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

- 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  - Draft Guidance published and received comments under consideration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.
• 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!*
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
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<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Speaker</th>
<th>NOTES/Action Items</th>
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</thead>
<tbody>
<tr>
<td>8:30-8:40</td>
<td>Welcome</td>
<td>Paulien Ravenstijn, Ph.D., Janssen R&amp;D</td>
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<tr>
<td>8:40-9:00</td>
<td>Introduction – set the stage &amp; link topics</td>
<td>John N. Van Den Anker, M.D., Ph.D., Children’s National Medical Center</td>
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<td>9:00-12:00 (incl break)</td>
<td>Session moderator: Joga Gobburu, PhD, FCP, MBA University of Maryland</td>
<td>Overview of ICH E11 Process: Describe process, understand what it takes, plan how to move forward and organize dedicate meeting to address this process.</td>
<td>PANELISTS: Dr. Gilbert Burckart (FDA) Dr. Lynne Yao (FDA) Dr. Dianne Murphy (FDA) Dr. Dianne Murphy (FDA) Dr. Jean Temeck (FDA) Dr. Jeff Barrett (Sanofi) Ms. Janet Jenkins-Showalter (Genentech-Roche) Dr. George Giacola (NIH) Dr. Cecile Ollivier (EMA) Dr. Paolo Tomasi (EMA) Dr. Ralf Herold (EMA) Dr. Efthymios Manolis (EMA) - tentative</td>
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**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.)**
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<tr>
<th>Time</th>
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<tr>
<td>12:00-13:00</td>
<td>Lunch</td>
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<td>13:00 – 14:00</td>
<td>Highlight of relevant FDA meetings:</td>
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<td></td>
<td>• FDA seeking input on how to incorporate PBPK in trial design and regulatory decision making (1-hr session on Pediatrics) (March2014)</td>
<td>Gilbert J. Burckart, Pharm.D., FDA</td>
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<td></td>
<td>• FDA (OCP) Workshop – PBPK applications to pediatric drug development in (May2014)</td>
<td>Jeffrey Barrett, Ph.D., FCP Sanofi Pharmaceuticals,</td>
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<td>14:00-15:00</td>
<td>How do we translate Juvenile toxicity data on a drug to pediatric clinical trial design?</td>
<td>Karen Davis Bruno, Ph.D., FDA</td>
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<td>Judith W. Henck, PhD, DABT Eli Lilly &amp; Co</td>
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<td>15:00-15:30</td>
<td>Coffee/tea break</td>
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<td>15:30-16:00</td>
<td>New Journal: Frontiers in obstetric and pediatric pharmacology</td>
<td>Anne Zajicek, M.D., Pharm.D NIH</td>
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<td>16:00-17:00</td>
<td>Ideas/discussion on future collaboration (vision/mission of Pediatric WG)</td>
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SUMMARY

• 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

- 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?
• 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.