



# 10th Annual FDA/AdvaMed Medical Devices & Diagnostics Statistical Issues Conference

Washington Marriott at Metro Center | Washington, DC  
April 26 – 27, 2017

## Wednesday, April 26, 2017

- 8:45 – 9:15 am**                    **Registration Check-In and Breakfast**
- 9:15 – 9:20 am**                    **Welcome and Introduction of Keynote Speaker**  
Ram Tiwari, Division Director, Division of Biostatistics, CDRH/FDA
- 9:20 – 10:00 am**                   **Keynote Address - Innovation and Statistics in Medical Devices**  
Robert Califf, Former Commissioner, FDA
- 10:00 – 10:30 am**                 **Break**
- 10:30 – 12:00 am**                **Perspectives on the Use of RWE from FDA and Industry**

### Co-organizers:

Nelson Lu, Team Leader, Division of Biostatistics, CDRH/FDA  
Terri Johnson, Acting Branch Chief, Division of Biostatistics, CDRH/FDA  
Jim Lesko, Johnson & Johnson  
Liz Galle, CVRx, Global Clinical Research

### Speakers/Panelists

Myoung Kim, Executive Director, Johnson & Johnson Medical Devices & Diagnostics  
Lilly Yue, Deputy Director, CDRH/FDA

### Additional Panelists:

Ling Zheng, Associate Professor of Research Neurology, Director of Quality Informatics  
Keck School of Medicine, University of Southern California  
Roseanne White, Director of Pragmatic Clinical Trial Statistics, Duke Clinical Research  
Institute  
Greg Campbell, Principal Statistician, GCStat Consulting  
Meijuan Li, Chief, Diagnostic Statistics Branch II, Division of Biostatistics, CDRH/FDA  
Lakshmi Vishnuvajjala, Chief, Diagnostic Devices Branch 1 / Division of Biostatistics,  
CDRH/FDA  
Jean Cooper, Associate Office Director for Surveillance and Outreach, OIVD/CDRH

There are great opportunities to use real-world data to potentially reduce the cost and duration of clinical trials, but challenges arise concerning how to use the data to draw reliable statistical inferences. Speakers will present FDA and industry perspectives on the use of RWE in both pre and post-market settings, and share specific ways to use current RWD sources. Following presentations, speakers will be joined by additional representatives from academia, FDA and industry for a panel discussion.

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12:00 – 1:30 pm

**Lunch**

1:30 – 3:00 pm

**FDA Guidance Update in a Global Market – Paradigm Shift or Status Quo**

**Co-organizers:**

Jie (Jack) Zhou, Mathematical Statistician, Division of Biostatistics, OSB/CDRH/FDA  
Boguang (Bo) Zhen, Branch Chief, Therapeutics Evaluation Branch, Division of Biostatistics, CBER/FDA

Mailin Hesse, Head Statistician, Design Quality/Statistics, Abbott

H. Terry Liao, Fellow Biostatistics, Division of Peripheral Interventions, Boston Scientific

**Speakers:**

Ram Tiwari, Director, Division of Biostatistics, FDA/CDRH

Estelle Russek-Cohen, Former Director, Division of Biostatistics, FDA/CBER

**Panelists:**

Meijuan Li, Acting Deputy Director, Division of Biostatistics, CDRH/FDA

Li Wei, Director, Center for Cardiovascular Diseases, Fuwai Hospital, China

Mingdong Zhang, CMO and Vice President, Medical & Regulatory Affairs, Boston Scientific Greater China

While paradigm shifts are widely recognized in the current political environment around the world, manufacturers need to be aware of changes in regulatory requirements to stay competitive internationally. In many cases, regulatory authorities will issue or update guidance documents to help manufacturers understand current laws and expectations. As the health care industry continuously evolves and device technology rapidly changes, so do the needs and expectations of the regulators and manufacturers. While the guidelines from different authorities are often complementary, they can sometimes be conflicting. Ideally, manufacturers figure out ways to design a single study to meet the needs of different regulators but this is not always realistic. In this session, speakers will address key FDA guidelines and provide an update on the recent development of an addendum to the ICH E9 guideline. Additionally, panelists will discuss the challenges in trying to simultaneously meet the expectations from ISO, CFDA, PMDA, the EU and other international regulators. Audience members will be encouraged to ask questions and participate in the discussion.

