



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Report from the Focus group on the practical application of principles relevant for the PIP framework

8th Industry Stakeholder Platform on Research and Development support

11 July 2022

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An agency of the European Union





Focus group meetings and participants

Constitution of the Focus group agreed at the 7th Industry stakeholder platform on research and development support in November 2021:

- 5 Video Conferences (March – July 2022)
- Participants
 - Industry representatives from trade associations
 - Vice-Chair PDCO, PDCO and EMA representatives



Objective and expected outcomes

The objective of this group is to develop further the principles that were established in the Focus group on the concept of an 'evolutionary' PIP in order to guide the practical application. The primary focus is on the 'evolutionary' PIP to support the preparation for piloting and testing of the concept. Furthermore, the initial discussion on key elements for a PIP in general should be matured to support a review of the applicable guidance. The following outcome is expected:

- **Concise description of the 'evolutionary' PIP model** including elements to guide a scientific justification to support a case-by-case discussion on the application of the concept;
- **Outline of practical arrangements and pathways that support integrated dialogue** on an 'evolutionary' PIP, including multi-stakeholder dialogue as required;
- **Comprehensive review and identification of suitable key elements for a PIP** ('evolutionary' and regular), to describe and agree a paediatric development programme robustly from a scientific and regulatory perspective;
- **Development of milestone terminology for PIPs** that ensures clarity of activities and dependencies and reduces unnecessary modifications.

Merged Opinion and Key element form

Study identifier(s)	<i>E.g., study identifier if available (company protocol code)</i>
Study design features and main objectives and study population	<i>A short summary of the study design features and study population. Age, sex and condition to be included and any other study population detail as considered necessary.</i>
Number of study participants by paediatric subset (e.g. age, sex, severity or stage)	<p><i>Number of subjects evaluable for the primary analysis (or enrolled, randomized, followed up until x etc. as appropriate).</i></p> <p><i>Randomisation and number per subset as appropriate.</i></p> <p><i>Depending on the type of study e.g. PK, the sample size can be precisely defined. In other cases where many elements are not known (e.g. the effect size in adults) and it is difficult to define, it may be appropriate to define the sample size in the most vulnerable groups (e.g. very young children) as a percentage of the overall sample size.</i></p> <p><i>A condition can be added here if a sample size cannot be defined (e.g. the sample size to be defined once data from studies x, y are available). The sample size could be expressed in terms of power e.g. sample size to achieve 80% power</i></p>

Study duration for participants	<p><i>In cases where the study duration cannot be defined at the time of agreement of the PIP, a condition can be added: e.g. in line with adult phase 3 studies, or milestone agreed for PDCO discussion/agreement. It may be appropriate to define a minimum duration in certain cases.</i></p> <p><i>In this section a bullet point can be included for long term follow- up studies if appropriate specifying that this is not part of the PIP.</i></p>

Dosage, treatment regimen, route of administration	<i>Doses to be studied only if known. Otherwise, if dose not known, it should be mentioned on what basis the dose will be selected (e.g., based on results from the PK study).</i>
Control(s)	<i>e.g., placebo or active comparator (dosage, route of administration). If external control, source of data. In cases where a control cannot be defined at the time of agreement of the PIP, a condition can be included e.g. the control must be agreed with the PDCO once data from x study are available, or the control could be a class of products, or it must match control used in adult studies, or milestone agreed with PDCO.</i>
Key objectives and outcomes	<p><i>This section should include only the critical objectives and outcomes important for establishing the paediatric indication. These are usually the primary endpoint but not necessarily limited to this. In cases where a primary endpoint cannot be defined it may be acceptable to include a primary objective here e.g. to collect efficacy information and further details on the primary endpoint to be added following a certain milestone (e.g. from a study in adults, or an earlier phase study in children). For small open label studies it may be appropriate to not define endpoints as primary or secondary as such studies are not powered for primary endpoint.</i></p> <p><i>When secondary endpoints are required to be included in the opinion only the most relevant should be added here. This is not intended to be a copy from all endpoints included in the protocol but a summary of the most relevant.</i></p>

Statistical plan including study conduct and analysis	<i>This section should be kept at a high level without too many details e.g. superiority study, descriptive statistics, Bayesian decision making, etc. and further details to be included only in cases where there is a justified need to do so.</i>
Date of initiation	<i>A date or milestone should only be included in exceptional circumstances. In these cases the deferral (or not) must be specified</i>
Date of completion (last patient, last visit)	<i>There must be a date or optionally, if measure is not deferred it can be a milestone, such as "before submission of the MAA".</i> <i>By the end of Quarter 1,2, 3, or 4 of <Year>.</i> <i>The deferral (or not) must be specified</i>



Next steps

Key elements

- Finalisation of Merged Opinion / Key element Form
- Implementation of updated opinion form with revised key elements end of 2022 / early 2023

Evolutionary PIP

- First draft Guidance document for ePIP in September for further discussion
- Pre-pilot to help with drafting the guideline and try out how the evolutionary PIP can work in practice. The pre-pilot would use the usual PIP application and evaluation framework. Call for candidates in the pipeline for pre-pilot.
- ePIP-pilot start end of 2022



Thank you

Further information

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