Session 1

Perform studies to develop optimal PK (and PD) designs in children to support extrapolation from adults

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Perform studies to develop optimal PK (and PD) designs in children to support extrapolation from adults

Co-moderators

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EMA

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HMA Heads of Medicines Agencies

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EMA Regulatory Science Research Needs – today's topic

2.4. Research needs to foster technologies for development of specific types of medicines

Focus area: New approach methodologies (NAMs) / Non-animal models / 3Rs				
NT11	Research on modelling and simulation methods to support regulatory decisions	1. Develop models and designs for characterisation of exposure response throughout drug development to support dose selection and posology claims in SmPC, with a focus on special populations (F; G) 2. Perform studies to develop optimal PK (and PD) designs in children to support extrapolation from adults (A; D; E; F) 3. Develop modelling approaches including PBPK for renal/hepatic impairment in elderly patients (A; D; E; F) 4. Develop methods to quantify and report uncertainties in complex models, such as diagnostic and reporting tools to facilitate regulatory decision based on these models (D; F)	• Modelling and simulation • Dose selection • Posology • Special populations	Human medicine

Sections with Research needs to …	**Number of research needs**	**Number of priority topics**
2.2. …improve clinical research	9	24
2.3. …improve regulatory system evolution	9	23
2.4. … foster technologies for development of specific types of medicines	14	35
2.5. … advance specifically animal health and the regulation of veterinary medicines	15	27
Total	49	109

(A) Natural sciences: disciplines such as biology, chemistry, physics, which make use of rigorous scientific methods, including observation, controlled experiments, analysis, mathematical models and empirical evidence.

(D) Applied sciences: disciplines such as medicine, biomedical engineering and genetic epidemiology, where scientific knowledge and research are applied to achieve tangible goals, solve real-world problems and improve systems and technologies.

(E) Wet-lab research: experimentation in laboratory settings.

(F) Dry-lab research: computational and theoretical research, in other words by using computer systems, coding and data analysis to generate new information and data outputs.

Breaking this down

- Performs **studies to develop optimal PK (and PD)** designs in children to support extrapolation from adults
- Picking the dose in paediatrics is key
- Some models work best in certain age group
  - Biggest gaps in the very youngest age groups
- *Degree of differences in efficacy, safety and benefit-risk balance per relevant subgroups in the target population should be described and when possible predicted by means of quantitative synthesis or meta-analysis of existing treatment data, or disease response models, PK-PD-response models or systems pharmacology approaches.*
- *When mechanism-based models are used, they should be qualified for the intended use. Expectations for qualification of a model used to reduce or to replace prospective data generation will be higher than those for a qualification of a model used to inform the design of a clinical study in the target population.*

Different questions to fill gaps

- Knowledge gaps
  - Can we develop better models of physiological processes?
- Theory gap
  - Do we understand the functioning of the human body from pre-term to child and adolescents, including in terms of receptors and enzymes, to be able to build an appropriate model?
- Data gap
  - The underlying model and the processes it represent are agreed, but there is insufficient data to be able to validate it, or populate the model.
  - Competing data sources giving less stable results
- Practice gap
  - Models are well understood and agreed but a reluctance to use them
- *Where can regulators proactively help to fill these gaps?*
  - *Where and when does regulatory science fill that gap?*