White Paper

Drug Development 2022

BlueReg
A ➤ PHARMALEX COMPANY

5 Must-Knows About Paediatric Investigation Plan in the EU

Introduction

A Paediatric Investigation Plan (PIP) or Pediatric Study Plan (PSP) is a development plan intended to support the authorization of a medicine for children by ensuring data are obtained through studies in the paediatric population during clinical trials.

In Europe, PIPs are described in Regulation (EC) No 1902/2006 which came into force in the EU on 26 January 2007. This paediatric regulation put in place the PIP to be agreed upon by a new expert committee (the EMA Paediatric Committee [PDCO]); it also regulates a system of obligations and rewards and different transparency/information measures. The objectives are to improve and better protect the health of children with high-quality & ethical research, increasing availability of appropriately authorized medicines for children specific information on the use of medicines in the paediatric population.

Why do we need an EU PIP?

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The EU paediatric regulation (1901/2006 and 1902/2006): A system of obligations and rewards

For:

- New medicines, or
- Medicines already authorised:
  - Covered by intellectual property rights (patent) if is added:
    - New indication
    - New pharmaceutical form
    - New route of administration
  - Not covered by intellectual property rights and exclusively developed for use in children (PUMA)

Need an agreed PIP, Waiver, Deferral (PDCO opinion + EMA decision)

EMA decisions are made public

PIP Compliance Check vs. EMA PIP decision (studies/ measures and timelines)

The outcome is made public

MAA submission validated only if:

- Results of paediatric studies per agreed PIP (CSR), and/or,
- EMA decision for waiver and/or deferral

Product to be placed on the market with the paediatric indication within 2 years

A full compliance check will lead to a reward (all studies completed with results in the label)

New medicine or on-patent authorised medicine	+ 6-month extension to the SPC (patent) (SPC extension application should be done latest 2 years prior to SPC expiry date)
Orphan medicine	+ 2 additional years of market exclusivity (in addition to the 10 years)
PUMA	10-year market protection (including 8 years of data exclusivity)

CSR=Clinical Study Report; EMA=European Medicines Agency; MA=Marketing Authorisation; PDCO = Paediatric Committee; PIP=Paediatric Investigation Plan; PUMA= Paediatric-use marketing authorisation; SPC=Supplementary Protection Certificate

Is a PIP required ?

PUMA => PIP

Assess the patent status and the product type

Is it an off-patent product already authorised in EU?

→ **Yes**

Is the product a generic? Hybrid product? Biosimilar? Planned for well-established use approval? Herbal? Homeopathic?

→ **Yes**

Define the target MA indication + Check the class-waiver list

Is the targeted indication part of the class waiver list?

→ **Yes:** full waiver (Request EMA confirmation)

Define if the medicinal product submission is in the regulation's scope

Is it for:

- **A new MA? (see Art. 7)**
- **A new indication, route of administration or formulation, with a SPC or patent qualifying for a SPC? (see Art. 8)**

→ **No**

No PIP required

Yes

For Art. 7 of 1901/2006 amended:

