IMPLEMENTATION ON THE PAEDIATRIC REGULATION EMEA VIEWS

2007 EMEA- EFPIA INFO DAY

Nathalie Seigneuret

Objectives of the Regulation entered into force 26 January 2007

- 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

- New EMEA Committee: Paediatric Committee
- **An agreed (evolutive) paediatric development: the Paediatric Investigation Plan (PIP)**
- **A mix of rewards and incentives**
  - **For on-patent products**
  - **For off-patent products**
- A series of other tools for information, transparency, and stimulation of research

Currently unauthorised products

18 months after entry into force of the Regulation, i.e 26 July 2008

- Obligation to submit **results** of agreed Paediatric Investigation Plan at time of marketing authorisation application

X If not: Invalid application for MA

- Results reported in SmPC
- Authorisation in all Member States
- **Reward**:
  - 6-month extension of the Supplementary Protection Certificate

Patent-protected authorised products

24 months after entry into force of the Regulation, i.e. 26 January 2009

- Obligation to submit **results** of agreed Paediatric Investigation Plan at time of change (variation/extension) for new indication, route of administration, or pharmaceutical form
- Results reported in SmPC
- Authorisation in all Member States
- **Reward:**
  - 6-month extension of the Supplementary Protection Certificate

Orphan drugs

- Same obligations
- Need for PIP and compliance
- **Reward:**

  2 years of market exclusivity added to existing 10 years

For off-patent products

Paediatric Use Marketing Authorisation (PUMA)

New type of MA

- Covers paediatric indication(s) and formulation(s)
- Optional but need for PIP (considering whether therapeutic need in each paediatric subset) and compliance

  – No need for MA in all Member States
  – Brand name may be retained
  – 10 years of data protection: (8+2) +1

Applicant's Request for PIP

- Timing of submission:
  - for new product: end of pharmacokinetic studies in adults (~ end of Phase I)
  - for variation or PUMA no legal deadline

- Available information may not be complete, but procedure for modification(s) foreseen

- Full information expected for products primarily intended in the paediatric populations

➡ **Early dialogue engaged with PDCO**

Paediatric Investigation Plans

- Details of timing and measures proposed (i.e studies, trials and pharmaceutical development) necessary to obtain a paediatric indication with an age appropriate formulation in all paediatric subsets affected by the condition

  - Quality
  - Safety
  - Efficacy

Marketing Authorisation criteria

Paediatric Investigation Plans

- Reference to ICH E11
- To be agreed and/or amended by the Paediatric Committee
- Binding on company & EMEA Decision published
- Follows scientific guidance/pharmaceutical legislation
- Combination of waivers and PIP possible according to condition, product, and significant therapeutic benefit/paediatric needs
- For variation/extension: application covering existing and new indications, pharmaceutical forms & route of administration

Commission Guideline

- Draft Commission guideline on applications for agreement or modification of PIP and request for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies

- Published 31 January 2007 for public consultation till 30 March 2007

- Scientific input given from PEG, other CHMP Working Parties

Commission Guideline

- Administrative and Product Information

  e.g. applicant/manufacturer, type and details of product, regulatory status in/out Community, condition(s), proposed indication

- Overall development of the product including information on the target disease(s)/condition(s)

  e.g. similarities disease(s) between adult/children and between the paed subsets, anticipated effect of the product, prevalence/incidence, current methods, significant therapeutic benefit/fulfilment of the therapeutic needs

Commission Guideline

- Significant therapeutic benefit

e.g expected improved efficacy, substantial improvement in safety, improved dosing scheme or method of administration, new clinically relevant age-appropriate formulation, new mechanism of action

- Therapeutic needs

e.g inclusion in the inventory

Commission Guideline

Product specific waiver

- **Scope product specific waiver**

  e.g one and more subset(s), indication(s)

- **Grounds**

  e.g based on efficacy and safety, disease or condition occurring only in adults population, lack of significant therapeutic benefit

\+ list of class waivers published by EMEA

Commission Guideline

PIP

- Overall strategy proposed for paediatric development

  e.g. proposed paediatric PIP indication, selected age group, outline quality/non-clinical, clinical data, extrapolation/inter-relation, existing paed bata

- Strategy in relation:
  - Quality aspects
  - non-clinical aspects
  - clinical
- Planned measures for the paediatric development

  e.g. synopsis of protocol of each study planned

- Proposed timelines

Commission Guideline

PIP

- Application for deferral
- Annexes

Modification of an agreed PIP

- Same structure but only relevant sections completed

Application forms to be developed

Commission Guideline

Significant studies

- Studies initiated before entry into force of Regulation but completed after
- If compliance, reward/incentives possible
- Assessment of significance on case-by case basis
- Transitional measure

