

Global Pediatric Drug Development and The European Pediatric Initiative: A Brief Overview

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The European context: regulatory framework

- **27 Member States:**

(Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, The Netherlands, Portugal, Spain, Sweden, United Kingdom, Estonia, Latvia, Lithuania, Czech Republic, Slovak Republic, Poland, Hungary, Slovenia, Malta, Cyprus, Bulgaria & Romania)

- **EEA countries:** Norway, Iceland, Liechtenstein

- **Observers:** Bulgaria, Romania

- **EFTA Switzerland**

23 languages!



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The European context: regulatory framework

- EMEA is not an FDA for Europe!
- Member States have pooled their sovereignty for authorisation of medicines
- EMEA coordinates the existing scientific resources of Member States
- An interface with all partners
- All parties linked by an IT network (EudraNet)

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The European Regulatory Framework

Centralized procedure



1 MAA

Max 210 days

**1 Evaluation by
scientific
committee
(CHMP)**



1 authorisation

**1 product information
(Summary of Product
Characteristics, Labelling,
Package Leaflet)**

23 languages!

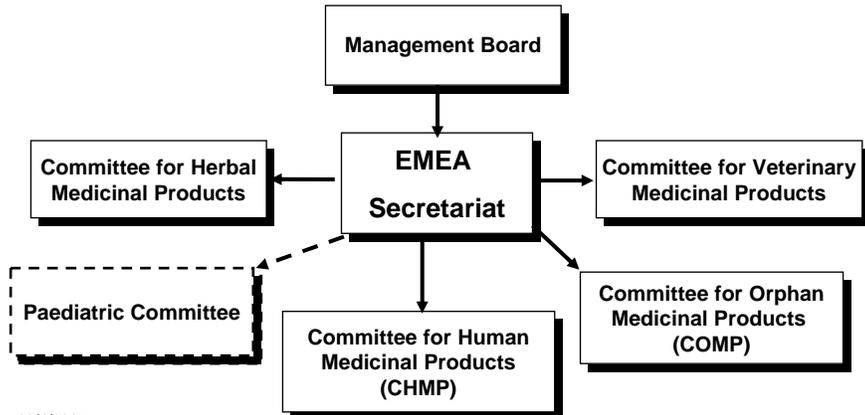
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How is the EMEA organized?

28 National Competent Authorities
+ 4000 European experts

EU institutions:
Commission - Parliament



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Outline of the proposed Paediatric Regulation

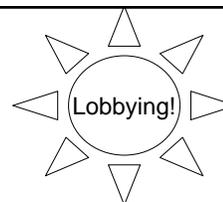
Chronology

- 1997 – EC Round Table, EMEA
- December 2000 Council Resolution; European Parliament also calling for action
- 2000-2003 – Proposal researched and Extended Impact Assessment conducted
- 2004 – Consultation
- September 2004: proposal adopted by the Commission

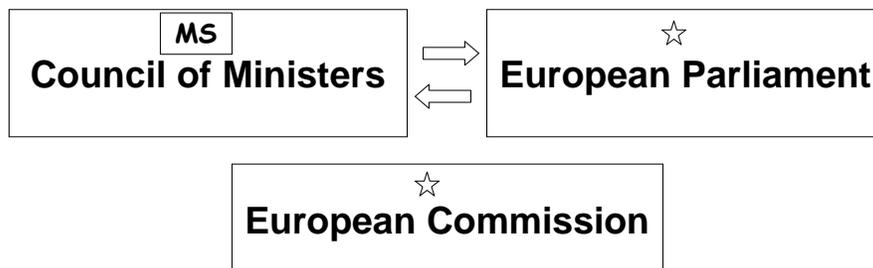
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What next?



Co-Decision process



- First reading in European Parliament and Council ended with Political Agreement (8 December 2005).
- Second reading in 2006

■ **Implementation beginning of 2007**

■ **2/4/07** *no transition phase until implementation!*

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Timelines: EU paediatric legislation

- **From entry into force (EIF): 26 January 2007**
 - Free Paediatric Scientific Advice
- **6 months from EIF (26 July 2007)**
 - Establishment of Paediatric Committee
 - Submissions of PIP/waiver requests
- **18 months from EIF (26 July 2008)**
 - Obligations for applications for Marketing Authorisation (new products), or waiver or deferral
- **24 months from EIF (26 January 2009)**
 - Obligations for application for new indications, new routes of administration, new pharmaceutical forms, or waiver or deferral

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Main pillars Of European Paediatric Development

- **Measures for patented medicinal products**
- **Measures for off-patent medicinal products**
- **Creation of a standing paediatric committee to review the paediatric plan that is now required by law for all applications**
- **Other measures (EMEA Network, Transparency, free Scientific Advice)**

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EMEA: The main areas of implementation

- The Paediatric Committee
- Paediatric Investigation Plan (PIP) and Waiver submission, process
- Paediatric Scientific Advice
- Transparency of information: trials and products
- Stimulation of research:
 - EMEA Network
 - Funding of off patent medicines studies
- Others

