CONFERENCE OVERVIEW
The FDA Critical Path Initiative has stimulated interest in new tools and ways to improve the efficiency and success rates of drug development programs, including their planning and analysis. Among the opportunities being explored is the increased use of quantitative modeling and computer simulation (M&S) tools and approaches. Although mechanistic and stochastic modeling and/or computer simulation have long been used for the design and analysis of clinical trials by different stakeholders within drug development, such as statisticians and clinical pharmacologists, the recent trend is to expand the joint understanding of how M&S can be better integrated and utilized into the drug development process. This trend has been associated with some level of confusion in terminology and understanding of the role and scope of M&S. There is, however, broad consensus that M&S has an enormous potential, in many cases already realized, to greatly improve drug development through better clinical study and program design, more effective approaches to dose selection and regimen optimization, as well as better assessment of the risk/benefit of new and existing treatments.

This M&S conference will provide an opportunity for different stakeholders to learn, create greater awareness, share good and bad experiences, identify gaps and opportunities, and clarify terminology and understanding of M&S and its role in clinical drug development.

LEARNING OBJECTIVES
At the conclusion of this meeting, participants should be able to:
- Demonstrate a common understanding of what modeling and simulation is, and is not, and of the terminology used in the field;
- Apply, share and learn about both successful and unsuccessful case studies illustrating the benefits and pitfalls of the use of modeling and simulation in drug development and for regulatory applications;
- Discuss the role and scope of modeling and simulation in decision making at various stages of the drug development process, for example dose/regimen selection, patient population selection, clinical trial and program design choices, supporting information for regulatory application; and
- Recognize the value of collaborative multi-disciplinary interactions (across statistical, clinical, pharmacometrics, and clinical pharmacology areas) as a centerpiece to effectively realize the benefits of modeling and simulation.

WHO SHOULD ATTEND
This program will benefit individuals involved in
- Statistics
- Clinical pharmacology
- Epidemiology
- Regulatory affairs
- Clinical research
- Pharmacometrics
- Health economics
- Pharmacokinetics

CONTACT INFORMATION
Conference: Ben Zaitz, Program Manager, Phone +1-215-293-5803
e-mail Benjamin.Zaitz@diahome.org

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Recording of any DIA tutorial/workshop information in any type of media, is prohibited without prior written consent from DIA.

TUESDAY • OCTOBER 27
4:00-6:00 PM
CONFERENCE REGISTRATION

WEDNESDAY • OCTOBER 28
7:30-8:15 AM
REGISTRATION AND CONTINENTAL BREAKFAST
8:15-8:30 AM
WELCOME/OPENING REMARKS
José Pinheiro, PhD
Senior Biometrical Fellow, Biostatistics
Novartis Pharmaceuticals Corporation

KEYNOTE INTRODUCTION
Rajesh Krishna, PhD, FCP
Director, Clinical Pharmacology and Head, Quantitative Clinical Pharmacology
Merck and Company, Inc.

8:30-9:15 AM
SESSION 1
MODELING AND SIMULATION IN EARLY DEVELOPMENT
SESSION CO-CHAIRPERSONS
Rajnikanth Madabushi, PhD
Pharmacometrics Reviewer
CDER, FDA

Rajesh Krishna, PhD, FCP
Director, Clinical Pharmacology and Head, Quantitative Clinical Pharmacology
Merck and Company, Inc.

In this session, gaps and opportunities on the use of strategic modeling and simulation in the early clinical development space will be examined. Two specific areas of value include the use of modeling and simulation for utilizing adaptive designs in Phase I/II studies enabling dose selection and the use of the end of phase (EOP)2A mechanism to better leverage regulatory feedback on these early clinical opportunities for designing pivotal registration trials.

Nitin Patel, PhD
Chairman and Chief Technology Officer, CTO
Cytel, Inc.

