The Paediatric Regulation

Paediatric Team

Scientific Advice, Paediatrics

& Orphan Drugs Sector

EMEA

2007

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The current situation

- 20% of the EU population, i.e. 100 million, is aged less than 16 years

  ⇒ premature neonate, term neonate, infant, child, adolescent

- 50-90% of paediatric medicines have not been tested and evaluated

Risks:

- *adverse effects (overdosing)*
- *inefficacy (underdosing)*
- *improper formulation*
- *delay in access to innovative medicines*

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The paediatric background

- “A child is not a small adult”
- Clinical trials in children are more difficult, take longer and cost more; said to be unethical
- Children require specific formulations
- Paediatric indications are not profitable
- Liability of use in children

Studies of medicinal products are performed by industry mostly in young adults, but not in children

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Objectives of the Regulation

- 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

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Main pillars of the Regulation

- An expert committee:
  the Paediatric Committee (PDCO)
- An agreed (evolving) paediatric development:
  the Paediatric Investigation Plan (PIP)
- A set of rewards and incentives
  - For new and on-patent products
  - For off-patent products
- A series of other tools for information, transparency, and stimulation of research

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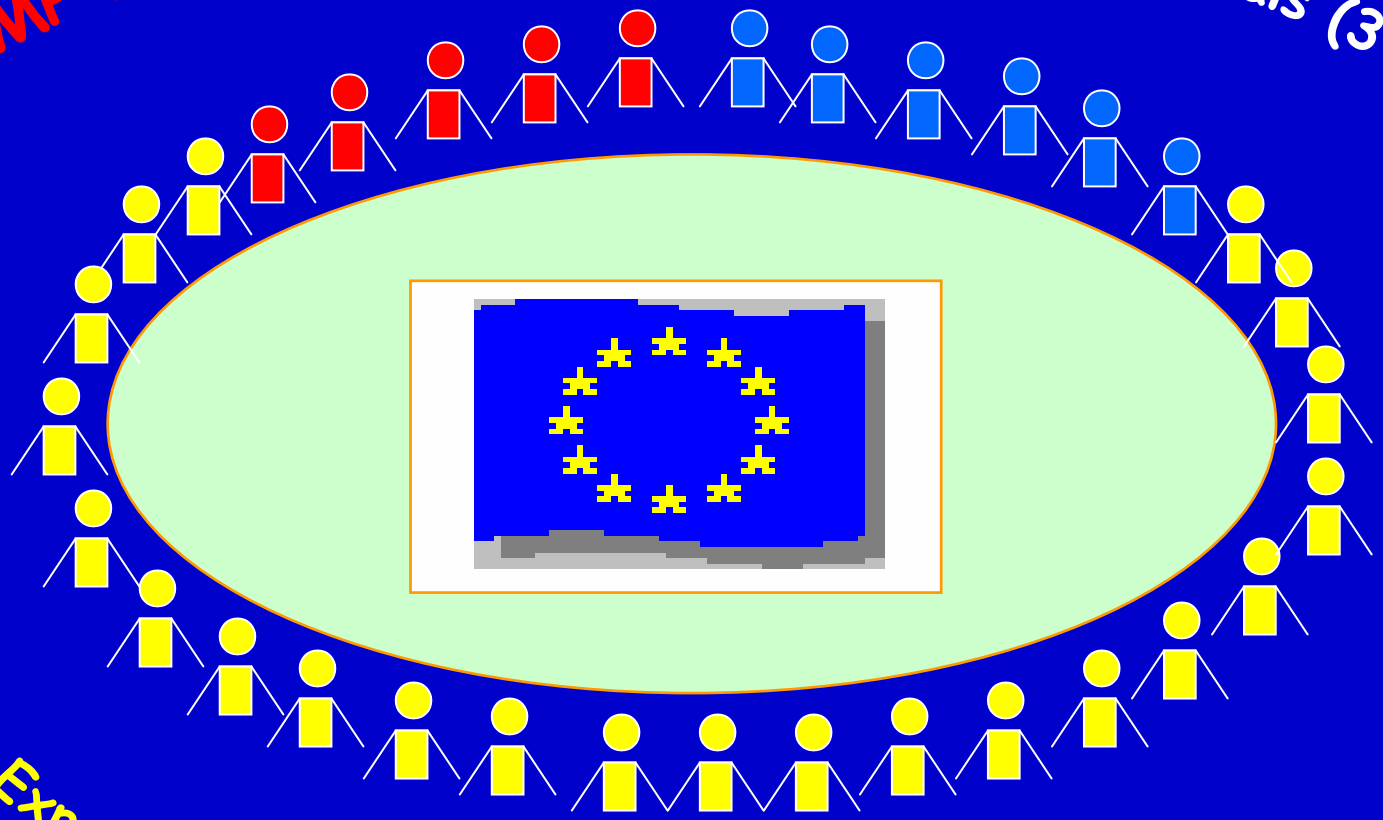
Paediatric Committee (PDCO)