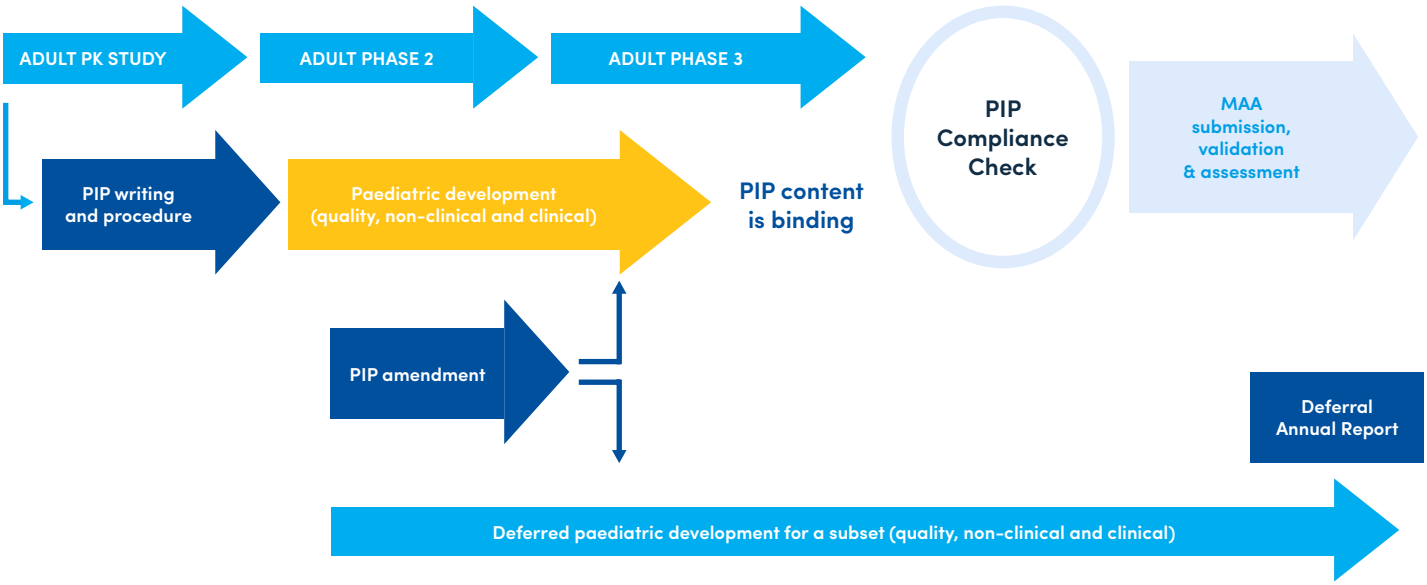
PIP required for all indications developed

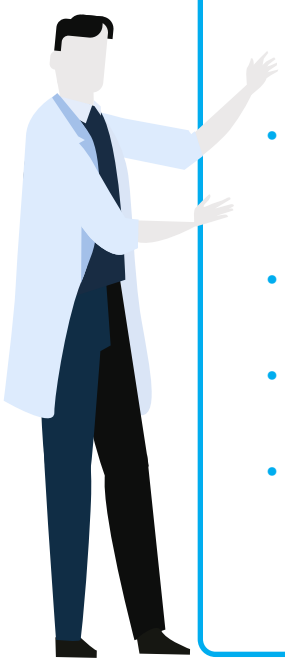
Art.8 of 1901/2006 as amended:

PIP required for all existing and new indications, routes of administration, formulations developed

EMA=European Medicines Agency; EU = European Union; MA=Marketing Authorisation; PIP=Paediatric Investigation Plan; PUMA= Paediatric-use marketing authorisation; SPC=Supplementary Protection Certificate