Pravin R. Jadhav, PhD
Pharmacometrician
Clinical Pharmacologist
Office of Clinical Pharmacology, CDER

10:30-11:00 AM
SESSION 2
MODELING AND SIMULATION TO INFORM DESIGN AND ANALYSIS OF CONFIRMATORY TRIALS
SESSION CO-CHAIRPERSONS
Dionne Price, PhD
Statistician
Office of Biostatistics, CDER, FDA
José Pinheiro, PhD
Senior Biometrical Fellow, Biostatistics
Novartis Pharmaceuticals Corporation

This session will discuss and illustrate the use of model-based methods and simulations to design and analyze clinical studies aimed at producing confirmatory evidence and labeling information. Case studies will be used to illustrate the benefits and challenges of this approach in clinical drug development.

Brenda L Gaydos, PhD
Senior Research Adviser, Center for Applied Statistical Expertise
Eli Lilly and Company

H.M. James Hung, PhD
Director, Division of Biometrics I
Office of Biostatistics
CDER, FDA
This session will provide an overview of how modeling and simulation can bridge the gaps between early phase trials and late phase drug development. Challenges are often encountered in integrating all available information to support and guide further drug development after the proof-of-concept trials. Modeling and simulation can serve as a powerful tool to integrate information from many sources in an objective and quantitative way to justify key decisions. The speakers in this session will briefly present case studies to demonstrate successful implementation of modeling and simulation for this purpose and also share examples where appropriate application of modeling and simulation could have shortened the drug development cycle and avoided unnecessary trials. An extended question-and-answer period and audience discussion will follow.

### BREAKOUT SESSION 1: MISSING DATA

**Session Co-Chairpersons**

- **Philip Dinh, PhD**
  - Statistician, Division of Biometrics I
  - Office of Biostatistics
  - CDER, FDA

- **Peter Lane**
  - Director of Consultancy & Training
  - Research Statistics Unit
  - GlaxoSmithKline

This session will focus on three aspects of missing data. The first is the level of model complexity that can reasonably be employed in the analysis of longitudinal trials. The second is the use of simulation to study missing value problems: of particular interest is the way missing data are simulated with specific characteristics relative to a given model (e.g. MCAR, MAR, MNAR). The third is the acceptability of the multiple-imputation approach, which simulates data and thereby adds an element of randomness into the analysis of trials.

- **Ohidul I. Siddiqui, PhD**
  - Mathematical Statistician
  - Division of Biometrics I, CDER, FDA

### BREAKOUT SESSION 2: MODELING AND SIMULATION IN THE LEARN-AND-CONFIRM PARADIGM

**Session Co-Chairpersons**

- **H.M. James Hung**
  - Director, Division of Biometrics I, Office of Biostatistics
  - CDER, FDA

- **Vladimir Dragalin, PhD**
  - Assistant Vice-President and Research Fellow
  - Head of Statistical Research and Applications
  - Wyeth Research

The role and scope of modeling and simulation in the exploratory (“Learn”) and confirmatory (“Confirm”) phases of clinical drug development are quite different. This session will include two presentations emphasizing that learning and confirming require different model-based approaches to clinical trial and program design and analysis. The specifics of statistical simulations in trial planning and design operating characteristics evaluation will be discussed. Two panelists will provide regulatory and industry perspectives on the key issues, followed by a floor discussion.

- **H.M. James Hung**
  - Director, Division of Biometrics I
  - Office of Biostatistics, CDER, FDA

### BREAKOUT SESSION 3: MODEL DEVELOPMENT USING ACCUMULATING DATA, WHAT ABOUT MODEL VALIDATION?

**Session Co-Chairpersons**

- **Lei Nie, PhD**
  - Mathematical Statistician
  - Division of Biometrics
  - Office of Biostatistics
  - CDER, FDA

- **Sue-Jane Wang, PhD**
  - Biostatistician
  - Office of Biostatistics
  - CDER, FDA

