31st PAGE Meeting
28 June 2023

Pediatric Extrapolation – Opportunities and Challenges

Kristin Karlsson
Swedish Medical Products Agency

LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Disclaimer

The views expressed in this presentation are those of the speaker and are not necessarily those of MPA or EMA.

History of Pediatric Extrapolation in EU

- 2007 EU Pediatric Regulation
  - Pediatric investigation plans (PIPs)
- 2017 ICH E11(R1) – Revision of the Guideline on clinical investigation of medicinal products in the pediatric population
  - The need for a guidance on Pediatric Extrapolation identified
- 2018 EMA Extrapolation Reflection Paper
  - Highlights the role of quantitative approaches
- 2022 ICH E11A Pediatric Extrapolation Guideline – Published draft

Paediatric Extrapolation

ICH E11A

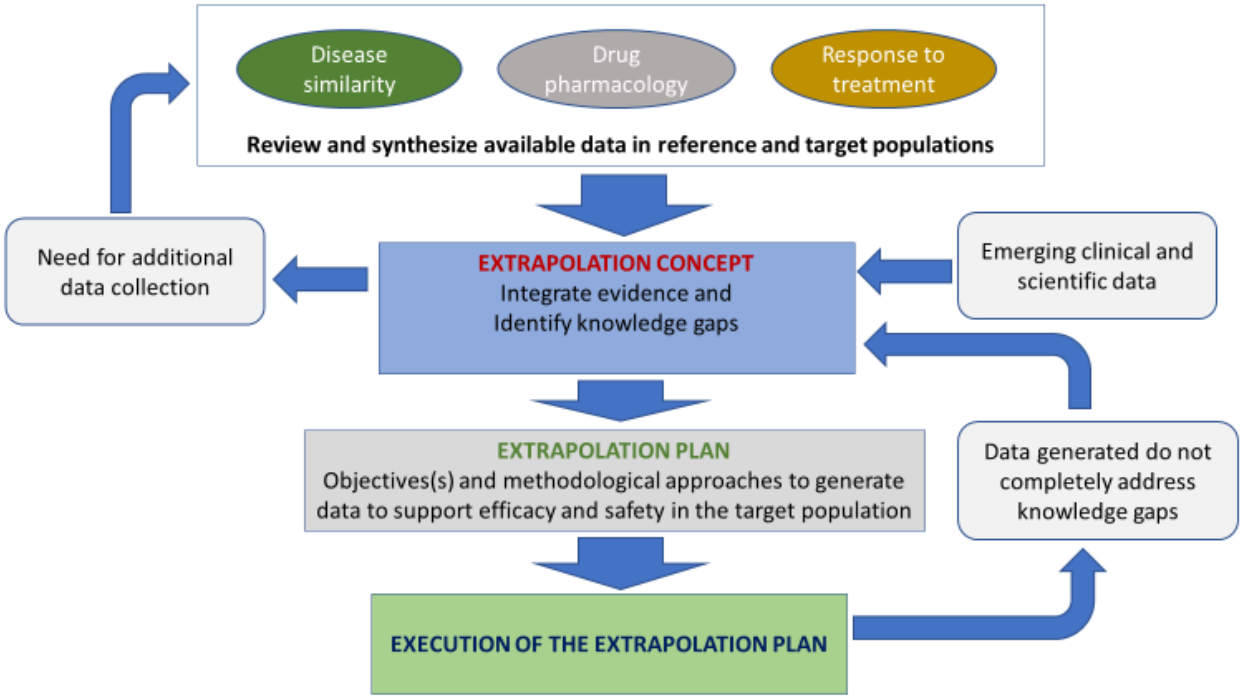
The concept of "extrapolation" is used in different ways in drug development. "Pediatric extrapolation" is defined as an approach to providing evidence in support of effective and safe use of drugs in the pediatric population when it can be assumed that the course of the disease and the expected response to a medicinal product would be sufficiently similar in the pediatric and reference (adult or other pediatric) population.

EMA RP

It is appropriate to take advantage of existing information when planning and evaluating clinical studies in children. A more targeted generation of evidence should help to ensure that children only participate in clinical trials with specific objectives that further the scientific understanding of a medicinal product for use in children and, address the requirements for regulatory decision-making.

