EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/PDCO approach to Neonatology: Opportunities !

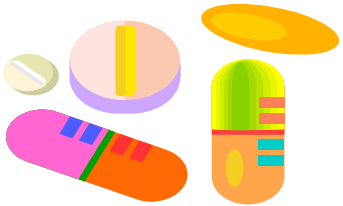
EnprEMA/EMA-PDCO Meeting
Collaboration on Challenges in development of medicines for neonates

London 17 March 2015

Presented by Ralph Bax
Paediatric Medicines | Product Development Scientific Support Department

An agency of the European Union

Why is there a EU Paediatric Regulation?



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Challenges drug development in neonates

- Highly complex
  - Developing organism (metabolism, detoxifying pathways)
  - Complex setting with up to 60 medicines administered simultaneously
- 'Traditional' high "off-label" use
  - Clinical practice, 'academic' studies – not necessarily without evidence

Objectives of the EU Paediatric Regulation

- Improve the health of children:
  - Increase high quality, ethical **research** into medicines for children
  - Increase **availability** of authorised medicines for children
  - Increase **information** on medicines
- Achieve the above:
  - Without unnecessary studies in children
  - Without delaying authorization for adults

EU Legislation - reminder

- **PIP** needed for the initial authorisation of new products (including only-adults indications) in the EU.

- Studies in neonates and children need not necessarily be done at the same time as in adults (**deferrals** > 80% of cases).

- Reasons to **waive** studies in children:
  - Likely to be ineffective or unsafe
  - Condition does not occur
  - No significant therapeutic benefit over existing treatments

Approach to neonatal population in PIPs

- PIPs are applicant triggered!
- Specific consideration for neonates:
  - **Condition / indication** applied for (in adults, older children) - Neonatal condition
  - **Properties** of the medicinal product
  - Paediatric and neonatal **needs**
  - Age-appropriate **formulation**
  - Specific juveniule **non-clinical** studies
  - Innovative design (PK, Mod and sim, (partial) extrapolation)
- Age-staggered approach – adequate?

Outcome analyses

- 1 in 4 PIPs specifically mention neonatal development (2007-2011)
- Inclusion of neonates increased in PIPs: from 15% to 28% (2008) and from 24% to 32% (2011).

→ outcome analysis for neonates across therapeutic areas ongoing

Further activities

- Funding: FP7 off-patent programme: over 50% of all funded programmes concerned specifically development in neonates.
- Paediatric inventory

Challenges

- Need matched with authorised medicines?
- Clinical community: level of evidence needed to change practice?
- Generation of high quality data ("academic ***and*** regulatory")
- Use of existing data
- Increased collaboration

