Joint Adaptive Design and Bayesian Statistics Conference: Drivers of Efficiency in Modern Medical Product Development

Tutorials: February 10 | Conference: February 11– 12
Doubletree by Hilton Washington DC – Crystal City | Arlington, VA

PROGRAM CHAIRS

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Executive Director
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OVERVIEW

As the complexity of pharmaceutical development escalates, researchers must leverage increasingly sophisticated statistical tools for design and analysis, including broader use of Bayesian methods and adaptive designs. There has been an upturn in interest and application of adaptive design and Bayesian statistics, in part due to their inclusion within the FDA's *Critical Path Opportunities List.*

While these methods have already contributed in many ways to reductions in risk, time, and cost of medical product development, and to overall improvements in decision making; for many drug developers, device, and diagnostic manufactures adaptive design and Bayesian statistics are still buzz-words. Per a recent survey conducted by DIA's Bayesian Scientific Working Group, education continues to be a significant gap in a broader appropriate uptake of Bayesian methods, including their use in adaptive designs. In order to improve the implementation of adaptive design and Bayesian statistics, we must demystify the practice and application of these proven methodologies.

February 2015 marks the 5th anniversary of the publication of the FDA's draft guidance on adaptive clinical trials and the final guidance of the use of Bayesian statistics in medical device clinical trials. Join us to celebrate these important milestones for clinical trials as well as to engage FDA representatives in discussions regarding the progress of both adaptive design and Bayesian statistics and to speculate the future for this science.

This conference will present the latest advancements in the application of adaptive design and Bayesian statistics to include critical aspects such as a better understanding of methodologies, identifying opportunities for when to apply them, analysis, and improved decision making. Presentations will be given from statistical, clinical, and regulatory viewpoints to provide a more complete picture of appropriate adaptive design and Bayesian statistics implementation.

Sessions will consist of joint and independent adaptive design and Bayesian statistic plenaries as well as concurrent breakout sessions for each class of methods. Case studies will be presented throughout the conference to encourage discussions and debates regarding the use of Bayesian and adaptive design methods within modern medical product development from presenters across industry, regulatory, and academia.

This program has been developed in collaboration with the DIA Adaptive Design Scientific Working Group and the Bayesian Statistics Scientific Working Group.

LEARNING OBJECTIVES

At the conclusion of this conference, participants should be able to:

- Apply concepts related to adaptive design and Bayesian methods
- Identify opportunities for improving pharmaceutical, device, and diagnostic product development by application of adaptive design and/or Bayesian statistics
- Assess whether the application of adaptive design and/or Bayesian methods would improve metrics such as cost, time of development, and probability of success, compared to the application of more traditional methods.

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- Bayesian Methods for Drug Safety Evaluation and Signal Detection: .3 IACET CEUs

- Using Historical Data in Clinical Trials: .3 IACET CEUs

Conference:
1.2 IACET CEUs

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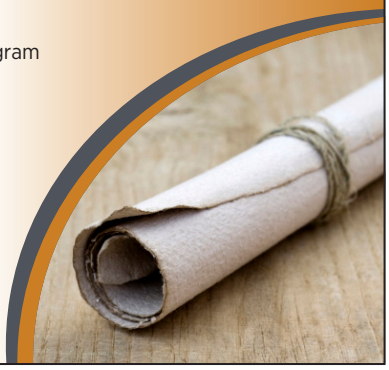

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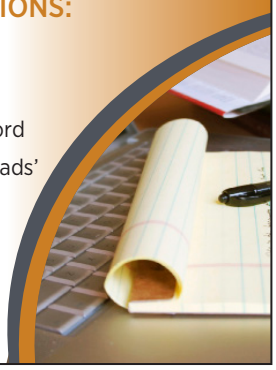

TUESDAY, FEBRUARY 10

1:30–5:00PM **CONCURRENT HALF DAY TUTORIALS**

Bayesian Methods for Drug Safety Evaluation and Signal Detection

INSTRUCTORS:

David Ohlssen, PhD
Senior Expert Methodologist
Novartis Pharmaceuticals Corporation

Amy Xia, PhD
Executive Director
Biostatistics
Amgen, Inc.

