DIA/FDA Biostatistics Industry and Regulator Forum

Virtual Event: May 27-29

PROGRAM CO-CHAIRS

Karen Lynn Price, PhD
Senior Research Advisor, Statistical Innovation Center
Eli Lilly and Company

Mat Soukup, PhD
Deputy Director, Division of Biometrics VII
OB, OTS, CDER
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Statistical Methodologist
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Associate Director of Biometrics II, Office of Biostatistics,
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Executive Director, Clinical Safety Statistics, Biostatistics and Research Decision Sciences (BARDS)
Merck Research Laboratories

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Aloka Chakravarty, PhD
Deputy Director, Office of Biostatistics, Office of Translational Sciences, CDER
FDA

Overview

The *DIA Biostatistics Industry and Regulator Forum* is focused on statistical thinking to inform policy, regulation, development, and review of medical products in the context of the current scientific and regulatory environments including pharmaceuticals, biologics and biosimilars, combination products and devices, and generics. Each session will be co-chaired by an FDA/Industry team working side-by-side with today's experts to present a 360-degree perspective of statistical design, analysis, and methodological approaches to building evidence for pharmaceutical, biologic and biosimilar, combination product and device development, and approval.

The forum fosters open discussion of timely topics of mutual theoretical and practical interest to statisticians and clinical trialists who develop new drugs, biologics, and combination products. This unique forum advances the dialogue between industry, regulatory agencies, and academia.

Who Should Attend

Professionals involved in:

- Biostatisticians
- Bioinformaticists, Medical Informaticists
- Mathematical Statisticians
- Regulatory Scientists
- Clinical Pharmacologists
- Clinical Trial Design and Clinical Trial Optimization Specialists
- Clinical Research Physicians
- Epidemiologists
- Health Economists

Highlights

- In-depth discussions on new and revised guidances
- Town Hall: An open discussion lead by an expert panel of leaders from industry and regulatory agencies

Schedule At-A-Glance

DAY ONE | WEDNESDAY, MAY 27

10:45-11:00AM	DIA Remarks
11:00AM-12:30PM	**Session 1:** Challenges with Global Development and Satisfying Regulatory Requirements
12:30-1:30PM	Break
1:30-3:00PM	**Session 2:** Statistical, Regulatory, and Operational Considerations for the Use of Digital Health Technologies and Endpoints in Clinical Trials
3:00-3:30PM	Break
3:30-5:00PM	**Session 3:** Technology Advances for Design and Analysis of Complex Innovative Designs Issues

DAY TWO | THURSDAY, MAY 28

8:30-10:00AM	**Session 4:** The Evolution of MID3 and the Intersection of Biostatistics and Clinical Pharmacology in MID3 Clinical Trials Registration
10:00-10:30AM	Break
10:30AM-12:00PM	**Session 5:** The Role of Pragmatic Trials for Regulatory Problems
12:00-1:00PM	Break
1:00-2:30PM	**Session 6:** Safety and Benefit-Risk Assessment

DAY THREE | FRIDAY, MAY 29

9:30-11:00AM	**Session 7:** A Community of Networks, Creating, and Leveraging a Network of Distributed Data Supporting Medical Product Development
11:00AM-12:00PM	Break
12:00-1:30PM	**Session 8:** Senior Leaders Town Hall Session
1:30-2:00PM	Break
2:00-3:30PM	**Session 9:** Therapeutic Area Focused Session: Diabetes with a Focus on NASH

Learning Objectives

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

- Describe the challenges and opportunities in applying Complex Innovative Designs and the role of simulation
- Identify the opportunities and challenges arising in patient-focused drug development
- Discuss the role that statisticians play in patient-focused drug development
- Explain how patient preferences and clinical outcome assessments can inform and influence regulatory submissions
- Discuss the unique challenges in the assessment of complex generics from statistical, clinical, and regulatory perspectives
- Identify GDUFA II enhancements for complex generics
- Describe the most common designs using Master Protocols and their utility in solving clinical development challenges
- Identify the operational challenges and considerations in executing Master Protocols
- Discuss the pros, cons, and common mistakes for Master Protocol designs through a panel discussion
- Discuss the estimand challenges and opportunities arising in oncology drug development
- Evaluate the differences among stakeholder views on clinically meaningful estimands
- Apply the estimand framework to the learner's own clinical investigations
- Describe the collaboration of statistical science with data science in drug development
- Identify what has changed in the role of the statistician
- Describe opportunities for drug development based on advancements in new technologies and data analytics
- Identify common clinical issues that arise when characterizing the safety and benefit-risk of a pharmaceutical product
- Apply good statistical practice for safety-related topics

