FDA-University of Maryland CERSI Meeting

"Analgesic Clinical Trial Design, Extrapolation, and Endpoints in Patients from Birth to less than Two Years of Age"

Speaker Bio's

Elizabeth Little Durmowicz, MD is a general pediatrician by training who joined the FDA in 2008. Dr. Durmowicz has worked as a medical officer in the Division of Pediatric and Maternal Health in the Office of New Drugs in the Center for Drug Evaluation and Research, a medical officer and team leader in the Office of Science in the Center for Tobacco Products, and currently is the medical officer on the Pediatric Ethics Team in the Office of Pediatric Therapeutics in the Office of the Commissioner. Dr. Durmowicz is a graduate of the University of Cincinnati College of Medicine and completed her pediatric internship and residency at the University of Colorado Health Sciences Center. Before joining FDA, Dr. Durmowicz practiced in academic and indigent care settings, focusing her practice on children with special health care needs and their families.

Suellen Walker MBBS MMed MSc PhD FANZCA FFPMANZCA FPMRCA is Professor of Paediatric Anaesthesia and Pain Medicine at UCL GOS Institute of Child Health and Great Ormond Street Hospital, London UK. She is Principal Investigator of the Paediatric Pain Research Group at ICH and has research interests in developmental neurobiology of pain, spinal analgesic toxicty, long-term effects of pain in early life, and neuropathic pain in children.

Ricardo Carbajal, MD, PhD, is a pediatrician and professor of pediatrics at Sorbonne University in Paris, France. He is the chief of the Pediatric Emergency Department at the Armand Trousseau University Hospital in Paris. He is the former Director of the National Center of Resources to Fight Pain in France (2002- 2008), and the former chief of the Pediatric Intensive Care Unit at Trousseau Hospital. He has conducted numerous epidemiological and randomized controlled trials in the field of pediatric pain going from the neonate to older children. Most of these studies have been published in high rank peer-review journals. He has been twice an elected council member of the Special Interest Group on Pain in Childhood.

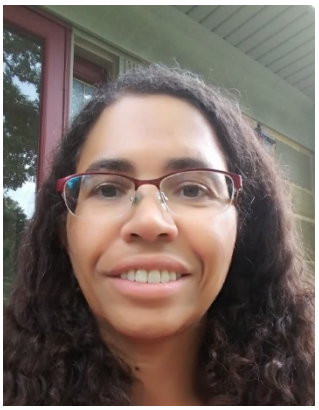
Christopher McPherson, PharmD, BCPPS graduated from the University of North Carolina School of Pharmacy and completed a fellowship in Neonatal Pharmacotherapy at The Women's Hospital of Greensboro. He is currently a clinical pharmacist in the neonatal intensive care unit at St. Louis Children's Hospital in St. Louis, Missouri and an associate professor in the Department of Pediatrics at Washington University School of Medicine.

John N. van den Anker, MD, PhD, FAAP, FCP is a Professor of Pediatrics, Pharmacology, Physiology, Genomics and Precision Medicine at the George Washington University School of Medicine and Health Sciences, Washington, DC and holds the Evan and Cindy Jones Endowed Chair in Pediatric Clinical Pharmacology. He also is the Eckenstein-Geigy Distinguished Professor of Pediatric Pharmacology at the University Children's Hospital of Basel, University of Basel, Switzerland.

Dr. van den Anker has been the President of the American College of Clinical Pharmacology (2016-2018) and twice the President of the European Society of Developmental, Perinatal and Paediatric Pharmacology (2006-2008 and 2017-2019). His awards include the Distinguished Investigator Award from the American College of Clinical Pharmacology (2008), the Distinguished Researcher award of the George Washington University (2012), and the Sumner J. Yaffe Lifetime Achievement Award in Pediatric Pharmacology and Therapeutics (2019) from the Pediatric Pharmacy Association.

Over the past 30 years, Dr. van den Anker' research has focused on developmental, neonatal and pediatric pharmacology. He has authored over 500 peer reviewed publications and has received NIH funding as well as funding from the European Union to support his research and the development of training programs in Pediatric Clinical Pharmacology.

