DIA/FDA Statistics 2016 Forum

Tutorials (AM): April 25 | Forum: April 25-27 | Bethesda North Marriott Hotel and Conference Center | North Bethesda, MD

PROGRAM CO-CHAIRS:

Aloka Chakravarty, PhD
Director, Division of Biometrics VII, Office of Biostatistics, Office of Translational Sciences
CDER, FDA

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

PROGRAM COMMITTEE:

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Quintiles

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

Nevine Zariffa
Vice President and Head Biometrics and Information Sciences
AstraZeneca Pharmaceuticals

Who Should Attend

Professionals from industry, academia, and government involved in all phases of medical product development who are interested in learning the latest state of the art techniques for pharmaceutical development:

- Biostatisticians
- Clinical Pharmacologists
- Epidemiologists
- Physicians
- Health Economists
- Regulatory Scientists

Highlights

KEYNOTE SPEAKERS:

Robert M. Califf, MD
Commissioner of Food and Drugs
FDA

Ronald Wasserstein
Executive Director
American Statistics Association

NEW CLOSING SESSION WITH:

Martin Posch, PhD
Professor
Medical University of Vienna

- 2016 marks the 10 year anniversary of the DIA/FDA Statistics Forum! Join us for celebration cake April 25, 2:30–2:45PM
- Poster Presentations on April 26, 5:00–6:30PM
- Luncheon Round Table Discussions on April 26, 12:00-1:30PM
- Town Hall with Leaders from Industry and FDA on April 27, 2:30–3:30PM
- Access to the DIA Statistics Community and Multiple Scientific Working Groups
- Numerous Networking Opportunities

Learning Objectives

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

- Discuss the latest trends and updates from regulatory agencies, including the US FDA and EMA
- Introduce innovative and state of the art statistical solutions to assess safety and efficacy of new medical products in development
- Assess the impact of new and upcoming regulations and guidances on statistical practice
- Propose recommendations for improving the communication between industry statisticians and reviewers
- Discuss the latest information about new ICH guidance developments related to statistics and clinical trials
- Describe the qualification of biomarkers to include the standards for biomarkers, validation, framework, and statistical requirements

Message from Program Co-Chairs

Dear Colleagues,

On behalf of the Program Committee, we are pleased to welcome you to the *DIA/FDA Statistics 2016 Forum*. We are honored to co-chair the 10th anniversary of this highly valuable statistics forum, co-sponsored by both FDA and DIA.

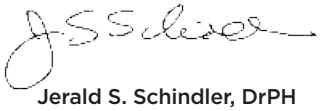
This forum is unique in setting the stage for an open, collaborative discussion of important statistical topics related to drug development among representatives from industry, academia, and regulatory agencies.

We will kick off with two preconference tutorials on Monday morning and the main forum will begin in the afternoon, and will feature our two keynote speakers. Our first address will be given by the new FDA's Commissioner of Food and Drugs, Dr. Robert M. Califf, followed by Ronald Wasserstein, Executive Director for the American Statistical Association.

We hope you take advantage of the many opportunities to actively engage in discussions and with each other. Be sure to join us Tuesday evening for the Networking Reception and Poster Session, and Wednesday during the luncheon for Round Table Discussions.

Best Regards,

Aloka Chakravarty, PhD
Director
Division of Biometrics VII
Office of Biostatistics,
Office of Translational Sciences
CDER, FDA



Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and
Adjunct Professor, Biostatistics
Harvard School of Public Health

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Schedule At-A-Glance

DAY ONE | MONDAY, APRIL 25

7:30AM–12:00PM	Tutorial Registration	Brookside AB Foyer
7:30–8:30AM	Tutorial Continental Breakfast and Networking	Brookside AB Foyer
8:30AM–12:00PM	Tutorial 1: Signal Detection from Drug Safety Databases Using Likelihood Ratio Tests	Brookside A
8:30AM–12:00PM	Tutorial 2: Recurrent Event Data Analysis in Clinical Trials	Brookside B
11:00AM–6:00PM	Forum Registration	Salon D Foyer
1:00–1:10PM	Welcome and Opening Remarks	Salon D
1:10–2:30PM	Keynote Addresses and Panel Discussion	Salon D
2:30–2:45PM	Celebration Cake! 10th Forum Anniversary	Salon D Foyer
2:45–4:15PM	Session 1: Real-World Evidence: Examples of Today and Tomorrow	Salon D
4:15–4:30PM	Refreshment Break and Networking	Salon D Foyer
4:30–5:30PM	Session 2: Single-Arm Trials and Use of Historical Data	Salon D
5:30–7:00PM	DIA Statistics Community: Open Meeting	Brookside AB

