, MBA	CEO, FLUIDDA
	Markus Fridén, PhD	Senior Principal Scientist, Biopharmaceutics, Inhalation Product Development, AstraZeneca
	Abdullah Hamadeh, PhD	Research Associate, School of Pharmacy, University of Waterloo, Canada
	Jay Mowli, MS	Director, Scientific Affairs, Capstone Development Services Co, LLC
	Jessica Spires, PhD	Principal Scientist, Simulation Plus Inc
	Mingliang Tan, PhD	Senior Pharmacologist, DQMM, ORS, OGD, FDA
	Flora Musuamba Tshinanu, PhD	Professor, University of Namur; Belgian FAMHP
	Ross Walenga, PhD	Senior Chemical Engineer, DQMM, ORS, OGD, FDA
1:25 PM – 1:30 PM	**Closing Remarks for Virtual Attendees**	
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, FDA

Session 3: Small Group Discussions (in-person only)
(Moderator: Dr. Eleftheria Tsakalozou)

1:30 PM – 1:45 PM	***Spectrum of Model Master File Options: Commonalities, Differences, Range of Ownerships***	
	Amin Rostami-Hodjegan, PhD, FCP	Professor, Systems Pharmacology, CAPKR, University of Manchester, UK & Senior VP, R&D and CSO, Certara, Princeton, USA

1:45 PM – 3:30 PM ***Discussion Topics***

- What are the potential benefits/incentives for stakeholders to develop and use an MMF in the area of new drugs and generic locally acting drug products?
- What are relevant considerations in the MMF life cycle: MMF versioning?

3:30 PM – 3:40 PM	**Workshop Summation/Closing Remarks**	
	Liang Zhao, PhD	Director, DQMM, ORS, OGD, FDA

Appendix of Abbreviations

AAPS	American Association of Pharmaceutical Scientists
ADME	Absorption, Distribution, Metabolism, and Excretion
AIML	Artificial Intelligence and Machine Learning
ANDA	Abbreviated New Drug Application
Anvisa	Brazilian Health Regulatory Agency
ASCO	American Society of Clinical Oncology
ASCPT	American Society for Clinical Pharmacology and Therapeutics
BA	Bioavailability
BCS	Biopharmaceutics Classification System
BE	Bioequivalence
BE	Bachelor of Engineering
BLA	Biologics License Application
CAMD	Computer-aided Medical Diagnosis
CAPKR	Centre for Applied Pharmacokinetic Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CEO	Chief Executive Officer
CMC	Chemistry, Manufacturing, and Controls
CPP	Clinical Pharmacology and Pharmacometrics
CRCG	Center for Research on Complex Generics
CRO	Contract Research Organization
CRL	Complete Response Letter
CSO	Chief Scientific Officer
DB III	Division of Bioequivalence III
DB VIII	Division of Biostatistics VIII
Dept	Department
DMF	Drug Master Files
DMPK	Drug Metabolism and Pharmacokinetics
DPM	Division of Pharmacometrics
DPQA	Division of Product Quality Assessment
DRL	Dr. Reddy's Laboratories Limited
DQMM	Division of Quantitative Methods and Modeling
ETT	Emerging Technology Team
EU	European Union
FAAPS	Fellow of the American Association of Pharmaceutical Scientists
FAMHP	Belgian Federal Agency for Medicines and Health Products
FBPS	Fellow of the British Psychological Society
FBPhS	Fellowship British Pharmacological Society
FCCP	Fellowship in the American College of Clinical Pharmacy
FDA	United States Food and Drug Administration
FHEA	Fitzgerald Health Education Associates
FJSSX	Fellow of the Japanese Society for the Study of Xenobiotics

GCM	Global Clinical Management
GDUFA	Generic Drug User Fee Amendments
GI	Gastrointestinal
GLP	Good Laboratory Practice
HDL	High-Density Lipoprotein
ICCM	Institute of Computational Comparative Medicine
ICH	International Council for Harmonisation
IND	Investigational New Drug
IO	Immediate Office
IPDO	Integrated Product Development Organization
IQ	Innovation & Quality
ISoP	International Society of Pharmacometrics
ISI	Institute of Scientific Information
IVIVC	In Vitro In Vivo Correlations
IVIVE	In Vitro In Vivo Evaluations
Ltd.	Limited
LAI	Long Acting Injectable
MBA	Master of Business Administration
MBMA	Model Based Meta-Analysis
MD	Doctor of Medicine
MDLC	Model Development Lifecycle
MFPM	Member Faculty of Pharmaceutical Medicine
MHRA	Medicines and Healthcare Products Regulatory Agency
MIDD	Model Informed Drug Discovery and Development
MIT	Massachusetts Institute of Technology
MMF	Model Master File
MPharm	Masters of Pharmacy
M&S	Modeling and Simulation
MS or MSc	Master of Science
MWP	Methodology Working Party
NDA	New Drug Application
NIMH	National Institute of Mental Health
OB	Office of Biostatistics
OCP	Office of Clinical Pharmacology
OGD	Office of Generic Drugs
OIDP	Orally Inhaled Drug Product
OLDP	Office of Lifecycle Drug Product
OPQ	Office of Pharmaceutical Quality
OPQA	Office of Pharmaceutical Quality Assessment
ORS	Office of Research and Standards
ORISE	Oak Ridge Institute for Science and Education
OTC	Over the Counter
OTS	Office of Translational Sciences
PBBM	Physiologically Based Biopharmaceutics Modeling
PBPK	Physiologically Based Pharmacokinetic Modeling

PD	Pharmacodynamics
PharmD	Doctor of Pharmacy
PhD	Doctor of Philosophy
PK	Pharmacokinetics
PKPD	Pharmacokinetics Pharmacodynamics
PQ	Pharmaceutical Quality
Prof	Professor
QSP	Quality Selection Process
QT-IRT	QT-Interdisciplinary Review Team
R&D	Research and Development
RLD	Reference Listed Drug
SAWP	Scientific Advice Working Party
SOM	School of Medicine
SOP	School of Pharmacy
SUPAC	Scale-Up and Post-Approval Changes
SVP	Senior Vice President
UCSF	University of California, San Francisco
UK	United Kingdom
USA	United States of America
USP	United States Pharmacopeia
VBE	Virtual Bioequivalence
VP	Vice President