Highlights of MCERSI/IQ/EuPFI workshop Challenges and Strategies to Facilitate Formulation Development of Pediatric Drug Products June 8-9, 2016 College Park, MD

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On behalf of M-CERCI 2016 Pediatric formulation workshop organizing committee

Organizational Details

- Organized through M-CERSI (**Centers of Excellence in Regulatory Science and Innovation**) in collaboration with IQ and EuPFI
- Conference Logistical support provided by M-CERSI and IQ
- Four IQ member companies provided sponsorship to support travel of 10 European participants
  - Lilly, Abbvie, BMS, Takeda
- 11 FDA, 4 EU Regulatory, 6 EuPFI, and 1 NIH representatives, along with 13 IQ members, served as either co-chairs or speakers.
- In total there were 85 registrants including over 20 FDA and 4 EU Regulatory

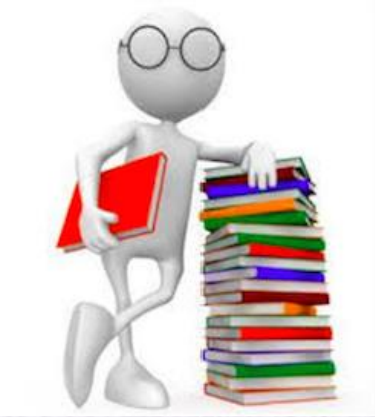
Workshop Topics

Six Sessions

1) Overview of Pediatric Formulations and Key Considerations
2) Age-Appropriate Formulations – Swallowability
3) Age-Appropriate Formulations – Palatability
4) Use of Excipients in Pediatric Formulations - Safety Considerations
   - Existing Excipients
   - Novel Excipients
5) Understanding of food effect for pediatric formulations co-administered with food
6) Biopharmaceutical considerations
   - PBPK modeling
   - BCS

Workshop Format

- Each session had introductory presentations followed by discussions in smaller breakout sessions
  - Pre-work provided (IQ and EuPFI)
  - Expectation set early with participants to be prepared to discuss
  - Breakouts facilitated and extensive notes taken



Age appropriate Session Swallowability- Outcomes

- Define swallowability from drug development point of view
- Develop quantifiable method and criteria to measure the key parameters based on definition
- Align on how the impact of swallowability on compliance and adherence could be assessed
- Create foundational data sets that would reduce the level of product specific data that needed to be generated
- Develop risk mitigation strategy to reduce impact of difficulty in swallowing
  - Training and education of patients and their caregivers
    - Explore how orthogonal disciplines can be used to train patients– e.g. physical therapy, psychology etc…
  - Evidence based directions for manipulation of dosage forms

Age appropriate Session Palatability-Outcomes

- Develop specific definitions for palatability in the pharma context
  - Integrate patient, product, cultural, and behavioral issues to understand palatability
  - Need consistent methodology for evaluation – facial monitoring in young children was discussed as an interesting idea
    - In-vitro techniques such as the use of e-tongue seems to be limited to risk screening at best and thus not used extensively anymore
- Is the goal elimination of taste or getting to taste neutral ?
  - Formulation options such as Coated multi-particulates are taste neutral but other attributes of multi-particulates such as particle size could affect overall palatability
  - Use of after market product modification (eg. FlavoRx) poses its own challenges
    - Federal Regulations versus State Pharmacy Laws
    - Concerns over stability, general lack of risk evaluation

Workshop Outcomes

3 Manuscripts published in International Journal of Pharmaceutics, Volume 536, Issue 2

- Assessment of swallowability and palatability of oral dosage forms in children: Report from an M-CERSI pediatric formulation workshop

  Robert Ternik et al

- Food effects in paediatric medicines development for products Co-administered with food

  Hannah Batchelor et al

- Challenges and strategies to facilitate formulation development of pediatric drug products: Safety qualification of excipients

  Lorrene A. Buckley et al

Common themes

- Common definitions/methodology needs to be developed based on industry, academia and regulatory experts input
- Specific tools needed to help evaluate the key attributes of pediatric formulations
- Collaboration needs to continue on increasing the understanding in new areas of development
- Platform to share the knowledge gained through these activities/collaborations

What have we done since?

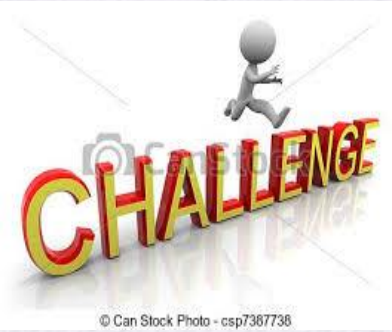
- Formed more multifunctional teams-for example IQ Pediatric WG has representatives from clin pharm, drug safety and analytical areas including FDA representative, Jian Wang
- Developed decision trees (included in manuscripts), contributed to tool kit development to help address the availability of resources for specific issues
  - IQ, EuPFI contributed to WHO's toolkit for research and development of pediatric antiretroviral drugs and formulations Module 5 on Acceptability, published July 2018
  - Joint drug product and analytical team discussing selection, quantity and type of supportive data that needs to be generated when food is used as administration aid
- Platform for sharing-workshops, manuscripts, webinars and commenting on regulatory guidance
  - Survey was conducted to collect regulatory feedback on pediatric plans and this data and was presented at IQ consortium as well as EuPFI annual meeting.
  - Webinars organized by IQ PWG, GRiP, EuPFI on pertinent topics

What have we done since?

- Discussing/Provide collective comments on regulatory guidance
  - For example, multidisciplinary IQ team working discussing FDA guidance on Assessing the Effects of Food on Drug in IND and NDAs-Clinical Pharmacology Considerations
- Innovative approaches are being looked at for solving these problems-patient centric approach, ideas canvas for excipients etc
  - Create a collaborative framework (in conjunction with IPEC-Americas and FDA) for improving development and regulatory acceptance of novel excipients
  - Explore the possibility of creating a new process for regulatory acceptance of novel excipients during early development

2019 Workshop Themes

- Build on discussions and collaborations initiated in 2016
- Share new findings and collective understanding in these key areas
- Tackle challenges that still need to be addressed



Remember who is at Stake
Let's make a difference !!