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DAY ONE | WEDNESDAY, MAY 27

10:45-11:00AM — **DIA Remarks**

11:00AM-12:30PM — **Session 1:** Challenges with Global Development and Satisfying Regulatory Requirements

Session Chair
Mouna Akacha, PhD, Statistical Methodologist, Novartis Pharma AG, Switzerland

Session Co-Chair
Aloka Chakravarty, PhD, Deputy Director, Office of Biostatistics, Office of Translational Sciences, CDER, FDA

In this session we will provide an overview of the changes in the regulatory landscape driven by the development of various ICH guidance documents (E8, E9, E11, E17, E19, E20). The key statistical challenges and opportunities that are in scope of the ICH guidelines will be discussed. Furthermore, the link and the overlap of some of the guidelines will be highlighted and the role of the Bayesian framework in these developments will be discussed.

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

Gregory Levin, PhD, Deputy Director, DBIII, OB, OTS, CDER, FDA

John Scott, PhD, MA, Director, Division of Biostatistics, OBE, CBER, FDA

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

Andrew Thomson, MA, MS, PhD, Statistician, Biostatistics and Methodology Support Office European Medicines Agency

Greg Ball, PhD, Clinical Safety Statistics, Merck & Co., Inc

12:30-1:30PM — **Break**

1:30-3:00PM — **Session 2:** Statistical, Regulatory, and Operational Considerations for the Use of Digital Health Technologies and Endpoints in Clinical Trials

Session Chair
Jonathan Haddad, MPH, Senior Director, Clinical Statistics, GlaxoSmithKline

Session Co-Chair
Scott Komo, DrPH, Mathematical Statistician, Office of Translational Sciences, CDER, FDA

This session will briefly review the digital health technology landscape as it pertains to clinical trials. Examples of where digital health technology data/endpoints are incorporated in clinical trials and the statistical, regulatory, and operational considerations will be presented. Representatives from Working Groups in this space will discuss key challenges and next steps to realize greater integration of digital data (the future).

Presentation Title
Andrew Potter, PhD, Mathematical Statistician, OB, OTS, CDER FDA

Presentation Title
Luis Garcia-Gancedo, Director, Digital Biomarkers, GSK

Presentation Title
Tyler Reynolds, Digital Health Consultant, PA Consulting

3:00-3:30PM — **Break**

3:30-5:00PM

Session 3: Technology Advances for Design and Analysis of Complex Innovative Designs Issues

Session Chair
Karen Lynn Price, PhD, Senior Research Advisor, Statistical Innovation Center, Eli Lilly and Company

Session Co-Chairs
Dionne Price, PhD, Director, Division of Biometrics IV, Office of Biostatistics, OTS, CDER FDA

The Food and Drug Administration launched the Complex Innovative Trial Design (CID) Pilot Program as a deliverable under the sixth iteration of the Prescription Drug User Fee Amendments. The goal of the program is to facilitate the advancement and use of complex adaptive, Bayesian, or other innovative clinical trial designs requiring simulations to estimate operating characteristics. Given the extent of simulations required and computational intensity associated with the number of simulations needed, it is important that we leverage and advance cutting-edge technology to enable efficient conduct and evaluation of simulations for CIDs. In this session, we will discuss the latest technological advances further enabling CIDs and explore gaps still existing and ways to potentially meet those gaps.

