DIA/FDA Advancing Complex Innovative Clinical Trial Designs to Efficiently Deliver Medicines to Patients

Conference: March 2-3 | Tommy Douglas Conference Center | Silver Spring, MD

PROGRAM CO-CHAIRS

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Overview

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Complex Innovative Trial Designs (CID) have the potential to increase the efficiency and lower the cost of drug development which will accelerate patient access to life altering therapies. The 21st Century Cures Act (Cures Act) and the sixth iteration of the Prescription Drug User Fee Act (PDUFA VI) recognize the need for CID and include provisions to advance their use to enhance medical product development. One such provision within PDUFA VI is the launch and implementation of the FDA CID Pilot Meeting Program which aims to foster discussions and education of the use and value of CID within drug development programs.

In an effort to promote CID, this unique conference will provide a platform for extensive scientific exchange among the FDA, other global health authorities including EMA, PMDA, and CFDA, patient advocates, and drug development innovators on CID topics such as master protocols, complex adaptive design, and Bayesian techniques, highlighting also the potential of alternative data sources.

Each session will begin with an introductory presentation by an FDA representative to set the stage followed by presentations and perspectives from a diverse group of expert speakers and panelists. The suitability of each CID topic and the proposed innovations from a US and global regulatory perspective, their usefulness from a patient perspective, and how challenges in the designs can be overcome, will be explored.

This conference is designed for key drug development decision-makers including clinicians, regulatory scientists and reviewers, and other key stakeholders, in addition to statistical specialists. Join us in this unique forum that will catalyze progress in advancing innovation in drug development.

The program is developed in collaboration with BIO, PhRMA and FDA.

Bio Biotechnology Innovation Organization

PhRMA RESEARCH + PROGRESS + HOPE

Who Should Attend

Professionals involved in:

- Biostatistics, Including Adaptive Design and Bayesian Statistics
- Clinical Research
- Research and Development
- Trial Design
- Clinical Operations
- Therapeutic Area Development, Management, and Operationist
- Rare disease, Oncology, Immunology, Alzheimer's disease
- Medical Affairs
- Medical Science Liaisons
- Medical Writing
- Regulatory Affairs

Schedule At-A-Glance

DAY ONE | MONDAY, MARCH 2		ROOM
7:00AM-5:00PM	Registration	Mezzanine
7:00-8:00AM	Continental Breakfast and Networking	Mezzanine
8:00-8:30AM	**Welcome and Opening Remarks**	Ballroom AB
8:30-9:00AM	**Keynote Address**	Ballroom AB
9:00-10:30AM	**Session 1:** PDUFA VI Pilot Program and Discussion	Ballroom AB
10:30-11:00AM	Refreshment and Networking Break	Mezzanine
11:00AM-2:15PM	**Session 2:** CID - Master Protocols	Ballroom AB
12:20-1:15PM	Luncheon and Networking	Cafeteria
2:15-5:05PM	**Session 3:** Flexible, Efficient Decision-Making: Complex Adaptive Design	Ballroom AB
3:00-3:30PM	Refreshment and Networking Break	Mezzanine
5:05-6:05PM	Networking Reception	Mezzanine
DAY TWO | TUESDAY, MARCH 3		
7:30AM-5:00PM	Registration	Mezzanine
7:00-8:00AM	Continental Breakfast and Networking	Ballroom AB
8:00-8:10AM	**Welcome to Day Two**	Ballroom AB
8:10-8:40AM	**Day 2 Keynote**	Ballroom AB
8:40-11:30AM	**Session 4:** Bayesian Designs: Continuous Learning and Decision-Making	Ballroom AB
9:40-10:10AM	Refreshment and Networking Break	Mezzanine
11:30AM-12:30PM	Luncheon and Networking	Cafeteria
12:30-3:20PM	**Session 5:** Alternative Data Sources and Historical Controls	Ballroom AB
1:50-2:20PM	Refreshment and Networking Break	Mezzanine
3:20-4:50 PM	**Session 6:** Global Regulatory Affairs	Ballroom AB
4:50-5:15PM	Closing Remarks	Ballroom AB

