EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Views of the PDCO and EMA Paediatric Medicines on discussing and using M & S as a tool to bridge pharmacokinetics, efficacy and safety data

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Paediatric Medicines section

M & S as part of a paediatric investigation plan

Proposed for medicines across most of the paediatric therapeutic areas

- Anticoagulants
- HIV medicines
- Anti-convulsants
- …

PDCO working on extrapolation

- PDCO working group on extrapolation
  - PDCO members and experts (Christoph Male, Gerard Pons, Peter Bauer, Wolfgang Köpcke, Birka Lehmann, Paolo Paolucci, Agnes Gyurasic, PEI)
  - CHMP members (Rob Hemmings, Tomas Salmonsson)
  - EMA (Cecile Ollivier, Julia Saperia, Martin Posch, Efthymios Manolis, Ralf Herold)
  - Work plan includes concept paper
- Some general work published (Manolis et al. 2011)

Problems with evaluating and using M & S approaches

- Endpoints relevant for paediatrics and needed for bridging are not documented in adult trials
- Few mechanistic models are proposed for learning
- Lack of standardised model how to go down in age studying children
- Can approaches used for paediatrics be generalised (and be further credited) for use in other population subsets?
- Gaps in proposed developments (e.g., youngest age ranges)
- Lack of simulation and of understanding of operating characteristics of proposed paediatric trials
- Decision to extrapolate efficacy does not rest on quality and statistical properties alone

Wish list for M & S approaches

- To routinely suggest paediatric starting dose using modelling
- To model safety in conjunction with activity/efficacy, in order to add to the benefit / risk assessment for concerned paediatric subsets
- To model outcomes more often, in a more sophisticated approaches and to validate outcomes
- To model and compare benefit / risk relationship between population subsets
- To include additional mechanistic models
- To describe the iterative / circular process of learning by adding new data and refining approach and decision-making

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