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Paediatric Investigation Plan

- Is basis for the development and authorisation of a medicinal product for the paediatric population subsets
- Includes details of the timing and the measures proposed to demonstrate:
  - Quality
  - Safety
  - Efficacy

Marketing Authorisation criteria

- Is to be agreed upon and/or amended by the Paediatric Committee (PDCO)
- Is binding on company

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Paediatric Investigation Plan/ Waiver Guideline

A Commission Guideline:

Includes modalities on

- PIP requests
- Waiver requests
- Deferrals
- Key elements for PIP Decision
- Proposal for Significant Studies
- Compliance check

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PIP request outline

- Information (administrative, condition, product)
- Waiver request
- Overall strategy for development in children
- Details of individual studies
- Proposed timelines (and request for deferral)
- References

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Paediatric needs

- Preliminary lists established by Paediatric Working Party (PEG), on EMEA web
- To be reviewed by Paediatric Committee in 2007
- Update of Paediatric needs by Paediatric Committee on basis of inventory (2009) following survey by Member States

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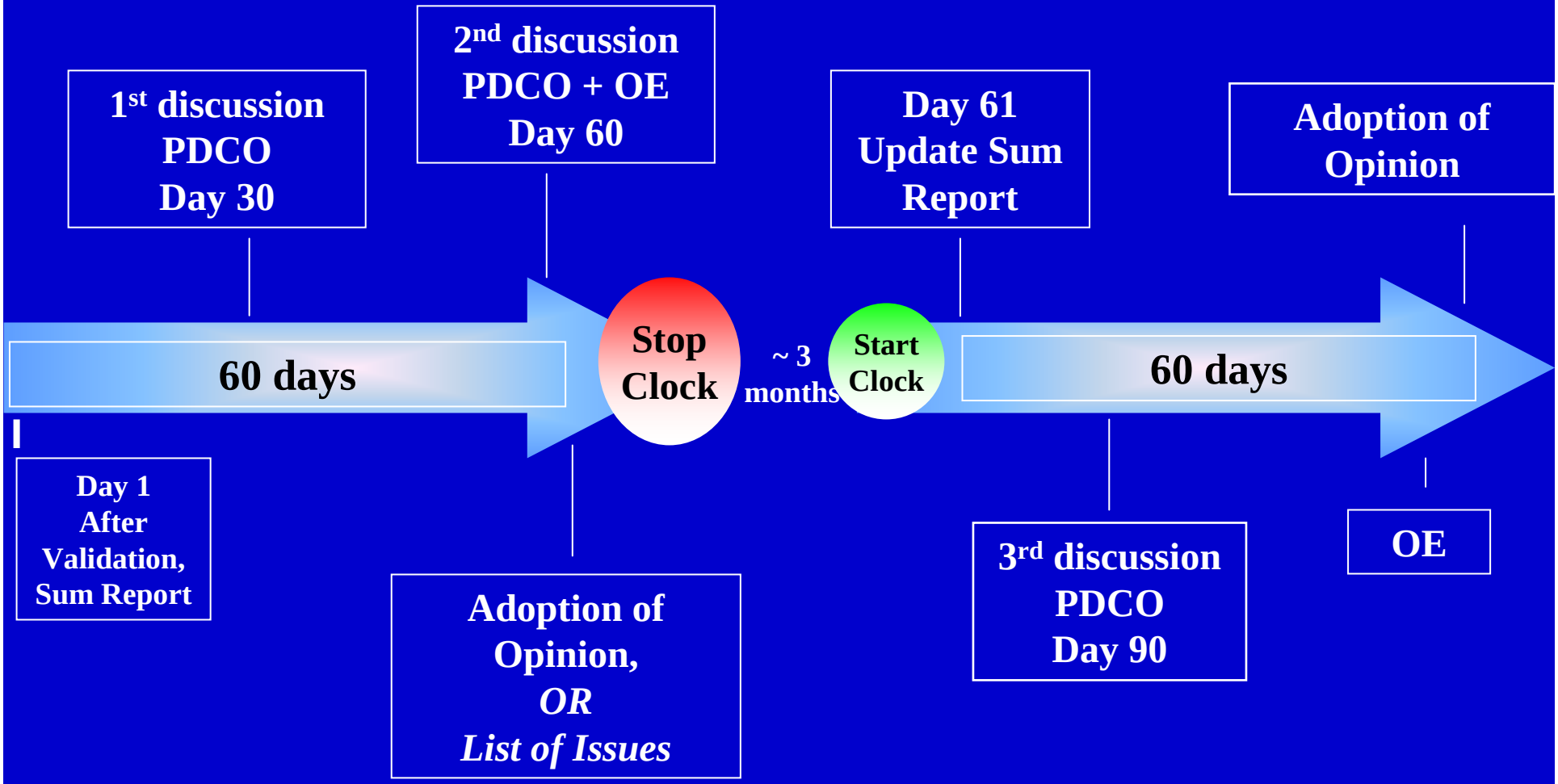
Overview PIP procedure



