Science and Ethics of Paediatric Research
Regulators’ perspective

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Better Medicines for Children

Children should be given medicines appropriately evaluated for their use

ICH E 11 Guideline: Clinical Investigation of Medicinal Products in the Pediatric Population
European Paediatric Regulation

Improve the health of children

• Increase high quality research into medicines for children
• Increase availability of authorised medicines for children
• Without unnecessary studies in children
• Without delaying authorisation for adults

• Main Pillars of the Regulation:
  - the paediatric investigation plan (PIP)
  - the paediatric committee (PDCO)
Challenges
Paediatric Drug Development

- Small population
- Recruitment of patients
- Design of clinical studies
- Lack of validated endpoints
- Lack of adequate training and expertise in conducting clinical trials for drug approval
- Ethical considerations
Better Medicines for Children

Children should not be protected from research but through research

Council of Canadian Academies
http://www.scienceadvice.ca
Protecting children in research

Paediatric Investigation Plans include:

- DSMB as standard requirement
- Measures to minimise pain, distress, fear
- Advocating sparse sampling
- Innovative methodology for design and analysis
- Modelling and simulation where possible
Ethical Consideration for clinical trials on Medicinal Products Conducted with the Paediatric population

EMA approach: How to address challenges

Diabetes Care 2014: Joining forces: A call for greater collaboration to study new medicines in children and adolescents with t2DM.
Paediatric medicines: Workshops

The European Medicines Agency regularly organises workshops on topics related to paediatric medicines.

2014

- Expert meeting on the clinical investigation of medicines for the treatment of paediatric hepatitis C (09/12/2014)
- Paediatric osteoporosis expert meeting (02/06/2014)
- Pharmacovigilance in the paediatric population workshop (28/04/2014)

2013

- Workshop on paediatric investigation plans in type-2 diabetes mellitus (25/02/2013)

2012

- Paediatric anticoagulation therapy expert meeting (06/11/2012)
- Joint European Medicines Agency / Food and Drug Administration workshop for paediatric Gaucher disease type I: exploring the way forward (17-18/10/2012)
- Workshop on endpoints for cystic fibrosis clinical trials (27-28/09/2012)
The purpose of this Collaborative Approach document is to increase - the chances of rapid and smooth agreement of the Paediatric Investigation Plan (EMA) / Pediatric Study Plan (FDA). In addition, this document discusses the possibility of a multi-arm, multi-company clinical trial for the treatment of Gaucher disease, as one approach to address the feasibility of developing multiple products for a rare disease in a limited timeframe.
Enpr-EMA

- A network of research networks, investigators and centres with recognised expertise in performing clinical trials in the paediatric population
- Members perform research with children (newborns to adolescents), in multiple therapeutic areas, and ranging from pharmacokinetics to pharmacovigilance
Recognition criteria

- Networks to be recognised by quality of paediatric research
- 6 recognition criteria and quality standards for self-assessment
  - Research experience and ability
  - Efficiency requirements
  - Scientific competencies and capacity to provide expert advice
  - Quality management
  - Training and educational capacity to build competences
  - Involvement of patients, parents or their organisations
- Each criterion composed of several sub items
- Set of minimum criteria to be fulfilled
Ad hoc Working Groups:

- Methodological approaches to priority setting (PDCO)
- How to establish communication between Enpr-EMA, networks and industry
- Sharing good practices within Enpr-EMA and with industry
- Dialogue and interaction with Ethics Committees
- Neonatology (PDCO)
- Strategies for funding and maintaining a paed. CT network
- FP7 projects (PDCO, EC)
- Joint ENCePP and Enpr-EMA WG on Pharmacovigilance
- GCP Training
- Young people (advisory) groups across Europe
5 years Paediatric Regulation – What has been achieved?

More information on medicines:
• 87 changes to product information
• 89 additions of dosing information, 77 of new study data and 134 of safety information

More medicines for children:
• 34 new medicines with paediatric indication
• 72 medicines with an extension of indication to children
• 26 medicines with new age appropriate formulation
The PUMA concept: a disappointment

- Incentive (data and market exclusivity) not working
- Market opportunities in this sector insufficient to outweigh economic risks of development
- Researchers not engaging in trials with medicines that have been on the market for year
- PUMA concept has failed to fulfil the initial expectations

PIP for a PUMA to cover only certain age groups and not the entire paediatric population
European law is failing children with cancer

Paediatric oncology drug development

Stakeholders flag public health issues
Oncology PIPs as of 9/2014

- **Paediatric patients targeted** – PIPs still driven by adult disease:
  - Only 7 PIPs exclusively/primarily for paediatric use (not or rare in adults)
  - 10 PIPs for to-be-found paediatric malignancy ("solid malignant tumour")
- First MA applications (by 10/2013): 38 under Paediatric Regulation
  - 18/38 using class waiver (with or without PDCO confirmation)
  - 4/38 using product-specific waiver (PDCO: disease does not exist)
  - 3/38 using product-specific waiver (PDCO: lack of safety or benefit)
  - 13/38 with agreed PIPs (Paediatric investigation plan, agreed by PDCO)
- **PIPs agreed** for 63 different anti-cancer medicines
- **Timelines**
  - For 13 MAAs (2008-2013) with agreed PIP: 6.5y from MA to PIP completion
Paediatric oncology drug development

- PDCO: Revision of the class waivers intended
- Close collaboration with Oncology networks
- Extending Addendum on paediatric oncology of anti-cancer guideline
- Standard PIP: Rhabdomyosarcoma and AML
- Call for multicompny multistage trials
Conclusions

- Paediatric Regulation strong tool to change way medicines are developed for children
- Addressing challenges requires
  - global cooperation
  - continuous education of regulators, clinical investigators, parents/patients, ethics committees
  - continuous early dialogue, exchange and collaboration with all stakeholders involved to achieve aim:

Better Medicines for children!
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Thank you

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