As the era of "big data" arrives in full force for health care and pharmaceutical development, researchers in these areas must turn to increasingly sophisticated statistical tools for their proper analysis. Bayesian statistical methods, while dating in principle to the publication of Bayes' Rule in 1763, have only recently begun to see widespread practical application due to advances in computation and software. This tutorial, sponsored by the DIA Bayesian Scientific Working Group, will provide an overview of Bayesian statistical methods and computation, and then explore their use in meta-analysis and hierarchical modeling especially with regard to drug safety. We will demonstrate methods via case examples and discuss the impact of utilizing these approaches throughout pharmaceutical development.

Learning Objectives:

At the completion of this tutorial, participants should be able to:

- Demonstrate knowledge of the key concepts behind Bayesian statistical methods, hierarchical modeling, computation and software
- Utilize meta-analysis and Bayesian meta-analysis in the context of safety evaluation
- Identify how Bayesian methods may be used in conjunction with an adaptive clinical trial designs that continuously monitor an adverse event of interest
- Examine techniques for safety signal detection that apply Bayesian hierarchical modeling to clinical trial adverse event data

Using Historical Data in Clinical Trials

INSTRUCTOR:

Heinz Schmidli, PhD, MSc
Biometric Fellow
Novartis Pharma AG, Switzerland

Making full use of available information leads to more efficient drug development. This tutorial will provide an overview on how to use historical data for design and analysis of clinical trials. We will describe Bayesian methods for evidence-synthesis that allow transparent quantification and integration of historical information. The concepts will be illustrated through applications and case studies, covering all phases of drug development.

Learning Objectives:

At the completion of this tutorial, participants should be able to:

- Apply evidence-synthesis approaches for non-inferiority, biosimilar, and historical-control trials
- Discuss how to mitigate conflicts between historical and current trial data
- Use historical information to evaluate probability of success

This program is being marketed in collaboration with the International Society for Bayesian Analysis (ISBA).

ISBA
INTERNATIONAL SOCIETY FOR BAYESIAN ANALYSIS

WEDNESDAY, FEBRUARY 11

7:00–8:00AM REGISTRATION / CONTINENTAL BREAKFAST

8:00–8:30AM WELCOME REMARKS AND OVERVIEW OF THE 1ST JOINT ADAPTIVE DESIGN AND BAYESIAN STATISTICS CONFERENCE

Zoran Antonijevic, MSc
Senior Director
Cytel Consulting

Karen Price, PhD, MA
Research Advisor
Eli Lilly and Company

8:30–9:25AM KEYNOTE ADDRESS: GLOBAL R&D OPERATING CONDITIONS DRIVING THE NEED FOR ADAPTIVE AND FLEXIBLE STUDY DESIGN MANAGEMENT AND PRACTICE

Kenneth A. Getz
Director of Sponsored Research; Chairman, CISCRP
Tufts Center For the Study of Drug Development

This keynote presentation discusses the results and implications of several recent studies conducted by the Tufts Center for the Study of Drug Development. The presentation will provide an overview and a characterization of current global operating conditions and challenges that the drug development enterprise faces. Strategies and new practices to transform and optimize study design, improve success rates, lower cost and accelerate development speed will be highlighted.

9:25–9:30AM CALL FOR PAPERS: *THERAPEUTIC INNOVATION & REGULATORY SCIENCE* (TIRS), THE OFFICIAL JOURNAL OF DIA

Richard C. Zink, PhD
Section Editor, Statistics, TIRS
Principal Research Statiscian Developer
JMP Life Sciences and SAS Institute, Inc.

DIA's official peer-reviewed journal, Therapeutic Innovation & Regulatory Science (TIRS) publishes papers on advancements and innovation in the field of medical product development in the areas of Biostatistics, Clinical Trials, Product Development and Innovation, Global Perspectives, Policy, Regulatory Science, Product Safety and Special Populations. Richard Zink, Section Editor for Statistics for TIRS will discuss publication opportunities with DIA at the conclusion of the meeting's plenary address.