DAY TWO | TUESDAY, APRIL 26

7:30AM–6:00PM	Registration	Salon D Foyer
7:30–8:30AM	Continental Breakfast and Networking	Salon D Foyer
8:30–8:35AM	Welcome to Day Two	Salon D
8:35–10:05AM	Session 3: Endpoints and PROs	Salon D
10:05–10:30AM	Refreshment Break and Networking	Salon D Foyer
10:30AM–12:00PM	Session 4: Data Analysis of Recurrent Events	Salon D
12:00–1:30PM	Networking Luncheon and Round Table Discussions	White Oak
1:30–3:00PM	Session 5: Biomarkers	Salon D
3:00–3:30PM	Refreshment Break and Networking	Salon D Foyer
3:30–5:00PM	Session 6: Analytical Similarity Assessment for Biosimilars	Salon D
5:00–6:30PM	Networking Reception and Poster Session	Salon D Foyer

DAY THREE | WEDNESDAY, APRIL 27

7:30AM–4:00PM	Registration	Salon D Foyer
7:30–8:30AM	Continental Breakfast and Networking	Salon D Foyer
8:30–8:35AM	Welcome to Day Three	Salon D
8:35–10:05AM	Session 7: Innovative Designs and Strategies for Rare Disease Clinical Trials	Salon D
10:05–10:30AM	Refreshment Break and Networking	Salon D Foyer
10:30AM–12:00PM	Session 8: ICH Guidance Updates – Part 1	Salon D
12:00–1:00PM	Networking Luncheon	White Oak
1:00–2:30PM	Session 9: ICH Guidance Updates – Part 2	Salon D
2:30–3:30PM	Session 10: Town Hall	Salon D
3:30–4:00PM	Closing Session	Salon D
4:00PM	Forum Adjourned	

Continuing Education

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As an IACET Authorized Provider, DIA offers CEUs for its programs that qualify under the ANSI/IACET Standard. DIA is authorized by IACET to offer 1.9 CEUs for the program (and tutorial, if applicable). Participants must attend the entire forum in order to be able to receive an IACET statement of credit. No partial credit will be awarded.

Continuing Education Credit Allocation

- **Tutorial 1:** ***Signal Detection from Drug Safety Databases Using Likelihood Ratio Tests:*** .3 CEUs
- **Tutorial 2:** ***Recurrent Event Data Analysis in Clinical Trials:*** .3 CEUs
- **Forum:** 1.6 CEUs

If you would like to receive a statement of credit, you must attend the forum (and tutorial, if applicable), sign in at the registration desk each day, and complete the online credit request process through My Transcript. Participants will be able to download a statement of credit upon successful submission of the credit request. My Transcript will be available for credit requests on **Wednesday, May 11, 2016**.

To access My Transcript:

- Visit DIAglobal.org, select "Sign in" and you will be prompted for your user ID and password
- Choose MENU, found in the upper left corner
- Under CONFERENCES select "Continuing Education"
- Select the blue "My Transcript" button followed by "Credit Request" to process your credit request for the forum

The online evaluation closes on Wednesday, May 18, 2016.

