Challenges in Conducting Trials Involving Children: Sponsor's view

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ebe european biopharmaceutical enterprises

This is a joint industry presentation on behalf of the trade associations shown

efpia European Federation of Pharmaceutical Industries and Associations

EuropaBio™ The European Association for Bioindustries

Discussion points

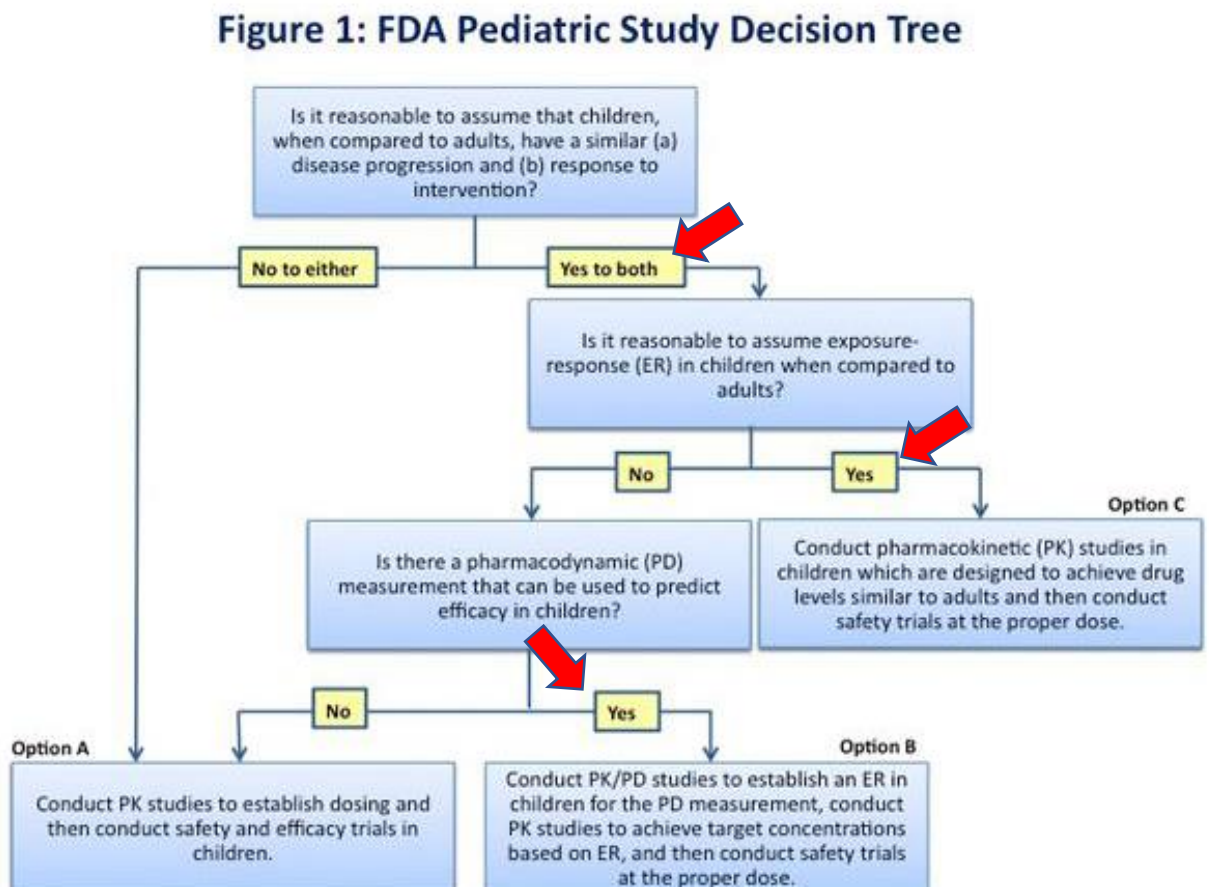
- Planning and execution best practices
- Improving movement along a Pediatric Program decision tree

- The paradigm shift in antibiotic drug development and its implications
- Current and near future challenges

