

FDA Workshop AGENDA

Pediatric Trial Design and Modeling: Moving into the next decade

Friday, September 8, 2017 Great Room, US FDA White Oak

Moderators:

Gilbert J. Burckart, Pharm.D., Associate Director for Pediatrics, Office of Clinical Pharmacology

Ann McMahon, M.D., Deputy Director of Science, Office of Pediatric Therapeutics, Commissioner's Office

Yaning Wang, Ph.D.
Acting Director, Division of Pharmacometrics, Office of Clinical Pharmacology

U.S. Food and Drug Administration

8:30-8:35 a.m. Welcome / Quality and Innovation in Drug Development

Susan McCune, M.D.

Director, Office of Pediatric Therapeutics

Commissioner's Office, US FDA

8:35-9:00 a.m. The Current State of Pediatric Drug Development

Lynne Yao, M.D.

Director, Division of Pediatric and Maternal Health, OND, CDER

U.S. Food and Drug Administration

9:00-9:25 a.m. Drug Development Through Modeling and Simulation – The Business Case

Patrick Smith, Pharm.D.

Chief Scientific Officer, Certara Strategic Consulting

Research Professor, Un. of Buffalo School of Pharmacy

9:25-9:50 a.m. Industry Approach to Innovative Pediatric Trial Design

Edress Darsey, Pharm.D.

Global Pediatric Medical Director, Pediatric Center of Excellence

Office of the Chief Medical Officer, Pfizer Inc

9:50-10:10 a.m. **Break**

10:10-10:35 a.m. **Use of Enrichment in Drug Development Trial Design**

Issam Zineh, Pharm.D., M.P.H.

Director, Office of Clinical Pharmacology, Office of Translational Sciences
CDER, U.S. Food and Drug Administration

10:35-11:00 a.m. **Pediatric Trial Design and Endpoint Considerations**

Dionna Green, M.D.

Pediatric Clinical Pharmacology; Guidance and Policy Team

Office of Clinical Pharmacology, Office of Translational Sciences

CDER, U.S. Food and Drug Administration

11:00 a.m.-12:00 p.m. **Moderated Panel Discussion**

Panelists: Susan McCune, M.D. (FDA), Maura O'Leary, M.D. (CBER, FDA), and speakers Dr.'s Lynne Yao (FDA), Edress Darsey (Pfizer), Patrick Smith (Certara), Issam Zineh (FDA), Dionna Green (FDA)

12:00-1:00 p.m. **Lunch**

Model Informed Pediatric Drug Development and Simulation

1:00-1:15 p.m. **Introduction to Modeling and Clinical Trial Simulation in Drug Development**

Carl Peck, M.D.

Chairman, NDA Partners, and former Director of CDER

San Luis Obispo, CA

1:15-1:40 p.m. **Application of Model Informed Drug Development in Study Design and Analysis**

Yaning Wang, Ph.D.

Acting Director, Division of Pharmacometrics

Office of Clinical Pharmacology

1:40 – 2:05 p.m. **A Bayesian Approach for Incorporating Adult Clinical Data into Pediatric**

Clinical Trials

James Travis, PhD, Staff Fellow

Jingjing Ye, PhD, Mathematical Statistician

Office of Biostatistics, Office of Translational Sciences

CDER, US Food and Drug Administration

2:05 - 2:30 p.m. Modeling and Simulation to Support Pediatric Clinical Trials

Matthew D. Rotelli, Ph.D.

Director, Global PK/PD and Pharmacometrics

Eli Lilly and Company, Lilly Corporate Center, Indianapolis IN

2:30 – 2:45 p.m. BREAK

2:45 – 3:10 p.m. ICH E11 Revisions and Pediatric Model Informed Drug Development and Simulation

Solange Corriol Rohou, M.D.

Senior Regulatory Affairs Director

AstraZeneca

3:10-4:00 p.m. Moderated Panel Discussion

Panelists: Daniel Gonzalez, Pharm.D., Ph.D. (Un. of North Carolina), Gary Rosner, Ph.D. (Johns Hopkins), Margaret Gamalo-Siebers, PhD (Eli Lilly), and speakers Dr.'s Peck, Wang (FDA), Travis (FDA), Ye (FDA), Rotelli (Eli Lilly), and Corriol Rohou (AstraZeneca).

4:00-4:15 p.m. Pediatric Trial Design and Simulation – What have we learned and next steps?

Dr. Gilbert Burckart

Speaker Biographical Sketches

GILBERT BURCKART, Pharm.D.