If studies already completed, not eligible for reward but data taken in account for PIP

Commission Guideline

Compliance check (# assessment of data)

STEP 1 AT VALIDATION

- By competent authority (reference MS)
- By PDCO at EMEA (60 day procedure)
- Before or during Validation

non-compliance ➡ non-validation

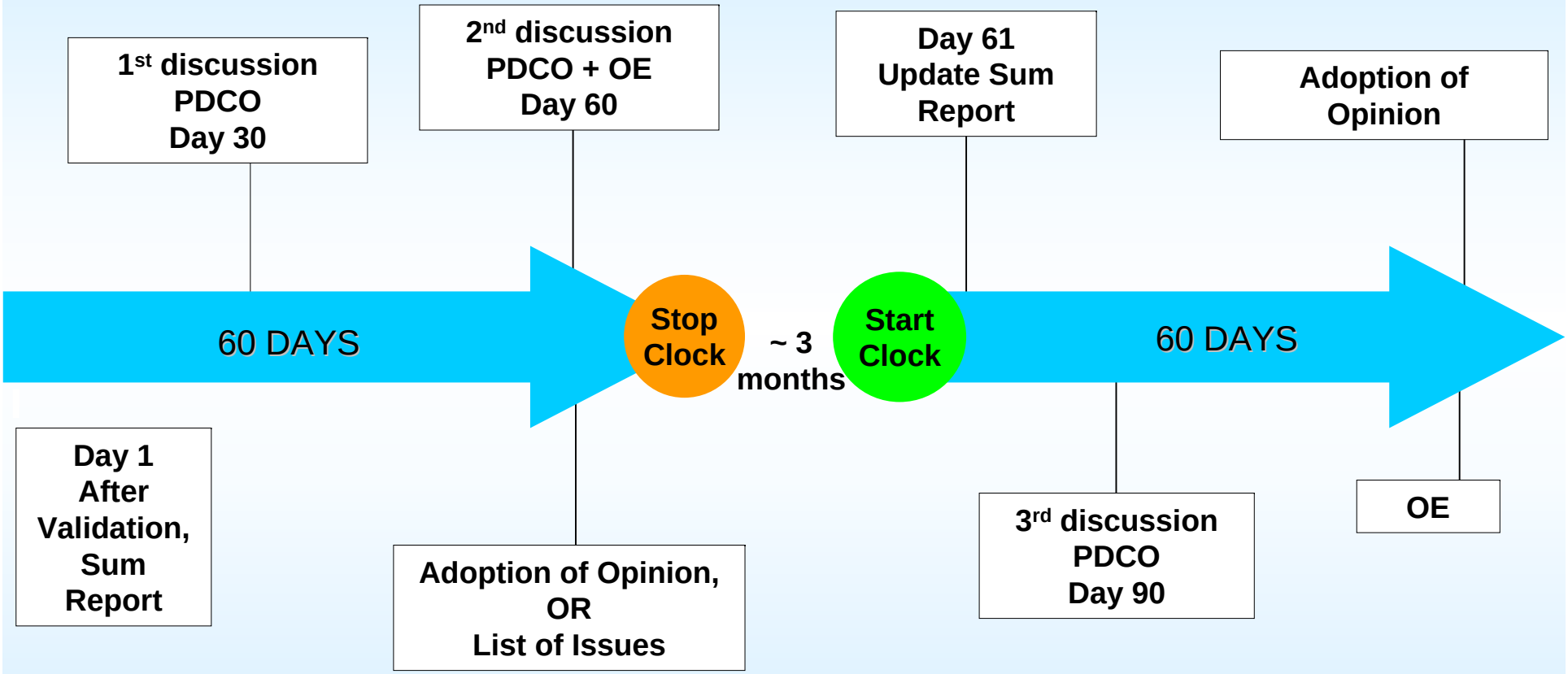
STEP 2 (DURING ASSESSMENT)

- Checking facts

Non inclusion in MA of compliance statement ➡ ineligibility for rewards/incentives