Lisa Wiltrout, MD is a clinical reviewer in the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) at the United States Food and Drug Administration (FDA). She received her medical degree (MD) from Washington University School of Medicine in St. Louis, Missouri and completed her pediatric internship and residency at Children's National Medical Center in Washington, DC. During her clinical career, Dr. Wiltrout worked as a general pediatrician and as a pediatric hospitalist in suburban Maryland. She transitioned from clinical practice to her position at the Food and Drug Administration in 2016. Dr. Wiltrout is board certified in General Pediatrics.



Caroline Donado MD, MBI is a Biomedical Informatician in the Department of Anesthesiology, Critical Care, and Pain Medicine at Boston Children´s Hospital. She received her medical degree from the Universidad de los Andes in Bogotá, Colombia in 2011. In 2013, Dr. Donado moved to the U.S. and began working at Boston Children's Hospital as a research fellow in pediatric pain management. In 2019, she received her Master's in Biomedical Informatics from the Harvard Medical School. Dr. Donado's research focuses on sensory physiology in children, meta-analyses of analgesic trials in pediatrics, and clinical outcomes of chronic and acute pediatric pain management, using a combination of electronic data capture and electronic health records. Her overarching goal is to improve clinical care by providing clinicians and patients with high quality data to improve and personalize pain management treatment.

Joe Kossowsky PhD, MMSc. is a clinical investigator in the Division of Pain Medicine in the Department of Anesthesiology, Critical Care and Pain Medicine at Boston Children's Hospital. Following his graduate studies in Clinical Psychology and Neuroscience, Dr. Kossowsky obtained his PhD in Clinical Psychology at the University of Basel, Switzerland and a Master's degree in Biomedical Informatics from Harvard Medical School. He completed postdoctoral fellowships in the areas of pediatric pain, placebo research and biomedical informatics at Boston Children's Hospital and Harvard Medical School. He is currently an Assistant Professor of Anaesthesia at Harvard Medical School.

Dr. Joe Kossowsky's research revolves around the evaluation of progression of acute and chronic pain and comorbid psychiatric conditions, including the benefits of interventions (i.e., medications, multi-modal pain interventions, invasive procedures). There are three core areas:

Network meta-analyses of existing intervention studies

Development and implementation of a comprehensive and dynamic framework for assessing pain, functional, emotional and behavioral outcomes using clinical questionnaires and surveys, electronic health records, digital phenotyping and wearables

Bioinformatic approaches focused on mapping associations between behavioral and clinical phenotypes with genotypes and genetic variants

Edress Darsey, PharmD, graduated with her Doctorate of Pharmacy Degree from Mercer University.

She completed a Clinical Pharmacy Practice Residency at the University of Alabama in Birmingham followed by a Specialty Residency in Clinical Pharmacokinetics at Mercer University. Following her training, Edress spent eight years developing and leading clinical pharmacy services and a pediatric pharmacy residency program at Children's Healthcare of Atlanta. During this time, she researched and published studies around pediatric pharmacokinetics, pain management and other areas of need. In 2000, Edress joined Pfizer Pharmaceuticals where she worked on a variety of medical teams until January 2014 when she was offered an opportunity to help build Pfizer's Pediatric Center of Excellence in the office of the Chief Medical Officer. Edress has served as a Global Pediatric Medical Director/Pediatric Clinical Director at Pfizer for the last 8 years. In this position, Edress works internally across many Pfizer medicine teams to provide end to end support of pediatric studies, including study protocol development, regulation, pediatric pharmacology and formulations. In addition, Edress works externally with Children's Hospitals to build and maintain relationships with a network of major children's hospitals and pediatric research centers in order to facilitate pediatric clinical trial site identification and to optimize clinical trial process execution for investigators and patients.

Edress has served on the Board of Directors for the Pediatric Pharmacy Association (PPAG) and is current chair of the Drug Development Committee. She is a member of the American College of Clinical Pharmacologists (ACCP) and the American Academy of Pediatrics Section on Advances in Therapeutics and Technology.

