Report from the Focus group on the concept of an 'evolutionary' PIP

7th Industry Stakeholder Platform on Research and Development support

23 November 2021

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Focus group meetings and participants

Constitution of the Focus group agreed at the 5th Industry stakeholder platform on research and development support in November 2020: [5th Industry Stakeholder Platform on R&D support 16.11.20 - highlight report (europa.eu)]

- 8 Video Conferences (April – November 2021)
- Participants
  - Industry representatives from trade associations
  - Vice-Chair PDCO, EMA representatives

Objective and expected outcomes

To explore a PIP model that allows, in certain cases, the paediatric development programme to become more defined over time as more evidence becomes available. The group should discuss possibilities for and limitations of such PIP model that allows to develop along with the evolution of scientific knowledge. ✓

- Reflections on a scientifically sound basis and in compliance with the regulatory requirements
- Consideration should be complemented with illustrative examples.

Criteria for the identification of paediatric developments that would qualify for a step-wise approach to agree the binding elements in the PIP	✓
Concepts for planning milestones on the basis of available evidence, with resulting binding elements and commitment for future interaction	✓
Analysis of risks inherent of such model(s), including potential delays of paediatric development, as well as resource investment	✓
Outline of a supporting framework for dialogue in context of such PIP submissions	✓

Relevance for the EMA-EC paediatric action plan

4.1 Explore possibilities for a PIP model that allows, in certain cases, for changes to be made to PIPs as more evidence becomes available over time

4.2 Explore opportunities for enhanced dialogue with sponsors in the context of PIP procedures

4.3 Improve processes for compliance checks

4.5 Review key elements (structure and granularity) of PIP opinions

Overview of criteria discussed

Examples for criteria for „evolutionary PIPs“:

- Not fully characterised Mechanism of Action (‘first in class’)
- Tumour/tissue agnostic therapies
- Gene therapies
- Programmes supported by extrapolation or innovative trial designs
- “First in disease”, paediatric only
- Challenges with standard of care (e.g. not existing, recently changed, heterogenous across regions)
- Programs with challenges e.g. due to patient scarcity

Discussion:

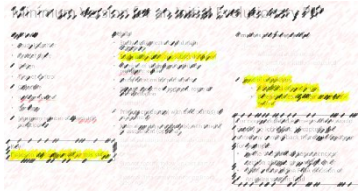
- Combination of criteria? No ‘tick-box exercise’!
- Case by case discussion and scientific justification needed
- To be further reflected.

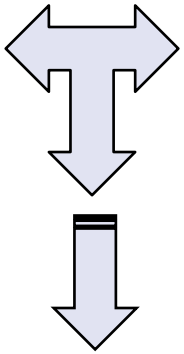
„Evolution" of a PIP

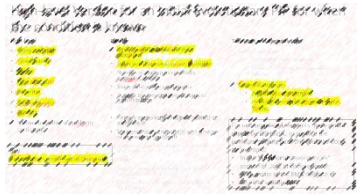
- Discussion on models
  - Integration into the current framework
  - ‚multi-step PIP'
  - Enhanced possibilities for interaction

- Risks
  - Keeping agreed timelines
  - Resources?

→ Common responsibility!







Final Version for the Evolutionary PIP

High-level
- Study identifier
- Type of study
- Design
- Type of control
- Objective
- Randomisation
- Blinding
- Minimum number of paediatric participants

Details
- Study design features and main objectives
- Study population and subset definition
- Number of study participants by paediatric subset
- Study duration for participants
- Dosage, treatment regimen, route of administration
- Control(s)
- Primary endpoint(s) with time point(s) of assessment
- Main secondary endpoint(s) with time(s) of assessment (optional)

Statistical plan including study conduct and analysis

Other

Plan for specific follow-up (not part of completion of this study)

External Data safety monitoring Board (yes / no)

Timelines and dependencies
- Data of initiation
  - Additional dependencies
  - Deferral for initiation requested – Yes/no
- Date of completion
  - Additional dependencies
  - Deferral for completion requested – Yes/no

Potential Milestone Terminology

- Wherever possible, milestones should be linked to activities and dependencies, rather than specific dates → reducing unnecessary modifications
- Utilized currently in key elements of agreed PIPs
- Examples
  - <details/data/outline, sample size etc> to be agreed by
    - X months after availability of pre-clinical data (e.g. tumour models / tox studies)
    - X months of adult [Study Identifier] Phase 2 study
    - X weeks following results of multi-stake holder meeting
    - X months of scientific advice….
- → Milestone terminology is planned to be explored further as the updated key elements are developed

Conclusion

- Very constructive and engaged discussions of the whole group
- Integration into discussion with the EC
- Discussion and work at PDCO level with a view on developing a pilot
- Further work and refinement required in the areas of
  - Details of the model and its implementation e.g. in a pilot
  - Further development of key elements, improved PIP guidance

Thank you

Further information

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