The Paediatric Regulation

Paediatric Team

Scientific Advice, Paediatrics

& Orphan Drugs Sector

EMEA

2007

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*

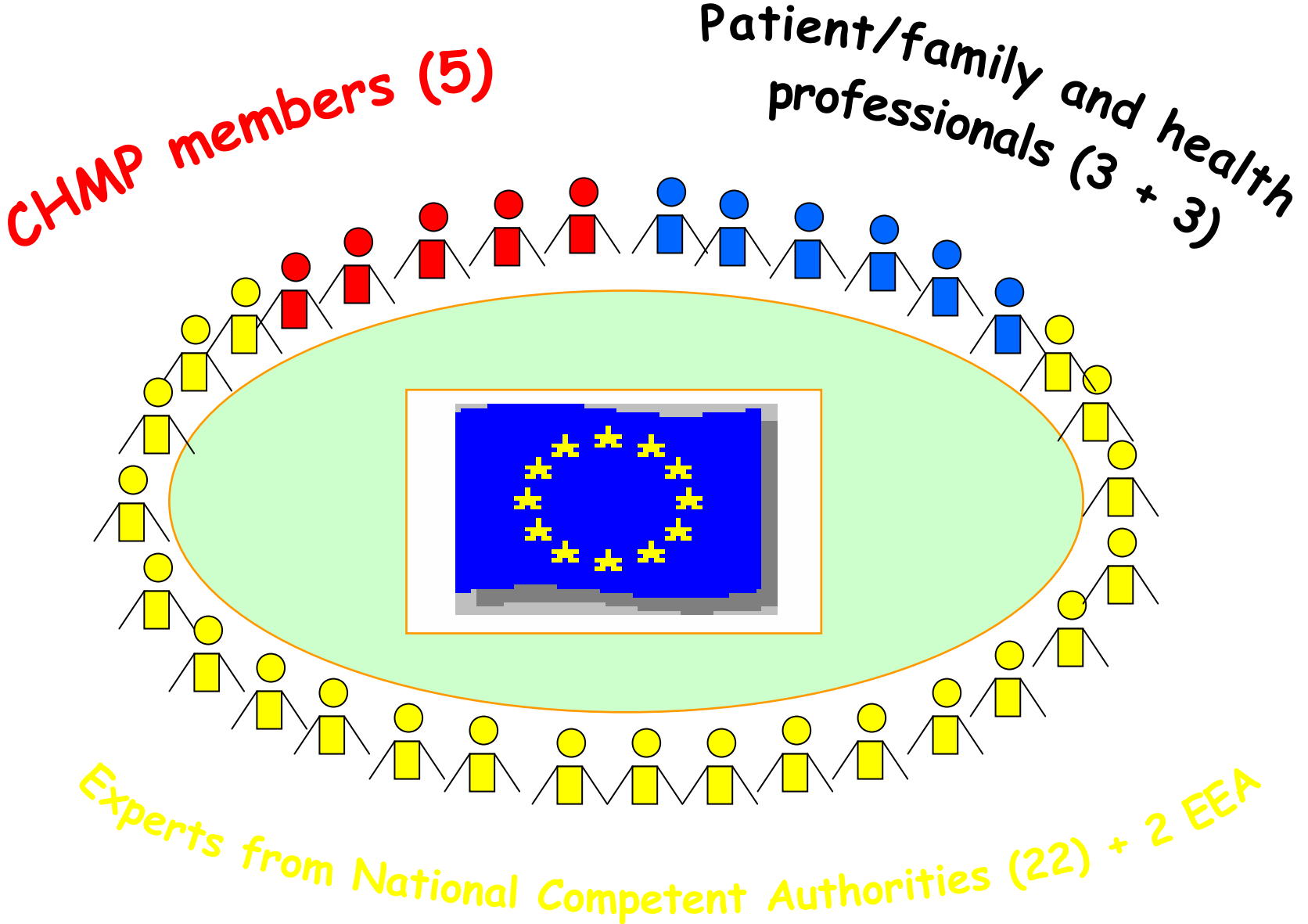
Objectives of the Regulation

- 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

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

Paediatric Committee (PDCO)



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

Paediatric Investigation Plan Guideline

Draft Commission Guideline includes modalities on:

- PIP requests
- Waiver requests
- Deferrals of studies
- ‘Key elements’ for PIP Decision
- Proposal for ‘Significant Studies’
- Compliance check

