CPLG Pediatric Working Group – 2014 Accomplishments and Path Forward

9 October 2014

IQ Symposium 2014 – “Pre-competitive Collaboration for Innovation”

CPLG Pediatric Working Group

- Formed in 2011
- 2012: Industry mini symposium as part of a Pediatric workshop organized by Children's Hospital of Philadelphia
- Currently: representatives from 22 pharmaceutical companies, NIH, academia, FDA & EMA/PDCO

PWG Leadership:

- Chair: Paulien Ravenstijn, Janssen R&D (J&J)
- Vice Chair: Konstantina M. Vanevski, Bayer
- Immediate-past Chair: Mohamed El Mouelhi, Novartis
- Special Advisor and avid supporter: Jim Keirns, Astellas

Short Term Objective – 2014

- Organized Pediatric Symposium and brought together the industry, academia, NIH, FDA and EMA/PDCO in an effort to establish closer collaboration, address the current challenges and seek new venues to improve the existing pediatric drug development paradigm.

- PWG Organizing Committee was led by:
  - Paulien Ravenstijn, Janssen R&D (J&J).
  - Konstantina Vanevski, Bayer
  - Dionna Green, FDA

- Approximately 50 participants
  - 12 from FDA, 4 from EMA, 2 from NIH
  - 2 academic, 1 BIO, 1 Pediatric Clinical Pharmacology Fellow
  - rest from IQ member companies

SUMMARY

- Overall evaluation of this meeting: **Satisfaction level – very positive**
- Main Meeting Objective was **ACHIEVED**
  - Starting point to discuss challenges of Pediatric Drug Development with all involved parties

- **Newborn represents a high unmet need**; more consideration to involve this forgotten population into clinical studies
  - How to share information with involved parties?
  - **What is new/currently ongoing at FDA and PWG**

- Update / Revision of ICH- E11 under consideration:
  - Revised Draft with collected comments under consideration

SUMMARY (2)

- When communicating with FDA:
  - Pediatric Clinical Pharmacology Staff in OCP at FDA is now in place
  - Always advisable to request participation of Ped expert (from Pediatric ClinPharm or Pediatric Maternal Health) in the Review of Ped Plan

- Initial Pediatric Study Plan (iPSP)
  - Draft Guidance published and received comments under consideration

- Common Commentary Pilot Program: (Pediatric Cluster Group):
  - Not equivalent to Scientific Advice, rather an Informal process requested by regulator, only Regulators participate at this stage
  - A brief (max 2 pages) common commentary document agreed upon by both FDA & EMA
  - Aim is ensure single pediatric development study (plan) realizing remaining differences due to legislative and cultural differences.

SUMMARY (3)

- General advice:
  - Earlier discussion of pediatric plans with EMA/FDA encouraged; although PIP is required at EOP1, a request for a preliminary meeting may be justification to delay the PIP submission to later
  - EMA is receptive to modifications to the PIP as more is learned about a compound
  - Ask for a meeting with the Division or ask the Division to put the issue on the Pediatric Cluster Group for discussion when facing some differences between EMA & FDA recommendations
  - Include relevant M&S in PIP application

  - *Always make the argument as it may be accepted!*

SUMMARY (4)

In the spirit of precompetitive collaboration:

- Collaborating with government agencies to take advantage of the government's knowledge about industry-wide issues is very valuable and should be encouraged

NEXT STEPS:

- Pediatric Symposium 2015 – Washington DC – either at the FDA or same venue as in June 2014
- Any topic to consider for future meeting?
  - Neonatal Clinical Pharmacology
  - Pediatric Biomarkers
  - Possible collaborations (academia, other groups)?
  - Plans to organize a webinar –
    - Neonatal drug development under consideration
    - Best practices in pediatric research and clinical trials

Long-term objectives of the CPLG Pediatric Working Group

- Hold similar symposia every 12-18 months
- Collaborate with the Pediatric WGs from IQ Consortium
- Become “the voice of industry” when it comes to pediatric clinical pharmacology

Thank you!