Learning Objectives

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

- Explain how complex innovative clinical trial designs (CIDs) contribute to increased efficiency and other enhancements of medical product research in order to ultimately accelerate patient access to innovative therapies
- Describe the purpose, anticipated outcomes, and progress to date of the FDA CID Pilot Program
- Discuss the views of global regulatory authorities (e.g., FDA, EMA, PMDA, and NMPA) on CIDs and their suitability/applicability for clinical research in their respective regions
- Explore aspects and further opportunities for alignment among global regulatory agencies in regard to CID adoption
- Examine several examples of CIDs, including master protocol designs, complex adaptive designs, and designs using Bayesian techniques, and discuss their regulatory suitability, potential challenges, and benefits for patients and medical product developers.

Continuing Education Credit

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DAY ONE | MONDAY, MARCH 2 — ROOM

7:00AM-5:00PM — **Registration** — Mezzanine

7:00-8:00AM — **Continental Breakfast and Networking** — Mezzanine

8:00-8:30AM — **Welcome and Opening Remarks** — Ballroom AB

Session Chair and Speakers
Bill Allman, Chief Technology Officer, DIA

Robert A. Beckman, MD, Professor of Oncology, Biostatistics, Bioinformatics, & Biomathematics, Georgetown University Medical Center

Fanni Natanegara, PhD, Principal Research Scientist, Eli Lilly and Company

Richard Moscicki, MD, Executive Vice President, Science and Regulatory Advocacy, Chief Medical Officer, Pharmaceutical Research and Manufacturers of America (PhRMA)

E. Cartier Esham, PhD, Executive Vice President, Emerging Companies Senior Vice President, Science and Regulatory Affairs, Biotechnology Innovation Organization (BIO)

8:30-9:00AM — **Keynote Address** — Ballroom AB

Abby Bronson, MBA, Senior Vice President of Research Strategy, Parent Project Muscular Dystrophy

9:00-10:30AM — **Session 1:** PDUFA VI Pilot Program and Discussion — Ballroom AB

Session Chair
Dionne Price, PhD, Director, Division of Biometrics IV, Office of Biostatistics, OTS, CDER, FDA

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

The Complex Innovative Trial Design (CID) Pilot Program was launched in August 2018 with the goal of advancing the use of novel designs when appropriate. The CID Pilot Program will achieve this goal through increased interactions between regulatory staff, industry, and public discussion of case examples for learning and information sharing. In this session, we will discuss the goals and progress of the program and set the stage for subsequent sessions by introducing case examples.

The Complex Innovative Trial Design Pilot Program: Setting the Stage
Dionne Price, PhD, Director, Division of Biometrics IV, Office of Biostatistics, OTS, CDER, FDA

Panelists
William H. Dunn, MD, Director, Division of Neurology Products, OND, CDER, FDA

Danise Subramaniam, PhD, Senior Director, Global Regulatory Affairs, Eli Lilly and Company

May Mo, Executive Director, Biostatistics, Amgen Inc

Abby Bronson, MBA, Senior Vice President, Research Strategy, Parent Project Muscular Dystrophy

10:30-11:00AM — **Refreshment and Networking Break** — Mezzanine

11:00AM-2:15PM — **Session 2:** CID - Master Protocols — Ballroom AB

Session Chair
Zoran Antoijevic, Msc, Head of Biometrics, MedSource

Min (Annie) Lin, MD, PhD, Mathematical Statistician, Division of Biostatistics, CBER, FDA

Rui (Sammi) Tang, PhD, Head of US Biostatistics and Programming Department and Medical Writing, Servier Pharmaceuticals

Master Protocols test multiple therapies in one indication, one therapy for multiple indications, or both. They also allow for discontinuation or addition of treatment arms and the concept known as platform trial. Master Protocols can significantly improve the efficiency of drug development when appropriately

designed and implemented. In this session we will discuss how to manage Master Protocols design and implementation complexities. We will present one case study and then follow up with novel approaches that focus on the confirmatory stage of development.

