# ICH E11A: Pediatric Extrapolation

Step 2

## *Step* 2 document – to be released for comments

**4 April 2022**

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

# Legal Notice




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# Background

- **This document has been signed off as a *Step 2* document (4 April 2022) to be issued by the ICH Regulatory Members for public consultation**
- **This document was developed based on a Concept Paper (17 October 2017) and a Business Plan (17 October 2017)**
- **Anticipating finalization as a *Step 4* document to be implemented in the local regional regulatory system: Q2 2024**

# Guideline Objectives

- **Address and align terminology related to pediatric extrapolation**
- **Provide information on various approaches that can be utilized to support the use of pediatric extrapolation**
- **Discuss a systematic approach on the use of pediatric extrapolation**
- **Discuss study designs, statistical analysis, modeling and simulation analyses and respective methods**

# Key Principles

- **Development of a Pediatric Extrapolation Concept**
- **Development of a Pediatric Extrapolation Plan**
- **Statistical/modeling methods that can be used to support a Pediatric Extrapolation Concept and Plan**
- **Discussion of safety considerations in the Pediatric Extrapolation Concept and Plan including the Extrapolation of Safety**
- **Discussion of timing of adolescent patient enrollment in the context of a Pediatric Extrapolation Plan**

# Table of Contents

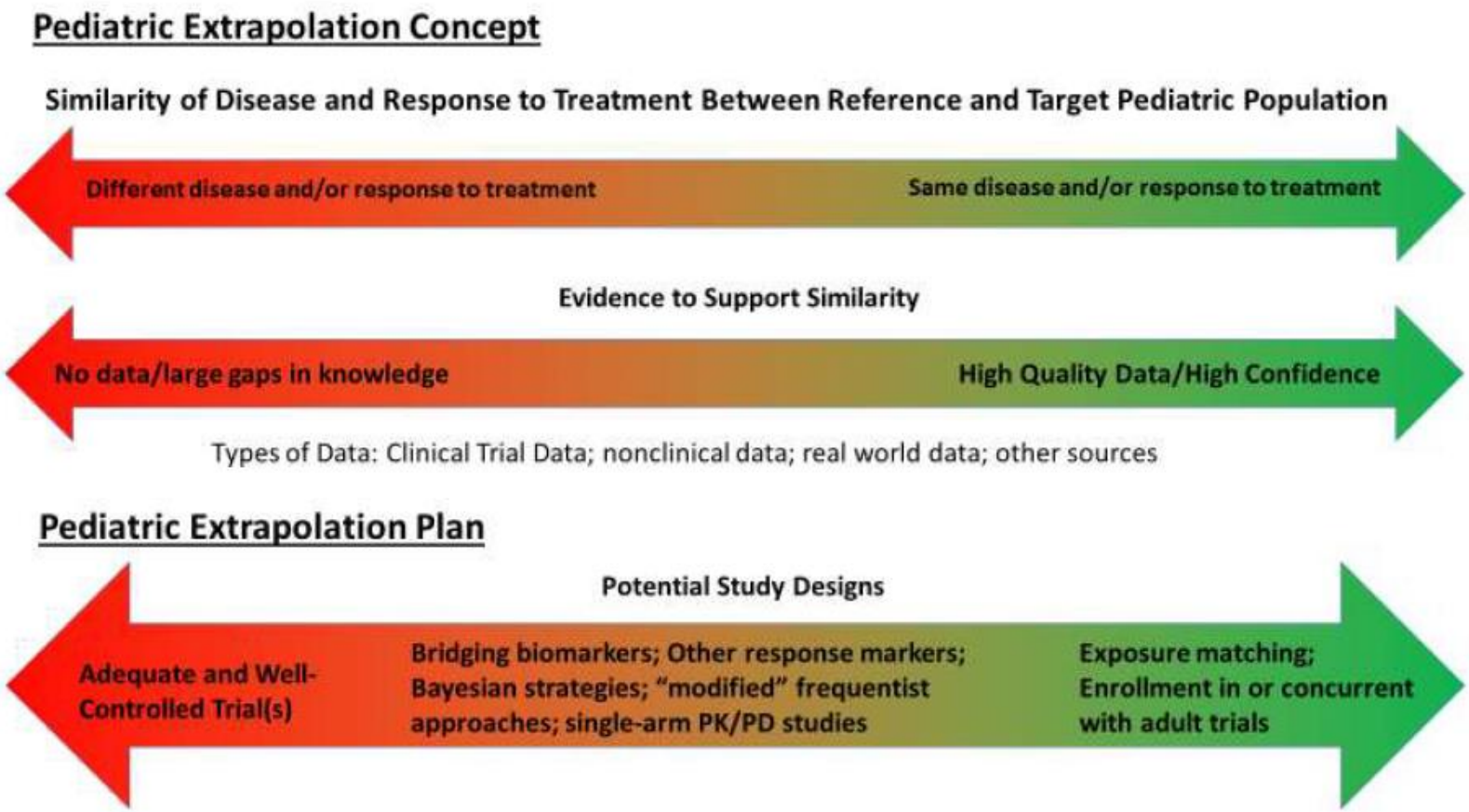
# Table of Contents (continued)