Monique van Dijk PhD, worked as a nurse for 9 years after which she studied Psychology specializing

in Methodology and Statistics. She finished her PhD thesis in 2001 on Pain assessment in neonates and infants. June 2017 she was appointed as Professor in Nursing Science at the Erasmus Medical Center in Rotterdam, The Netherlands. Since 2005 she collaborates with the Red Cross Children's Hospital in Cape Town, South Africa. Her research interests are pain assessment in preverbal and nonverbal patients, non-pharmacological interventions, patient- and family centered care, and basic nursing care.

Kanecia Zimmerman, MD, MPH, is an Associate Professor of Pediatrics at Duke University School of Medicine, where she specializes in pediatric critical care medicine. She has served as chair of the Pediatric Trials Network Steering Committee, where she has helped guide the vision of the Network, oversee the development and execution of all research protocols and personnel, and interact directly with site investigators, the NICHD, FDA, and other stakeholders. She is the principal investigator and IND holder for four multicenter trials, including trials to evaluate the pharmacokinetics, safety, and efficacy of analgesics in children. She is also the principal investigator for an FDA-sponsored program to evaluate and validate outcomes and endpoints for trials of acute pain therapeutics in infants and young children. Dr. Zimmerman is committed to patient and family voice in research, and has developed and led the PTN's program of participant and family engagement, including return of results to research participants. Moreover, she has a sincere commitment to educating future scientists through leadership of the NICHD-funded Unified Program for Therapeutics in Children (UPTiC) T32 program and co-PI for the Duke Summer Training in Academic Research (STAR) Program. Dr. Zimmerman attended Duke University for medical school and residency training in Internal Medicine and Pediatrics. Following residency, she served as Chief Resident in Pediatrics prior to completing fellowships in pediatric critical care medicine and clinical research at the Duke School of Medicine and Duke Clinical Research Institute, respectively.

Rebeccah Slater, PhD, MSc, BSc is Professor of Paediatric Neuroscience at the University of Oxford and a Senior Wellcome Fellow. She is also a Professorial Fellow at St John's College.

Rebeccah studied Physics (BSc) at Imperial College and Neuroscience (MSc) at UCL, and in 2007 was awarded her PhD (UCL). Since 2013 she has led the Paediatric Neuroimaging Research Group, which focuses on understanding the mechanisms that underlie the development of pain perception. She uses a range of non-invasive brain imaging tools, including EEG and fMRI, to explore the development of pain perception in the human nervous system and has developed new approaches to measure the efficacy of analgesics in neonates.

She has published many articles about infant pain and has been enthusiastically involved in science communication and public engagement with science. Rebeccah holds an honorary research position in the Neonatal Care Services at the John Radcliffe Children's Hospital, NHS Foundation Trust and is a Principal Investigator at the Wellcome Centre for Integrative Neuroimaging.

Brian Anderson, MB ChB, PhD, FANZCA, FCICM is a specialist paediatric anaesthesiologist and intensivist at Auckland Children's Hospital, New Zealand. A PhD in paediatric clinical pharmacology was completed in 2002. He is Professor of Anaesthesiology at Auckland University where his primary research interests center around pharmacokinetic maturation and effects of simple analgesic drugs. He has published over 250 peer-reviewed papers as well as many book chapters and editorials. Editorial work includes Associate Editor-in-Chief for the journal *Pediatric Anesthesia.* Cote, Lerman and Anderson's book "A Practice of Anaesthesia for Infants and Children" is now undergoing its 7th edition.

S. Y. Amy Cheung, PhD is a Senior Director at Certara, leading a Quantitative Science Group (with scientists from UK, Italy and Nordic regions) in Integrated Drug Development and is on the leadership team of the Pediatric Integrated Practice Area. She is also a mentor of the Certara-Monash University Fellowship programme. She obtained her PhD from the University of Manchester. After receiving her PhD, she worked at the Centre for Applied Pharmacokinetic Research (CAPKR) at The University of Manchester. Before joining Certara, she gained over a decade of experience at AstraZeneca (AZ), where she was a Senior Pharmacometrician. She was also a Project Manager and functional representative at the AZ Pediatric Working Group that consisted of 22+ cross-functional pediatric experts. During this time, she was also the company representative on IMI DDMoRe, co-led WPs e.g. PMX-workflow, cardiovascular training. She has been a member of the EFPIA MID3 workgroup since the 2011 EMA M&S workshop, which resulted in several white papers. She has expertise in pediatric/geriatric drug development, oncology, infection, CNS, pain, vaccine, mAb, MIDD, structural identifiability, PBPK, and extrapolation.