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This program is part of DIA's Certificate Program and is awarded the following:

- Clinical Research Certificate Program: 10 Elective Units
- Regulatory Affairs Certificate Program: 10 Elective Units

For more information go to **DIAglobal.org/certificateprograms**

MONDAY, APRIL 25

7:30AM–12:00PM **Tutorial Registration**

7:30–8:30AM **Tutorial Continental Breakfast and Networking**

11:00AM–6:00PM **Forum Registration**

8:30AM–12:00PM Half Day Tutorials

Tutorial 1: Signal Detection from Drug Safety Databases Using Likelihood Ratio Tests

Instructors:

Ram Tiwari
Associate Director, Office of Biostatistics, Office of Translational Science
CDER, FDA

Lan Huang, PhD
Mathematical Statistician, Office of Biostatistics, Office of Translational Science
CDER, FDA

Jonathan G. Levine, PhD
Senior Scientist, Office of Critical Path Programs, OC
FDA

The statistical methods used for data-mining or signal detection of drug-adverse event combinations from large drug safety databases, such as FDA's Adverse Event Reporting System (FAERS), consisting of spontaneous reports on adverse events for postmarket drugs are called passive surveillance methods. On the other hand, the statistical signal detection methods for longitudinal data, as the data accrues in time, are called active surveillance methods. A review of the most commonly used passive surveillance statistical methods, along with a likelihood ratio test (LRT) based method, developed by the instructors, will be discussed in detail. A live demo of the LRT in OpenFDA tool that uses the FAERS data will be presented. Extensions of LRT, such as the LRT for a drug-class (Ext-LRT), the LRT for longitudinal safety data (Long-LRT), used for active surveillance, and the LRT for handling excessive number of zeros (ZIP-LRT) will also be presented in detail. Finally, use of the LRT in meta-analysis, when there are several studies, will be given.

The tutorial will consist of three modules:

- **Module-I**: A quick review of commonly used Bayesian and Frequentist methods for signal detection in passive surveillance will be given; then the basic LRT method will be discussed in detail and extensions of the LRT methodology to a drug-class and data with excessive zeros
- **Module-II**: A live demonstration of the LRT in OpenFDA tool (available for public use) to certain drugs or adverse events (AEs) from the FAERS database
- **Module-III**: The LRT for longitudinal clinical database and the use of the LRT in meta-analysis, when there are several studies

Who Should Attend:

Professionals who already have a basic knowledge of statistics.

Learning Objectives:

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

- Demonstrate familiarity with data-mining in a drug-safety database
- Explain commonly used methods for disproportionality analysis in drug safety databases
- Apply a new likelihood ratio test (LRT) based method with different extensions for disproportionality analysis that controls false positive and false discovery rates

Tutorial 2: Recurrent Event Data Analysis in Clinical Trials

Instructors:

Mouna Akacha, PhD
Statistical Methodologist
Novartis Pharma AG, Switzerland

H. M. James Hung, PhD
Director, Division of Biometrics I, Office of Biostatistics, Office of Translational Science
CDER, FDA

Recurrent events are repeated occurrences of the same type of event over time and are often encountered in clinical trials. Examples include relapses in multiple sclerosis and heart failure hospitalizations in chronic heart failure patients. In such studies, interest usually lies in understanding the underlying recurrent event process and how this is impacted by explanatory variables such as treatment. This includes the investigation of the rate at which events occur and the inter-individual variation.

We will review the objectives and challenges of recurrent event data approaches. Different statistical methods and modelling approaches including parametric and semi-parametric models will be discussed. We will illustrate the approaches with case studies, discuss own experiences, and provide SAS code snippets.

Learning Objectives:

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

- Discuss objectives, advantages, and limitations of recurrent event endpoints and approaches
- Apply appropriate statistical methods and modelling approaches to recurrent event endpoints
- Interpret the results based on different approaches

Who Should Attend:

All statisticians with interest in the design and analysis of clinical trials with recurrent event endpoints.

1:00–1:10PM

Welcome and Opening Remarks

Aloka Chakravarty, PhD
Director, Division of Biometrics VII, Office of Biostatistics, Office of Translational Science
CDER, FDA

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

Barb Jones, PhD
Associate Director, Scientific Collaboration, Strategic Communications
DIA

1:10–2:30PM

Keynote Addresses and Panel Discussion

Session Co-Chairs:

Aloka Chakravarty, PhD
Director, Division of Biometrics VII, Office of Biostatistics, Office of Translational Science
CDER, FDA

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

Keynote Addresses

Robert M. Califf, MD
Commissioner of Food and Drugs
FDA

Why Does it Hurt When I *p*?

