



IQ/ M-CERSI Pediatric Workshop

Breakout Session Questions

Clinical Sub-Group

Clinical Break-out Schedule

9:00:00 AM	0:15:00	Clinical: Clinical Pharmacology Approaches/Practices in Pediatric Drug Product Development from Industry Perspective – Jack Cook (Pfizer)
9:15:00 AM	0:15:00	Clinical: Value of Pharmacokinetics in Pediatric Clinical Development – Hao Zhu (FDA)
9:30:00 AM	0:45:00	Clinical Break-out 1
10:15:00 AM	0:15:00	Break
10:30:00 AM	0:45:00	Clinical Break-out 2
11:15:00 AM	0:45:00	Clinical Break-out 3
12:00:00 PM	0:45:00	Lunch and Networking
12:45:00 PM	1:00:00	Clinical Summary and Panel Discussion

Speakers

- **Jack Cook:**
 - Title: Clinical Considerations in Pediatric Drug Product Development from an Industry Perspective
- **FDA (OCP): Hao Zhu**
 - Title: Value of Pharmacokinetics in Pediatric Clinical Development

Break-out session Format

- Each break-out session facilitated by respective moderators

	Moderator 1	Moderator 2	Notetaker
Topic I: PK	Jian Wang	Shailly Mehrotra	Mei Khong
Topic II: Study design	Hari Sachs	Jing Liu	TBD
Topic III: Biostudies to support formulation	Elimika Fletcher	Karen Thompson	Beth Galella

- Attendees divided into 3 groups and will rotate through the 3 break-out session
- Panel discussion and Wrap-up after break out sessions

Panel Discussion and Wrap-up

- Session Moderator: Jack Cook (Pfizer)
- Panelist:
- Hao Zhu (FDA)
- Justin Pittaway-Hay (MHRA)
- Jing Liu (Pfizer)
- Karen Thompson (Merck),
- Elimika Fletcher (FDA),
- Jian Wang (FDA)

Pre / Post-Meeting

Meetings	Date/day	Purpose
Pre-workshop	17 June/Monday 3:00 to 5:00 pm	<ul style="list-style-type: none">• To ensure readiness and tie some last minute loose ends.• Plan outline for potential publication
Post-workshop	20 June/Thursday 9:00am to 12:00pm	<ul style="list-style-type: none">• To recap the workshop discussions and lessons learnt from various break-out sessions• Align and prepare the framework for the deliverables (assign action items)

Scope of Break-Out Topics

- Topic I: Pediatric PK Prediction and its Influence on Formulation Design
 - Initial prediction / data collation activities and collaborations
- Topic II: Pediatric Drug Development Strategy Considerations
 - Overarching clinical strategies in pediatric DP development
- Topic III: Clinical Strategies to Support Formulation Design
 - Specific needs for formulation changes to suit clinical needs

Objectives of Discussion

- Identify the gaps/challenges with respect to bridging clinical and formulation needs in pediatric drug development
- Streamline activities between pediatric formulation development and clinical execution
- Understand how pediatric formulation development can help or hinder clinical program
- Propose best practices in pediatric formulation development which aligns with industry standards and regulatory requirements
- Identify opportunity for future collaboration between stakeholders

Break-out Topic I: Pediatric PK Prediction and its Influence on Formulation Design

Background:

- Pediatric PK predictions typically utilize adult data for modelling; however, due to the small pediatric population, the variability used in the predictions may result in large dose tables, which increases formulation burden.
- PK predictions get more challenging particularly for neonates and can significantly impact formulation design.
- Close collaboration between clinical and formulation is desirable to ensure appropriate formulation and dose flexibility is built in to enable successful clinical execution.

Focus: The focus of this breakout session is to explore the collaboration between PK prediction and formulation design and to address the gaps and needs for each function, addressing dose selection, dosing flexibility and safety. It is desirable to share best practices experience for different pediatric age groups particularly neonates.

Break-out Topic 1: Pediatric PK Prediction and its Influence on Formulation Design

- **Question 1:** Can we apply the same variability / uncertainty used for adults in pediatric PK prediction? How does this influence dose selection?
- 1) How does this apply to neonates?
 - 2) How does dosing recommendations change after final pediatric PK is available?
 - 3) How does exposure-response relationship influence dose selection/ formulation design and inform safety?