- **Ted Grasela, PharmD, PhD**
  - President and CEO
  - Cognigen Corporation

Model development is often data-driven and labor intensive. To meet project deadlines, it is sometimes desirable to start model development before database lock. Even if the modeler is allowed access to randomization codes, the data still accumulate and change as modeling proceeds. And sometimes even after database lock, data can change if late corrections are made. In addition, the validation of the developed model is of paramount importance for the model to be useful. In this session, participants will hear some case scenarios on strategies for proactive use of accumulating...
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<th>Breakout Session 1: Missing Data (Continued)</th>
<th>Breakout Session 2: Modeling and Simulation in the Learn-and-Confirm Paradigm (Continued)</th>
<th>Breakout Session 3: Model Development Using Accumulating Data, What about Model Validation? (Continued)</th>
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<td>Peter Lane</td>
<td>Vladimir Dragalin, PhD</td>
<td>data, to be followed by discussion on validity with late changes in the data and proper model validation.</td>
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| Director of Consultancy and Training        | Assistant Vice-President and Research Fellow                                   | Ted Grasela, PharmD, PhD
| Research Statistics Unit                    | Head of Statistical Research and Applications                                  | President and CEO, Cognigen Corporation |
| GlaxoSmithKline                             | Wyeth Research                                                                  | James Rogers, PhD
| Panel Discussion                            |                                                                                | Principal Scientist, Metrum Research Group |
|                                            |                                                                                | Stephen Ruberg, PhD
|                                            |                                                                                | Senior Research Fellow, Global Statistical Sciences and Clinical Data Management |
|                                            |                                                                                | Eli Lilly and Company |
|                                            |                                                                                | Sue-Jane Wang, PhD
|                                            |                                                                                | Associate Director for Adaptive Design and Pharmacogenomics, Office of Biostatistics |
|                                            |                                                                                | Office of Translational Sciences, CDER, FDA |

5:00-6:00 PM NETWORKING RECEPTION

THURSDAY • OCTOBER 29

7:30-8:30 AM CONFERENCE REGISTRATION AND CONTINENTAL BREAKFAST

8:30-9:00 AM FEEDBACK/RESPONSE FROM BREAKOUT SESSIONS

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<th>Session Co-Chairpersons</th>
<th>FDA Representative</th>
<th>Industry Representative</th>
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9:00-10:30 AM SESSION 5

MODELING AND PHARMACOGENOMICS

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10:30-11:00 AM MORNING REFRESHMENT BREAK

11:00-12:30 PM SESSION 6

PRODUCT DIFFERENTIATION

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Early-phase drug development provides a learning space to explore whether treatment effects are potentially limited to patients possessing genomic characteristics or whether there is a favorable utility of the genomic profile adding to the existing clinical model. In early- to mid-phase clinical trials, both the genomic and clinical modeling could be explored via simulation studies to learn the variability of the treatment effects due to, e.g., genomic factors and/or joint clinical-genomic factors, and to address the clinical utility of the genomic biomarker. In contrast, when the genomic model outperforms clinical model or the joint clinical/genomic models provide favorable benefit/risk profile, confirmatory pharmacogenomics clinical trials can be designed to incorporate the model. Use of such model/simulations would allow prospective testing of the treatment effect and demonstrate the clinical utility of the genomic associated model. This session will include three presentations. The utility of modeling and simulation in early- and late-phase clinical trials will be illustrated via some case examples.

Samir Lababidi, PhD
Statistician
CDRH, FDA

Andrew Vickers, PhD
Associate Attending Research Methodologist
Memorial Sloan-Kettering Cancer Center

Patrick Kelly, PhD
Senior Lecturer, Biostatistics
The University of Sydney

This session will provide an overview of the current landscape of the economics of drug discovery and development, a model of valuation of pharmacotherapies, and how product differentiation can play a key component in pricing and reimbursement. Various methodologies and tools that can be used in evaluating / predicting differentiation will be emphasized. Lastly, a discussion will be provided about the strategic thinking that one should consider when setting a development plan around product differentiation.

Linda Harpole, MD
Vice President, Global Health Outcomes
GlaxoSmithKline
To address the challenges arising from conducting a thorough evaluation of drug safety, different perspectives need to be integrated that could overcome the difficulties arising from this process. For this reason, safety tools have become increasingly integrated into the design and analysis of drug development strategies. For example, these tools could be useful in assessing a major safety concern associated with drugs under the same class. The session will feature how modeling and simulation can provide insights into the development of quantitative methodology associated with the assessment of drug safety, and open new directions into the assessment of safety via modeling and simulation.