Best practices for planning

- Involvement of all stakeholders
  - Therapeutic experts, investigators, regulators **and parents**
- Defining the sponsor's position early
  - Sponsor accepting the role as the definitive expert of their asset
  - Recognizing the temporal components of medical practice – identifying impending changes in SOC
- Collaborative development of PIP/PRSPs
  - Infeasible = unethical
- Potential contributions of c4c and I-ACT
  - Consultation – early
  - Improving clinical trial infrastructure
  - Socializing the importance of conducting pediatric clinical trials

Pediatric Antibacterial Drug Development and the Decision Tree



http://www.fda.gov/ScienceResearch/SpecialTopics/PediatricTherapeuticsResearch/ucm106614.htm

Improving movement along the decision tree

- Extrapolation of efficacy from adult experience to children
  - Understanding pathogenesis of disease in adults, children, infants and neonates
  - Importance of defining exposure/response relationships in initial efficacy trials
- Borrowing data
  - Potentially unique toxicity in children suggested by preclinical studies
  - Safety profiles of drugs from the same class
- RWE
  - Assessing experience based on information collected in children included in health care databases

A paradigm shift

- Previously, acquisition of biotech by pharma brought big pharma resources
  - Acquisitions and licensing opportunities often underestimate impact on resources required to complete plans
  - Acquisitions and sponsor changes delay activities/timelines; disruptive to development
- Development and commercialization of antibiotics have shifted from big pharma to biotechs
- Now, big pharma is not buying small pharma/biotech; actually divesting antibiotics

Shift of antibiotic development and commercialization brings new challenges

- Huge resource differences
- All of the issues flagged by colleagues from big pharma are magnified many fold in small pharma/biotech
  - Resource-constrained enterprises delay early planning for pediatric development
    - Often can do one big thing at a time
    - Focus can be regional—how to best harmonize globally
  - Biotech unlikely to have internal expertise in pediatrics, CMC, tox, PK, regulatory (no regional resources)
  - External resources (c4c*, I-ACT*) may be limited in providing expertise to biotech not supporting these networks
  - Although they will bear the brunt of the work going forward, biotech/small pharma are typically not at the table during discussions of antibiotic development
    - They are not members of EFPIA or PhRMA

*c4c=conect (**Co**llaborative **N**etwork for **E**uropean **C**linical **T**rials for Children) for children

*I-ACT= **I**nstitute for **A**dvanced **C**linical **T**rials for Children

Disclaimer: QUICK SUMMARY!

Summary of EMA Recent PIPs (PSPs)*

IPOUND	Year PSP agreed	COMPLETION	treatment study	EUDRACT	Sponsor shift
bavancin	2008, modified 2013, 2014, 2015, 2016	2021	neonatal sepsis	NA	X
			3mo-18 patients requiring hospitalization and IV ABX	X	
			CSSTI	X	
Ceftaroline	2010; modified 2011, 2012, 2013, 2014, 2015, 2016	2018	CSSTI and CABP 2mo-18	X	X
			neonatal sepsis	X	
Tedizolid	2013, modified 2014, 2016, 2018	2020	age 3mo-12, 12-18 gram positive infection	X	X
			neonatal sepsis birth-90 d	NA	
Oritavancin	2013; modified 2017	2022	SSTI birth-18	NA	X
Meropenem-vaborbactam	2015	2025	UTI/IAI age 3mo-18	NA	X
			neonatal sepsis birth-90d	NA	
Omadacycline	2017	2024	CABP 8-18	NA	
Eravacycline	2015; modified 2016	2026	UTI age 8-18	NA	
Lefamulin	2017	2025	CABP 2mo-18 y; suspected bacterial infection birth-18	NA	
Plazomicin	2018	TBD	TBD	NA	

*Source: EudraCT, EMA pediatrics webpage

Current and near term challenges

- Understanding the changing antibiotic development and commercialization environment with its impact on pediatric plans
- Defining global pediatric development plans
  - Aligning regulatory timing and opinion
  - Consideration of extrapolation and alternative methods of data collection
  - The impact on timing and resources associated with amending plans
- Challenging studies
  - Wasting precious resources
  - The ethics of enrolling vulnerable patients in trials that can never be completed