# Summary of Guideline Content

- **Pediatric Extrapolation Introduction and Framework**
  - Provides overarching description of the three parts of the Pediatric Extrapolation Framework
    1. Pediatric Extrapolation Concept
    2. Pediatric Extrapolation Plan
    3. Execution of the Pediatric Extrapolation Plan
  - Provides detailed expansion of the information provided in the ICH E11(R1) Guideline
  - Distinguishes the use of Pediatric Extrapolation from other forms types of extrapolation used in drug development

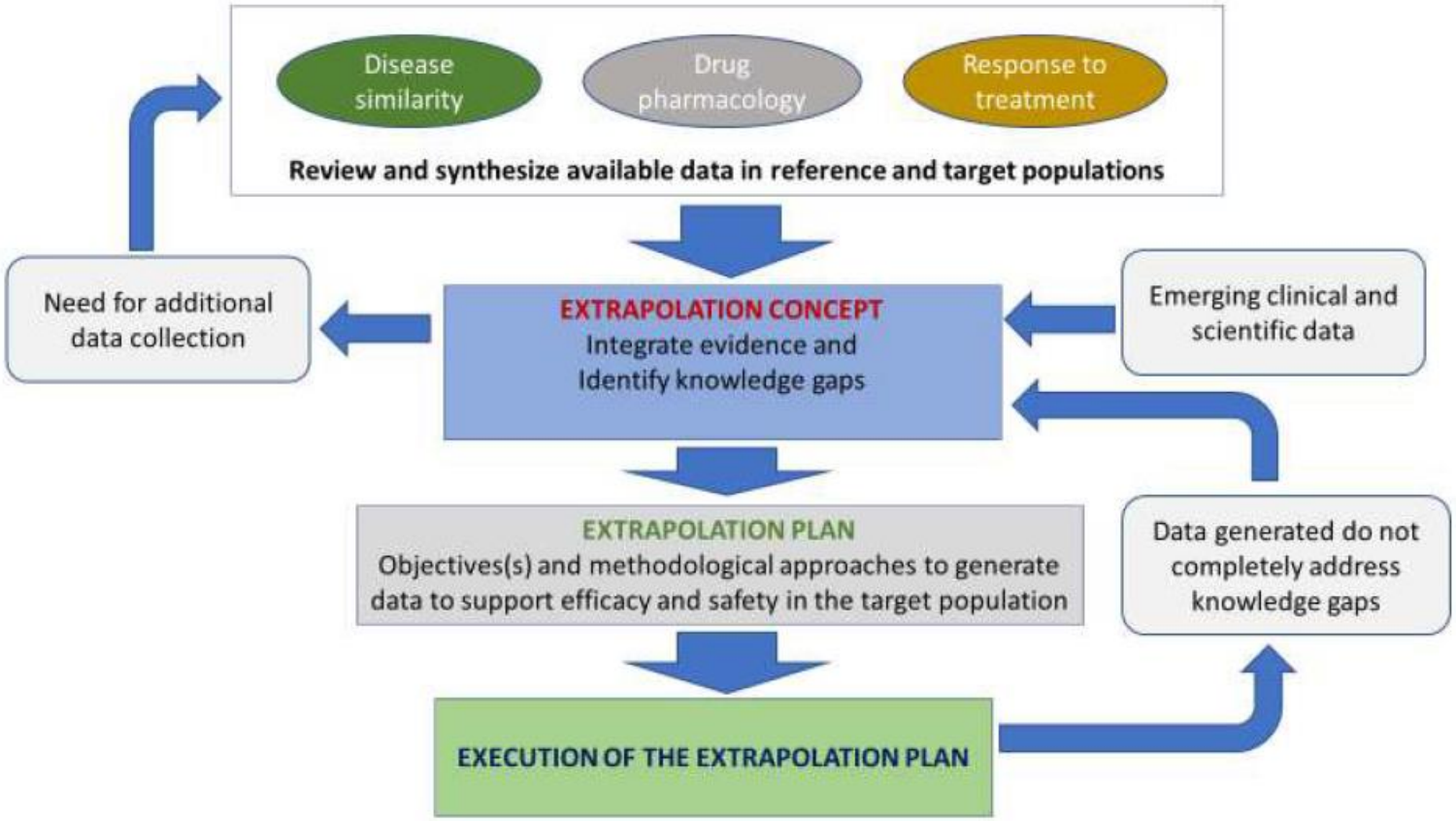
# Summary of Guideline Content

**Figure 1: Pediatric Extrapolation Approach**



# Summary of Guideline Content

**Figure 2: Pediatric Extrapolation Framework**



# Summary of Guideline Content

- **Pediatric Extrapolation Concept**
  - This section reviews the sources and types of data that can be used to evaluate disease and response to treatment similarity between a reference and target pediatric population
  - This section also provides a list of key questions that should be asked in evaluating the data used to support similarity of disease and response to treatment
  - This section also puts forth considerations for extrapolation of safety as part of the Pediatric Extrapolation Concept, including key questions that should be asked
  - This section also explains how the data reviewed can be integrated to finalize a Pediatric Extrapolation Concept
    - Identification of knowledge gaps that need to be addressed as part of the Pediatric Extrapolation Plan
    - Overview of how the Pediatric Extrapolation Concept should be presented

# Summary of Guideline Content

- **Creation and Execution of the Pediatric Extrapolation Plan**
  - This section provides the types of studies that can be used as part of a Pediatric Extrapolation Plan based on the final Pediatric Extrapolation Concept and the gaps in knowledge that have been identified
