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
  \[\Rightarrow\] 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
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)

CHMP members (5)

Patient/family and health-care professionals (3 + 3)

Experts from National Competent Authorities (22) + 2 EEA
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

• Is to be agreed upon and/or amended by the Paediatric Committee (PDCO)

• Is binding on company
Paediatric Investigation Plan Guideline?

A Commission Guideline *under preparation*:
Includes modalities on

- PIP requests
- Waiver requests
- Deferrals
- 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), 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
Overview PIP procedure

1st discussion
PDCO
Day 30

2nd discussion
PDCO + OE
Day 60

Day 61
Update Sum Report

Stop Clock

~3 months

Start Clock

3rd discussion
PDCO
Day 90

Adoption of Opinion

OE= oral explanation

60 days

Day 1
After Validation, Sum Report

Adoption of Opinion,
OR
List of Issues

OE
Applicant’s request for a Waiver

Full Waiver

PDCO

YES

Waiver

NO

REFUSAL

PIP

Partial waiver

± deferral

NB: full waiver= no reward

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Applicant’s request for a PIP

- PIP ± Partial waiver
- PDCO
  - YES ± Partial waiver
  - NO Full WAIVER

- PIP ± Partial waiver
  - new PDCO agreement ± Partial waiver

NB: full waiver = no reward
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
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
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
Timing Consultation of Paediatric Committee

- **Non-clin**
  - Phase 1
  - Phase 2
  - Phase 3
  - Post approval

- Paed. Investig. Plan
- PIP Amendments
- Compliance
- Deferral
- Waiver

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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
Compliance check: Possible scenarios (new products)

**PIP Decision**

- MA validation
- MA

**Completion measures**

- Waiver
- Completion of Measures at MAA
- Deferral
- Partial deferral

**Annual reports on deferral**

**Partial completion measures**

**Reward:** If compliant
- + Results in SPC
- + Authorisation in all MSs
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
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
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)
Transparency Measures

- **Database of Paediatric Trials (EudraCT)**
  - Protocols
  - Results
  - Studies previously performed (+/- published)

- **Database of authorised Products in EU (EudraPharm)**
  - Link to results of studies

- **Medicinal Product information**
  (waivers & deferrals, compliance, results)

- **Name and Praise/Name and Shame by European Commission**
Other measures

- Inventory of use in children in Member States
- Inventory of Paediatric Needs by Paediatric Committee

- 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
Timeline of Implementation

- **Immediate (as of Entry into force, 26 January 2007)**
  - Free Scientific Advice

- **6 months from entry into force (26 July 2007)**
  - Establishment of Paediatric Committee
  - Submission of PIP request
  - Paediatric Use Marketing Authorisation provisions apply

- **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
Conclusions

... better medicines for children!