9:30–10:00AM REFRESHMENT BREAK AND NETWORKING

10:00–11:30AM SESSION 1: 5TH ANNIVERSARY OF THE DRAFT GUIDANCE FOR ADAPTIVE DESIGN

SESSION CHAIR:

Zoran Antonijevic, MSc
Senior Director
Cytel Consulting

Sue-Jane Wang, PhD, MA, MS
Associate Director
Adaptive Design & Pharmacogenomics, OB, OTS
CDER, FDA

FDA and industry speakers will report on the progress made in implementing adaptive trials since the FDA Draft Guidance on Adaptive Design Clinical Trials for Drugs and Biologics release in 2010. The session will then continue with a panel discussion that will address topics such as: opportunity, experience, learnings, and issues related to adaptive design.

FDA's Perspective

Robert T. O'Neill, PhD
Senior Statistical Advisor
Office of Translational Sciences
CDER, FDA

Industry's Perspective of the Progress Made Implementing Adaptive Trials and the Potential for the Future

Jerald S. Schindler, DrPH
Head
Global Late Development Statistics
Merck Research Laboratories

Q&A Panel Discussion

JOINING THE SPEAKERS:

Christy Chuang-Stein, PhD
Vice President
Head of Statistical Research and Consulting Center
Pfizer

Martin Posch, PhD, DrSc
Professor of Medical Statistics
Center for Medical Statistics
Medical University of Vienna

Lisa M. LaVange, PhD
Director
Office of Biostatistics, Office of Translational Science
CDER, FDA

11:30AM–1:00PM **LUNCH AND NETWORKING**

1:00–2:30PM **SESSION 2: 5TH ANNIVERSARY OF THE GUIDANCE FOR BAYESIAN STATISTICS**

SESSION CHAIR:

Laura Thompson
Mathematical Statistician
CDRH, FDA

It has been five years since the release of the final Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials. In this session, prominent speakers from FDA and industry discuss the impact of the guidance on marketing submissions to the Center for Devices and Radiological Health, including benefits and lessons learned. The second half of the session contains a Q&A panel with Bayesian statisticians from FDA, industry, and academia.

An FDA Perspective on the 5th Anniversary of the Guidance on the Use of Bayesian Statistics in Medical Device Clinical Trials

Gregory Campbell, PhD
Director, Division of Biostatistics
CDRH, FDA

Industry's Perspective

Roger J. Lewis, MD, PhD
Professor of Medicine
Department of Emergency Medicine
Harbor UCLA Medical Center

Q&A Panel Discussion

JOINING THE SPEAKERS:

Donald Berry, PhD
Professor, Department of Biostatistics
University of Texas
MD Anderson Cancer Center

Karen Price, PhD, MA
Research Advisor
Eli Lilly and Company

Estelle Russek-Cohen
Director
Division of Biostatistics, OBE
CBER, FDA

2:30–3:00PM **REFRESHMENT BREAK AND NETWORKING**

3:00–4:30PM **SESSION 3: BAYESIAN AND ADAPTIVE DESIGN APPROACHES IN SPECIAL POPULATIONS**

SESSION CHAIR:

Estelle Russek-Cohen
Director
Division of Biostatistics, OBE
CBER, FDA

This session will focus on the use of Bayesian methods and adaptive designs in the context of special populations, including pediatrics and rare diseases. We will demonstrate the impact and value of the use of Bayesian methods and adaptive designs via case examples, with perspectives from regulatory and industry. The session will conclude with two discussions and a panel discussion to explore opportunities and ways to overcome hurdles.

