Extrapolation plan and statistical tools
Panel discussion

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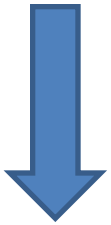
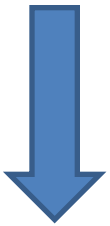
Choice of tools to be used for extrapolation

Only PK and safety studies in children



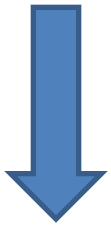
M&S should be used for study design and PK data analysis

PK, PK/PD and safety studies in children



M&S should be used for study design and PK/PD data analysis

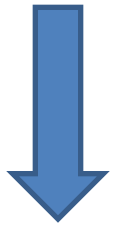
Bridging efficacy trial/data in children



- M&S and/or statistics could be used for study design (**Prior**?)
- M&S should be used for PK/PD data analysis when applicable(for learning)

- Statistics should be used efficacy data analysis (confirming)

Fully powered efficacy trial in children



- M&S should be used for study design and PK/PD data analysis when applicable (for learning)
- Statistics should be used for efficacy data analysis (confirming)

How we use Modelling and Simulations and statistics in a more complementary manner?

Choice of tools to be used for extrapolation

Different methods were described in the presentions:
- Empirical modelling and simulations
- Meta-analysis
- Bayesian statistics

And other methods might apply
- PBPK, QSP
- Adaptive designs
- Etc.

Do we have the right tools to implement the extrapolation framework to the pediatric development, can we identify the gaps?

Choice of tools to be used for extrapolation

Possible gaps wrt Bayesian statistics

- How do we deal with the prior for the Bayesian distribution not matching the observed data?
- How do we decide how strong a prior is acceptable?
- Bayesian approaches are not a singular way of doing things. How can we decide which Bayesian approach is best?
- Etc.

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How do we best align between pharmaceutical Industry and regulators which tool is most appropriate/serve the purpose for acceptable extrapolation efficacy/safety data for children?

How to evaluate and quantify the impact of uncertainties and assumptions, i.e. the probability of violating assumptions and the clinical consequences?

How can we communicate these models to clinicians?