THE UNIVERSITY OF MARYLAND CENTER FOR EXCELLENCE IN REGULATORY SCIENCE AND INNOVATION AND THE FOOD AND DRUG ADMINISTRATION PRESENT:

DISSOLUTION AND TRANSLATIONAL MODELING STRATEGIES ENABLING PATIENT-CENTRIC PRODUCT DEVELOPMENT

FINANCIAL ASSISTANCE PROVIDED BY ABBVIE, MERCK, AND NOVARTIS

UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY
MAY 15-17, 2017
BALTIMORE, MD
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<th>TIME</th>
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<td>8:00-8:30 a.m.</td>
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<td>8:30-8:35 a.m.</td>
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<td>James Polli, PhD</td>
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<td>Shangraw/Noxell Endowed Chair in Industrial Pharmacy and</td>
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<td>University of Maryland School of Pharmacy</td>
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<td>Sandra Suarez Sharp, PhD</td>
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<td>8:35-8:45 a.m.</td>
<td>OPENING REMARKS</td>
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<td>Lawrence Yu, PhD</td>
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<td>8:45-9:00 a.m.</td>
<td>INTRODUCTION AND OBJECTIVES OF THE WORKSHOP</td>
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<td>Andreas Abend, PhD</td>
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<td>Director Merck</td>
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<td>Rob Ju, PhD</td>
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<td>Head, Dissolution Sciences AbbVie</td>
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<td>THE ROLE OF DISSOLUTION TESTING IN DRUG PRODUCT DEVELOPMENT</td>
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<td>Challenges and Opportunities in Developing in vitro Methods to</td>
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<td>Successfully Guide Product Development and Justification of QC Method</td>
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<td>9:00-9:30 a.m.</td>
<td>THE FUTURE OF DISSOLUTION TESTING : KEY ELEMENT FOR THE NEED OF</td>
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<td>PATIENT-CENTRIC ASSESSMENT OF QUALITY - REGULATORY PERSPECTIVE</td>
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<td>Sarah Pope Miksinski, PhD</td>
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<td>Office Director CDER/FDA</td>
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<td>9:30-10:00 a.m.</td>
<td>INDUSTRY PERSPECTIVE ON THE CURRENT STATUS AND FUTURE OF DISSOLUTION</td>
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<td>TESTING FOR PRODUCT DEVELOPMENT AND QUALITY CONTROL</td>
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Rob Ju, PhD  
Head, Dissolution Sciences  
AbbVie

Haiyan Grady, PhD  
Associate Scientific Director  
Takeda Pharmaceuticals

10:00-10:15 a.m. **BREAK**

10:15-11:00 a.m. **USE OF BIO-PREDICTIVE METHODS DURING EARLY FORMULATION SCREENING WITH CASE STUDIES**  
Jesse Kuiper, PhD  
Principal Scientist  
Merck

11:00-12:00 p.m. **DISSOLUTION METHODOLOGIES FROM BIORELEVANT TO QUALITY CONTROL: CHALLENGES AND GAPS**  
Xujin Lu, PhD  
Senior Principal Scientist  
Bristol-Myers Squibb

Jian-Hwa Han, PhD  
Section Manager  
AbbVie

Danna Mattocks, PhD  
Senior CMC Project Manager  
TherapeuticsMD

12:00-12:50 p.m. **LUNCH**

12:50-1:35 p.m. **THE USE OF SURROGATES FOR DISSOLUTION TESTING FOR IR FORMULATIONS: WHEN IS IT FEASIBLE? -- CASE STUDIES**  
Limin Zhang  
Senior Research Scientist  
Bristol-Myers Squibb

Andre Hermans, PhD  
Principal Scientist  
Merck

1:35-2:15 p.m. **STATUS AND CHALLENGES OF DISSOLUTION MODELS FOR REAL TIME RELEASE TESTING**  
Hanlin Li, PhD  
Associate Director  
Vertex

German Drazer, PhD  
Associate Professor  
Rutgers University
BREAKOUT SESSIONS (CHOOSE ONE)
10-Minute Presentation Followed by Discussion on Pre-Selected Questions

DEFINITION/DISCUSSION OF TERMINOLOGIES (E.G., QC VS. PHYSIOLOGICALLY RELEVANT VS. CLINICALLY RELEVANT VS. BIO-PREDICTIVE VS. DISCRIMINATING DISSOLUTION TESTING)

Speakers: Dorys Argelia Diaz, MBA, Associate Director, Pfizer, and Pramod Kotwal, PhD, Director, Merck
Facilitators: Cindy Buhse, PhD, Director, FDA; Angelica Dorantes, PhD, Acting Branch Chief, FDA; Johannes Kraemer, PhD, CEO, Phast GmbH; Dorys Argelia Diaz, MBA, Associate Director, Pfizer; Pramod Kotwal, PhD, Director, Merck; and Haiyan Grady, PhD, Associate Director, Takeda
Questions for Discussion: (TBD)