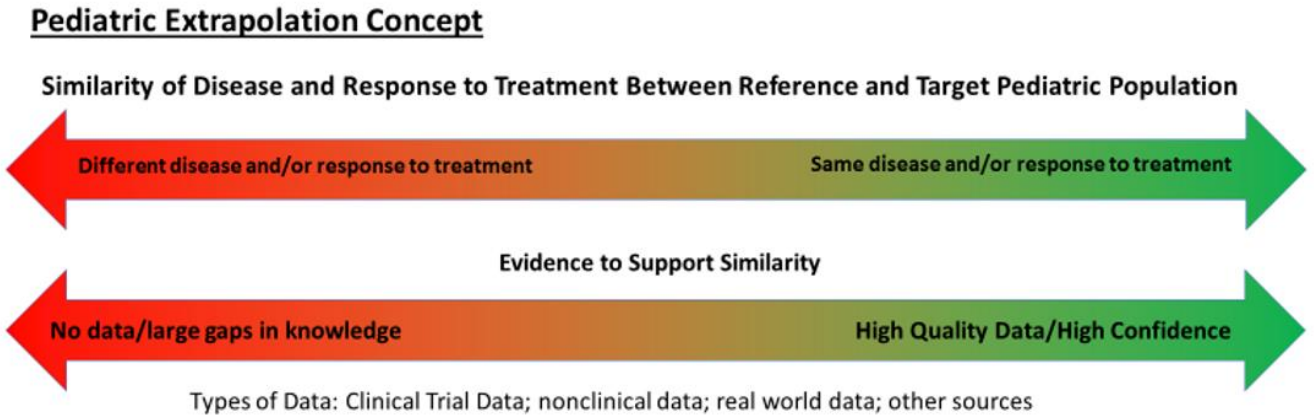
ICH E11A

Pediatric Extrapolation Framework



ICH E11A

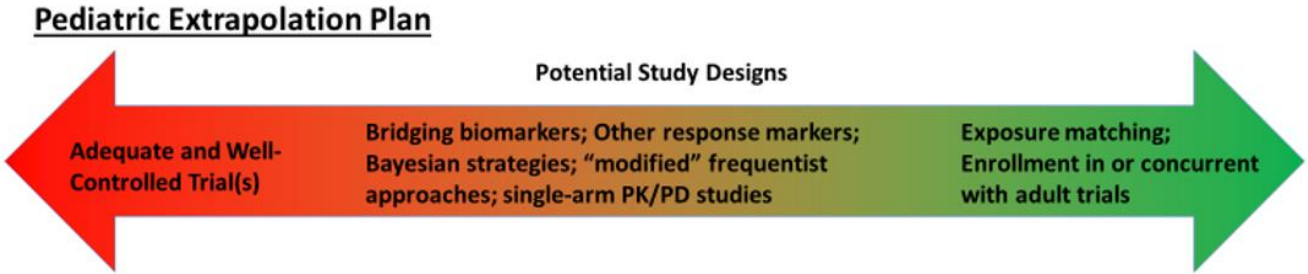
Pediatric Extrapolation Concept



Quantitative methods can be used to synthesize and integrate existing evidence

ICH E11A

Paediatric Extrapolation Plan



- Examine appropriate study designs
- Dose selection
- Perform sensitivity analyses

Challenges

- ✓ How similar is similar?
- ✓ Provide sound quantitative evidence to support disease similarity and response to treatment in small populations.
- ✓ Models used in early drug development often come with high uncertainty.
- ✓ Design informative clinical trials in situations with feasibility and ethical constraints.
- ✓ Extrapolation does not equal “collect less data” or just smaller trials.

Opportunities

- ✓ Model-informed approaches to justify the extrapolation concept
- ✓ Model-informed approaches play a key role in designing pediatric clinical trials to ensure collection of informative data
  - Study size
  - Dose selection
  - Duration of treatment
  - Define “success criteria”
- ✓ Model-informed analyses are often essential in support of dosing recommendations in pediatric patients
  - Exposure matching
  - Simulation based dosing recommendations

Conclusion

MIDD is recognised as an essential part of pediatric drug development, and in particular to support extrapolation approaches!