Planning for the PIP procedure



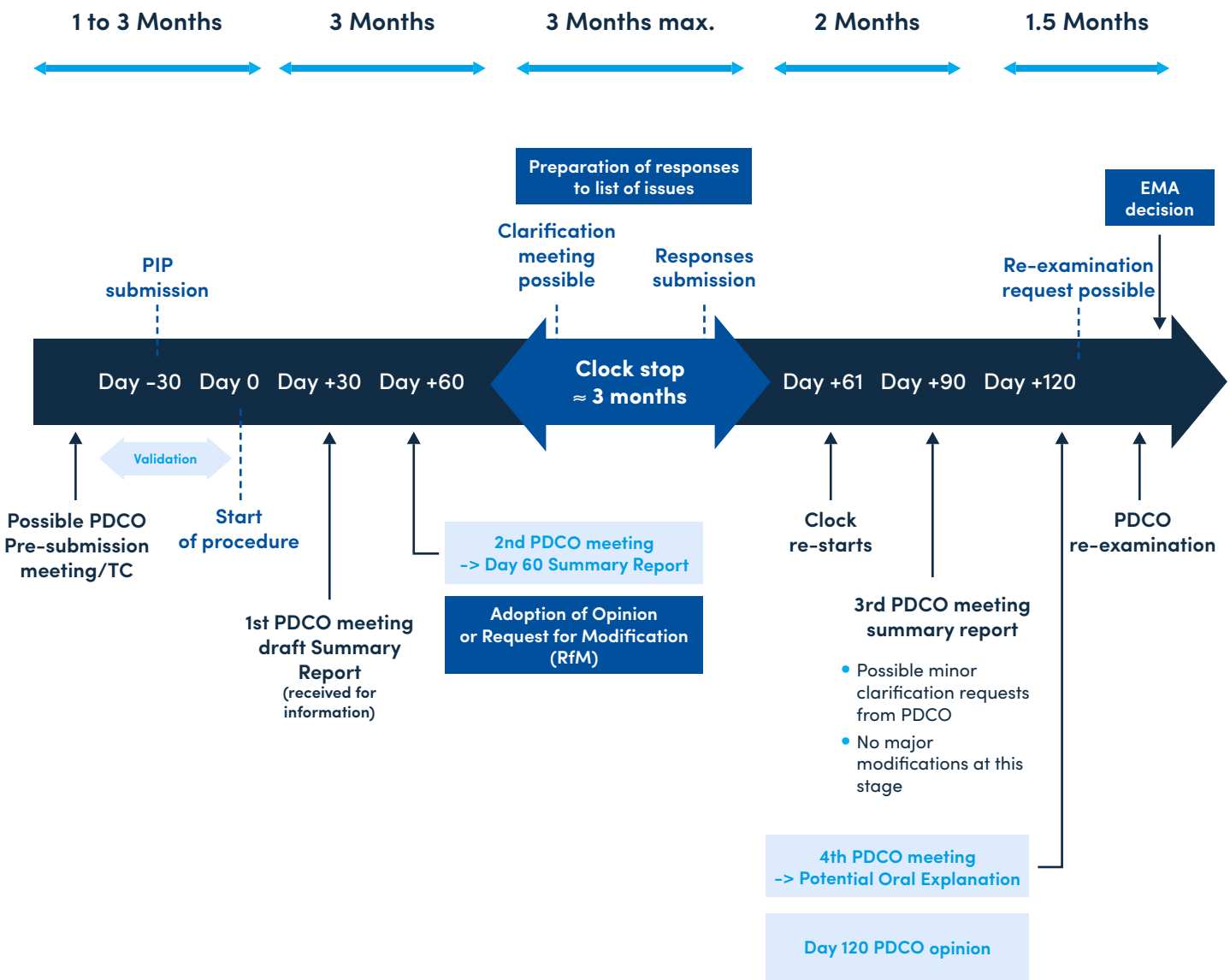


- PIP submission required not later than upon completion of adult PK studies -> justification required if the PIP submission is late
- Plan 3-6 months for the PIP writing + 1 year for the PIP procedure
- Pre-submission meeting possible (regulatory and administrative)
- PDCO re-examination possible after Day 120 upon request

