EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Paediatric investigation plans for medicines to treat high-grade glioma (HGG)

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EMA scope and mission

- > 500 Mio EU residents
- ~ 100 Mio children (:= 0-18 years)

- Promoting and maintaining public health
- Evaluating, ensuring and supervising the quality, safety and efficacy of medicinal products

- Paediatric Regulation (EC) 1901/2006 http://ec.europa.eu/health/human-use/paediatric-medicines/index_en.htm

Aims of the EU Paediatric Regulation

- *Make paediatric medicines available*

- Improve the health of children
  - Increase high quality, ethical research into medicines for children
  - Increase availability of authorised medicines for children
  - Increase information on medicines
- Achieve the above
  - Without unnecessary studies in children
  - Without delaying authorisation for adults

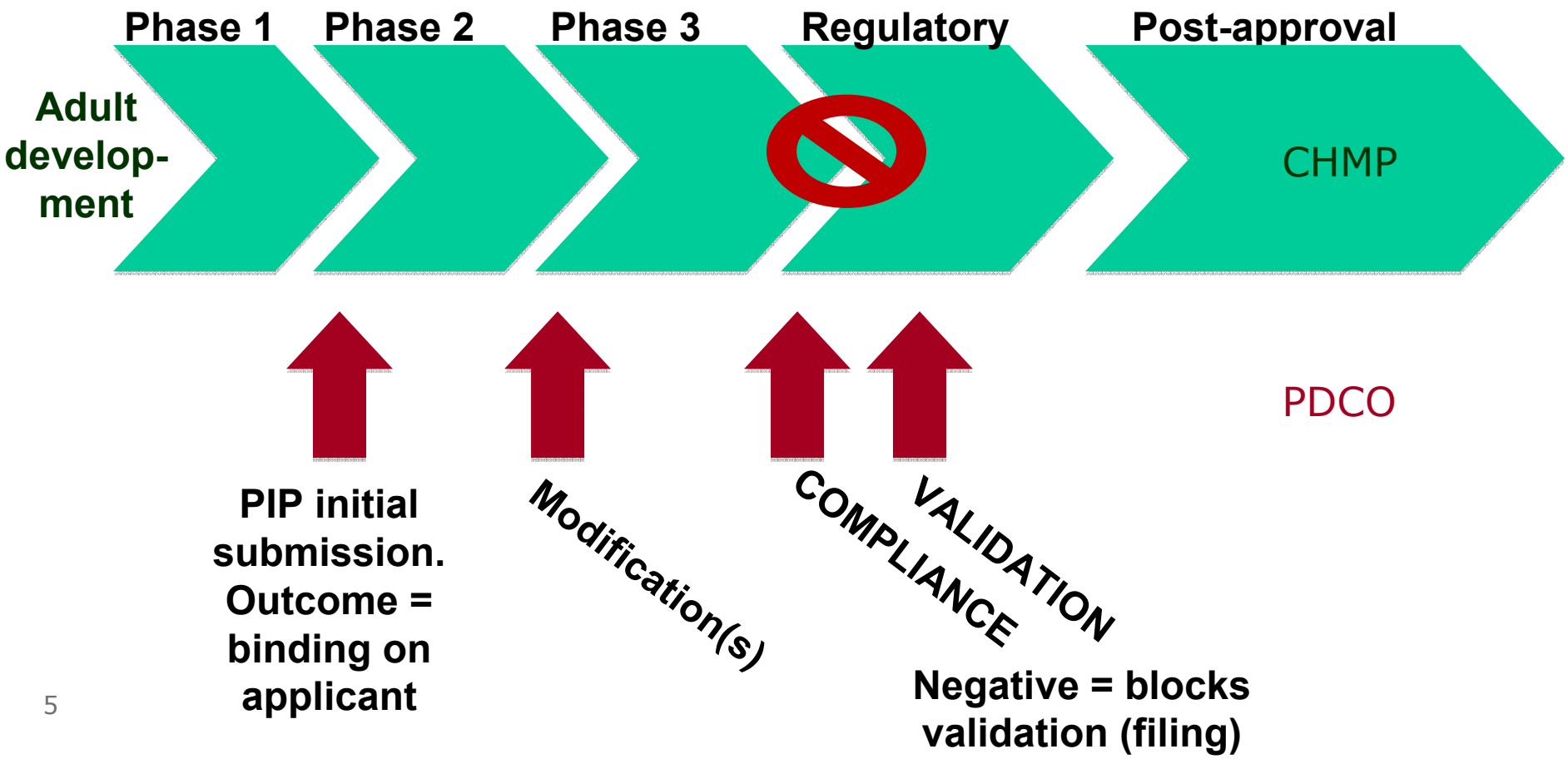
- Since January 2007

Main pillars of paediatric regulation

- Scientific expert committee = PDCO
- Paediatric investigation plans = PIPs
- If paediatric interest, PIPs are required for
  - New medicinal product
  - New: indication, form or route for authorised medicine
- Paediatric requirements based on condition (disease)
- PIP decisions are binding on companies