3:00 – 3:30 pm

**Break**

3:30 – 5:00 pm

**Effective FDA/Industry Communication**

**Co-organizers:**

Laura Lu, Mathematical Statistician, Division of Biostatistics, CDRH/FDA

Xuan Ye, Mathematical Statistician, Division of Biostatistics, CDRH/FDA

Crystal Williams, Manager, Biostatistics, Roche Tissue Diagnostics

Ted Lystig, Director, Corporate Biostatistics, Medtronic

**Speakers:**

Tracy Bergemann Carr, Senior Principal Statistician, Medtronic

Malinka Jansson, Manager, Biostatistics, Agilent Technologies

Sherry Yan, Branch Chief, Therapeutics Statistics Branch III, CDRH/FDA

Lakshmi Vishnuvajjala, Chief, Diagnostic Devices Branch 1 / Division of Biostatistics, CDRH/FDA

This session will be composed of two speakers followed by a two person panel. Malinka Jansson, a speaker from Agilent technologies, will discuss FDA/Industry communication

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within the context of the successes and failures encountered in recent submissions. This includes specific examples and discussion around the impact of failing to provide comprehensive information regarding the limitations in IHC. Dr. Sherry Yan, an FDA speaker, will provide guidance on writing pre-sub or IDEs in order to obtain useful feedback from the FDA; as well as encountered issues in study design when reviewing Q-sub or IDE, including EAP submissions. The two panelists, Dr. Lakshmi Vishnuvajjala from FDA, and Dr. Tracy Bergemann Carr from Medtronic will discuss examples of positive statistical communication experiences from the point of view of both FDA and sponsor. This will be followed by a question and answer session open to the audience.

**5:00 – 6:00 pm**                    **Poster Session and Networking Reception**

## **Thursday, April 27, 2017**

**8:15 – 8:45 am**                    **Breakfast**

**8:45 – 4:30 pm**                    **Concurrent Sessions - Therapeutic Device Track and Diagnostics Track**

### **Therapeutic Device Track**

**8:45 – 9:00 am**                    **Welcome**

**9:00 – 10:30 pm**                    **Bayesian and Adaptive Designs**

#### **Co-organizers:**

Shabnam Azadeh, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Zhen Zhang, Director, Worldwide Clinical Research, Abbott Vascular

#### **Speakers:**

Mohammad Hossein Rahbar, Professor and Director of  
Biostatistics/Epidemiology/Research Design (BERD), Core Center for Clinical and  
Translational Sciences, University of Texas Health Science Center at Houston  
Hong (Laura) Lu, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Adam Himes, Sr. Principal Engineer, Medtronic

It has been 11 years since the FDA introduced the draft “Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials”. In addition, the FDA guidance on “Adaptive Designs for Medical Device Clinical Studies” has been finalized in 2016. Thanks to the pioneer work of the FDA and the collaborations with academia and industry, we have seen increased applications of both designs in clinical trials (Campbell, G., 2013 and Yang, X., et al., 2016). Although progress has been made, due to the challenges associated with both designs, adoption remains relatively low in real practice. In this session, representatives from the FDA, academia, and industry will provide their perspectives on the advantages and challenges of both designs and discuss on how to better utilize both in clinical trials.