OE= oral explanation

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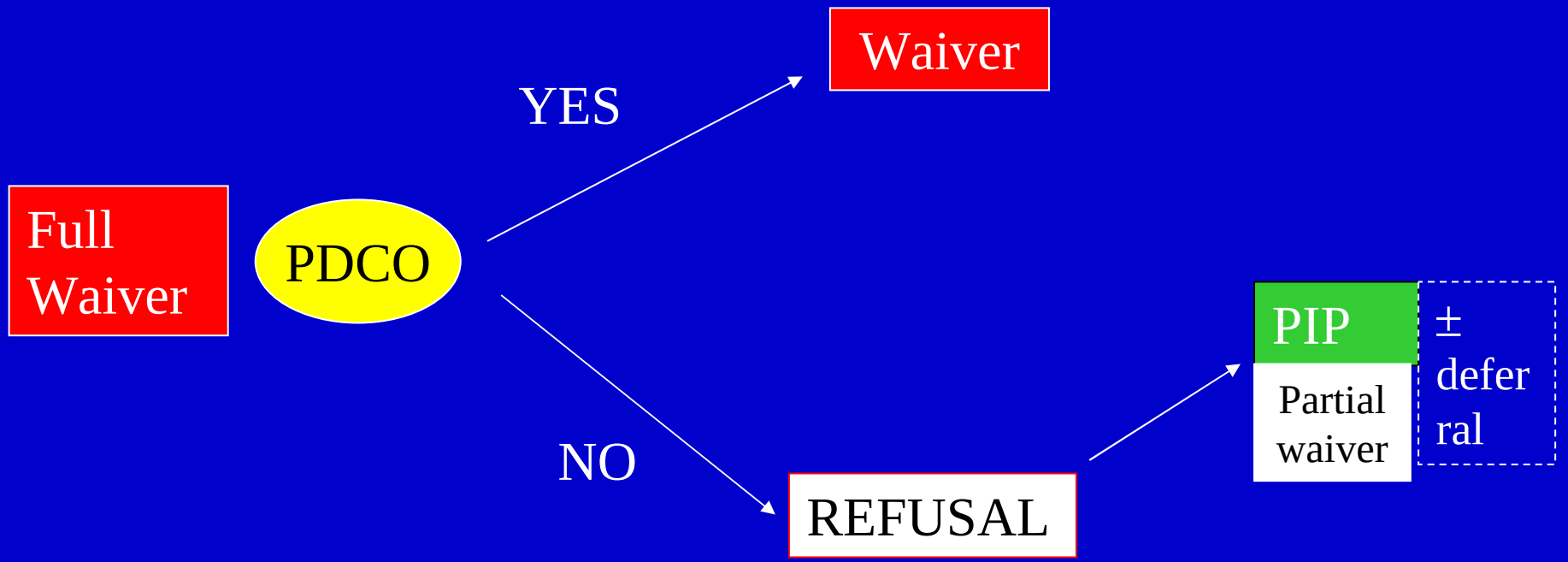
Applicant's request for a Waiver