Leveraging Adult Data to Make Statistical Inferences about the Effectiveness of Medical Devices in a Pediatric Population

Laura Thompson
Mathematical Statistician
CDRH, FDA

Case Study: Use of Bayesian Statistics and Adaptive Design in Rare Diseases

Melanie Quintana, PhD
Statistical Scientist
Berry Consultants, LLC

Q&A Panel Discussion

JOINING THE SESSION SPEAKERS:

DISCUSSANT

Robert A. Beckman, MD
Professor of Oncology and of Biostatistics, Bioinformatics, and Biomathematics (Adjunct Track)
Lombardi Cancer Center, Georgetown University Medical Center

DISCUSSANT

Ram Tiwari, PhD
Associate Director
Office of Biostatistics, OTS
CDER, FDA

4:30–5:30PM **NETWORKING RECEPTION**

THURSDAY, FEBRUARY 12

7:00–8:00AM REGISTRATION AND CONTINENTAL BREAKFAST

8:00–8:10AM WELCOME TO DAY 2

Zoran Antonijevic, MSc
Senior Director
Cytel Consulting

8:10–9:40AM SESSION 4: MASTER PROTOCOL

SESSION CHAIR:

Lei Nie
Lead Mathematical Statistician
CDER, FDA

Tired of high failure rate, slow process to marketing, and spending so much time in planning for each drug? Master protocol is revamping trial designs by bringing pharmaceutical companies together to test multiple agents under a single master protocol. Experts from academia, industry, and regulatory agencies are ready to share their experience, considerations, as well as excitement with you in a session that requires very basic statistical background from the audience.

Platform Trials with Bayesian Adaptive Design

Donald Berry, PhD
Professor, Department of Biostatistics
University of Texas
MD Anderson Cancer Center

Regulatory Perspectives on Platform Trials: Lung Map Master Protocol

Hui Zhang, PhD
Mathematical Statistician
FDA

Operational Aspects of Platform Trials: Challenges and Opportunities

Ohad Amit, PhD
Senior Director, Clinical Statistics
GlaxoSmithKline

Q&A Panel Discussion

JOINING THE SPEAKERS:

DISCUSSANT

Mary Redman, PhD
Lead Biostatistician
SWOG Lung Committee/LungMap
Fred Hutchinson Cancer Research Center

9:40–10:00AM REFRESHMENT BREAK AND NETWORKING

10:00–11:30AM **CONCURRENT BREAKOUT SESSIONS 1**

CONCURRENT BREAKOUT SESSION 1A

Adaptive Design Case Studies

SESSION CHAIR:

Yili Pritchett, PhD
Senior Director
Global Development
Astellas Pharma Inc.

The use of adaptive designs in clinical development for new drug products has gained momentum in recent years, with the applications in both learning and confirmatory phase of development. As a result of this exciting new trend, more and more completed adaptive clinical trials have emerged and some of them have delivered compounds to the finish line. In this session, three clinical development programs that have used adaptive designs to eliminate uncertainty and generate pivotal data for new drug applications will be shared. These cases covered drug development in therapeutic areas from oncology, gastroenterology to diabetics, and all have successfully obtained the approval of marketing authorization by the FDA. The speakers will share trial designs, operational challenges and regulatory interactions, while the discussant will discuss the three cases from a regulatory perspective.

Sequential Stage Design in the Gazyva Registration Trial

Chia-Wen Ko
Mathematical Statistician
FDA

2-Stage Design in the Crofelemer Pivotal Program

M. Scott Harris, MD, MS, FACP, AGAF
Principal
Middleburg Consultants

Moving Drugs from Phase 2 into Phase 3

Brenda Gaydos, PhD
Head of Clinical Trial Optimization
Eli Lilly and Company

Q&A Panel Discussion

JOINING THE SPEAKERS:

DISCUSSANT

Sue-Jane Wang, PhD, MA, MS
Associate Director
Adaptive Design & Pharmacogenomics, OB, OTS
CDER, FDA

CONCURRENT BREAKOUT SESSION 1B

Bayesian Methods for a Better Decision Making Process

SESSION CHAIR:

Brad Carlin, PhD
Professor and Head of Biostatistics
University of Minnesota

This session will focus on the importance/use of Bayesian methods for decision making, in design, analysis, and approval process. The presentations will include examples of case studies of specific trial designs that utilize Bayesian methods to enable Bayesian decision making from industry's perspective, and the benefit-risk assessment in making regulatory determinations for medical devices. The session will have a discussant and then conclude with a panel discussion to answer questions and discuss broader implementation.