Speakers
Paul Schuette, PhD, MS, Mathematical Statistician, OB, OTS, CDER FDA

Maria Matilde S. Kam, PhD, Associate Director Analytics & Informatics, FDA

Roger J. Lewis, MD, PhD, Professor and Chair, Department of Emergency Medicine Harbor-Ucla Medical Center

Eric Nantz, DrSc, MSc, Principal Research Scientist, Eli Lily and Company

DAY TWO | THURSDAY, MAY 28

8:30-10:00AM

Session 4: The Evolution of MID3 and the Intersection of Biostatistics and Clinical Pharmacology in MID3 Clinical Trials

Session Chair
Jonathan Haddad, MPH, Senior Director, Clinical Statistics, GlaxoSmithKline

Session Co-Chair
Lei Nie, PhD, Associate Division Director in Division of Biometrics II, OTS, CDER, FDA

This session will briefly describe the intent and potential benefits of the MID3 approach. We will share current activities to pilot MID3 and to develop guidelines for the use of MID3 in clinical trials. Opportunities for best working practices and collaboration between the biostatistics and clinical pharmacology functions within both the agency and industry will be explored. It is assumed that the audience will have a basic familiarity with MID3.

Speaker
Lei Nie, PhD, Associate Director of Biometrics II, Office of Biostatistics, OTS, CDER, FDA

Speaker
Hao Zhu, PhD, Deputy Division Director, Division of Pharmacometrics, Office of Clinical Pharmacology, FDA

Speaker
Anubha Gupta, PhD, Pharmacometrician/Clinical Pharmacologist, GSK

10:00-10:30AM

Break

10:30AM-12:00PM

Session 5: The Role of Pragmatic Trials for Regulatory Problems

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

Session Co-Chairs
Frank W. Rockhold, PhD, MSc, Professor of Biostatistics, Duke Clinical Research Institute, Duke University Medical Center

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

Regulators and industry are actively exploring the use of real world evidence (RWE) to address important regulatory problems. Randomized pragmatic trials provide a promising source of RWE. This session considers the role of pragmatic trials for regulatory problems and focuses on the clinical and statistical objectives of pragmatic trials and their appropriateness for regulatory problems.

Per-Protocol Analyses of Pragmatic Trials
Miguel Hernan M.D., Dr. P.H., Professor, Departmend of Epidemiology, Harvard T.H. Chan School of Public Health

ITT Analyses of Pragmatic Trials: Is the 21st Century Different from the Past?
Janet Turk Wittes, PhD, President, Statistics Collaborative Inc.

Panelists
Peter Stein, MD, Director, Office of New Drugs, CDER, FDA

12:00-1:00PM **Break**

1:00-2:30PM **Session 6:** Safety and Benefit-Risk Assessment

Session Chair
William Wang, PhD, Executive Director, Clinical Safety Statistics, Biostatistics and Research Decision Sciences (BARDS), Merck Research Laboratories

Session Co-Chairs
Brenda Crowe, PhD, Senior Research Advisor, Global Statistical Sciences, Eli Lilly and Company

Gregory Levin, PhD, Deputy Director, DBIII, OB, OTS, CDER FDA

Several documents, such as the International Conference on Harmonization (ICH) M4E (R2) and ICH E2 series give guidance on what should be included in safety and benefit risk assessments for new drug applications and post marketing evaluation. These documents set good objectives for safety and benefit-risk evaluation during drug development. How to achieve these goals is an active topic of discussion for regulators and drug developers. This session will focus on the current regulatory landscape, industry practice and emerging trends for safety and benefit risk evaluation throughout the drug development lifecycle, with a particular focus on improved planning.

Benefit-Risk Assessment Along the Product Lifecycle
Sara Eggers, PhD, Director, Decision Support and Analysis Team, Office of Program and Strategic Analysis/ Office of Strategic Programs, CDER, FDA

Improved Safety and Benefit-Risk Planning
Gregory Levin, PhD, Deputy Director, DBIII, OB, OTS, CDER, FDA

Aggregate Safety and Benefit-Risk Assessment Planning: Multi-Disciplinary Approach
Lothar Tremmel, PhD, Head Biostatistics and Medical Writing, CSL Behring

DAY THREE | FRIDAY, MAY 29

9:30-11:00AM **Session 7:** A Community of Networks, Creating, and Leveraging a Network of Distributed Data Supporting Medical Product Development

Session Chair
Rima Izem, PhD, Biostatistician, Division of Biostatistics and Study Methodology Children's Research Institute at Children's National Medical Center

Session Co-Chairs
Pallavi Mishra-Kalyani, Mathematical Statistician, FDA

The size, number and diversity of healthcare data sources increases at a faster pace than the speed of this information's use in regulatory and business decisions necessary in the drug development lifecycle. The innovation leverages common goals to share resources and advance public health more efficiently than any member of the network could feasibly accomplish alone. The innovation is also in creating standards, processes, designs and analyses which account for the distributed nature of the information and is fair to stakeholders in the network. This latter set of innovation can be borrowed and adapted by future networks

and partnerships. This panel will discuss the promise and accomplishments of networks in designing clinical trials or observational studies to assess drug safety, and efficacy in rare diseases and oncology. Panelists will discuss lessons learned in creating these networks, their accomplishments and promising current/future work.

