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Forum on Regulatory Science and Biomedical Innovations

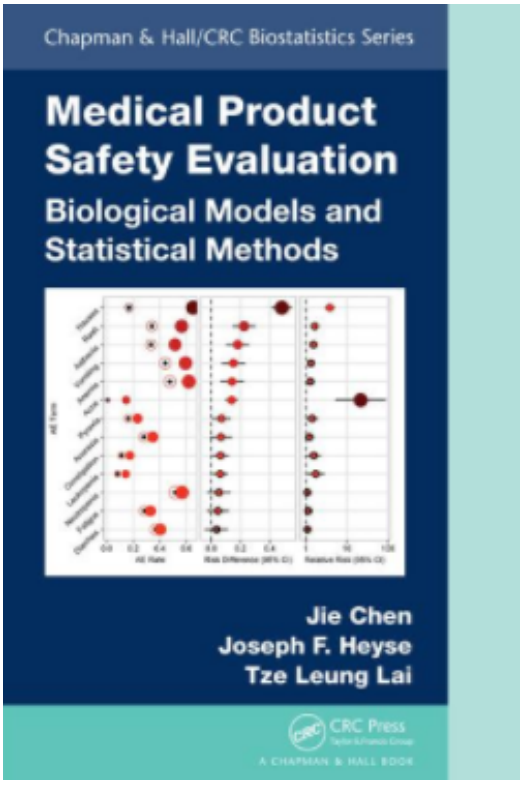
Program (06/10/2018)

A Half-Day Short Course

Statistical Methods for Medical Product Safety Evaluation

7:30-8:30am	**Registration**
8:30-12:30pm	**Instructors:** Jie Chen, PhD: Distinguished Scientist, Merck Research Laboratories Joe Heyse, PhD: Scientific AVP at Merck Research Laboratories Tze Leung Lai, PhD: The Ray Lyman Wilbur Professor of Statistics, and by courtesy, of Biomedical Data Science and Computational & Mathematical Engineering, and Co-director of the Center for Innovative Study Design at Stanford University

This half-day short course is based on the forthcoming book published by Chapman & Hall (available July 9, 2018): Medical Product Safety Evaluation: Biological Models and Statistical Methods



Abstract: Over the past decade there has been a greatly increased focus on the safety evaluation of medical products. Safety data are routinely collected throughout preclinical in-vitro and in-vivo experiments (e.g., living cells and animal models), clinical development (e.g., randomized clinical trials) and post-approval studies and monitoring. While the majority of clinical studies are designed to investigate the hypothesized efficacy of a compound, safety outcomes, on the other hand, are not generally defined *a priori* (with exceptions to be discussed in the short course). This brings a number of challenges to statisticians on how to best analyze the high-dimensional safety data, in order to detect safety signals earlier, and at the same time, reduce the rates of false signals and false non-signals. Depending on the questions of interest and the systems for collecting safety data, statistical methods applied to safety data analysis could differ dramatically. This half-day short course will present cutting-edge biological models and statistical methods that are tailored to specific objectives and data types for safety analysis and benefit-risk assessment. Some frequently encountered issues and challenges in the design and analysis of safety studies are discussed with illustrative applications and examples.

Background knowledge: Some background in drug development including basic concepts, practice, and regulation on safety data reporting, analysis and result interpretation in nonclinical and clinical studies is helpful. Basic knowledge of commonly used statistical methods (e.g., categorical data analysis, survival analysis, Bayesian methods, meta-analysis, etc.) and machine learning techniques is assumed. The course will begin with a review of fundamental concepts in safety data analysis with regulatory guidelines and scientific plausibility of drug-induced safety concerns (e.g., QTc

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prolongation, hepatotoxicity, nephrotoxicity, etc.) and continue to statistical methods for pre-licensure safety analysis and post-licensure safety surveillance.

Course learning objectives: The audience will learn the commonly used as well as cutting-edge statistical methods that are tailored for specific safety questions, safety data types and benefit-risk assessment. Examples are given throughout the presentation to illustrate the applications of the methods.

Instructors' background:

1. Jie Chen, PhD: Distinguished Scientist, Merck Research Laboratories, more than 24 years of experience in biopharmaceutical research and development with research interest in the areas of innovative trial design, data analysis, Bayesian analysis, multiregional clinical trials, data mining, machine learning and medical product safety evaluation; most recently focusing on sequential testing and monitoring of safety signals; over 30 publications in peer reviewed journals (and book chapters).

2. Joe Heyse, PhD: a Scientific Assistant Vice President at Merck Research Laboratories, Fellow of the ASA and AAAS, and founding editor of *Statistics in Biopharmaceutical Research*. He has more than 40 years of experience in pharmaceutical R&D with research interest in safety evaluation and health economics and has more than 70 publications in peer reviewed journals. He is an editor of *Statistical Methods in Medical Research*.

3. Tze Leung Lai, PhD: The Ray Lyman Wilbur Professor of Statistics, and by courtesy, of Biomedical Data Science and Computational & Mathematical Engineering, and Co-director of the Center for Innovative Study Design at Stanford University. He is a Fellow of the IMS and ASA. His research interest includes sequential experimentation, adaptive design and control, change-point detection, survival analysis, time series and forecasting, multivariate analysis and machine learning, safety evaluation and monitoring. He has published 12 books and 300 articles in peer reviewed journals, and has supervised over 70 PhD theses at Columbia and Stanford Universities.