NB: full waiver= no reward

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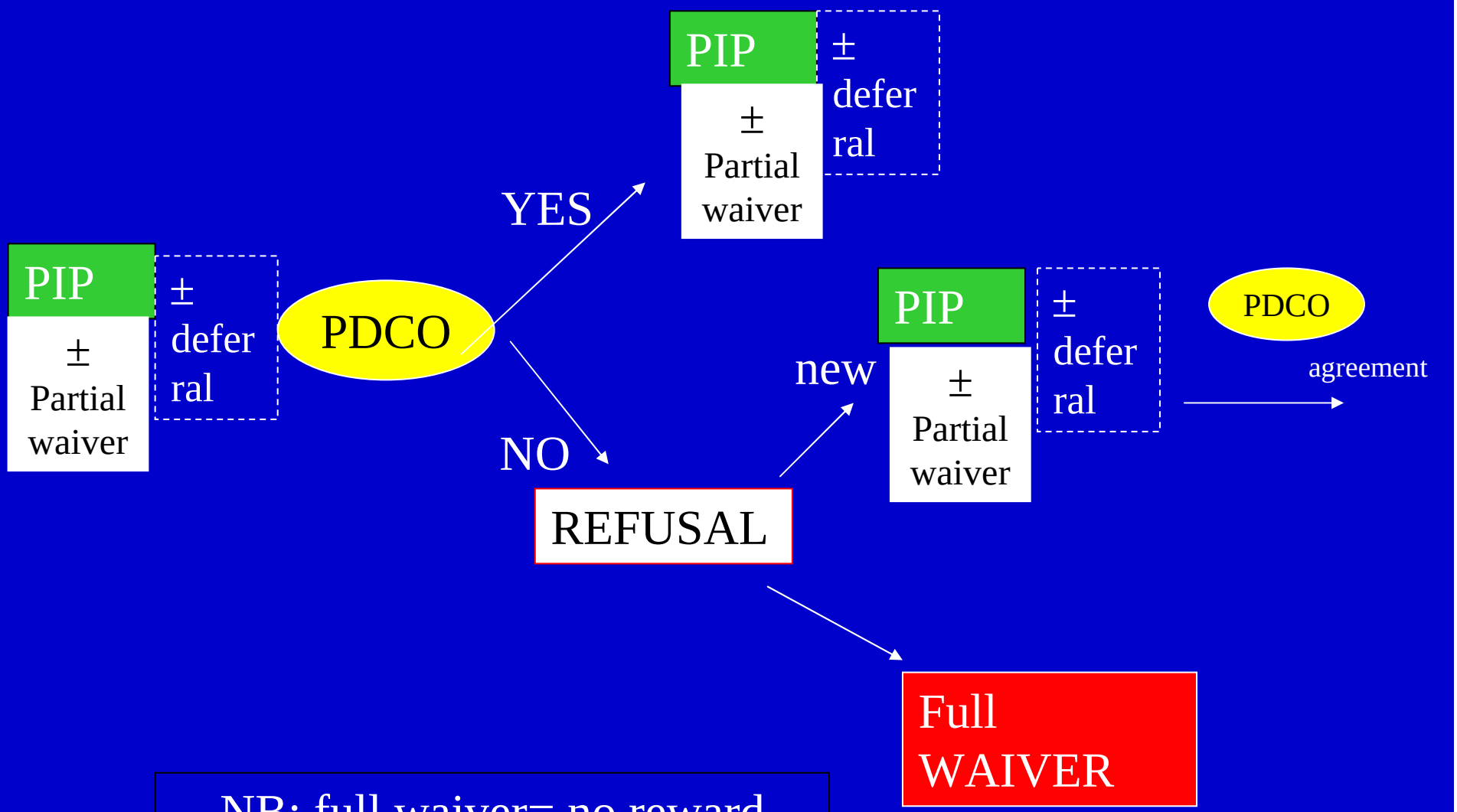
Applicant's request for a PIP