Dr. Gilbert Burckart is presently Associate Director for Pediatrics, Office of Clinical Pharmacology, U.S. Food and Drug Administration. Dr. Burckart has served on the faculties of four universities (Buffalo, Tennessee, Pittsburgh, Southern California) as a Professor of Pharmacy, Pediatrics and Surgery for 33 years prior to coming to the FDA. He moved to the US FDA in 2008, and his duties include the direction of the Pediatric Clinical Pharmacology program within the Office of Clinical Pharmacology, and participation in the FDA's Pediatric Review Committee.

ANN MCMAHON, MD, MS

Ann McMahon, MD, MS is Deputy Director of Science and the Director of Kidnet in the Office of Pediatric Therapeutics in the Office of the Commissioner at the FDA. She received a Master's of Science in Health Policy and Management from the Harvard School of Public Health, and went on to receive an MD from the Case Western Reserve University School of Medicine. She completed her residency in Pediatrics at the Johns Hopkins Children's Center, and continued with post-doctoral training both at the National Institutes of Health and Johns Hopkins Children's Center in Virology and Pediatric Infectious Diseases, respectively. After an Assistant Professorship at the University of Chicago, she joined the Food and Drug Administration in 2002. Since joining the FDA, she has focused primarily on post-marketing safety.

YANING WANG, Ph.D., M.S.

Dr. Yaning Wang is currently the Director (acting) and Deputy Director in the Division of Pharmacometrics in the Office of Clinical Pharmacology at FDA. Before joining FDA, Dr. Wang received his Ph.D. in Pharmaceutics and master's degree in Statistics from the University of Florida from 1999 to 2003.

SUSAN MCCUNE, MD, M.S.

Dr. Susan McCune is the Director in the Office of Pediatric Therapeutics (OPT) in the Office of the Commissioner at the Food and Drug Administration (FDA). She joined the Agency in 2003 in the Division of Pediatric Drug Development, Office of Counter-Terrorism and Pediatric Drug Development, in the Center for Drug Development and Research (CDER). From 2005 through 2009, Dr. McCune held the positions of Associate Director and team leader in the Office of Counter-Terrorism and Emergency Coordination in CDER. She joined the Office of Translational Sciences in CDER in February, 2010 as the Deputy Director, staying in that position until January, 2017. Dr. McCune received her medical degree from George

Washington University following her undergraduate degree at Harvard University. She completed her internship, residency, chief residency, and neonatal fellowship at Children's National Medical Center in Washington, D.C.

LYNNE YAO, MD

Lynne Yao, M.D., is the Director, Division of Pediatric and Maternal Health in the Office of New Drugs, Center for Drug Evaluation and Research. She has held this position since 2012. The Division of Pediatric and Maternal Health oversees quality initiatives which promote and necessitate the study of drug and biological products in the pediatric population; and improve pregnancy and lactation-related information in product labeling. Dr. Yao started at FDA as a Medical Officer and primary reviewer on the Inborn Errors of Metabolism team in the Division of Gastroenterology and Inborn Errors Products (DGIEP) in 2008, and was a team leader in DGIEP from 2009-2012. Dr. Yao graduated from the George Washington University School of Medicine, completed residency in Pediatrics at Walter Reed Army Medical Center, and fellowship in Pediatric Nephrology at the Georgetown University Children's Medical Center. Dr. Yao is board certified in both Pediatrics and Pediatric Nephrology.

PATRICK SMITH, Pharm.D.

Dr. Patrick Smith currently serves as Chief Scientific Officer for d3 Medicine and Certara Strategic Consulting. He has ~20 years of diverse drug development experience and more than 120 peer-reviewed publications. He received his PharmD degree from UCSF, completed a clinical residency at Duke University Medical Center, and served on the faculty for 10 years at the University at Buffalo School of Pharmacy working in the areas of infectious disease and oncology clinical pharmacology and modeling and simulation. He then joined Roche in clinical pharmacology and translational medicine, and was the U.S. Administrative Head of Roche Clinical Pharmacology prior to co-founding d3 Medicine in 2012, a drug development consulting organization, which was successfully acquired by Certara in 2016.

EDRESS DARSEY, Pharm.D.

Edress Darcey is Global Pediatric Medical Director, Pediatric Center of Excellence, Office of the Chief Medical Officer, Pfizer, Inc.