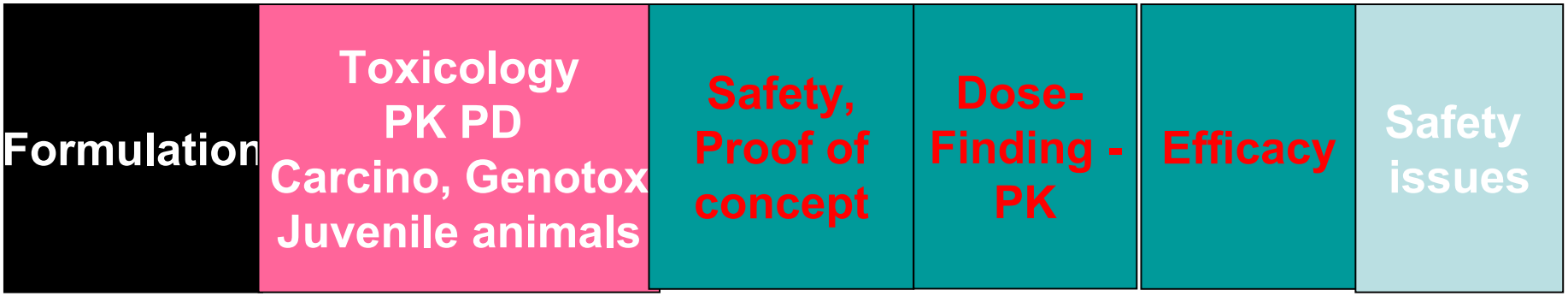
- Catch-up by assessing old studies
- Transparency

Time lines and relation of PIPs to MAAs



Paediatric Investigation Plans (PIPs)

- Intended to support an **indication** ("paediatric use") in relevant subsets of the paediatric population
- Define **required data** on efficacy, safety and age-appropriate formulation (and ethical aspects)
- **Timelines** for study start and completion (ICH E11)
- **Binding** on applicants (but trial authorisation remains to be independently requested)



Evaluating and defining oncology PIPs

- Existing knowledge:
  - Disease: What are the paediatric patient subsets with unmet therapeutic needs? How do children compare to adults?
  - Medicine: Pharmacology? Proof of concept?
- Potential use and significant benefit for children?
- Needed paediatric data:
  - Non-clinical data? Age-appropriate formulation?
  - Clinical data? Strategy? Trial methodology? Biomarkers? Long-term?
- Summary report template
  http://www.ema.europa.eu/docs/en_GB/document_library/Templates_and_Form/2009/09/WC500003740.doc

Example PDCO opinion

EMA/PDCO/98975/2010

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and on the refusal of a waiver

EMEA-000477-PIP01-08

Scope of the application

Active substance(s):

Cediranib maleate

Condition(s):

High-grade glioma

Pharmaceutical form(s):

Tablet

Route(s) of administration:

Oral use

http://www.ema.europa.eu/docs/en_GB/document_library/PIP_decision/WC500095040.pdf

3.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1: Development of a 5 mg strength tablet that can be dispersed for oral use.
Non-clinical	0	Not applicable.
Clinical	3	Study 2: Open-label, multicentre, multiple dose trial to evaluate pharmacokinetics, safety and activity of cediranib in children from 2 years to less than 19 years age with refractory or recurrent solid tumours. Study 3: Open-label, multicentre, multiple dose trial to evaluate pharmacokinetics and safety of cediranib in children from 1 year to less than 18 years of age with refractory or recurrent solid tumours of the central nervous system Study 4: Double-blind, randomised, parallel-group, placebo-controlled add-on, multi-centre trial to evaluate pharmacokinetics, safety and efficacy of cediranib added to temozolomide in children from birth to less than 18 years with newly-diagnosed high-grade glioma, including a run-in period and an open-label stratum with children with first progression or first relapse of high-grade glioma

4. Follow-up, completion and deferral of pip

Measures to address long term follow-up of potential safety issues and efficacy in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	By December 2015
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Motivation for HGG workshop

Shared objectives and science, complementary activities:

- Academic scientists
  - Medicine users and paediatric oncology experts
  - Running networks making trials feasible
- Regulators
  - Have access to all data (incl. unpublished, negative)
  - Assess to provide impartial and exhaustive scientific view
  - Involve experts from several fields
  - See all medicinal products
  - Want to make medicines available (prescr., reimburs.)

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Motivation for HGG workshop (cont.)

- Understand the current state of the art
- Learn about interpretations of recent data
- Discuss consequences for PIPs for HGG:
  - Characteristics of interesting medicines
  - Paediatric trials informed by adult experience
  - Opportunities for extrapolation of efficacy
  - Endpoints – specific paediatric, shared
  - Standard of care in paediatric age subsets

→ Work along the questionnaire