BRIDGING BIO-PREDICTIVE → QC METHODS: FRAMEWORK, APPROACHES, AND INFORMATION SUGGESTED TO REACH FOLLOWING SCENARIOS:

1. SCENARIO WHERE QC METHODS CAN BE BIO-PREDICTIVE
2. SCENARIO WHERE IT IS CHALLENGING FOR QC METHODS TO BE BIO-PREDICTIVE (PARALLEL R&D BIO-PREDICTIVE AND QC METHODS)

Speakers: David Curran, Scientist, GlaxoSmithKline, and Yiqing Lin, PhD, Senior Scientist, Biogen
Facilitators: Erika Stippler, PhD, Director, USP; Kimberly Raines, PhD, Acting Branch Chief, FDA; Danna Mattocks, PhD, Senior Manager, TherapeuticsMD; Yiqing Lin, PhD, Senior Scientist, Biogen; David Curran, PhD, Scientist, GSK; and Banu Zolnik, PhD, Biopharmaceutics Reviewer, FDA
Questions for Discussion: (TBD)

SUMMARY OF BREAKOUT DISCUSSIONS

SPeaker/Facilitators/Note Takers Day 1 CLOSE-OUT

TUESDAY, MAY 16

TIME
8:00-8:30 a.m. REGISTRATION
8:30-8:35 a.m. WELCOME AND LOGISTICS

Tycho Heimbach, PhD
Director
Novartis
Rob Ju, PhD
Head, Dissolution Science
AbbVie

THE NEED FOR ESTABLISHING IN VITRO-IN VIVO LINK
Novel Approaches and in silico Tools in the Development of Bio-Predictive Dissolution and Permeability Testing (BCS 2/4)

8:35-9:05 a.m.

CHALLENGES AND STRATEGIES IN ESTABLISHING AN IN VITRO-IN VIVO LINK
Paul Seo, PhD
Division Director
CDER/FDA

9:05-9:35 a.m.

NOVEL APPROACHES IN HUMAN PK STUDY DESIGN (E.G., STABLE ISOTOPES TECHNIQUE) TO OVERCOME THE CHALLENGES IN THE CONDUCT OF DEDICATED BA/BE STUDIES (CASE STUDIES)
Timothy H. Montague, PhD
Clinical Statistics ADD TA Head
GSK

9:35-10:10 a.m.

DEVELOPMENT OF CANAGLIFLOZIN: MECHANISTIC ABSORPTION MODELING DURING LATE-STAGE FORMULATION AND PROCESS OPTIMIZATION
Nico Holmstock, PhD
Scientist, Preformulation and Biopharmaceutics
Janssen R&D, Johnson and Johnson

10:10-10:25 a.m.

BREAK

10:25-11:00 a.m.

APPLICATION OF STOCHASTIC DECONVOLUTION IN IVIVC DEVELOPMENT
Maziar Kakhi, PhD
Staff Fellow
CDER/FDA

11:00-11:35 a.m.

PBPK ABSORPTION MODELING CHALLENGES IN PREDICTING CLINICAL OUTCOMES ACROSS BCS/BDDCS CLASSES (PPI EFFECTS, FORMULATION ASSESSMENTS, FOOD EFFECTS): CASE STUDIES FROM INDUSTRY PERSPECTIVE
Tycho Heimbach, PhD
Director
Novartis

11:35-12:10 p.m.

CASE STUDIES OF MECHANISTIC ABSORPTION MODELING AND IVIVC USED IN DEVELOPMENT PROJECTS
Andres Olivares-Morales, PhD
Project Leader, M&S Scientist
Roche

12:10-1:00 p.m.

LUNCH
1:00-2:10 p.m.
The Utility of in silico PBPK Absorption Modeling and Simulation as a Tool to Increase the Success of Developing Bio-Predictive Dissolution Methods: Success and Limitations (Case Studies from Regulatory Perspective)
HoPi Lin, PhD
Biopharmaceutics Reviewer
CDER/FDA

Liang Zhao, PhD
Division Director
CDER/FDA

2:10-2:45 p.m.
Applications of PBPK Modeling for the Development of Biorelevant Dissolution Methods with Case Studies – Industry Perspective
Xavier Pepin, PhD
Principal Scientist, Biopharmacy
AstraZeneca

3:00-5:00 p.m.
Gaps in Knowledge to Increase the Confidence in the Use of in silico PBPK Absorption Models for Regulatory Decision Making: Space of API and Formulation Attributes Where in silico PBPK May Have Limited Utility