ISSAM ZINEH, Pharm.D., MPH

Issam Zineh is Director of the Office of Clinical Pharmacology (OCP) at the U.S Food and Drug Administration (FDA). He has held various leadership positions at FDA including Associate Director for Genomics in OCP (2008-2012), Co-Director of the CDER Biomarker Qualification

Program (2009-2015), and voting member of the CDER Medical Policy Council (2016-present). He is an experienced pharmacist and applied clinical pharmacologist who was formerly on the faculty of the University of Florida (UF) Colleges of Pharmacy and Medicine and Associate Director of the UF Center for Pharmacogenomics. Dr. Zineh received his PharmD from Northeastern University and completed his residency at Duke University Medical Center. He completed a fellowship in cardiovascular pharmacogenomics at UF where he also obtained his MPH in Health Policy and Management. He is a recognized expert in the fields of drug development and evaluation, clinical pharmacology, pharmacotherapy, and precision medicine. As Director of OCP, Dr. Zineh leads a staff of 230 regulatory, research, program/project management, and administrative staff in FDA's efforts to enhance drug development and promote regulatory innovation through clinical pharmacology and experimental medicine.

DIONNA GREEN, MD

Dionna Green, M.D. is presently a Medical Officer and Policy Lead in the Guidance and Policy Team (GPT) in the Office of Clinical Pharmacology, Center for Drug Evaluation and Research, US FDA. She joined the Agency in 2009 in the Pediatric Clinical Pharmacology Staff, Office of Clinical Pharmacology where she engaged in regulatory science research and review activities focused on pediatric product development. Dr. Green graduated from Howard University School of Medicine, received her training in pediatric medicine from the Herman and Walter Samuelson Children's Hospital at Sinai, and completed a clinical pharmacology fellowship at Georgetown University.

MAURA O'LEARY, MD

Maura O'Leary is a Medical Reviewer and Team Leader in the Hematology Branch of the Office of Tissues and Advanced Therapies (OTAT) in CBER at the Food and Drug Administration. Dr. O'Leary works with other reviewers to manage the Branch's portfolio of genetically engineered T-cell products, cytotoxic T lymphocytes, hemophilia factor products, and combination products. Dr. O'Leary graduated from Georgetown University School of Medicine in 1975 and received her pediatric hematology-oncology training at the University of Minnesota. She was in clinical practice in pediatric hematology-oncology primarily at the Children's Hospitals and Clinics in Minneapolis (1989-2005). From 2006-2010, Dr. O'Leary was the Administrative Officer for the Children's Oncology Group (NCI sponsored Pediatric Cooperative Group). Dr. O'Leary started at the FDA in 2011 and her focus has been engineered T cell products.

CARL PECK, MD

Dr. Peck obtained a B.A. in mathematics and chemistry from the University of Kansas in 1963 and the M.D. in 1968. Following training in internal medicine, he undertook a research fellowship in clinical pharmacology at the University of California San Francisco (1972-74). From

1974 to 1980, Dr. Peck was employed at the Letterman Army Institute of Research, San Francisco, CA, as Chief of the Army Blood Preservation Research Program. In 1980, Dr. Peck became Director of the Division of Clinical Pharmacology and, Professor, Departments of Medicine and Pharmacology, Uniformed Services University, Bethesda, Maryland. Dr. Peck joined the FDA as Director, Center for Drug Evaluation and Research, in October 1987. He was promoted to Assistant Surgeon General in the Public Health Service in October 1990.

Dr. Peck received the 2012 ASCPT Gary Neal Prize for Innovation in Drug Development and the 2017 Sheiner-Beal Pharmacometrics Award. Dr. Peck's research interests center on optimizing informativeness, efficiency, speed and economy of drug development and regulation using advanced concepts and techniques of clinical pharmacology, trial designs, and pharmacostatistical modeling and simulation to generate causal evidence of effectiveness and safety.

JAMES TRAVIS, Ph.D.

James Travis received his PhD from the University of Maryland, Baltimore County. He is a statistical reviewer in Division of Biometrics II, Office of Biostatistics, Center for Drug Evaluation and Research and primarily supports the Division of Anesthesia, Analgesia, and Addictions Products. He is a member of the Pediatric Review Committee.

JINGJING YE, Ph.D.

Jingjing Ye received her PhD in Statistics from University of California, Davis. She has more than 10 years of experience in pharmaceutical industry and regulatory agency of US FDA. She is currently a mathematical statistician in Division of Biostatistics V in office of Biostatistics, CDER, FDA. Division V is supporting the drug approvals in oncology and hematology products.

MICHAEL ROTELLI, Ph.D.