Ronald Wasserstein
Executive Director
American Statistical Association

Panel Discussion

Joining the Keynotes

Panelists:

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

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

John Scott, PhD
Deputy Director, Division of Biostatistics
CBER, FDA

2:30–2:45PM Celebration Cake: 10th Forum Anniversary

2:45–4:15PM

Session 1: Real-World Evidence: Examples of Today and Tomorrow

Session Co-Chairs:

Nevine Zariffa
Vice President and Head Biometrics and Information Sciences
AstraZeneca Pharmaceuticals

Mark Levenson, PhD
Deputy Director, Division of Biometrics VII, Office of Biostatistics
CDER, FDA

Electronic medical data systems and other health care data sources have the potential to enhance our understanding of medical interventions. While the randomized clinical trial continues to have an established place in the realm of evidence generation, these new data sources also warrant recognition. Clinical, bioinformatic, statistical, and epidemiological experts will address how these data sources can be used to provide real-world evidence to address clinical and regulatory questions. They will also discuss how real-world evidence can most productively be used in the short term and more ambitious uses in the future, as well the challenges to making this happen.

Human-Machine Synergy for Effective Classification of Health and Health Events

Alec Walker, MD, DrPH
Drug Safety Epidemiologist
World Health Information Science Consultants

Oncology Real-World Evidence in Action: What Does it Take to Make the Promise of RWE a Reality?

Amy Abernethy, MD, PhD
Chief Medical Officer and Senior Vice President Oncology
Flatiron Health

Differentiating Real-World Information Versus Real-World Evidence

Frank Shen, PharmD, PhD
Vice President, Data and Statistical Sciences, GPRD
AbbVie Inc.

Use of Real-World Evidence in Regulatory Decision-Making: FDA Perspective

Jonathon Jarow, PhD
Director (Acting), Office of Medical Policy
CDER, FDA

Panel Discussion

4:15–4:30PM Refreshment Break and Networking

4:30–5:30PM

Session 2: Single-Arm Trials and Use of Historical Data

Session Co-Chairs:

Pandu Kulkarni, PhD
Vice President, Biometrics and Advanced Analytics
Eli Lilly and Company

Rajeshwari Sridhara, PhD
Director, Division of Biometric V, Office of Biostatistics, Office of Translational Science
CDER, FDA

Single-arm trials are on their way back in oncology and continue to be present in rare diseases. We will discuss the reasons for this shift, the circumstances in which single-arm trails are useful, and how to utilize the historical control data in such trials – in an appropriate practical and statistical sense. Examine the pitfalls of using single-arm trials and historical controls especially around Exchangeability (with or without controlling for covariates and time) and obtaining adequate data to assess inter-study variability (with or without controlling for covariates and time) and possible solutions to address these pitfalls.

A Prospective Retrospective Approach for Single-Arm Oncology Trials

Ralph D'Agostino Jr., PhD, FASA
Professor
Wake Forest University School of Medicine

Statistics, Rabbits, and Hats

Andrew Stone, MSc
Head of Statistical Innovation
AstraZeneca, United Kingdom

Single-Arm Trials in Hematology and Oncology Drug Applications: FDA Review Examples

Yuan-Li Shen, DrPH
Biostatistician, Office of Biostatistics, Office of Translational Science
CDER, FDA

Panel Discussion

Joining the Speakers

Discussant

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

5:30–7:00PM

DIA Statistics Community: Open Meeting

Whether you are already a member, or are interested in learning more about DIA's Statistics Community and its Data Hubs, this is great opportunity to network and to learn more about on-going projects and future initiatives.

Led by:

Joan Buenconsejo, MPH, PhD
Statistics Team Leader, Inflammation, Neuroscience and Respiratory TA, B and I Science
AstraZeneca Pharmaceuticals LP

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

THREE PART WEBINAR SERIES

Rare Diseases: On the Road to Approval: The Impact of Patient-Driven Data

While rare disease product approvals are held to the same evidentiary standards as common diseases, rare diseases faces unique challenges in designing and conducting the clinical trials to meet these standards.

Buy More and Save!

MAY 25 | 11:00AM–12:30PM ET
Part 1: Conducting Clinical Research in Collaboration with Patients and Patient Advocacy Groups

Explore the benefits and challenges associated with patient-focused approaches throughout clinical trial design and execution.