  - This section reviews important tools that can be used as part of a Pediatric Extrapolation plan, including the use of biomarkers, the use of model-informed approaches, and the use of various efficacy study designs to address the gaps in knowledge

# Summary of Guideline Content

- **Additional Considerations**
  - This section includes important considerations when creating and executing a Pediatric Extrapolation Plan, including important safety considerations
  - This section also includes a brief section about considerations related to enrollment of adolescent patients in adult trials

# Considerations

- **There is a need to obtain multidisciplinary expertise in the development of a Pediatric Extrapolation Concept and Plan (e.g., clinical, clinical pharmacology, biostatistics)**
- **Development of a Pediatric Extrapolation Concept and Plan should start early in adult drug development in order to obtain data that can support the concept and approach**
- **Obtaining feedback from regulatory authorities is important to achieve agreement on any Pediatric Extrapolation approach. Generally, such plans should be submitted during adult drug development (depending upon the region)**
- **Other issues relevant to pediatric extrapolation are referred to in the Guideline (ICH E11(R1), E2, E5, E6, E17, E9(R1))**

# Conclusions

- **This Guideline is intended to provide important considerations regarding the development of a Pediatric Extrapolation approach**
- **A hypothetical case example will be included with the document during the public consultation period**
- **Additional training materials will be developed to complement the Guideline**

# Contact

- **For any questions please contact the ICH Secretariat:**

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