

**Final Business Plan  
Pediatric Extrapolation  
3 October 2017**

*Endorsed by the Management Committee on 17 October 2017*

**1. The issue and its costs**

• **What problem/issue is the proposal expected to tackle?**

An expert working group (EWG) was formed to revise the ICH E11 guideline, Clinical Investigation of Medicinal Products in the Pediatric Population. The E11(R1) addendum recently completed *Step 4*. This revision includes a high level discussion of pediatric extrapolation. However, there is a need to provide more detailed guidance about how pediatric extrapolation can be used in pediatric product development. There is also a need to provide harmonized approaches to pediatric extrapolation. As noted in the E11(R1) addendum, successful pediatric drug development is increasingly multiregional and regional differences in some instances limit the ability of health authorities to align requirements. Development of more detailed guidance about pediatric extrapolation will help to increase the timely and efficient pediatric product development.

• **What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with “non action”?**

Pediatric extrapolation, when used appropriately, can improve the feasibility of pediatric product development. There is also an ethical imperative to consider the appropriate application of pediatric extrapolation because children should only be enrolled in a clinical trial if the scientific and/or public health objectives cannot be met through enrolling subjects who can provide informed consent personally (i.e., adults). Where applicable, it will also serve to reduce the unnecessary enrollment of children in clinical trials.

This topic is important for international harmonization because use of pediatric extrapolation can be used to optimize and increase the efficiency of pediatric medicinal product development. In both the US and EMA, pediatric legislation has increased the number of approved drugs with specific efficacy and safety data in pediatric populations. However, in many cases, there is still an unacceptably long gap (between 7-8 years) between the initial adult approval and incorporation of pediatric-specific labeling. Harmonization of methodologies and strategies to incorporate pediatric extrapolation into overall drug development plans will improve the speed of access to new drugs for pediatric patients. The social/health and financial costs of non-action will allow this unacceptably long gap between adult approval and pediatric-specific labeling to persist.

## 2. Planning

- **What are the main deliverables?**

The main deliverables of this expert working group will be the development of a stand-alone ICH E guideline for Pediatric Extrapolation under the E11: Clinical Investigation of Medicinal Products in the Pediatric Population guideline (e.g., E11A: Pediatric Extrapolation).

- **What resources (financial and human) would be required?**

The financial and human resources that will be required include the need to meet face-to-face on a regular basis to come to alignment on this topic across expert working group members. Additional pediatric experts in statistical and clinical pharmacology (including experts in pharmacometrics and modeling and simulation) may need to be added on an as needed basis to address certain technical components of the guideline.

- **What is the time frame of the project?**

It is expected that this guideline would take a minimum of 3 years to be developed (based on overall experience from the E11 EWG).

- **What will be the key milestones?**

The key milestones will include the following:

- Creation of specific subgroups to begin work on sections of the guideline based on the topics included in the finalized concept paper
- Regularly scheduled conference calls to discuss and develop sections of the guideline
- Regularly scheduled face-to-face meetings to come to agreement on sections completed by each subgroup
- Submission of drafts to the ICH for advancement through each Step.

## 3. The impacts of the project

- **What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?**

As stated above, harmonization of methodologies and strategies to incorporate pediatric extrapolation into overall drug development plans will improve the speed of access to new drugs for pediatric patients. The social/health and financial costs of non-action will allow this unacceptably long gap between adult approval and pediatric-specific labeling to persist.

- **What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?**

This topic is clearly implementable in different regions from a regulatory standpoint and would allow for better alignment of global pediatric medicinal product development plans.

## 4. Post-hoc evaluation

- **How and when will the results of the work be evaluated?**

The result of the work will be the publication and implementation of a harmonized guideline on pediatric extrapolation. The success of this publication can be evaluated based on feedback on regulators and industry as well as evaluation of certain metrics such as the successful use of pediatric extrapolation in pediatric medicinal product development, and the amount of time between adult approval of a medicinal product and the addition of pediatric-specific labeling information.