CDRH's Perspective: Bayesian Quantitative Benefit-Risk

Telba Irony, PhD
Chief
Biostatistics: General Surgical Devices Branch
CDRH, FDA

Bayesian Decision Making: Industry's Perspective

David Ohlssen, PhD
Senior Expert Methodologist
Novartis Pharmaceuticals Corporation

Bayesian Approach to Personalized Benefit-Risk Assessment: A Perspective

Ram Tiwari, PhD
Associate Director
Office of Biostatistics, OTS
CDER, FDA

Q&A Panel Discussion

11:30AM–1:00PM **LUNCH AND NETWORKING**

1:00–2:30PM **CONCURRENT BREAKOUT SESSIONS 2**

CONCURRENT BREAKOUT SESSION 2A:

Adaptive Design: Optimization of R&D Programs and Portfolios

SESSION CHAIR:

Zoran Antonijevic, MSc
Senior Director
Cytel Consulting

This session will discuss approaches that maximize values of Pharmaceutical R&D programs and portfolios. The focus will be on how clinical trial design and decision criteria maximize parameters such as Expected Net Present Value (eNPV) and Return on Investment (ROI) at a development program or a portfolio level.

Simulating the Whole Development Program to Help Optimize the Design of a Phase 2 Trial in Oncology

Tom Parke, BSc
Consultant
Tessella

Extension of Neuropathic Pain Development Program Optimization Via Consideration of Including 1 or 2 Doses in Phase 3

Jim Bolognese
Senior Director of Clinical Trial Services
Cytel Inc.

Maximizing Return on Investment in Designing Clinical Trials

Cong Chen, PhD
Director
Merck & Co., Inc.

Q&A Panel Discussion

CONCURRENT BREAKOUT SESSION 2B:

Bayesian Evidence Synthesis

SESSION CHAIR:

John W. Seaman, PhD
Professor of Statistics
Baylor University

This session will focus on the use of Bayesian methods for meta-analytical approaches, including network meta-analysis, in the context of safety data. Case examples will be presented throughout, highlighting the impact of the use of Bayesian methods in decision making, and in designing and analyzing clinical trials. The session will conclude with a panel discussion to answer questions and identify opportunities for broader implementation.

Meta-analysis in Safety Data

Mark S. Levenson, PhD
Deputy Director
Division of Biometrics VI
Office of Biostatistics
CDER, FDA

Bayesian Meta-Analysis in Drug Safety Evaluation

Amy Xia, PhD
Executive Director
Biostatistics
Amgen

Bayesian Evidence Synthesis and Network Meta-Analysis

Brad Carlin, PhD
Professor and Head of Biostatistics
University of Minnesota

Q&A Panel Discussion

JOINING THE SPEAKERS:

John Scott, PhD
Deputy Director
Division of Biostatistics
Office of Biostatistics and Epidemiology
CBER, FDA

2:30–3:00PM **REFRESHMENT BREAK AND NETWORKING**

3:00–4:30PM **CLOSING SESSION – PANEL DISCUSSION - MOVING FORWARD: ADAPTIVE DESIGN AND BAYESIAN STATISTICS DRIVERS OF EFFICIENCY IN MODERN MEDICAL PRODUCT DEVELOPMENT**

SESSION CHAIRS:

Zoran Antonijevic, MSc
Senior Director
Cytel Consulting

A panel discussion of experts with different backgrounds will conclude this conference. The discussion will build on material presented during the event. It will address the necessity for application of Adaptive Design and Bayesian Statistics in order to achieve better and more efficient drug development, such as: better patient care, improved decision making, meeting requirements of regulatory agencies and payers, and industry's needs for the maximum outcome using the available resources.

PANELISTS:

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Principal
Middleburg Consultants

Donald Berry, PhD
Professor, Department of Biostatistics
University of Texas
MD Anderson Cancer Center

Robert Metcalf, PhD
Vice President
Global Regulatory Affairs
Eli Lilly and Company

Lisa M. LaVange, PhD
Director
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