**10:30 – 10:45 pm**                    **Break**

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10:45 – 12:15 pm

## **Heterogeneity in Medical Device Trials - Opportunities and Challenges**

### **Co-organizers:**

Rajesh Nair, Team leader, Division of Biostatistics, CDRH/FDA  
Chithra Sangli, Sr. Director, Biostatistics & Data Management, Johnson & Johnson

### **Speakers:**

Nelson Lu, Team Leader, Therapeutic Statistics Branch II, FDA/CDRH  
Jim Lesko, Biostatistics Director, Johnson & Johnson Medical Devices  
Ravi Varadhan, Associate Professor, Johns Hopkins University

Subjects in a study typically differ in their responses to treatment. The ability to identify meaningful heterogeneity of treatment effect among subgroups defined by important demographic and baseline characteristics is crucial for the development of individually tailored treatment regimens. Increasingly multi-region device studies are being conducted in order to gain simultaneous regulatory approval from different regulatory bodies. The potential differences in ethnicities and practice guidelines, and the resultant differences in response to treatment in different geographies have increased the challenges in design, conduct, analyses and outcome interpretation. In this session speakers will discuss the many challenging issues related to estimation and reporting of heterogeneity of treatment effects and the impact of recent guidances.

12:15 – 1:15 pm

**Lunch**

1:15 – 2:45 pm

## **Statistical Challenges in Evaluating Multiple Hypotheses**

### **Co-organizers:**

Vandana Mukhi, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Hung-Ir Li, Director, Global Biostatistics, THV, Edwards Lifesciences Inc.

### **Speakers:**

Peter Lam, Sr. Fellow, Biostatistics, Boston Scientific  
Frank Bretz, Global Head of Statistical Methodology and Consulting Group, Novartis  
Heng Li, Team Leader, Mathematical Statistician, CDRH/FDA

Clinical endpoints are an essential design component of pivotal clinical investigations for medical devices. Multiple endpoints (primary and secondary) considered may include composite endpoints and/or their individual components used to demonstrate the device performance. In the context of multiple endpoints, this session will explore the choice of non-inferiority and/or superiority hypothesis, study success criteria, multiplicity adjustment approaches and permissibility of superiority claim in a non-inferiority study.

2:45 – 3:00 pm

**Break**

3:00 – 4:30 pm

## **Data Quality Improvement: The Continuous Effort across the Clinical Study Lifestyle**

### **Co-organizers:**

Chu Jianxiong, Chief, Therapeutic Statistics Branch 2, Division of Biostatistics, CDRH/OSB  
Juanjuan Li, Senior Statistician, Abbott Vascular.

### **Speakers:**

Rajesh Nair, Team Leader, Therapeutic Statistics Branch II, CDRH/FDA  
Marc Buyse, Chief Scientific Officer, CluePoints Inc.  
Roseann White, Director of Pragmatic Clinical Trial Statistics, Duke Clinical Research Institute

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High-quality data is essential for statistical inference and regulatory decision-making. Each step in clinical study design, collection, monitoring, handling, and processing of data affects data quality. This session will discuss some common approaches to improve data quality across the clinical study lifecycle, including but not limited to such topics as: strategies to mitigate missing data, statistical methods for outlier and discrepancy identification, firewalls to insure data integrity and data standards (e.g., CDISC).

4:30 pm

**Adjournment**

### Diagnostics Track

8:45 – 9:00 am

**Welcome**

9:00 – 10:30 pm

**Statistics for in vivo Diagnostics**

**Co-organizers:**

Yuqing Tang, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Zengri Wang, Sr. Manager & Advisor, Medtronic

**Speakers:**

Bipasa Biwas, Mathematical Statistician, CDRH/FDA  
Xiaolong (Alex) Shih, Principal Biostatistician, Medtronic plc  
Haiwen Shi, Mathematical Statistician, CVM/FDA

In vivo diagnostic devices take measurements on the subjects (patients) in contrast to in vitro tests on specimens from the subjects. Examples of in vivo diagnostic devices include measurements of brain activity utilizing quantitative electroencephalogram (qEEG), pill cameras ingested to image polyps in colon, ophthalmic devices like optical coherence tomography system for the in-vivo imaging and measurement of the retina, retinal nerve fiber layer, and optic disc etc. In this session, we are going to discuss scientific issues related to evaluation of in vivo diagnostic devices. Specifically, the discussion will focus on issues from three different types of in vivo diagnostic devices, i.e. devices for monitoring/detecting traumatic brain injury, in vivo imaging devices including gastrointestinal camera, and ophthalmic diagnostic devices.