JUNE 9 | 11:00AM–12:30PM ET
Part 2: Developing Clinically Meaningful Patient Focused Outcome Measures

Define clinically meaningful endpoints that are relevant to the rare disease patient's definition of unmet medical needs while satisfying regulatory requirements and expectations.

JULY 14 | 11:00AM–12:30PM ET
Part 3: Evidentiary Standards for Rare Diseases: How Much Data is Enough?

Get a closer look at opportunities for registry data and natural history studies and join a frank discussion on registry data quality.

TUESDAY, APRIL 26

7:30AM–6:00PM **Registration**

7:30–8:30AM Continental Breakfast and Networking

8:30–8:35AM **Welcome to Day Two**

Aloka Chakravarty, PhD
Director, Division of Biometrics VII, Office of Biostatistics, Office of Translational Sciences
CDER, FDA

8:35–10:05AM **Session 3: Endpoints and PROs**

Session Co-Chairs:

Stephen E. Wilson, DrPH, CAPT, USPHS
Director, Division of Biometrics III
Office of Biostatistics, Office of Translational Science
CDER, FDA

Laura Lee Johnson, PhD
Associate Director, Office of Biostatistics, DB III, Office of Translational Science
CDER, FDA

FDA's effort to foster patient-focused drug development has several elements statisticians can leverage reaching from what was done in the past to where we see drug development moving. Three examples will be introduced and discussed. FDA's new Pilot Clinical Outcome Assessment (COA) Compendium collates and summarizes COA information for many different diseases and conditions into a single resource intended to facilitate communication and be used as a starting point for early drug development. CPATH's PRO Consortium and other consortia are working to fill critical measurement gaps with patent centric tools that will be used as primary and secondary endpoints in future clinical trials. PEDSnet is a multi-specialty pediatric learning health system including several of the United States' largest children's hospital health systems and is organized to quickly and inexpensively address important research questions using real-world data and common data models.

COA Compendium Pilot: An Update for Statisticians

Nikunj B. Patel, PharmD
Clinical Outcome Assessment Reviewer
Office of New Drugs
CDER, FDA

Using COAs from Electronic Health Records in Pediatric Clinical Care and Clinical Research

Charles Bailey, MD, PhD
Associate Professor of Pediatrics
Perelman School of Medicine at Children's Hospital of Philadelphia

PRO Consortium Activities Involving and Impacting Statistical Analyses in Trials

Laura Lee Johnson, PhD
Associate Director, Office of Biostatistics, DB III, Office of Translational Science
CDER, FDA

Panel Discussion

10:05–10:30AM Refreshment Break and Networking

10:30AM–12:00PM **Session 4: Data Analysis of Reccurrent Events**

Session Co-Chairs:

Mouna Akacha, PhD
Statistical Methodologist
Novartis Pharma AG, Switzerland

Peiling Yang, PhD
Statistics Team Lead, Division of Biometrics I, Office of Biostatistics, Office of Translational Science
CDER, FDA

In many chronic disease trials, treatment effects have been assessed through time-to-event endpoints; e.g. time to death or hospitalization in chronic heart failure trials or time-to-tumor occurrence in cancer trials. Traditionally, these time-to-event endpoints have been analyzed using a time-to-first-event analysis approach. A recurrent event approach, in which the first as well as subsequent events are included, would more accurately reflect the true burden of the illness on the patient. We will discuss the opportunities and challenges in the use of recurrent event endpoints from a statistical, regulatory, and clinical perspective. The focus will lie on cardiovascular outcome trials.

Recurrent Event Data Endpoints in Cardiovascular Outcome Trials: What is the Estimand of Interest?

Guenther Mueller-Velten, MS
Senior Global Group Head Biometrics and Statistical Sciences
Novartis Pharma AG, Switzerland

New Approaches to Capturing Disease Burden in Cardiovascular Studies

Brian Claggett, PhD, MA, MS
Instructor
Harvard Medical School

Panel Discussion

Joining the Speakers

Discussant

Norman Stockbridge, MD, PhD
Director, Division of Cardiovascular and Renal Products, OND
CDER, FDA

Panelists

H. M. James Hung, PhD
Director, Division of Biometrics I, Office of Biostatistics, Office of Translational Science
CDER, FDA.

