Challenges and Strategies to Facilitate Formulation Development of Pediatric Drug Products
Session 5: Excipient Safety

Organizing Committee:
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Session 5: Pre-Read Material

- EMA Guideline on Excipient Labeling (Review example of propylene glycol, esp Q&A)
  - http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000387.jsp&mid=WC0b01ac05808c01f6
- EMA Reflection paper on extrapolation of efficacy and safety in paediatric medicine development. 01Apr2016 DRAFT
  - http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2016/04/WC500204187.pdf
- IPEC Position paper on EU Risk Assessment Guidelines for Excipients (2015/C95/02)
  - http://ipecamericas.org/content/ipec-federation-publishes-position-paper-eu-risk-assessment-guidelines-excipients-2015c-9502
- Schmitt 2015 (*Children* **2015**, *2*, 191-197) "Safety of excipients in pediatric formulations – A call for toxicity studies in juvenile animals?" doi:10.3390/children2020191
- Loftsson 2015 (*Int J Pharm* **2015,** 480:48-54) "Excipient pharmacokinetics and profiling"
- Turner 2014 (*Adv Drug Deliv Rev* **2014** Jun;73:89-101) "Risk assessment of neonatal excipient exposure: Lessons from food safety and other areas" doi:10.1016/j.addr.2013.11.003
- Sources of information supporting excipient use
  - FDA inactive ingredients and IPEC Comments
    - http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm
    - http://www.pharmtech.com/ipec-america-suggests-improvements-fda-s-inactive-ingredients-database&topic=333&cid=PTE?eid=173028031&bid=1229925
  - STEP database (Safety and Toxicity of Excipients for Pediatrics)
    - http://pharmacyapp-a.ucl.ac.uk:8080/eupfi/appDirectLink.do?appFlag=login;
    - http://www.sciencedirect.com/science/article/pii/S037851731300848X
    - http://www.sciencedirect.com/science/article/pii/S0378517315005360

Session 5: Case Scenarios & Questions to Inform Development of a Risk Assessment Framework

Two Breakout discussion groups:

1. New/Novel excipients
   - "Inactive" vs biologically active agents (e.g. SNAC)
   - European vs. US approaches
2. Established/Standard excipients with incomplete information (eg new use: dose, duration, route, severity of diseases, age group, etc)
   - Clarification of known information in proposed setting
   - Identification of information gaps
   - Alternative sources of information and the appropriateness thereof

Session 5: Case Scenarios & Questions to Inform Development of a Risk Assessment Framework

- How to justify the use of excipients (novel, established) in paediatrics? What are the hurdles faced?
- Risk assessment of excipients in paediatrics
  - Can a common template or approach (framework) be developed for implementing risk assessments for individual excipients?
  - What minimum information is required? What additional data is required?
  - What circumstances and factors should be considered regarding the justification for junvenile tox studies?
  - Should toxicology studies with the final formulation be conducted? If so, when & which studies?
  - What alternative options are available if no additional information is available?
  - What clinical trial design factors can be incorporated to provide information on the safety of excipients?
  - Where are the knowledge gaps and how would you prioritize studies needed to approach the evaluation of excipients for paediatrics?
- Would the proposed framework help address the issues of use of excipients in paediatrics?
  - What are the pros and cons of the presented framework ?
  - What additional elements would you consider in the framework?
- Can we evaluate data on excipients and present in a format which will satisfy regulators.
  - Should a standardized template/monograph be created?
- Where to find the existing information?
  - extending the FDA inactive ingredient database to paediatrics
  - Platform to share information ? (eg, STEP database)