Break-out Topic 1: Pediatric PK Prediction and its Influence on Formulation Design

- **Question 2:** How does formulation address dosing flexibility – especially in younger children and neonates?
 - How do you get the required dosing flexibility? What is the compromise?
- **Question 3:** How does neonate maturation affect PK prediction and formulation development and mode of delivery? What are the ADME factors that can impact PK prediction, and formulation development?

Break-out Topic II: Pediatric Drug Development Strategy Considerations

Background:

- Recognizing that age-appropriate formulations are essential for safe pediatric use, what strategies can be adopted to ensure formulation development does not delay initiation of pediatric studies (and approval)?
- Potential pediatric development strategies, depending on the ability to extrapolate efficacy, knowledge of PK profile and safety of drug:
 - 1. Dedicated pediatric PK study (single and/or multiple dose) followed by pediatric efficacy and safety studies
 - 2. Pediatric PK or PK/PD study followed by pediatric safety study (pediatric efficacy can be extrapolated from adult efficacy, e.g. anti-infectives, HIV)
 - 3. Pediatric PK as part of the pediatric efficacy or safety studies
 - 4. Enroll pediatric patients in the adult phase 3 studies (e.g, asthma, rare diseases)
- **Focus:** The focus of break-out session is to discuss how to optimize pediatric formulation development for a given pediatric drug development strategy

Break-out Topic II: Pediatric Drug Development Strategy Considerations

- **Question I:** Do different pediatric drug development strategies entail different pediatric formulation needs?
 - What factors should be considered?
 - Should commercial formulations be developed first regardless of pediatric drug development strategy?
 - When is a preliminary pediatric formulation necessary? If so, what information is needed to bridge the preliminary and commercial pediatric formulations?

Break-out Topic II: Pediatric Drug Development Strategy Considerations

- **Question 2:** When is the best time for pediatric formulation and clinical scientists to start engaging each other?
 - During the discussion of pediatric clinical development plan?
 - During specific study design (PK, efficacy and/or safety)?
 - Before and during study execution?

Break-out Topic III: Clinical Strategies to Support Formulation Development

Background:

- Changes in formulation can impact the bioavailability of a drug and the impact of food on bioavailability. Therefore, timing of the development of clinical trial and/or the final age appropriate formulation and a bridging strategy are crucial.

Focus: In this break-out session, participants will discuss the types of and timing of studies to support clinical trial and age appropriate formulations. Participants will share strategies in considering formulation changes during drug development to suit clinical needs of pediatric patients.

Break-out Topic III: Clinical Strategies to Support Formulation Development

- **Question I:** What are the considerations for and impacts of the **timing** of development of age-appropriate formulation and performing bioavailability and food effect study in reference to the PK/efficacy/safety studies?

Break-out Topic III: Clinical Strategies to Support Formulation Design

- **Question 2:** What are the considerations for selecting dosage forms / clinical trial execution for the age-appropriate formulation to be developed considering different populations including neonates?

Break-out Topic III: Clinical Strategies to Support Formulation Design

- **Question 3:** What are the considerations for the impact of various types and amounts of food consumed in different pediatric populations? What factors or considerations would be most relevant to assess for impact on formulation?

Pre-read material

- Assessing the Effects of Food on Drugs in INDs and NDAs – Clinical Pharmacology Considerations (Draft Guidance for Industry), FDA – Feb 2019
- Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials Guidance for Industry (Guidance for Industry), FDA – March 2019.
- Pediatric HIV Infection; Drug Development for Treatment (Draft Guidance for Industry), FDA – May 2018.
- Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address pediatric-specific clinical data requirements, EMA – Mar 2018.
- Purohit, V.S., Biopharmaceutic Planning in Pediatric Drug Development, AAPS Journal, 14 (3), 2012.
- Barbour, A.M., Practical Considerations for Dose Selection in Pediatric Patients to Ensure Target Exposure Requirements, AAPS Journal, 16 (4), 2014.

Pre-read material

- FDA, Guidance for Industry: Bioavailability Studies Submitted in NDAs or INDs — General Considerations
<https://www.fda.gov/media/121311/download>
- Momper, J.D., et al. Adolescent Dosing and Labeling Since the Food and Drug Administration Amendments Act of 2007. JAMA Pediatr. 2013. 167(10): 926-932. doi:10.1001/jamapediatrics.2013.465
- FDA, Guidance for Industry: General Clinical Pharmacology Considerations for Pediatric Studies for Drugs and Biological Products. 2014. <https://www.fda.gov/media/90358/download>