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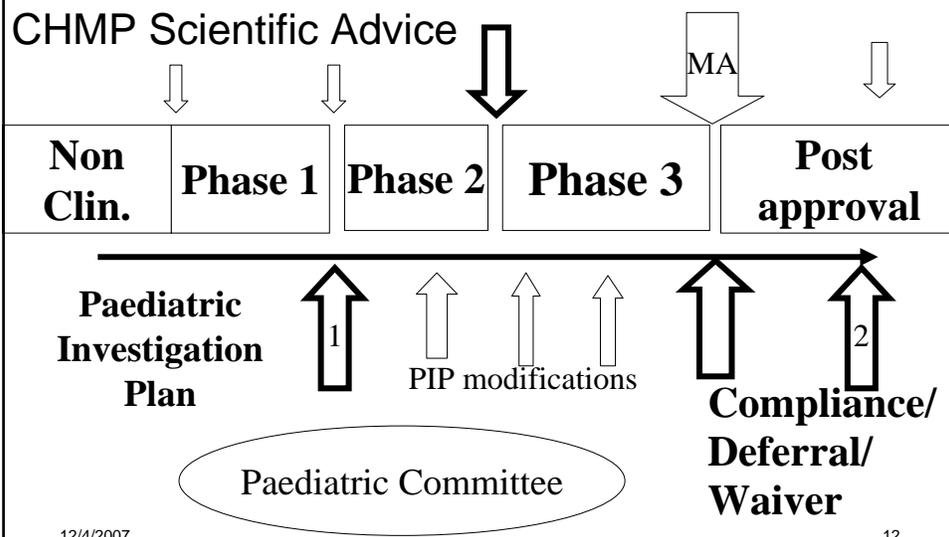
European Pediatric Legislation

- They require development of Pediatric Implementation Plan (PIP) at end of Phase 1
- A expert Pediatric Committee must approve the PIP
- Marketing Authorization Application will not be valid without an approved PIP
- PIP is required for products irrespective of Exclusivity!
- Europe does not want to subject children to trials for indications already studied in the US. They think this is unethical and a new or better questions should be asked in the PIP
- The US and Europe are implementing processes to address the need for close communication on pediatric trials.

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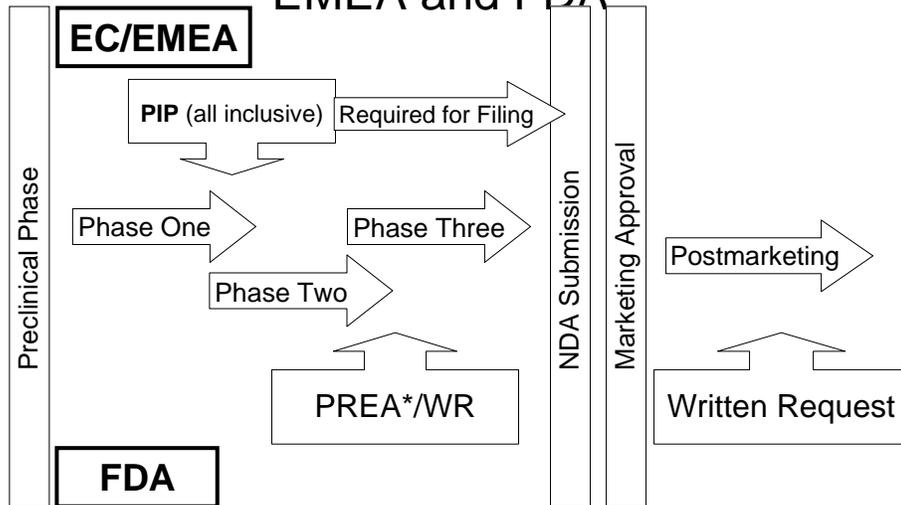
Timing of EMEA Paediatric Committee



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New Drug Development Process: EMA and FDA



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Patent-protected products

- Obligation to submit and agree upon a PIP before marketing authorisation, new indication, new pharmaceutical forms and routes of administration
- Reward:
 - 6-month extension of the Supplementary Protection Certificate (~ patent protection)
 - (Products to have Superscript of the letter "P")?