Dr. Rotelli has over 20 year of pharmaceutical development experience at Eli Lilly and Company, located in Indianapolis, Indiana. He has led statistical and modeling groups to bring medicines to patients in oncology, immunology, cardiovascular, endocrine, and neuroscience indications. Dr. Rotelli is currently the Director of Global Pharmacokinetics, Pharmacodynamics (PK/PD), and Pharmacometrics for the Bio-Medicines Business Unit of Eli Lilly and Company. Previously, he was a Research Advisor in the Advanced Analytics Hub focusing on Data Mining and Bayesian applications.

Dr. Rotelli earned his B.A. in Mathematics from Cornell University and his M.S. and Ph.D. degrees in Statistics from Virginia Tech. He is a member of the American Statistical Association (ASA), American Society for Clinical Pharmacology and Therapeutics, International Society of Pharmacometrics (ISoP), and the Drug Information Association. He co-chairs the joint ASA/ISoP Statistics and Pharmacometrics Scientific Interest Group.

SOLANGE CORRIOL ROHOU, MD

Solange Corriol-Rohou is a pulmonologist and an immuno-allergist by training. She joined AstraZeneca R&D in 2004 where she is currently Sr. Director Regulatory Affairs & Policy for Europe.

Solange in her role as the chair of the Clinical Development Expert Group at EFPIA (the European Federation of Pharmaceutical Industries and Associations) has organized several workshops with the European Medicines Agency (EMA). She has also experience working in EU Innovative Medicines Initiative (IMI) projects, such as PROactive in COPD; she is currently the deputy topic leader of the IMI ADAPT SMART project which has established a multi-stakeholder platform to facilitate and accelerate the availability of beneficial treatments for the right patient groups at the earliest appropriate time in the product life-span in a sustainable fashion (Adaptive Pathways). She joined ICH (International Conference of Harmonization), and is currently the EFPIA topic leader for the revision of the ICH E11 paediatric guideline, which is now almost complete.

DANIEL GONZALEZ, Pharm.D., Ph.D.

Daniel Gonzalez, PharmD, PhD, joined the UNC Eshelman School of Pharmacy in 2014 after completing a postdoctoral clinical pharmacology fellowship at the University of North Carolina and the Duke Clinical Research Institute. Gonzalez received his pharmacy degree from the University of Florida in 2008. He then obtained his PhD in pharmaceutical sciences from the University of Florida in 2012. Gonzalez is currently an Assistant Professor within the Division of Pharmacotherapy and Experimental Therapeutics (DPET). The primary goal of his research program is to optimize pharmacotherapeutic efficacy and safety through the use of innovative clinical trial designs and application of mathematical modeling and simulation techniques, with an emphasis in pediatric populations. Dr. Gonzalez has received funding from the National Institutes of Health as well as the Thrasher Research Fund, and has published over 65 publications and abstracts.

GARY ROSNER, Ph.D.

Gary Rosner is the Eli Kennerly Marshall Jr. Professor of Oncology at the Johns Hopkins University School of Medicine and Professor of Biostatistics, Bloomberg School of Public Health, Johns Hopkins University. He directs the Division of Biostatistics and Bioinformatics in the Department of Oncology and heads the Research Program in Quantitative Sciences at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

Dr. Rosner received his Sc.D. in Biostatistics from the Harvard School of Public Health in 1985. He was a member of the faculties of Yale University, Duke University, and The University

of Texas M. D. Anderson Cancer Center. His collaborations include the design and analysis of clinical studies in cancer and population modeling in pharmacokinetics and pharmacodynamics.

Dr. Rosner carries out research on Bayesian statistical methods to improve the design and analysis of complex cancer research studies. He is a Fellow of the American Statistical Association and an Associate Editor for the journals Biometrics and Clinical Trials.

MARGARET GAMALO-SIEBERS, Ph.D.

Margaret Gamalo-Siebers is a Principal Research Scientist in the Global Statistical Sciences – Immunology and is also a member of the Pediatric Steering Committee in Eli Lilly Co. She is the Program-Chair- Elect for the Biopharmaceutical Section of the American Statistical Association and co-leads the Bayesian Scientific Working Group for paediatric drug development. Prior to joining Eli Lilly and Co, she was a Mathematical Statistician at the Center for Drug Evaluation and Research (CDER) and then later at the Center for Food Safety and Applied Nutrition (CFSAN) within the Food and Drug Administration (FDA) from June, 2008 to January, 2016. She received her PhD and Master's degree in Statistics at the University of Pittsburgh and a Master's degree in Operations Research at the University of The Philippines. Meg has expertise in Bayesian Statistics, Meta-analysis, use of Propensity Scores in Historical Controls and has written numerous manuscripts in those research areas.