Speakers: Xavier Pepin, PhD, Principal Scientist, Biopharmacy, AstraZeneca, and Carrie Coutant, PhD, Principal Research Scientist, Eli Lilly
Facilitators: Marilyn Martinez, PhD, Senior Biomedical Research Scientist, FDA; Xavier Pepin, AstraZeneca; Carrie Coutant, PhD, Principal Research Scientist, Eli Lilly; and HoPi Lin, PhD, FDA
Questions for Discussion: (TBD)

Which Data Should be Submitted to Support the Validation/Verification of in silico PBPK Absorption Models for Regulatory Decision Making? What are the Recommended Validation Acceptance Criteria for PBPK M&S

Speakers: Nikunjkumar Patel, PhD, Senior Research Scientist (M&S), Certara, and Denise Morris, PhD, Assistant Director, SimulationsPlus
Facilitators: Ping Zhao, PhD, Lead, PBPK Program, FDA; Tycho Heimbach, Novartis; Filippou Kesisoglou, Merck; Min Li, FDA; Amitava Mitra, PhD, Associate Director, Sandoz
Questions for Discussion: (TBD)

5:00-5:30 p.m.
Summary of Breakout Discussions

5:45-6:30 p.m.
Speaker/Facilitators/Note Takers Day 2 Close-out
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| 8:30-8:35 a.m. | WELCOME AND LOGISTICS  
Sandra Suarez Sharp, PhD  
Master Biopharmaceutics Reviewer  
CDER/FDA  
Evangelos Kotzagiorgis, MSc  
Scientific Administrator  
European Medicines Agency |
| 8:35-9:35 a.m. | REGULATORY APPLICATIONS OF BIO-PREDICTIVE DISSOLUTION TESTING            |
| 9:35-10:05 a.m. | FRAMEWORK OF SETTING CLINICALLY RELEVANT SPECIFICATIONS:  
APPROACH, INFORMATION NEEDED, AND CRITERIA  
Sandra Suarez Sharp, PhD  
Master Biopharmaceutics Reviewer  
CDER/FDA  
Evangelos Kotzagiorgis, MSc  
Scientific Administrator  
European Medicines Agency  
Andreas Abend, PhD  
Director  
Merck |
| 10:05-10:20 a.m. | BREAK                                                                  |
| 10:20-11:00 a.m. | THE ROLE OF BIO-PREDICTIVE DISSOLUTION TESTING IN INCREASING THE SUCCESS RATE OF IVIVR/IVIVC: KEY APPROACH IN SUPPORT OF MAJOR POST-APPROVAL CHANGES (BIOWAIVERS) IN REFERENCE TO REGULATORY GUIDELINES  
Min Li, PhD  
Acting Biopharmaceutics Lead  
CDER/FDA |
The Utility of On Level CIVIVC for Setting Clinically Relevant Specifications: Case Studies and Implications
Filippos Kessoglou, PhD
Senior Principal Scientist
Merck

Establishing Clinical Relevant Specifications During Product Lifecycle: Case Studies
Barbara Davit, PhD, JD
Distinguished Scientist
Merck

Patrick Marroum, PhD
Senior Research Fellow
AbbVie

LUNCH

Breakout Sessions (Choose One)
10-Minute Presentation Followed by Discussion on Pre-Selected Questions

Similarities, Differences, and Shared Challenges in the EMA and U.S. FDA: Recommended Approaches to Setting Clinically Relevant Drug Product Specifications

Speakers: Nagesh Bandi, PhD, Executive Director, Merck, and Michael Cohen, Pfizer
Facilitators: Evangelos Kotzagiorgis, EMA; Sandra Suarez, FDA; Andreas Abend, Merck; Poonam Delvadia, PhD, Acting Biopharmaceutics Lead, FDA; and Nagesh Bandi, Merck
Questions for Discussion: (TBD)

Similarities, Differences, and Shared Challenges in the EMA and U.S. FDA: Recommended Use of In Silico PBPK Absorption M&S in Regulatory Decision Making in Relation to Biowaivers

Speakers: Erik Sjögren, PhD, Associate Professor in Biopharmaceutics, Uppsala University, and Barbara Davit, Merck
Facilitators: Paul Seo, Director, FDA; Shereeni Veerasingham, PhD, Assessment Officer, Health Canada; Erik Sjögren, Uppsala University; Xinyuan (Susie) Zhang, PhD, Clinical Pharmacology Reviewer, FDA; and Shinichi Kijima, MSc, Clinical Pharmacology Reviewer, PMDA
Questions for Discussion: (TBD)

Summary of Breakout Discussions
3:30-4:00 p.m.  MEETING WRAP-UP AND FOLLOW-UP ACTIONS
4:15-5:15 p.m.  SPEAKER/FACILITATORS/NOTE TAKERS DAY 3 CLOSE-OUT