Back Up

Final Agenda IQ CPLG Pediatric Symposium on June 4, 2014

	Time	Topic	Speaker	NOTES/Action Items
A.M.	8:30-8:40	Welcome	**Paulien Ravenstijn, Ph.D.,** Janssen R&D	
	8:40-9:00	Introduction – set the stage & link topics	**John N. Van Den Anker, M.D., Ph.D.,** Children's National Medical Center	
	9:00-12:00 (incl break)	Session moderator: **Joga Gobburu, PhD, FCP, MBA** **University of Maryland** **Overview of ICH E11 Process:** Describe process, understand what it takes, plan how to move forward and organize dedicate meeting to address this process. **International Regulations:** 1. **Extrapolation in pediatric drug development** – from FDA and EMA perspective (*approx. 35-40 mins.)* 2. **FDASIA update** – experience since the passage of FDASIA, including discussion of Pediatric Study Plans *(approx. 20 mins.)* 3. **Common commentary pilot program** – description of FDA/EMA common commentary program and experience to date (*approx. 10 mins.)* 4. **Q&A Session** addressing challenges in the development of a pediatric program *(approx. 30 mins.)* 5. **Panel discussion** *(approx. 45 mins.)*	Overview of ICH E11 Process **Joga Gobburu, PhD, FCP, MBA;** University of Maryland Int. Regs. Topic #1: **Dianne Murphy, M.D.** FDA **Cecile Ollivier,** EMA Int. Regs. Topic: #2: **Lynne Yao, M.D.** FDA Int. Regs. Topic # 3: **Jean Temeck, M.D.** FDA	PANELISTS: **Dr. Gilbert Burckart (FDA)** **Dr. Lynne Yao (FDA)** **Dr. Dianne Murphy (FDA)** **Dr. Jean Temeck (FDA)** **Dr. Jeff Barrett (Sanofi)** **Ms. Janet Jenkins-Showalter (Genentech-Roche)** **Dr. George Giacoia (NIH)** **Dr. Cecile Ollivier (EMA)** **Dr. Paolo Tomasi (EMA)** **Dr. Ralf Herold (EMA)** **Dr. Efthymios Manolis (EMA) - tentative**

	12:00-13:00	Lunch		
	13:00 – 14:00	Highlight of relevant FDA meetings: • FDA seeking input on how to incorporate PBPK in trial design and regulatory decision making (1-hr session on Pediatrics) (March2014) • FDA (OCP) Workshop – PBPK applications to pediatric drug development in (May2014)	**Gilbert J. Burckart, Pharm.D.** FDA **Jeffrey Barrett, Ph.D., FCP** Sanofi Pharmaceuticals,	
P.M.	14:00-15:00	How do we translate Juvenile toxicity data on a drug to pediatric clinical trial design?	**Karen Davis Bruno, Ph.D.** FDA **Judith W. Henck, PhD, DABT** Eli Lilly & Co	
	15:00-15:30	Coffee/tea break		
	15:30-16:00	New Journal: Frontiers in obstetric and pediatric pharmacology	**Anne Zajicek, M.D., Pharm.D** NIH	
	16:00-17:00	Ideas/discussion on future collaboration (vision/mission of Pediatric WG)	**ALL**	

SUMMARY (5)

- Extrapolation in Pediatric Drug Development:
  - No, Partial or Complete Extrapolation depending on product and indication...
  - Changing over time from “No” to “Complete Extrapolation” as new data /evidence/ knowledge become available
  - Cross Committee Working Group to evaluate extrapolation process (Gaucher’s disease a positive experience)
  - Next steps:
    - Reflection paper in preparation
    - EPWG to review individual submission
    - Algorithm (set of approaches)for Extrapolation
    - Harmonization between FDA & EMA
    - Guidance document for EP under discussion

Summary (6)

- Role of E-R in peds depends on the circumstances;
  - useful when it is unclear if peds will have the same E-R relationship as adults.
  - Similar disease pathology and therapeutic response →E-R data in peds may not be needed.
- Selection of relevant species, age and dose for Juvenile tox studies: a challenging matter
- Juvenile animal studies:
  - Is observed effect sufficiently robust to drive the decision to pursue evaluation of clinical maturation stage?
  - Is a complete weight of evidence approach being applied?

SUMMARY (7)

- Collaborating with government agencies to take advantage of the government's knowledge about industry-wide issues is very valuable and should be encouraged.
- PSP should include plans for a PPSR (if relevant). PSP and PPSR are separate regulatory documents, but should align with each other and with the general development plan; they are complimentary to each other
- Under PREA, the PSP is indication-specific, whereas the PIP specifies "Conditions of Use." COU is more general and may include the adult indication as well as other potential indications.
- Although the PSP is indication-specific, there are mechanisms in US to study other indications (if appropriate and needed) under BPCA