Paediatric Medicines
The New European Legislation

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The current situation in the EU

- 20% of the EU population is aged less than 18 years (100 million)
- Children are not one single population
- Premature and term neonates, infants, children, adolescents (ICH E11)
- > 50 % of medicines used in children have not been tested and evaluated in children
- Paediatric intensive care: 90%

The current situation in the EU

Consequences:

- Appropriate dose?
- Increased risk of adverse effects (overdosing)
- Ineffective treatment (underdosing)
- Use of improper formulations
- Delay in access to innovative medicines

Why do we need a legislation?

- A child is not a small adult
- Clinical trials in children are more complex (refusal parents, small populations, costly, "unethical)
- Children require specific formulations
- Paediatric indications not profitable

- The US example: incentives stimulate research
- US data not necessarily submitted in Europe

Legislative Process

- First European initiatives in 1997
- First and Second Reading in the European Parliament and Council between 2004-2006
- Final adoption 01 June 2006
- Entry into force autumn 2006
- Regulation directly applicable and obligatory in all its elements for all 25 EU Member States

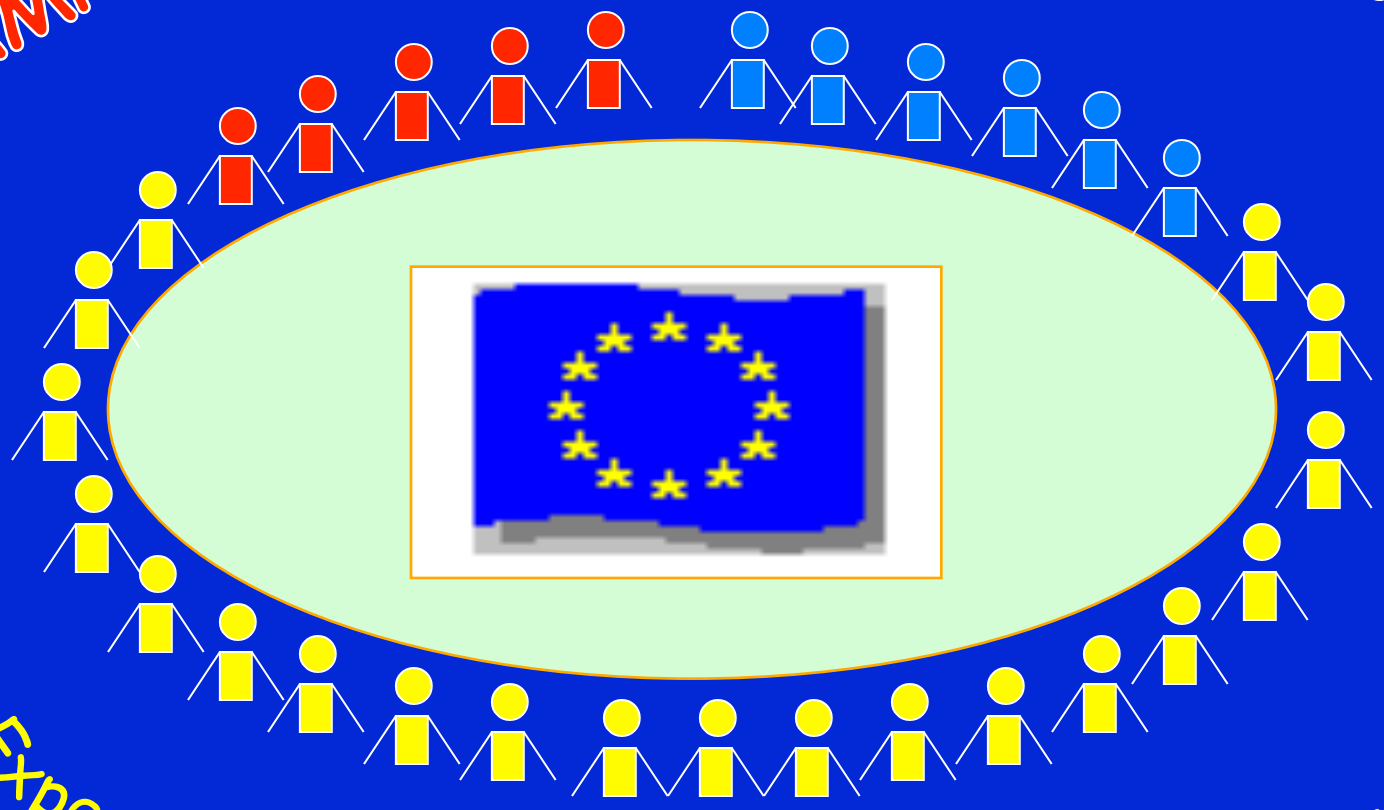
Objectives of the Regulation

- Improve the health of children
  - Increase high quality, ethical research into medicines for children
  - Increase availability of authorised medicines for children
  - Increase information on use of medicines in children
- Achieve the above
  - Without unnecessary studies in children
  - Without delaying authorisation for adults