Panelists

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. Dr. Yao received a B.S. degree in Biology from Yale University, and an M.D. degree from the George Washington University School of Medicine. She is board certified in both Pediatrics and Pediatric Nephrology. Prior to joining FDA, Dr. Yao was the Director of Dialysis and Associate Pediatric Residency Program Director at the Inova Fairfax Hospital for Children in Fairfax, VA. She has been with the FDA since 2008. 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 collection of data to support the safe use of drugs and biological products in pregnant and lactating individuals. She collaborates with numerous stakeholders both inside and outside of FDA to advance development of safe and effective therapies for children, and pregnant and lactating women.

Dr. John Alexander, PhD is a pediatrician who joined the US Food and Drug Administration as part of a joint fellowship in pediatric infectious diseases with FDA and Children's National Medical Center in Washington, DC. After completion of his fellowship, he became a full-time medical officer, and subsequently a team leader, in the Division of Anti-Infective Products. He has been involved in drug regulation and pediatric drug development for more than 20 years. Dr. Alexander is currently Deputy Director in the Division of Pediatric and Maternal Health in the Center for Drug Evaluation and Research at FDA.

Dina El-Metwally, MD, Ph.D., is the Chief of the Division of Neonatology, Professor of Pediatrics Department, University of Maryland, School of Medicine. As the Medical Director, she led the Drs. Rouben and JiJi NICU Neonatal Intensive Unit, a $33-million project which opened in 2015.

Dr. El-Metwally completed a Pediatrics residency and Perinatal-Neonatal fellowship at the Warren Alpert Brown University School of Medicine, Providence, RI, after graduation from the Faculty of Medicine, Suez Canal University in Egypt. She completed a Master's in pediatric visual evoked potentials and a Ph.D. in Neurodevelopment of ELBW with brain injury.

Dr. Metwally worked as a consultant to the World Health Organization (WHO) in program evaluation and health workforce development. She led national programs to decrease neonatal and childhood mortality in the Middle East and North region (MENA), as Child Survival (UNICEF), Integrated Management of Childhood Illness (WHO/UNICEF). As a MENA regional trainer, she disseminated neonatal resuscitation to prevent Hypoxic ischemic encephalopathy. In recognition of her efforts, she received the Sheila Wallace Award from the International Child Neurology Association.

Dr. El-Metwally's research is in two areas; 1) NICU Environmental Toxicants as heavy metals and volatile organic compounds, and 2)- neonatal opioid withdrawal syndrome (NOWS). She held workshops to raise awareness and advocacy for babies with NOWS among Judges at the Maryland Judicial College and Circuit Court for Baltimore, Interagency Coordinating Council (SICC) for infant and Toddler Program (ITP), Maryland State Department of Education. 'Ready at 5'. She is an Advisor on the Baltimore Network of Early Services and Training (B-NEST) board for opioid exposure. She presented at more than 75 national and international conferences.

Dr. El Metwally is the Co-Director of the UM Center of Excellence for Substance Use in Pregnancy (SUP). She collaborates with Departments of Neurobiology, the Institute for Genome Sciences (IGS), School of Pharmacy, and the Center of Health Information Decision System, Smith School of Business; in the use of artificial intelligence to study SNP arrays and small RNAs as biomarkers for withdrawal, and the impact of substance use in pregnancy on neurodevelopment.