NB: full waiver= no reward

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New products

- **Currently unauthorised products**
  - Obligation to submit results compliant with agreed Paediatric Investigation Plan (PIP) at time of marketing authorisation (or invalid application)
  - **Reward**: 6-month extension of the patent protection (Supplementary Protection Certificate) - if compliance, authorisation in all Member States, and information in Product Information

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Recent products

- **Authorised products with a patent**
  - Obligation to submit results compliant with agreed Paediatric Investigation Plan (PIP) at time of new indication, new route of administration, or new formulation (or invalid application)
  - **Rewards**: 6-month extension of the patent protection (Supplementary Protection Certificate) / 1-year extension of the market protection - if compliance, authorisation in all Member States, and information in Product Information

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Orphan drugs

- 15-20% of rare diseases only affect children, 55% affect both adult and children (orphan designation data)

- 2 years of market exclusivity added to existing 10 years

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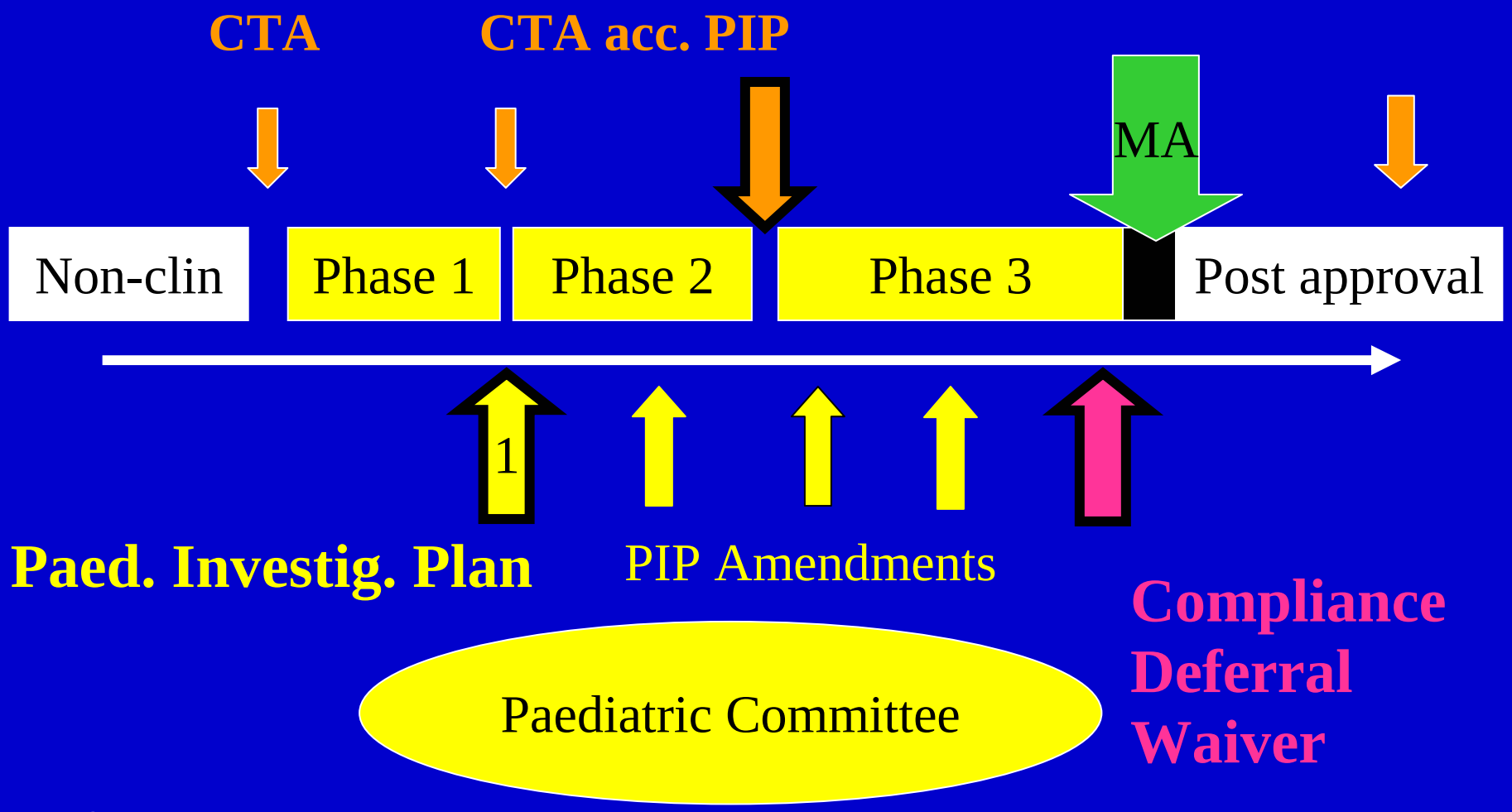
Timing Consultation of Paediatric Committee