Main pillars

- Creation of a Paediatric Committee at the EMEA
- Measures for patent protected medicinal products
- Measures for off-patent medicinal products
- Paediatric Investigation Plans (PIP)
- Additional measures

Paediatric Committee



Paediatric Committee

- Expertise in all aspects related to medicines for children (paediatric research, pharmacology, ethics…..)
- Potential therapeutic benefit of studies in children
- Avoid unnecessary studies in children
- Avoid any delay in the authorisation of medicines for other populations

Paediatric Committee

Assessment of:

- Paediatric Investigation Plans (PIP)
- Requests for waivers and deferrals
- Compliance with PIP's
- Assess data on Safety, Efficacy and Quality
- Support various additional measures laid down in the Regulation

Rewards, Incentives and Requirements

Dependent on the current status of the product

- Patent protected new products
- ‘Old’ products without patent protection
- Orphan drug

New products

Patent-protected products

- Obligation to submit results of studies according to an agreed Paediatric Investigation Plan (PIP)
- At time of marketing authorisation or variation application

Reward:

- 6-month extension of the Supplementary Protection Certificate (= patent protection)

‘Old’ products

Off-patent products not covered by a patent or supplementary protection certificate

- Paediatric Use Marketing Authorisation (PUMA)
- ***New type of MA!***
- Includes paediatric formulation
- PIP required
- Optional

Old products

Incentive:

- 10 years of data protection: (*as for new products*)
- Use of existing brand name (brand recognition)
- Superscript of a symbol (applies to all products with a paediatric indication)

Orphan Medicinal Products

- 15-20 % of rare diseases only affect children, 55 % affect adults and children

Requirement:

- Submission of studies according to an agreed Paediatric Investigation Plan

Reward:

2 years extra market exclusivity added to existing 10 years

Rewards, Incentives and Requirements

- Rewards will be granted even if results fail to lead to the authorisation of a paediatric indication

Obligation:

- Include study results in the SmPC and, if appropriate, in the package leaflet
- Authorisation in all Member States of the European Union mandatory

Paediatric Investigation Plan

- Document upon which the development and authorisation of a medicinal product for the paediatric population will be based
- Include details of the timing and the measures proposed to demonstrate:
  - Quality
  - Safety
  - Efficacy

MA conditions

Paediatric Investigation Plan

- Includes measures to adapt formulation
- Considering different subsets of the paediatric population
- Assessment and agreement by the Paediatric Committee
- Binding to receive reward
- Can be amended
- Justification for waivers and deferrals
- Reference ICH E11

Waivers

- Product likely to be ineffective or unsafe in all or part of the paediatric population
- Disease occurs only in adults
- No significant therapeutic benefit over existing treatments for children
- For one or more subsets of the paediatric population
- For one or more specified indications

Deferrals

- Request to defer initiation or completion of some or all the measures set out in the PIP
- Request from applicant or Paediatric Committee
- For part or all paediatric subpopulations
- To ensure that studies in children are safe and do not delay the authorisation for adults.

Other measures

Free scientific advice

- On design and conduct of studies, pharmaco-vigilance measures

Inventory of use in children

- EU Member States to collect available data on all existing uses of medicinal products in children (within 2 years)
- Assessment by the Paediatric Committee

Inventory of therapeutic needs

- Identifying research priorities in the EU

Other measures

European paediatric research network

- To link together existing networks, investigators and centres with specific expertise in the performance of studies in the paediatric population

European Database of clinical trials (EudraCT)

- Public access to paediatric information and study results
- Transparency of EudraCT for paediatric data

Other measures

Community funding for studies into off-patent medicinal products

- EU Framework Programmes
- Amount?
- Link to identified needs / research priorities

Intention to withdraw product from the market

- After having benefited from incentives/rewards
- Transfer of Marketing Authorisation
- Access to data

Post-authorisation requirements

- Place the product on the market within two years (taking into account the paediatric indication)
- Obligation to ensure the follow-up of efficacy and safety
- In cases of particular cause of concern
  - Long term follow-up of safety
  - Risk management system
  - Risk minimisation plan
  - Post-authorisation studies

Conclusions

- Slow regulatory process (8 years)
- Challenge for all stakeholders involved
- Fundamental progress towards better medicines for children in Europe
- Stimulation of innovation and research in Europe

Websites

- **EMEA**: www.emea.eu.int
- **European Union**: www.europa.eu.int
- **Legislation**: http://pharmacos.eudra.org (Regulation and explanatory texts)
- **DG Research**: www.cordis.lu

Abbreviations

CHMP	Committee for Human Medicinal Products
EP	European Parliament
EUDRACT	European Database on Clinical Trials
FP7	7th Framework Programme
ICH	International Conference on Harmonisation
NCA	National competent authorities
MA	Marketing authorisation
MS	Member States
PEG	Paediatric Expert Group/Working Party
PIP	Paediatric Investigation Plan
PUMA	Paediatric Use Marketing Authorisation
SmPC	Summary of Product Characteristics