GARY A. WALCO, PhD is a Professor of Anesthesiology and Pain Medicine (adjunct Pediatrics and Psychiatry) at the University of Washington School of Medicine and the Director of Pain Medicine at Seattle Children's Hospital. He has conducted multiple studies on pain treatment and assessment in children. Dr. Walco was the founder of the American Pain Society's first special interest group, focusing on Pain in Infants, Children, and Adolescents, and received their Jeffrey Lawson Award for Advocacy in Children's Pain Relief (2003) and their Distinguished Service Award (2019). Dr. Walco is a past chair of the Pain Committee for the Children's Arthritis and Rheumatology Research Alliance and served on the core committee for Palliative Care in the Children's Oncology Group. He was the president elect of the American Pain Society and is a past president of the special interest group on Pain in Childhood of the International Association for the Study of Pain. Dr. Walco currently sits on editorial boards for Pain, the Journal of Pain, the Clinical Journal of Pain (past associate editor), and did so formerly for the Journal of Developmental & Behavioral Pediatrics and the Journal of Pediatric Psychology. Dr. Walco is a founding member and currently on the Board of Directors for ChildKind International. He has consulted on analgesic trials for children and served on the FDA's Analgesic and Anesthetic Drug Products Advisory Committee.

Tamorah Lewis MD, PhD is a physician-scientist at Children's Mercy Hospital in Kansas City, MO. She is dual trained in neonatal/perinatal medicine and clinical pharmacology. Her research program focuses on developmental pharmacology and pharmacogenetics in the neonatal population. As an Associate Professor in the Department of Pediatrics at The University of Missouri, Kansas City School of Medicine, she practices clinical neonatology and works collaboratively to design, implement, and manage her clinical and translational research program in Neonatal Precision Therapeutics. The overarching goal of her research program is to bring individualized medicine to the NICU population using modern pharmacology tools. Her research career will focus on elucidating the pharmacokinetics, pharmacodynamics and pharmacogenetics of both old and new drugs used to treat neonatal disease, with an emphasis on optimizing and individualizing drug therapy in neonates.

Dr Lewis serves as the Director of Clinical Research Logistics for her Division. She has established the Maternal Neonatal Pharmacogenetic Repository at Children's Mercy Hospital and has multiple

prospective pharmacogenetic cohort studies enrolling and depositing diverse bio-samples to this repository. In addition, she has established research collaborations at UCSF (steroid pharmacogenetics), Vanderbilt (ductus arteriosus pharmacogenetics), and Univ of Buffalo (NSAID PK) and is actively engaged as site PI in multi-site studies assessing neonatal drug safety and efficacy.

Dr Lewis is actively engaged in research societies. She sits on the Board of Directors for the American Society of Clinical Pharmacology and Therapeutics and is on the Executive Committee of the American Academy of Pediatrics (AAP) Section on Clinical Pharmacology and Therapeutics. Dr Lewis is also a member of the International Neonatal Consortium, a multi-stakeholder collaboration run by the Critical Path Institute to advance neonatal therapeutics.

Ellen Fields, PhD is a pediatrician who joined the US Food and Drug Administration in 2005 after almost 20 years practicing as a general pediatrician. She started as a Medical Officer in the Division of Analgesics, Anesthetics, and Addiction Products, and advanced to Team Leader and Deputy Director of the division, focusing almost entirely on analgesic development, with a special interest in pediatric analgesic development. Dr. Fields retired from the FDA at the end of 2019, and since then has been a partner in Hertz and Fields Consulting, Inc. assisting sponsors in the regulatory and clinical aspects of analgesic development.

Lily Mulugeta, PharmD, is the Acting Associate Director for Policy and Research in the Division of Pediatrics and Maternal Health at the FDA. She engages in scientific and regulatory review and research related to pediatric drug development. Dr. Mulugeta serves as a representative for the Division on the FDA Pediatric Review Committee (PeRC). Prior to joining the Division in 2017, Lily was the Scientific Lead for Pediatrics in the Division of Pharmacometrics at the FDA. Prior to joining the FDA, Dr. Mulugeta practiced as a Critical Care Specialist at Children's National Medical Center in Washington D.C. She also served as a faculty member in the Department of Pediatrics at the George Washington School of Medicine and in the Department of Pharmacy at the University of Maryland College of Pharmacy School of Pharmacy. Dr. Mulugeta received her Pharm.D. degree from the University of Kentucky College of Pharmacy and completed a pediatric residency at Inova Fairfax Hospital in Falls Church, Virginia.