A Master Protocol for Chronic Pain: a Brief Overview and Lessons Learned
James Travis, PhD, Senior Staff Fellow, OB, OTS, CDER, FDA

Design and Analysis of Treatment Trials of Ebola Virus Disease
Michael Proschan, PhD, Mathematical Statistician, Biostatistical Research Branch, National Institute of Allergy & Infectious Diseases, NIH

Master Protocols and Clinical Trial Innovation
Lisa LaVange, PhD, Professor and Associate Chair Department of Biostatistics; Director of Collaborative Studies Coordinating Center, University of North Carolina at Chapel Hill

Complex Innovative Design for a Basket Trial
Vlad Dragalin, PhD, Vice President, Scientific Fellow, Janssen R&D at Johnson & Johnson

Panelist
Nora Carbine, Georgetown Breast Cancer Advocate

12:20-1:15PM **Luncheon and Networking** Cafeteria

2:15-5:05PM **Session 3:** Flexible, Efficient Decision-Making: Complex Adaptive Design — Ballroom AB

Session Chair
Yi Liu, PhD, Senior Director Biostatistics, Nektar Therapeutics

Cristiana Mayer, DrSc, PhD, Director, Statistics and Decision Sciences, Janssen Research & Development, LLC

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

Novel methods for planning decision-making in Complex Innovative Designs comprise different features of adaptive efficient trials. Efficiency can be viewed from different angles to balance correct decision-making as early as possible for a drug development program with cost effectiveness and quantification of multiple metrics to measure "success" of a trial. An example of a platform trial in the infectious disease area is presented to illustrate a Bayesian approach to utilize longitudinal data for developing a predictive model for the long-term clinical outcome. In confirmatory settings, the use of a basket trial will be used to illustrate the effect of adaptive trials on cost effectiveness and feasibility of drug development in rare diseases and/or subgroups of common diseases like cancer. A third presentation will address an optimal sample size adaptation rule that maximizes return on investment, a metric to balance time to market, trial costs, and probability of success.

Speaker
Cesar Torres, PhD, MS, Mathematical Statistician FDA

Improving Efficiencies in Drug Development Through a Platform Trial
Kyle Wathen, PhD, MS, Senior Directory Advanced Analytics, Gilead Sciences

Efficiency and Type I Error Control of a Generalized Confirmatory Basket Trial Design
Robert A. Beckman, MD, Professor of Oncology and of Biostatistics, Bioinformatics, & Biomathematics, Georgetown University Medical Center

Optimal Sample Size Re-estimation in Adaptive Design based on Return on Investment
Yi Liu, PhD, Senior Director Biostatistics, Nektar Therapeutics

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

Nora Carbine, Georgetown Breast Cancer Advocate

3:00-3:30PM **Refreshment and Networking Break** Mezzanine

5:05-6:05PM **Networking Reception** Mezzanine

DAY TWO | TUESDAY, MARCH 3 — ROOM

7:00AM-5:00PM — **Registration** — Mezzanine

7:00-8:00AM — **Continental Breakfast and Networking** — Mezzanine

8:00-8:10AM — **Welcome to Day Two** — Ballroom AB

Robert A. Beckman, MD, Professor of Oncology, Biostatistics, Bioinformatics, and Biomathematics, Georgetown University Medical Center

Fanni Natanegara, PhD, Principal Research Scientist, Eli Lilly and Company

8:10-8:40AM — **Day 2 Keynote** — Ballroom AB

Gianna McMillan, PhD, Bioethics Program Administrator, LMU Bioethics Institute

8:40-11:30AM — **Session 4:** Bayesian Designs: Continuous Learning and Decision-Making — Ballroom AB

Session Chair
Fanni Natanegara, PhD, Principal Research Scientist, Eli Lilly and Company

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

Through the CID Pilot Program afforded by PDUFA VI, FDA supports the advancement and use of Bayesian clinical trial designs. The Bayesian framework enables continuous learning from various data sources and provides decision-makers with straightforward probabilistic statements. This session will motivate the use of Bayesian approaches in CID by presenting case studies in broad therapeutic areas including rare diseases and highly prevalent chronic disease and discussing success stories, challenges, and opportunities to facilitate drug development.