Daniele Ouellet, PhD, MSc
Director, Clinical Pharmacology, Modeling & Simulation
GlaxoSmithKline

Bill Frame, BS, MS
President and CEO
Wolverine Pharmacometrics Corporation

Lingling Li, PhD
Assistant Professor and Biostatistician
Department of Ambulatory Care and Prevention
Harvard University

3:00-3:15 PM        AFTERNOON REFRESHMENT BREAK

PATH FORWARD AND NEXT STEPS FOR MODELING AND SIMULATION
SESSION CO-CHAIRPERSONS
Sue-Jane Wang, PhD
Associate Director for Adaptive Design and Pharmacogenomics
Office of Biostatistics, Office of Translational Science
CDER, FDA

José Pinheiro, PhD
Senior Biometrical Fellow, Biostatistics
Novartis Pharmaceuticals Corporation

Rajesh Krishna, PhD, FCP
Director, Clinical Pharmacology and Head
Quantitative Clinical Pharmacology
Merck & Company Inc.

This panel discussion session will review the key issues discussed at the meeting and the path forward for better understanding the benefits and pitfalls of M&S, expanding its appropriate use in clinical drug development, and improving the dialogue and collaboration among key stakeholders involved. Different perspectives will be considered, including regulatory, industry, and academic points of view.

Frank Bretz, PhD
Biometrical Fellow, Biostatistics
Novartis AG

Oscar Della Pasqua, PhD
Director, Clinical Pharmacology
GlaxoSmithKline

Richard L. Lalonde, PharmD
Vice President and Global Head of Clinical Pharmacology
Pfizer, Inc.

Jogarao (Joga) V. Gobburu, PhD
Pharmacometrics
Office of Clinical Pharmacology
CDER, FDA

John K. Jenkins, MD
Director, Office of New Drugs
CDER, FDA

Robert Temple, MD
Director of the Office of Medical Policy
Associate Director for Medical Policy
CDER, FDA

4:15-4:30 PM       CLOSING REMARKS AND CONFERENCE ADJOURNED

TRAVEL AND HOTEL
The most convenient airport is Reagan National Airport and attendees should make airline reservations as early as possible to ensure availability. The Marriott Bethesda, Pooks Hill is holding a block of rooms at the reduced rate below until October 6, 2009, for the DIA event attendees. Room availability at this rate is guaranteed only until this date or until the block is filled.

Single $189  Double $189

Please contact the Marriott Bethesda, Pooks Hill by telephone at +1-301-897-9400 and mention the DIA event. The hotel is located at 5151 Pooks Hill Road, Bethesda, MD 20814, USA.
Modeling and Simulation in Drug Development: Quantitative Approaches for Decision Making

Event ID #09024
Marriott Bethesda Pooks Hill Hotel
Bethesda, MD, USA
OCTOBER 28-29, 2009

Register online or fax this page to +1-215-442-6199

CONTACT INFORMATION

Contact Ben Zaitz, Program Manager, at the DIA office by telephone +1-215-293-5803, fax +1-215-442-6199 or email Benjamin.Zaitz@diahome.org

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Modeling and Simulation Drug Development: Quantitative Approaches and Decision Making

Meeting I.D. # 09024 – October 28-29, 2009
Marriott Bethesda Pooks Hill, Bethesda, MD, USA

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US $515

CANCELLATION POLICY: On or before OCTOBER 21, 2009

Administrative fee that will be withheld from refund amount:

Member or Nonmember = $200

Government or Academia or Nonprofit (Member or Nonmember) = $100

Tutorial (if applicable) = $50

Cancellations must be in writing and be received by the cancellation date above. Registrants who do not cancel by that date and do not attend will be responsible for the full registration fee paid. Registrants are responsible for cancelling their own hotel and airline reservations. You may transfer your registration to a colleague at any time but membership is not transferable. Substitute registrants will be responsible for nonmember fee, if applicable.

DIA reserves the right to alter the venue, if necessary. If an event is cancelled, DIA is not responsible for any airfare, hotel or other costs incurred by registrants.

I cannot attend but please keep me informed of DIA's future events.

(Please complete name, postal address and email address on this form)

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