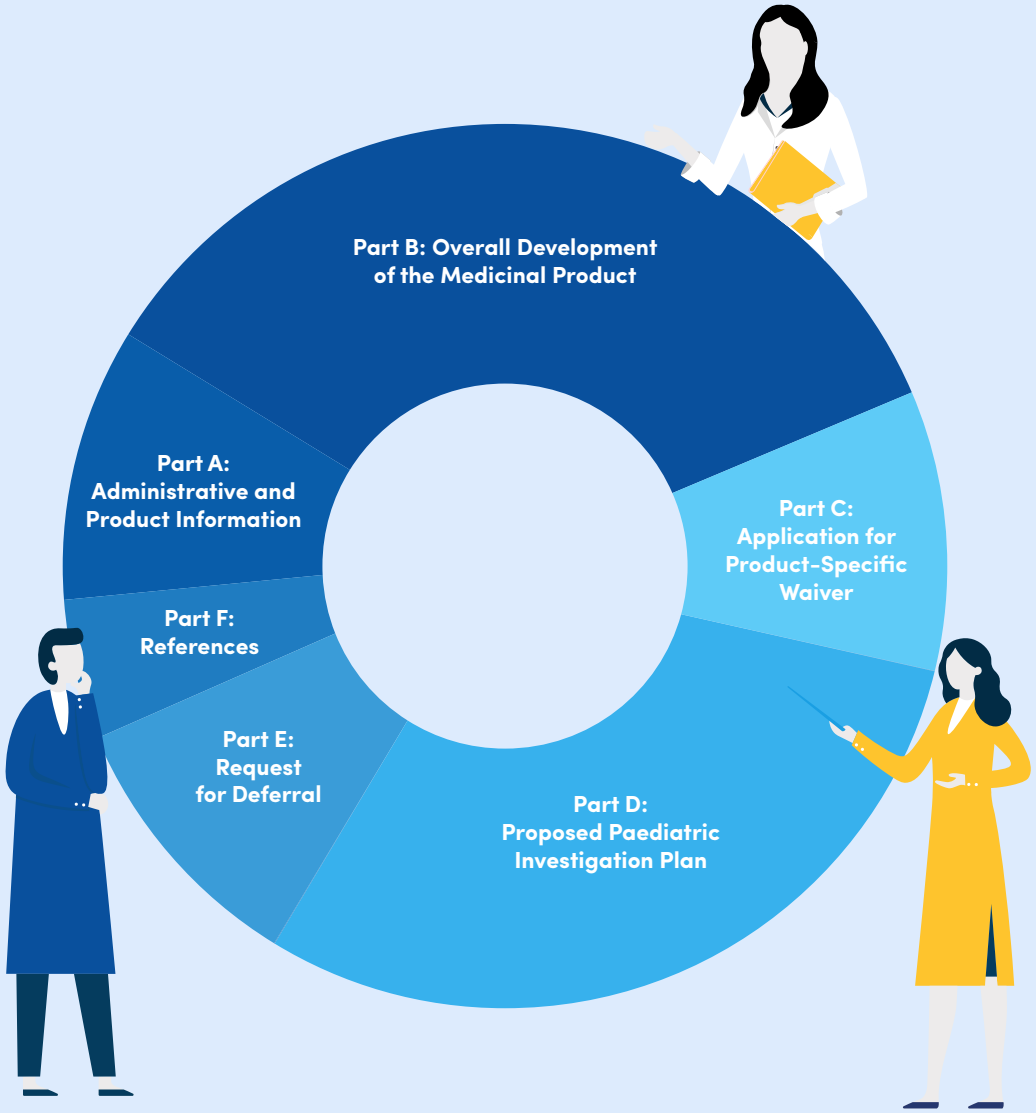
MAA= Marketing Authorisation Application; PK=Pharmacokinetic; PDCO=Paediatric Committee; PIP=Paediatric Investigation Plan

Overview of the PIP procedure 9 months to 1 year

Free of charge



Content of the PIP Application



Part A: Administrative and Product Information

- **Electronic application form**
- **Key Elements Form**
  Summarises the planned paediatric development

Parts B to F: Scientific Document

- **Development plan**
- **Waiver application**
- **Deferral request**

Conclusion

Some additional Tips

Make sure the PIP content is aligned with the implemented paediatric development:

- Submit draft synopsis in early development
- But amend the PIP with the final synopsisduring development before starting paediatric studies

Perform regular internal PIP compliance checks during development:

- Has the targeted indication been modified ?
- Are studies starting as planned ?
- Are study reports available as planned ?

Our consultants can advise whether a deferral or waiver may be appropriate and can provide a complete PIP writing service as well as any PIP modifications through the product lifecycle within the EU or US (especially during the development process).

Here is the Methodology Summary:

Regulatory Strategy - Is a PIP required? If so, you will need to

- Plan the reward strategy
- Plan the PIP procedure
- Define the PIP condition (indication, mechanism of action, paediatric needs, MedDRA)
- Define whether the PIP should include a paediatric development, a waiver, and/or a deferral (Assess competitors, epidemiology, existing treatments, advise on development plan)
- Prepare Part A of the PIP application

Writing the Paediatric Scientific Document:

- Complete the Application Summary, outlining the overall approach in paediatrics
- Complete part B with similarities and differences between adult's vs paediatrics and between paediatric subsets, and identification of a therapeutic benefit/need
- Complete part C for full/partial waiver
- Complete par D for paediatric development (Quality, non-clinical and clinical measures)
- Complete part E for deferral requests (to be justified)
- Compile part F with References/Annexes

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Any questions? Contact-us!

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