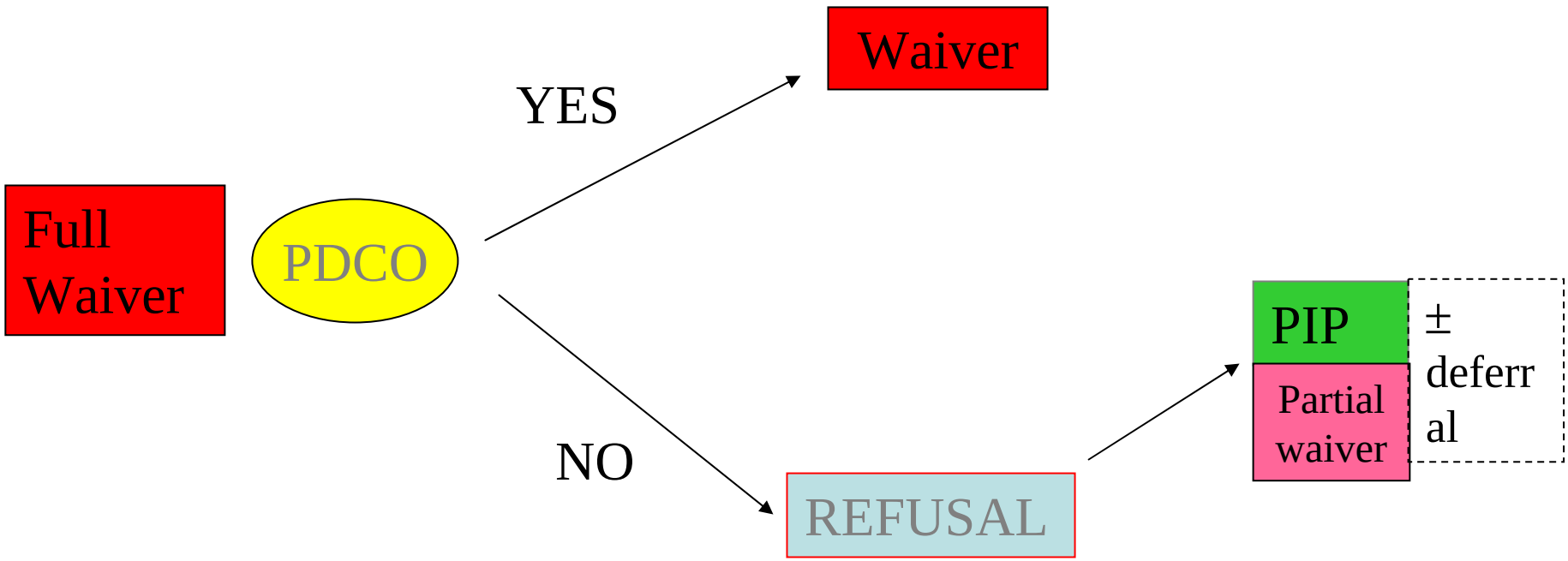
PIP request outline

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

Paediatric Needs

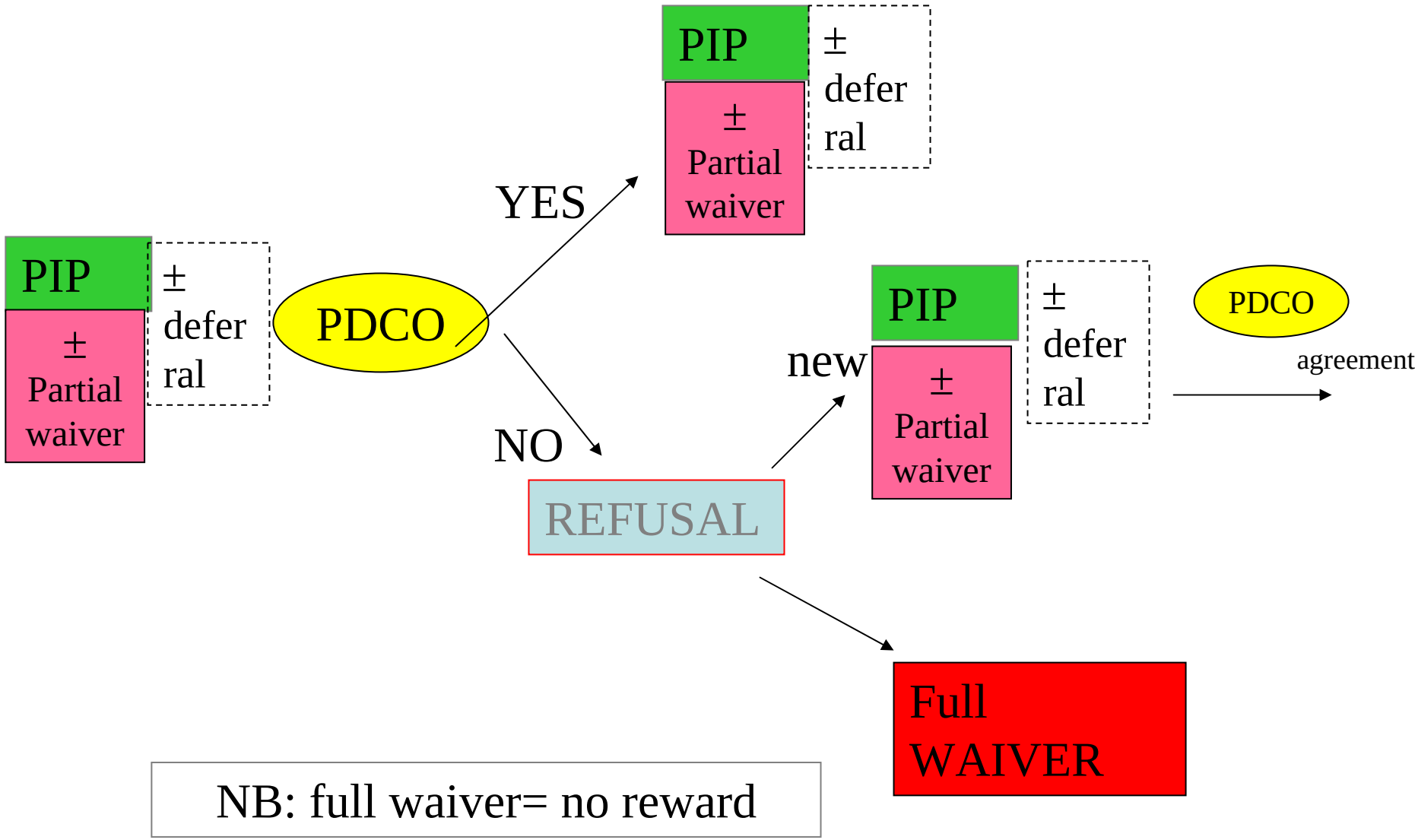
- Preliminary lists established by Paediatric Working Party (PEG), published on EMEA web
- To be reviewed by Paediatric Committee in 2007
- Update of Paediatric needs (in 2009) by Paediatric Committee, on basis of inventory, following survey by Member States

Applicant's request for a Waiver



NB: full waiver= no reward

Applicant's request for a PIP



NB: full waiver= no reward

New products

- **Currently unauthorised products**
  - Obligation to submit results compliant with agreed Paediatric Investigation Plan (PIP) at time of validation 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

Authorised products

- **Authorised products with a patent**
  - Obligation to submit results compliant with agreed Paediatric Investigation Plan (PIP) at time of validation of new indication, new route of administration, or new formulation (or invalid application)
  - **Rewards**: 6-month extension of the patent protection (Supplementary Protection Certificate)