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Patent-protected products (2)

- Absence of agreed PIP, or waiver or deferral
 - = Invalid application for Marketing Authorization (MA)
- Paediatric study results can be submitted either with Marketing Authorisation Application for adults, or later (deferral of initiation or completion of studies in children)

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Old products

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

- Paediatric Use Marketing Authorisation (PUMA) ***New type of MA!***
- Covering exclusively therapeutic indications relevant for use in paediatric population(s), including the appropriate strength, pharmaceutical form or route of administration

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Old products (2)

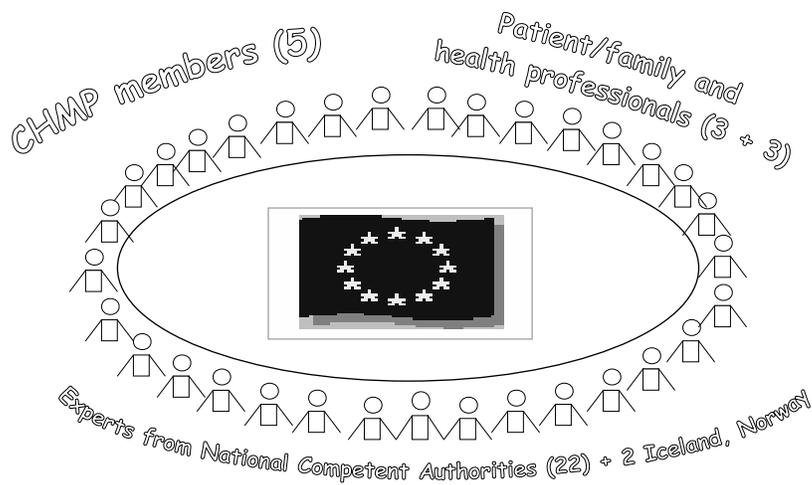
Incentive:

- 10 years data protection/exclusivity: (as for new products)
- Use of existing brand name (brand recognition)
- (Superscript of the letter “P”)?
- Refer to data in other packages without company permission

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Paediatric Committee (PDCO)



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Paediatric Committee Tasks

Assessment of:

- Paediatric Investigation Plans (PIP)
- Requests for waivers and deferrals
- Compliance with PIP
- Data for Safety, Efficacy & Quality of the medicinal product for use in paediatric population

Support:

- Survey of use, definition of paediatric needs
- Establishing of the European Paediatric Research Network
- Scientific contribution to documents, and advice on paediatric medicines

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Paediatric Investigation Plan

- Document upon which studies in children are based
- Research and development programme to ensure availability of data in the paediatric population
- To be agreed by the Paediatric Committee
- Binding to receive reward
- Can be amended



“Measures to allow the proper use of medicines in children including timing of studies and appropriate formulation”

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Other measures

Community database: transparency

- Public access to paediatric information from the European database of Clinical Trials and results (modified EUDRACT) (*not in the original proposal*) and authorised products ('Europharm')

Paediatric study programme:

- Development of European Networks
- Public funding of research into off-patent products through EU Framework Programmes (*not in the original proposal*)

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Transparency Measures

- **Database of Paediatric Trials (EudraCT)**
 - Protocols and Results
 - Submission of old studies (guidance released)
 - Guideline on paediatric fields and public fields released 3Q2007
- **Database of authorised Products in EU**
 - Pilot phase of EudraPharm, under development
- **Medicinal Product information**
(results, waivers & deferrals, compliance)
 - Guideline of Summary of Product Characteristics under revision

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A European Network

A network of existing networks

- Preliminary discussions with existing and developing networks over 2005-2006
- Proposal for Strategy to be released for public consultation soon
- Advice from Paediatric Committee when established
- Consultation with the European Commission
- Discussion and Adoption by Management Board in December 2007 (before 26 Jan 2008)

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Funding of paediatric research

- EU Community funding for studies into off-patent medicinal products
 - 7th Framework Programme
 - Current call: 6 million € max per project, total: 30 million € (deadline for bids: 18 Sept 2007)
 - Link with identified Priorities for research into off-patent medicines (List on EMEA website)

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Global Development

- Need for global development for children for ethical (and efficiency) reasons
- Under the confidentiality arrangements, preparation for systematic and regular exchange of information on Written Requests and Paediatric Investigation Plans/Waivers
- Monthly FDA-EMEA teleconferences in place
- Exchange of staff between agencies

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FDA-EMEA Exchanges

- Monthly t-con to review what PIPs have been submitted and what pediatric studies FDA does or does not have for the product
- Scientific issues relating to any of the products is developed from these t-cons
- From August to November:
 - 30 Products have been discussed
 - 6 Scientific issues have been identified in addition to a number of other important factual exchanges

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Abbreviations

- BWP: Biologicals Working Party (of CHMP)
- CHMP: Committee for Medicinal Products for Human Use
- EMEA: European Medicines Agency
- EUDRACT: European Database of Clinical Trials
- Eudrapharm: future Database of all authorised (national and Community) medicinal products in the EU EWP: Efficacy Working Party (of CHMP)
- FDA: Food and Drug Administration (USA)
- PEG: Paediatric Working Party (previously Expert Group)
- PhVWP: Pharmacovigilance Working Party
- PIP: Paediatric Investigation Plan
- QWP: Quality Working Party SA: Scientific Advice
- SAWP: Scientific Advice Working Party (of CHMP)
- SWP: Safety (non clinical) Working Party (of CHMP)

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Websites

- EMEA www.emea.eu.int (+ links to EU national agencies)
- European Union www.europa.eu.int
- DG Enterprise pharmacos.eudra.org
- DG Research www.cordis.lu