Bruce Binkowitz, PhD, MSc
Executive Director, Late Development Statistics
Merck Research Laboratories

12:00–1:30PM Networking Luncheon and Round Table Discussions

Session Co-Chairs:

Joan Buenconsejo, MPH, PhD
Statistics Team Leader, Inflammation, Neuroscience and Respiratory TA, B and I Science
AstraZeneca Pharmaceuticals LP

Brenda Crowe, PhD
Senior Research Advisor, Global Statistical Sciences
Eli Lilly and Company

Peiling Yang, PhD
Team Lead, Division of Biometrics I, Office of Biostatistics, Office of Translational Science
CDER, FDA

1:30–3:00PM

Session 5: Biomarkers

Session Co-Chairs:

Jeff Maca, PhD
Senior Director, Biostatistics, Advisory Services Analytics Quintiles

Sue-Jane Wang, PhD
Associate Director, Adaptive Design and Pharmacogenomics, OB, Office of Translational Science
CDER, FDA

The BEST (Biomarker, Endpoints, and other Tools) resources, developed through a collaboration of FDA and NIH, recently became available on the National Center for Biotechnology Information's Bookshelf. In light of this new development, we will introduce the BEST resources to clarify what we mean when we talk about biomarkers, present the roadmap to qualify biomarkers, and share a real case study utilizing biomarker in phase II to take a go/no-go decision with or without enrichment for phase III. The session will then open to the floor for discussion.

Harmonization of Terminology for Biomarkers and Endpoints To Strengthen Quality and Improve Efficiency of Translational Science

Lisa McShane, PhD
Mathematical Statistician
National Cancer Institute

Roadmap to Biomarker Qualification: Strategy and Process

Shashi Amur, PhD
Senior Genomics Reviewer, Office of Clinical Pharmacology
CDER, FDA

A Phase II/III Biomarker-Based Bayesian Design

Marc Buyse, DrSc
Founder, CluePoints
International Drug Development Institute (IDDI)

3:00–3:30PM Refreshment Break and Networking

3:30–5:00PM

Session 6: Analytical Similarity Assessment for Biosimilars

Session Co-Chairs:

Eric M. Chi, PhD
Executive Director
Amgen

Yi Tsong, PhD
Director, Division of Biometrics VI, Office of Biostatistics, Office of Translational Sciences
CDER, FDA

Analytical similarity plays a fundamental role in the evaluation of biosimilar application. A tiered approach has been recommended by the FDA. The method to assess similarity for Tier 1 critical quality attributes (CQAs) is an equivalence test with the objective to show the mean difference between test (biosimilar) and reference products is within a pre-specified margin, and the method to assess similarity for Tier 2 CQAs is by a justified quality range. In consideration of a small number of observations and for the comparisons to be uniform and objective, FDA recommends to use 1.5 as the equivalence margin and mean ± c as the quality range where c needs to be justified. They are so recommended such that the inferences could have sufficient power. Experts from the FDA, industry, and academia will share their experiences and research of issues related to assessing analytical similarity.

Development of Equivalence Test for Analytical Similarity

Yi Tsong, PhD
Director, Division of Biometrics VI, Office of Biostatistics, Office of Translational Sciences
CDER, FDA

Handling Heavily Unbalanced Sample Size of Analytical Similarity Equivalence Test

Xiaoyu (Cassie) Dong, PhD
Mathematical Statistician, Office of Translational Sciences
CDER, FDA

Issues of Correlated Values in Equivalence Test for Analytical Biosimilar

Meiyu Shen, PhD
Mathematics Statistician, Office of Translational Sciences,
CDER, FDA

Analytical Similarity Assessment: Practical Challenges and Statistical Perspectives

Richard O. Montes, PhD
Associate Director, Statistics (Biosimilars Pharmaceutical Sciences)
Hospira, a Pfizer Company

Panel Discussion

Joining the Speakers

Discussant

Shein-Chung Chow, PhD
Professor
Duke University School of Medicine

5:00–6:30PM Networking Reception and Poster Session

Session Co-Chairs:

Stephen E. Wilson, DrPH, CAPT, USPHS
Director, Division of Biometrics III, Office of Biostatistics, Office of Translational Sciences
CDER, FDA

William Wang, PhD
Executive Director, Clinical Safety and Risk Management Statistics
Merck Research Laboratories, Merck & Co., Inc.
Biostatistics and Research Decision Sciences (BARDS), China

Poster Topic Areas:

- Dissolutation Profiles
- Sample Size Determiniation
- Adaptive Design and Bayesian Design
- CMC
- Modeling
- Statistical Science
- Clinical Safety and Pharmacovigilance
- Patient Advocacy

Poster Competition

Don't Forget to Vote for Best Poster!