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

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

Complex Bayesian Primary Analyses in Confirmatory Trials
Scott Berry, PhD, President and Senior Statistical Scientist, Berry Consultants LLC

Bayesian Modeling in the CID Pilot Program: Lilly's Pain Master Protocol
Jon David Sparks, PhD, Principal Research Scientist, Eli Lilly and Company

Panelist
Gianna McMillan, PhD, Bioethics Program Administrator, LMU Bioethics Institute

9:40-10:10AM — **Refreshment and Networking Break** — Mezzanine

11:30AM-12:30PM — **Luncheon and Networking** — Cafeteria

12:30-3:20PM — **Session 5:** Alternative Data Sources and Historical Control — Ballroom AB

Session Co-Chairs
Pritibha Singh, MBA, MSc, Novartis

Maria Apostolaros, JD, MS, PharmD, RPh, PhRMA

Laura Lee Johnson, PhD, Director, Division of Biometrics III, Office of Biostatistics, Office of Translational Sciences, CDER, FDA

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

The CID program enables the exploration of the innovative use of alternative data sources. This exploration continues to be increasingly important as we encounter the emerging challenges with alternative data sources in methodological approaches to data collection, analysis, and benefit to the patients, regulators, and biopharmaceutical companies. This session will inspire and open you to the possibilities of utilizing alternative data sources, e.g. digital approaches to identify, screen, enroll, collect data on, and provide an intervention to patients.

Speakers
Pritibha Singh, MBA, MSc, Novartis

Data in the Wild: Design Lessons from the Apple Heart Study
Manisha Desai, PhD, Professor of Medicine, Biomedical Data Science, Stanford University School of Medicine

Borrowing Information from Historical Data: A Double-edged Sword
Ying Yuan, PhD, Bettyann Asche Murray Distinguished Professor, Deputy Chair, Department of Biostatistics, University of Texas MD Anderson Cancer Center

DIA Advancing Complex Innovative Clinical Trial Designs to Efficiently Deliver Medicines to Patients
Jackson Kempber Burton III, PhD, Scientific Director, Quantitative Medicine

Laura Lee Johnson, PhD, Director, Division of Biometrics III, Office of Biostatistics, Office of Translational Sciences, CDER, FDA

1:50-2:20PM **Refreshment and Networking Break** Mezzanine

3:20-4:50PM **Session 6:** Global Regulatory Affairs Ballroom AB

Session Chair
Cristiana Mayer, DrSc, PhD, Director, Statistics and Decision Sciences, Janssen Research & Development, LLC

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

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

This session will consist of two presentations from EMA and PMDA followed by a panel from FDA, EMA, and PMDA to discuss their perspectives on use of complex innovative designs (CID). We will highlight the regulatory principles, current thinking and activities related to utilization and evaluation of innovative designs in various regulatory agencies. Challenges, opportunities and best practices in applying CID will be described. Furthermore, we will discuss key aspects on how to interact with regulatory agencies in different regions on global trials with CID for the purpose of global registration.

European Reflections on Complex Innovative Designs
Frank Petavy, MS, Head of Biostatistics and Methodology Support, Human Medicines Development, European Medicines Agency, European Union

Yuki Ando, PhD, Senior Scientist for Biostatistics, Office of New Drug I, Pharmaceuticals and Medical Devices Agency

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

4:50-5:15PM **Closing Remarks** Ballroom AB

Dionne Price, PhD, Director, Division of Biometrics IV, Office of Biostatistics, OTS CDER, FDA

Fanni Natanegara, PhD, Principal Research Scientist, Eli Lilly and Company

Robert Beckman, MD, Professor of Oncology, Biostatistics, Bioinformatics, and Biomathematics, Georgetown University Medical Center