Speaker
Jeremy Rassen, DrSc, MS, Co-Founder, President and Chief Science Officer, Aetion

Arecelis Torres, PhD, MPH, Director, Quantitative Sciences, Flatiron Health

Klaus Romero MD, MS, Chief Science Officer, Executive Director, Clinical Pharmacology and Quantitative Medicine, Critical Path Institute

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

Yong Ma, PhD, Mathematical Statistician, OB, OTS, CDER, FDA

11:00AM-12:00PM **Break**

12:00-1:30PM **Session 8:** Senior Leaders Town Hall Session

Session Chair
Mat Soukup, PhD, Deputy Director, Division of Biometrics VII, OB, OTS, CDER, FDA,

Session Co-Chair
Karen Lynn Price, PhD, Senior Research Advisor, Statistical Innovation Center, Eli Lilly and Company,

If hindsight is 20/20, the year 2020 seems an opportune time to reflect on the past decades of clinical research to gain a clearer understanding of where we've been, key lessons we have learned, and apply learnings from the past to tackle tomorrow's challenges. In this session, senior leaders from the biostatistics community will share examples and provide insights from their own personal experiences on topics from the past that were innovative historically but are commonplace today. These leaders will reflect on the lessons learned and keys to the successful adoption of more innovative approaches to address challenges. Alternatively, innovative ideas that failed to progress may be discussed in an effort to learn for the future.

Panelists
Sylva Collins, PhD, Director, Office of Biostatistics, OTS, CDER, FDA

John Scott, PhD, MA, Director, Division of Biostatistics, OBE, CBER, FDA

Pandurang Kulkarni, PhD, Chief Analytics Officer-R&D / Vice President-Biometrics, Eli Lilly and Company

Lisa Lupinacci, PhD, MS, Vice President, Late Development Statistics, Merck and Co., Inc.

Amy Xia, PhD, Vice President, Biostatistics, Design & Innovation, Amgen Inc.

Ram Tiwari, PhD, Director, Division of Clinical Evidence and Analyses 2, Biostatistics, CDRH, FDA

1:30-2:00PM **Break**

2:00-3:30PM **Session 9:** Therapeutic Area Focused Session: Diabetes with a Focus on NASH

Session Chair
Mouna Akacha, PhD, Statistical Methodologist, Novartis Pharma AG, Switzerland

Session Co-Chairs
William Wang, PhD, Executive Director, Clinical Safety Statistics, Biostatistics and Research, Decision Sciences (BARDS), Merck Research Laboratories

George Kordzakhia, PhD, Mathematical Statistican, CDER FDA

Non-alcoholic steatohepatitis (NASH) is a liver inflammation and damage caused by a buildup of fat in the liver. With the growing burden of NASH, and the inherent limitations of transplantation both in terms of cost and number of livers available, it is critical to increase the pace of development of safe and effective therapies to prevent and treat NASH (see Liver Forum Project). In this session, we will discuss the challenges and opportunities that arise when developing drugs in NASH, e.g. what is the estimand of primary interest?

Speakers

Paul Imbriano, PhD, MSc, Mathematical Statistician, FDA

Veronica Miller, PhD, Executive Director, Forum for Collaborative Research and Professor at UC Berkeley School of Public Health

Peter Grant Mesenbrink, PhD, Executive Director Biostatistics, Novartis Pharmaceuticals Corporation, Global Drug Development- IHD Development Unit, Transplantation and Hepatology Therapeutic Area

Panelist

Michael Crutchlow, Distinguished Scientist, Clinical Research, Late Stage Development, Diabetes & Endocrinology, Merck Research Laboratories