

## FDA-University of Maryland CERSI

### **Analgesic Clinical Trial Designs, Extrapolation, and Endpoints in Patients from Birth to Less Than Two Years of Age**

**Wednesday October 13, 2021      10:00am – 1:30pm EST      All Virtual**  
**Thursday October 14, 2021      10:00am – 3:00pm EST      All Virtual**

The goal of the workshop is to address challenges related to evaluation of analgesic products in pediatric patients including population to study, endpoints, and extrapolation of adult efficacy data. The workshop will also provide a forum for discussion on the use of extrapolation as well as alternative trial designs and statistical methods. The focus of the workshop will be on well-established mechanism of actions (NSAIDs, acetaminophen, local anesthetics, opioids).

#### Day 1

- 10:00 – 10:15**      **Welcome/Introductory remarks: Setting the scene (DPMH )**  
Lily Mulugeta, PharmD (Division of Pediatrics and Maternal Health, FDA)
- 10:15 – 10:35**      **Introductory remarks**  
Peter Stein, MD (Office of New Drugs, FDA)  
Rigo Rocca, MD (Division of Anesthesiology, Addiction Medicine, and Pain Medicine, FDA)
- 10:35– 10:50**      **General landscape of extrapolation of efficacy in pediatric drug development and Ethical considerations in Pediatric Drug Trials**  
Beth Durmowicz, MD (Office of Pediatric Therapeutics, FDA)

#### **Session 1: Extrapolation of Efficacy (goals: To define an age limit for using PK-based extrapolation (i.e. exposure-matching))**

**Moderators: Lily Mulugeta (FDA) and Lisa Wiltrout (FDA)**

- 10:50 – 11:10**      **Development of nociception and pain--** Suellen Walker, PhD (UCL GOS Institute of Child Health)
- 11:10 – 11:30**      **Pain epidemiology in neonates and infant patients--**Ricardo Carbajal, MD (Hospital Armand Trousseau)
- Types of pain encountered in each age cohort as compared to older pediatric patients, number of patients available for clinical trials, etc.*
- 11:30 – 11:45**      **Developmental pharmacology of analgesics--**Chris Mcpherson, PharmD (Washington University School of Medicine, St Louis)
- What do we know about maturation of targets? Are there maturation related changes to drug disposition or targets that may suggest need for lower or higher drug exposures in this age group to achieve response similar to older pediatric patients?*
- 11:45– 12:05**      **Extrapolation of adult efficacy data to pediatric patients**  
John van den Anker, MD (Children’s Hospital, Washington DC)
- Given the available data, is there a biological reason to believe that drugs with well-established MOA (on drugs with well-established MOAs (opioids, NSAIDs, acetaminophen, and local anesthetics) would be less effective (at similar concentrations) in pediatric patients less than 2*

*years of age compared to older children? If so, in which age group and what are the uncertainties? Assessment of PK and safety would be required in all age groups.*

**12:05—1:20**

**Panel Discussion (Moderators: Lily Mulugeta and Charles Berde)**

**Q&A: All speakers**

**Panelists:** John Alexander (FDA), Yun Xun (FDA), Lisa Wiltout (FDA), Tamorah Lewis; Suellen Walker, Gary Walco, Ellen Fields, Kanecia Zimmerman, John Van Den Anker

**1:20—1:30**

**Closing Remarks – Charles Berde**

## Day 2

### Session 2: Trial design considerations in acute pain (goals: Trial design and endpoint considerations in age cohorts where exposure-matching cannot be used as the basis for extrapolation of efficacy)

**Moderators: Lily Mulugeta (FDA) and Charles Berde**

- 10:00 – 10:05**      **Welcome/Introductory remarks: Setting the scene (DPMH )**  
Lisa Wiltrout (Division of Anesthesiology, Addiction Medicine, and Pain Medicine, FDA)
- 10:05-10:55**      **Trial Design Considerations for Acute Pain in neonates and infants:**
- Academic Perspective**  
Carolina Donado-Rincon and Joe Kossowsky (Boston Children’s)
- Industry Perspective**  
Edress Darsey (Pfizer Pediatric Center of Excellence)
- Regulatory Perspective**  
Lisa Wiltrout, MD (FDA Division of Analgesics and Anesthetics, FDA)
- 10:55-11:10**      **Outcome measures in acute pain clinical trials in neonatal & infant populations**  
Monique van Dijk
- 11:10-11:25**      **PTN COA development and PTN/NICHHD trials for off patent drugs**  
Kanecia Zimmerman, MD (Duke University/Pediatric Trials Network)
- 11:25—11:40**      **Brain-derived approaches to assess neonatal & infant pain**  
Rebecca Slater, PhD (University of Oxford)
- 11:40-12:00**      **Innovative trial designs including Bayesian approaches**  
Brian Anderson
- 12:00-12:40**      **Lunch break**
- 12:40-1:00**      **Considerations for PK/PD studies**  
Amy Cheung, PhD (Certara)
- 1:00 – 2:50**      **Q&A and Moderated Panel Discussion (moderators: Lily Mulugeta and Charles Berde)**  
Q&A: All speakers  
Panelists: Rigo Roca (FDA), Gerri Baer (FDA), Lynne Yao (FDA), Jinglin Zhong (FDA), James Yates (GSK), Ellen Fields, Edress Darsey (Pfizer), Dina Metwally (UMD), Gary Walco, Kanecia Zimmerman, Tamorah Lewis
- 2:50– 3:00**      **Closing Remarks/Future Direction**  
Lynne Yao, MD—FDA