Voting cards are available at the DIA registration desk. Cards must be returned by 6:30PM on April 26.

WEDNESDAY, APRIL 27

7:30AM–4:00PM **Registration**

7:30–8:30AM Continental Breakfast and Networking

8:30–8:35AM **Welcome to Day Three**

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

8:35–10:05AM **Session 7: Innovative Designs and Strategies for Rare Disease Clinical Trials**

Session Co-Chairs:

Brenda Crowe, PhD
Senior Research Advisor, Global Statistical Sciences
Eli Lilly and Company

Cristiana Mayer, PhD
Scientific Director, Statistical Modeling and Methodology, Statistics and Decision Science
Janssen Research and Development LLC

Yeh-Fong Chen, PhD
Mathematical Statistician, Office of Translational Sciences
CDER, FDA

Approximately 30 million people worldwide are affected by a rare disease. However, of the nearly 7,000 rare diseases, only about 400 have therapies. Given the limited number of patients with a specific rare disease, enrolling patients in clinical studies and drawing conclusions about the efficacy and safety of a treatment can be challenging. One possible solution is to adjust the general standards in clinical trials that apply well to common diseases for rare diseases, but there is still no consensus on the specifics that can ensure both the quality of good trials and the efficacy of the approved drugs. In this session, three experts from public and private sectors will present their research, challenges, lessons learned, and possible solutions.

Rare Diseases and Orphan Drug Development: Challenges and Opportunities

Laurie Muldowney, MD
Lead Medical Officer
CDER, FDA

Informational Designs and Potential Applications to Rare Diseases

Robert A. Beckman, MD
Professor of Oncology and of Biostatistics, Bioinformatics, and Biomathematics
Lombardi Comprehensive Cancer Center and Innovation Center for Biomedical Informatics, Georgetown University Medical Center

Can We Optimize Rare Disease Trials?

Carl Frederick Burman, PhD
Associate Professor in Biostatistics, Chalmers University of Technology; Senior Principal Scientist
AstraZeneca R&D, Sweden

Panel Discussion

10:05–10:30AM Refreshment Break and Networking

10:30AM–12:00PM **Session 8: ICH Guidance Updates – Part 1**

Session Co-Chairs:

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

Aloka Chakravarty, PhD
Director, Division of Biometrics VII, Office of Biostatistics, Office of Translational Science
CDER, FDA

An Addendum was proposed to provide clarification on E9 and an update on the choice of estimand in clinical trials to describe an agreed framework for planning, conducting, and interpreting sensitivity analyses of clinical trial data. This Addendum focuses on statistical principles related to estimands and sensitivity analysis, not on the use or acceptability of specific statistical procedures or methods. While a variety of mid-stage and late-stage clinical trials may be in scope, the primary focus of the Addendum will be on confirmatory clinical trials. It will promote harmonized standards on the choice of estimand in clinical trials and describe on agreed framework for planning, conducting, and interpreting sensitivity analyses of clinical trial data.

You will hear firsthand from the Topic Leader, Dr. Estelle Russek Cohen, followed by a panel discussion, in which key players in this initiative will share their insight. Ample time will be left to allow a robust floor discussion.

