The Paediatric Regulation
a perspective from the European Medicines Agency

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Current paediatric 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 fully tested and evaluated

- Risks:
  - Inadequate dosing: adverse reactions, inefficacy
  - Improper formulation
  - Delayed access to innovative medicines
The background

- Clinical trials in children are more difficult
- Children require specific formulations
- Paediatric indications are not profitable for industry
- Fear of liability of use in children
The background

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

• “A child is not a small adult”, data in adults can not be extrapolated to children

• Many medicinal products are not authorised for use in children

• Therapeutic needs of children unmet by currently authorised medicinal products

Market force alone have proven insufficient
The Paediatric Regulation


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The Objectives

- Improve the health of children
  - Ensure high quality, ethical research into medicines for children
  - Increase availability of authorised medicines for children
  - Improve information available
- Without
  - subjecting children to unnecessary trials
  - delaying the authorisation of medicines for use in adults
Main pillars of the Regulation

• A set of obligations, rewards and incentives
  – For new and on-patent products
  – For off-patent products

• Paediatric Investigation Plan (PIP)

• Paediatric Committee (PDCO)

• A series of other tools
  for information, transparency, and stimulation of research

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Main pillars of the Regulation

• A set of obligations, rewards and incentives
  – future products, not yet authorised
  – products already authorised (on patent or off-patent)
New products

• Currently unauthorised products
  – **Obligation**
    to submit results compliant with agreed Paediatric Investigation Plan (PIP) at time of marketing authorisation application (unless waiver or deferral)

  – **Reward:**
    6-month extension of the patent protection (Supplementary Protection Certificate) - IF compliance, authorisation in all Member States, and information in Product Information
On patent products “Recent”

• Authorised products with a patent

  – Obligation
    to submit results compliant with agreed Paediatric Investigation Plan (PIP)
    at time of application for a new indication, new route of administration, or new formulation unless waiver or deferral

  – 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
Off-patent products “old”

- **Optional Procedure**
  Paediatric Use Marketing Authorisation (PUMA)
  - Paediatric indication and formulation
  - PIP and compliance
  - Brand name can be retained

- **Reward**: 10 years data protection/exclusivity

- **Community funding for studies into off-patent medicinal products**
  - Framework Programme(s) FP7 30 million Euros for the 2 first years
  - Link with priority list for studies into off-patent paediatric medicinal products (EMEA website)

  *i.e.*, long term safety of topical steroids used in atopic dermatitis

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Orphan drugs

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

- Reward: 2 years of market exclusivity added to existing 10 years
Incentive: Free EMEA scientific advice

- Prior to submission of a PIP or during PIP implementation process
- Including advice on pharmacovigilance and risk management systems
- Not binding on Paediatric Committee
Obligation

• to market,

• or transfer of MA or consent to use data if product withdrawn from the market
Main pillars of the Regulation

- Paediatric Committee (PDCO)
- Paediatric Investigation Plan (PIP)
Paediatric Committee (PDCO)

CHMP members (5)

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

Experts from National Competent Authorities (22) + 2 EEA

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Paediatric Committee (PDCO)

• Primarily responsible for the scientific assessment and agreement of the PIP

• First meeting held at the EMEA on 4-5 July 2007
Paediatric Investigation Plan

• Basis for the development and authorisation of a medicinal product for the paediatric population

• Provides detailed timing and measures to demonstrate:
  – Quality, Safety and Efficacy
  – In different paediatric subsets from birth to adolescence

• Ensure integration of the paediatric development in development program for adults
European Commission Guideline:

- on the **format and content** of applications for agreement or modification of a paediatric investigation plan
- and **requests for waivers or deferrals**, 
- and concerning the operation of the **compliance check**, and on criteria for assessing significant studies.

Overview PIP procedure

1st discussion
PDCO
Day 30

2nd discussion
PDCO + OE
Day 60

Stop Clock

Day 1
After Validation, Sum Report

Start Clock

~3 months

60 days

Adoption of Opinion, OR List of Issues

Day 61
Update Sum Report

3rd discussion
PDCO
Day 90

Adoption of Opinion

OE

60 days

OE= oral explanation
Applicant’s request for a Waiver

NB: full waiver = no reward

YES

Waiver

Full Waiver

PDCO

NO

REFUSAL

Partial waiver ±

Draft list of waivers i.e. Alzheimer disease

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Main pillars of the Regulation

• A series of other tools for information, transparency, and stimulation of research
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
Regulation reinforces existing measures to monitor adverse drug reactions especially long-term reactions

- Guideline on conduct of pharmacovigilance for medicines used by the paediatric population
- Guideline on risk management systems for medicinal products for human use
- Paediatric centres in the European Network of Centres of Pharmacoepidemiology and Pharmacovigilance (ENCEPP)
EMEA Paediatric Research Network

- link 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
Other measures

• Inventory of use in children in Member States

• Inventory of Paediatric Needs by Paediatric Committee Preliminary lists

• Symbol on any medicinal product authorised for children (pre and post Regulation)
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 PDCO (1st meeting July 2007)
- 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 (on-patent products)
- Or EMEA decision granting a waiver or deferral

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Conclusions

... better medicines for all children!
EMEA website: medicines for children

Questions on authorisation of paediatric medicines
Email to the Paediatric team at paediatrics@emea.europa.eu

Thanks to my colleagues from the EMEA Paediatric Team
Scientific Advice, Paediatrics & Orphan Drugs Sector
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