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‘Old’ products

Off-patent products (Optional Procedure)

- Paediatric Use Marketing Authorisation (PUMA)
  - Covers Paediatric indication and Formulation
  - Need for Paediatric Investigation Plan and Compliance
- **Reward**: 10 years data protection/exclusivity
- Brand name can be retained

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Paediatric Scientific Advice

- Free of charge from entry into force
- Prior to submission of a PIP or during PIP implementation process
- Including advice on pharmacovigilance and risk management systems
- Not binding on Paediatric Committee
- Link Paediatric Committee / Scientific Advice Working Party

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A European Network - a tool

EMEA Paediatric Research Network

- To link together existing networks, investigators and centres with specific paediatric expertise
- Build up competences at a European level
- Facilitate the conduct of studies
- Avoid duplication of studies

- New European Recommendations on Ethics of Clinical Trials in children

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Funding of paediatric research

- Community funding for studies into off-patent medicinal products
  - From Framework Programme(s)
  - FP7: in second call (dead line for bids: second half of 2007)
  - 30 million Euros for the 2 first years
  - Link with identified Needs and Priorities for research into off patent medicines (EMEA website)

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Transparency Measures

- **Database of Paediatric Trials (EudraCT)**
  - Protocols
  - Results
  - Studies previously performed (published or not)
- **Database of authorised Products in EU (EudraPharm)**
  - Link to results of studies
- **Data in the medicinal product Information (waivers & deferrals, compliance, results)**
- **‘Name and Praise’/’Name and Shame’ by European Commission**

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Other measures

- Inventory of use of medicines in children in Member States
- Symbol on any medicinal product authorised for children (all medicines with paediatric indication)
- Obligation to market products which benefited, or if product withdrawn from the market: Transfer of marketing authorisation, or Consent to use data

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Timeline of Implementation

- **Immediate (26 January 2007)**
  - Free Scientific Advice
- **6 months from entry into force (26 July 2007)**
  - Establishment of Paediatric Committee
  - Submissions of PIP and Waivers
- **18 months from entry into force (26 July 2008)**
  - Obligation to submit results of studies according to agreed PIP with applications for Marketing Authorisation (**new products**)
  - Or EMEA decision granting a waiver or deferral
- **24 months from entry into force (26 January 2009)**
  - Obligation to submit results of studies according to agreed PIP with application for **new indications, new routes of administration,**
    new pharmaceutical forms
  - Or EMEA decision granting a waiver or deferral

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Conclusions

- Better information for patients, families and prescribers
- Transparency of clinical trials
- More products available with appropriate formulation
- More research of high quality

… Better medicines for children!

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