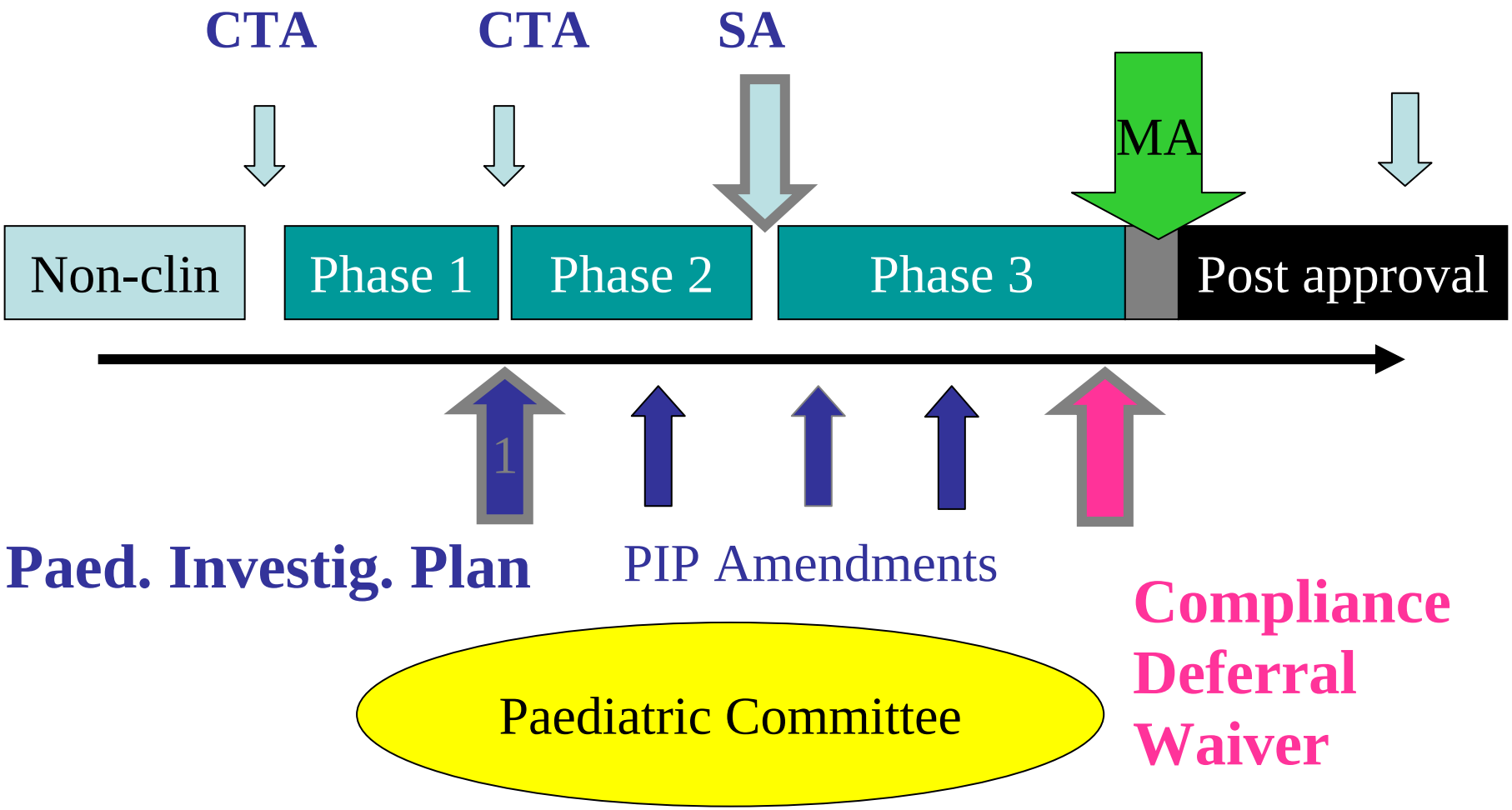
    If compliance, authorisation in all Member States, and information in Product Information

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 if compliance with PIP and information in Product information

Timing of PIP application (new 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
- Brand name can be retained

PUMA versus MA

- Both can use same legal basis for applications
- Stand-alone applications, OR
- Abridged application with cross-reference to adult product
- Covers (only) paediatric indication(s) and formulation(s)

- Need for agreed Paediatric Investigation Plan, and Compliance

Paediatric Scientific Advice

- Free of charge since January 2007
- 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 to ensure consistency

EMEA Paediatric Research Network

Objectives:

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

- Strategy to be adopted by EMEA Management Board in December 2007

European Funding

- Studies into off-patent medicinal products
  - From Framework Programme(s)
  - FP7: in second call (deadline: September 2007)
  - 30 million Euros for the 2 first years
  - Link with identified Priority List of off-patent medicines (published on EMEA website)

Transparency Measures

- **Database of Paediatric Trials (EudraCT)**
  - Protocols
  - Results
  - Studies previously performed (+/- published)
- **Database of authorised Products in EU (EudraPharm)**
- **Medicinal Product information (including results)**
- **‘Name and Praise’/’Name and Shame’ by European Commission**

Other measures

- Survey of paediatric use of medicines in Member States
- Inventory of Paediatric Needs by Paediatric Committee (on basis of survey)

- Symbol on any medicinal product authorised for children (pre and post Regulation)
- Obligation to market, OR Transfer of MA (or consent to use data) if product withdrawn from the market

Timelines of Implementation

- **Immediate (since 26 January 2007)**
  - Free Scientific Advice
- **6 months from entry into force (26 July 2007)**
  - Establishment of Paediatric Committee
  - Submission of PIP/waiver requests
  - Paediatric Use Marketing Authorisation provisions apply
- **12 months from entry into force (26 January 2008)**
  - Adoption of network strategy by Management Board
- **18 months from entry into force (26 July 2008)**
  - Obligation for Marketing Authorisation of new products
  - Or EMEA decision granting a waiver or deferral
- **24 months from entry into force (26 January 2009)**
  - Obligation for new indications, new routes of administration, new pharmaceutical forms
  - Or EMEA decision granting a waiver or deferral

Conclusions

- New and Older medicines are concerned
- Funding of research for academics and generic companies is available
- Need to answer DG Research calls!
- Transparency of information
- Support through the EMEA network

… Better medicines for children!