Submission of compliance report encouraged

Overview procedure

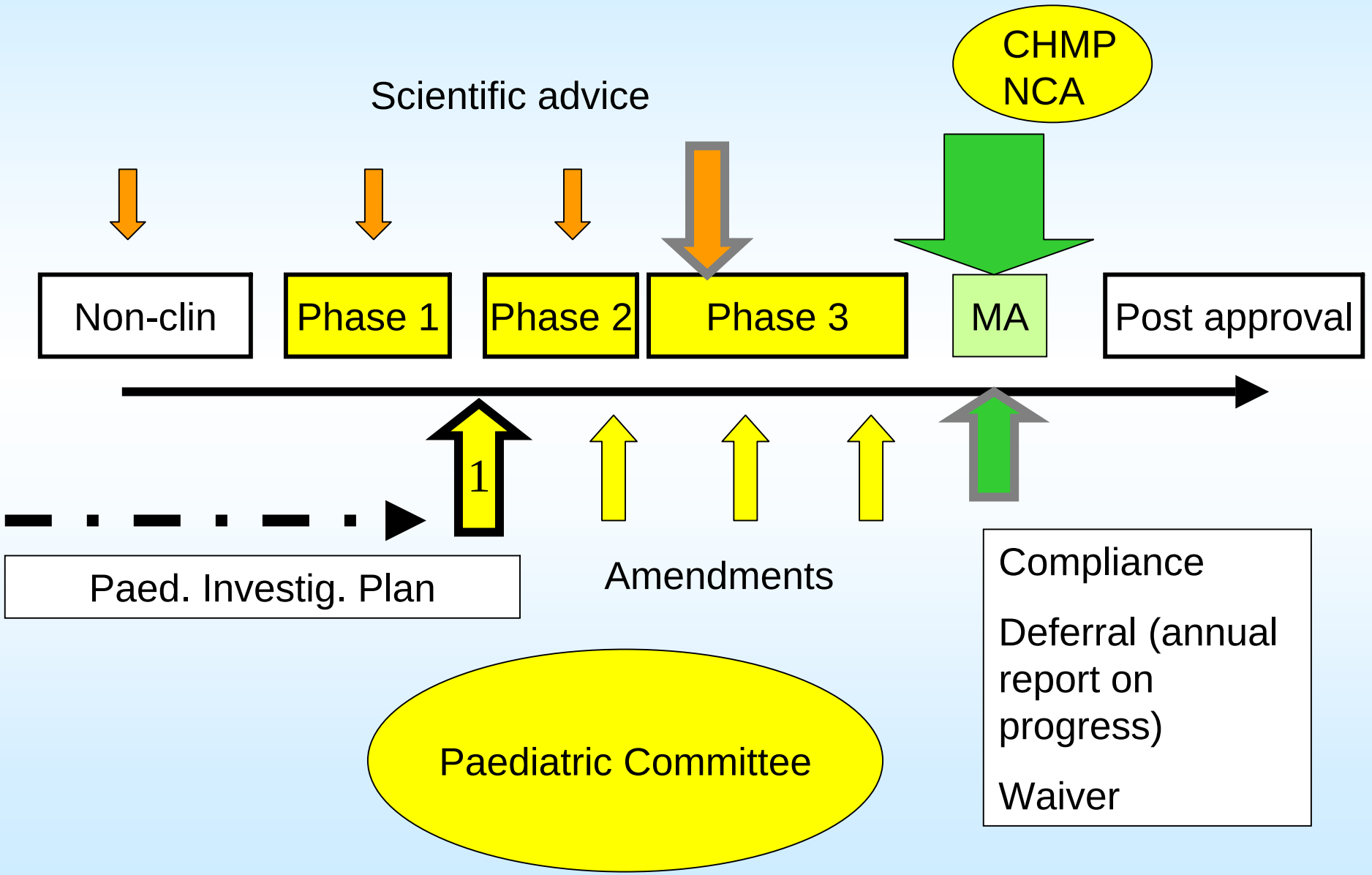


OE= oral explanation

SPC extension

- All measures as agreed in PIP completed
- Statement on compliance with agreed PIP included in marketing authorisation and ‘significant’ studies (*target: Patent office*) for those completed after entry into force
- Inclusion of study results in SmPC and PL, if appropriate
- Marketing authorisation in all Member States
- If waiver mention in SmPC and if appropriate in package leaflet but no reward

In Summary..


CHMP
NCA
Scientific advice
Non-clin
Phase 1
Phase 2
Phase 3
MA
Post approval
1
Paed. Investig. Plan
Amendments
Compliance
Deferral (annual report on progress)
Waiver
Paediatric Committee