

Multiple Comparisons in Clinical Trials

H.M. James Hung and Sue-Jane Wang
US Food and Drug Administration

Abstract For regulatory applications, each clinical trial is conducted almost surely to entertain multiple objectives. As such, multiple comparisons are often performed in a clinical trial. As a clinical trial is regarded as a human experiment, an adequate control of experimentwise type I error is traditionally thought important to contain false positives. Statistical methodologies for ensuring a proper control are affluent in decades. As the clinical development program for a tested medical product is increasingly evolved, the statistical framework of inference pertaining to each clinical trial alone in relation to a family of multiple trials and to the issue of level of evidence becomes fuzzy. This short course will focus on visiting the statistical framework and paradigm of inference for multiple doses, multiple endpoints, and multiple analyses within a single clinical trial or a family of clinical trials, which may be a multi-regional clinical trial or trials. Case examples will be presented to facilitate discussion. The topics to be covered are:

1. Early phase learning trials
2. Single versus multiple confirmatory placebo-controlled trials
 - Multiple endpoints
 - Multiple doses
 - Multiple analyses
3. Active-controlled trials
 - Placebo is present
 - Placebo is absent
 - Non-inferiority and superiority analyses
4. Adaptive design trials
 - Early phase trial
 - Pivotal trial

Short Course Instructors:

H.M. James Hung, PhD
Director, Division of Biometrics I, OB/OTS, CDER
U.S. Food and Drug Administration
10903 New Hampshire Avenue, Bldg 21 Room 4616
Silver Spring, MD 20993-0002
Tel: (301)-796-1092
Fax: (301)-847-8525
E-mail: hsienming.hung@fda.hhs.gov

Sue-Jane Wang, PhD
Associate Director, Office of Biostatistics, OTS, CDER
U.S. Food and Drug Administration
10903 New Hampshire Avenue, Bldg 21 Room 3562

Silver Spring, MD 20993-0002
Tel: (301)-796-0831
Fax: (301)-796-9734
E-mail: suejane.wang@fda.hhs.gov

About the Instructors

Dr. H.M. James Hung is Director of Division of Biometrics I, Office of Biostatistics, Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration (FDA). He is an author of over 90 papers and book chapters in statistical and medical literature. His research interests include factorial design clinical trials, utility of p-value distribution, adaptive design/analysis in clinical trials, and non-inferiority trials, multi-regional clinical trials. He made major contributions to regulatory reviews of many large mortality or morbidity clinical trials in cardiovascular and renal disease areas. He has presented over 180 invited talks and short courses in his research areas. Dr. Hung received two FDA/CDER Scientific Achievement Awards, one FDA Scientific Achievement Group Award and many other awards for the recognition of his scientific contributions to the US FDA. Currently, he serves as an Editor-in-Chief for Journal of Pharmaceutical Statistics and an Associate Editor for Statistics in Medicine and Journal of Biopharmaceutical Statistics. He is a Fellow of the American Statistical Association and an elected member of the International Statistical Institute.

Dr. Sue-Jane Wang is Associate Director for Pharmacogenomics and Adaptive Design, Office of Biostatistics, Office of Translational Sciences, CDER, FDA. Dr. Wang is an author of over 90 papers and book chapters in statistical, clinical, genetic, bioinformatics, and pharmacogenomics literature. She made major contributions to regulatory reviews in these areas. As a result, Dr. Wang received two FDA Outstanding Intercenter Scientific Collaboration Awards and was recently awarded the FDA level Scientific Achievement individual Awards in recognition of her sustained record of published regulatory research in statistical design and methodology advancing complex and emerging clinical trial designs and analysis that support regulatory guidance, policies and review. She has presented over 200 invited talks, discussion, and short courses in her research areas including non-inferiority, multi-regional trials. She is an elected member of the International Statistical Institute. She has served as an Editor-in-Chief for Pharmaceutical Statistics, and is an Associate Editor for Statistics in Medicine and Statistics in Biosciences. She is conference co-chair for MCP 2011 conference.