E9: Addendum to Statistical Principles for Clinical Trials: Missing Data, Estimands and Sensitivity Analysis

Estelle Russek-Cohen, PhD
Director, Division of Biostatistics, OBE
CBER, FDA
Frank Bretz, PhD
Global Head of Statistical Methodology
Novartis Pharma AG, Switzerland

Frank Bretz, PhD
Global Head of Statistical Methodology
Novartis Pharma AG

Panel Discussion

Joining the Speakers

Thomas J. Permutt, PhD
Director, Division of Biometrics II, Office of Biostatistics, OTS
CDER, FDA

12:00–1:00PM Networking Luncheon

1:00–2:30PM **Session 9: ICH Guidance Updates – Part 2**

Session Co-Chairs:

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

Aloka Chakravarty, PhD
Director, Division of Biometrics VII, Office of Biostatistics, Office of Translational Sciences
CDER, FDA

Session 9 will focus on two ICH guidelines:

E17 – Multi-Regional Clinical Trials (MRCTs)
With the increasing globalization of drug development, it has become important that data from MRCTs can be accepted by regulatory authorities across regions and countries as the primary source of evidence to support drug registration. The purpose of this guideline on MRCTs is to minimize the need to conduct single country, regional, or bridging studies. This guideline describes general principles for the planning and design of MRCTs with the aim of increasing the acceptability of the use of MRCTs in global regulatory submissions. It also addresses some strategic program issues as well as those that are specific to the planning and design of confirmatory MRCTs and should be used together with other ICH guidelines.

E14 – Q&A Document on QT prolongation study requirement; Update to allow use of concentration-response modeling
The hypothesis between a prolonged QT interval and Torsade de Pointes (TdP) cardiac arrhythmias is well-accepted by the medical development community and has been the subject of significant effort with regard to the safety of prescription drugs by the FDA. This effort has included the development by the International Conference on Harmonization (ICH) of the E14 Guidance (Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs). As the understanding of this phenomenon has progressed, the medical development community has been looking for improvements on this methodology. One popular alternative approach is the Concentration Response Relationship (CRR) method. Experiences by all parties with the implementation of the E14 Guideline have resulted in the need for some clarification. The questions and answers developed by the E14 Implementation Working Group (IWG) are intended to facilitate the implementation of the E14 Guideline by clarifying key issues.

The session will start with presentations by key players in these ICH guidance's, followed by a panel discussion to further elucidate major issues. Adequate time for floor discussion will allow participants to interact with the thought leaders.

E17: Multi-Regional Clinical Trials (MRCTs)

William Wang, PhD
Executive Director, Clinical Safety and Risk Management Statistics
Merck Research Laboratories, Merck & Co., Inc.

E14: Q&A Document on QT prolongation Study Requirement; Update to Allow Use of Concentration-Response Modeling

Yi Tsong, PhD
Director, Division of Biometrics VI, Office of Biostatistics, Office of Translational Science
CDER, FDA

Panel Discussion

2:30–3:30PM

Session 10: Town Hall

Session Co-Chairs:

Jerald S. Schindler, DrPH
Head, Translational Applied Statistics
Merck Research Laboratories and Adjunct Professor, Biostatistics
Harvard School of Public Health

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

Panelists will address questions posed by attendees:

- Via e-mail to Meredith.Kaganovskiy@DIAglobal.org
- During the forum, written questions may be turned in at the DIA registration desk
- By asking them live at the session

Topics may focus on the sessions held during this forum, but can also branch out into other areas of regulatory statistics.

Panelists:

Nevine Zariffa
Vice President and Head Biometrics and Information Sciences
Astrazeneca Pharmaceuticals

Pandurang M Kulkarni, PhD
Vice President, Global Biometrics and Advanced Analytics
Eli Lilly and Company

Eric Gibson, MS, PhD
Vice President, Global Head Biostatistical Sciences and Pharmacometrics
Novartis Pharmaceuticals Corporation

Gerry Gray, PhD
Acting Director, Division of Biostatistics, CDRH
FDA

Telba Irony, PhD
Deputy Director, Office of Biostatistics and Epidemiology
CBER, FDA

Thomas J. Permutt, PhD
Director, Division of Biometrics II, Office of Biostatistics, Office of Translational Science
CDER, FDA

3:30–4:00PM

Closing Session

Session Chair:

Jeff Maca, PhD
Senior Director, Biostatistics, Advisory Services Analytics
Quintiles

An Extrapolation Framework to Specify Requirements for Drug Development in Children

Martin Posch, PhD
Professor
Medical University of Vienna

4:00PM

Forum Adjourned