- → PDCO neonatology group since 2014

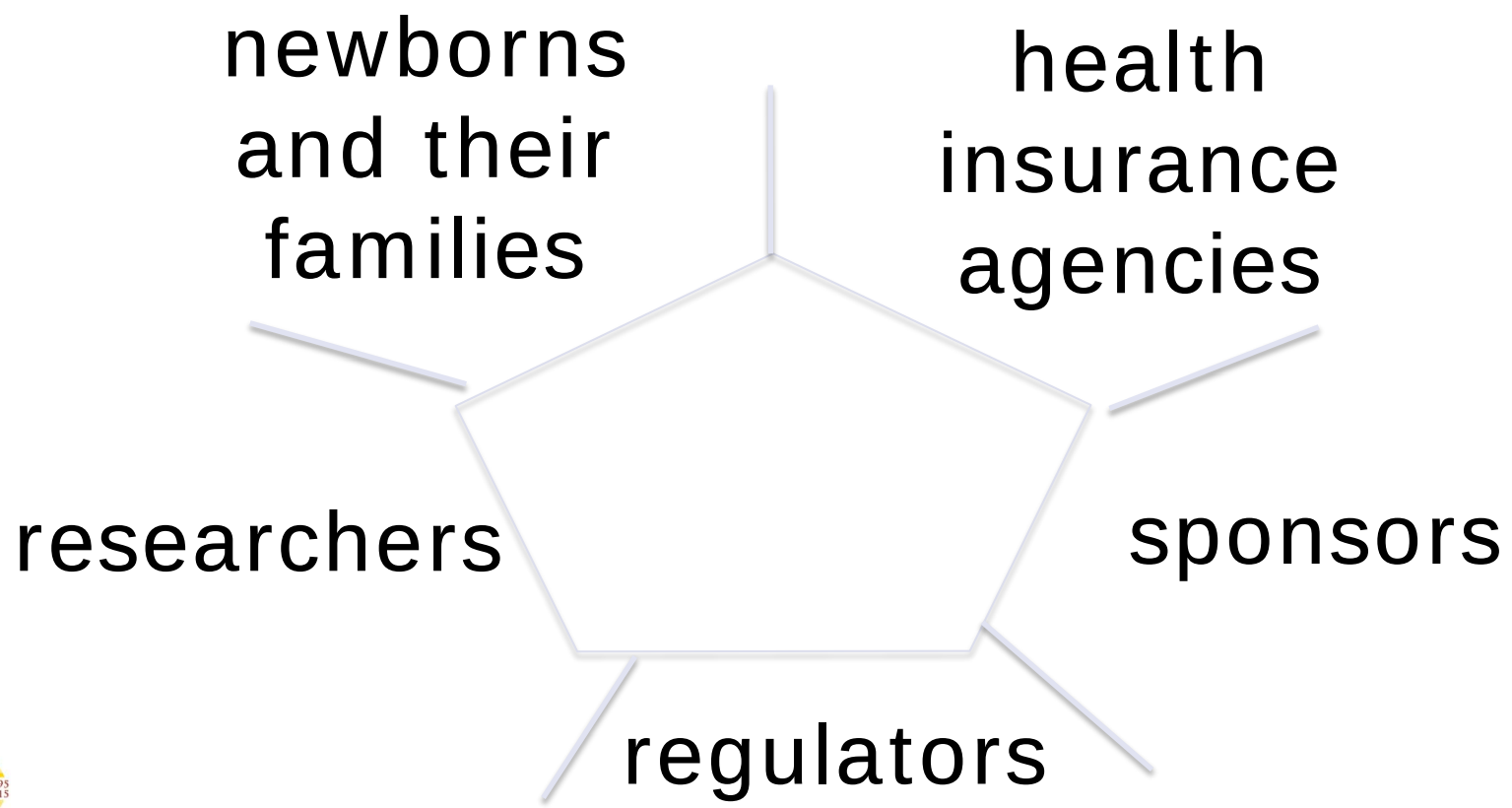
Collaboration

Product-specific
- Expert(s) (Declaration of interest, different levels)

Condition/therapeutic area:
- Directly with PDCO neonatology group
- Organisation of expert meeting

Scientific guideline
- e.g. neonatal guideline revision

Collaboration with existing groups
- e.g. Modelling Simulation, Extrapolation


newborns and their families
health insurance agencies
researchers
sponsors
regulators

Thank you

Further information

paediatrics@ema.europa.eu

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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Need for clinical trials in neonates

Vulnerable population, often treated with multiple medicines at the same time (up to 60)

Just like children are not small adults, neonates are not small children, therefore extrapolation of efficacy or safety from older children is very often inappropriate

Neonates are the paediatric population for which less data are available on the correct use of medicines

Gradual maturation of metabolic and detoxifying pathways during the first months of life cause different sensitivity and response to active substances and excipients

Ethical and scientific arguments in favour of protecting children through clinical trials, not from them

Higher incidence and severity of adverse drug reactions in “off-label” use of medicinal products

Efficacy cannot be assumed when prescribing medicines not tested in the appropriate population

Inclusion of a child in a clinical trial is likely to be associated with a better outcome than “off-label” use

Failure to conduct clinical trials in children is unethical as it forces physicians to do uncontrolled experiments almost every time they prescribe a medicine to a child