10:30 – 10:45 pm

**Break**

10:45 – 12:15 pm

**Analytical Studies for Diagnostic Tests - Standards Update and Case Studies**

**Co-organizers:**

Lan Huang, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Kristen Meier, Director of Biostatistics, Illumina

**Speakers:**

Marina V. Kondratovich, Associate Director for Clinical Studies, OIR/CDRH/FDA  
Leonard Buchner, Senior Director of IVD Study Design and Biostatistics, Illumina  
Tinghui Yu, Mathematical Statistician, Division of Biostatistics, CDRH/FDA

For diagnostic devices, establishment of analytical performance is a critical step in development and for product labeling. There are many different types of studies that are performed in order to characterize the different aspects of device performance including but not limited to limit of detection, precision, analytical accuracy and linearity. While consensus standards exist for these studies, existing standards do not always address the study design and statistical analysis challenges brought with new technologies such as next generation sequencing (NGS). This session will provide an update on CLSI Evaluation Protocols revisions in progress, highlight statistical issues associated with test detection capability and provide case examples for the evaluation of qualitative test performance. The session will conclude with a short panel discussion.

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12:15 – 1:15 pm

**Lunch**

1:15 – 2:45 pm

**Statistical Considerations and Development for Companion Diagnostics**

**Co-organizers:**

Yaji Xu, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Raj Chandra, Senior Statistician, ADD Statistics, Abbott Diagnostics

**Speakers:**

Gene Pennello, Team Leader, Division of Biostatistics, CDRH/FDA  
Junming Zhu, Director, Biostatistics and Data Management, Ventana Medical Systems  
Robert Abugov, Mathematical Statistician, Office of Biostatistics, CDER/FDA

A companion diagnostics (CDx) provides information that is essential for the safety and efficacy of a corresponding drug or biological product. It has been playing the key role in precisely identifying the targeted patient populations in precision medicine. Recently, diagnostic devices that may provide additional useful information of risk/benefit to patients have begun to be proposed. Similar to companion diagnostics, these complementary diagnostic tests can identify a biomarker-defined subset of patients that respond particularly well to a drug and aid risk/benefit assessments for individual patients. Work in both CDx and complementary diagnostics tests are relatively new and evolving. In this session we will discuss statistical considerations in predictive biomarker evaluation, and will demonstrate the development and validation of a CDx in a practical manner. A real-life case study will be used to show the differentiation between companion and complementary diagnostic tests.

2:45 – 3:00 pm

**Break**

3:00 – 4:30 pm

**Emerging Technologies and Precision Medicine**

**Co-organizers:**

Wei Wang, Mathematical Statistician, Division of Biostatistics, CDRH/FDA  
Svilen Tzonev, Director Business Development, Digital Biology Group, Bio-Rad Laboratories

**Speakers:**

Jincao Wu, Division of Biostatistics, CDRH, FDA  
Abha Sharma, Director, Biostatistics, Roche Molecular Systems  
Matija Snuderl, Assistant Professor of Pathology, Director of Molecular Pathology and Diagnostics, NYU Langone Medical Center  
Wei Wang, Mathematical Statistician, Division of Biostatistics, CDRH/FDA

The concept of Precision Medicine, where the right drug is delivered to the right patient at the right time and the right dose, is made possible by the development of several 'emerging' technologies. This session will focus on statistical aspects of such emerging technologies, including Next Generation Sequencing and Digital PCR, implemented in traditional tissue-based or novel liquid-biopsy formats. Development of sensitive tumor genotyping tests that can measure actionable driver or resistance mutations in non-invasive and cost-efficient fashion will continue to expand the practice of Precision Medicine.

4:30 pm

**Adjournment**

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