CONSORZIO PER LE VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE

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REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 12 December 2006

ON MEDICINAL PRODUCTS FOR PAEDIATRIC USE

and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

Prof. ssa Adriana Ceci

The current situation

Children are not little adults!

Less then 20-30% of marketed drugs are approved for use in children

The percentage is changing among drug categories and paediatric ages

Less than 30% of the paediatric approved drugs have included a paediatric development into registrative documentation.

Few paediatric ages are completely studied and Newborns are generaly excluded by the trials

FDA Iniziatives

- **1980 and 1990**
  - **Voluntary based initiatives to encourage the pharmaceutical industry to research medicines for children (unsuccessfully)**
- **1998 (overturned 2002 and passed again 2003)**
  - **Paediatric rule: requires companies to perform paediatric studies for new and already marketed medicinal products if the product is likely to be used in paediatric patients or if it would provide a meaningful therapeutic benefit over existing treatments.**
- **1997**
  - **Paediatric exclusivity (FDAModernisation Act) provides an incentive (6 months of further market exclusivity) for companies who perform clinical studies according to a written request submitted to the FDA. The incentive is granted irrespective of whether the results are positive or not.**
- **2002**
  - **Best Pharmaceuticals for Children Act includes a requirement to develop a prioritised list of medicines for which paediatric studies are needed. In addition, the act establishes a fund for the study of medicinal products for which there is no patent protection or market exclusivity.**

FDA Iniziatives Effects

- **1980 and 1990**
  - **none.**
- **1998**
  - **Paediatric rule: 12 labelling changes impacting on the safe and effective use of products**
- **1997**
  - **Paediatric Exclusivity: as of February 2004, 63 new paediatric labels and 661 studies requested**
- **2002**
  - **Best Pharmaceuticals for Children Act: more than 300 pediatric studies and more than 115 products have undergone labeling changes for pediatric use.**

Drugs to Which FDA has proposed/request studies

Review Division	Proposed Pediatric Study	Written Requests *
DCRP (Division of Cardiovascular Rental Drug Products)	50	35
DNP (Division of Neurology Products	67	46
DPP (Division of Psychiatry Products)	9	4
DDOP (Division of Drug Oncology Products)	36	40
DMIHP (Division of Medical Imaging and Hematology Products)	14	6
DAARP (Division of Analgesics, Anesthetics, and Rheumatology Products)	51	32
DGP (Division of Gastroentereology Products)	45	20
DMEP (Division of Metabolism and Endocrinology Products)	103	42
DAIOP (Division of Anti-Infective and Ophthalmology Products)	29	34
DAVP (Division of Anti-Viral Products)	30	35
DDDP (Divisioin of Dermatology and Dental Drug Products)	38	17
DNCE (Division of Nonprescription Evaluation)	8	5
DPAP (Division of Pulmonary and Allergy Products)	27	19
DRUP (Division of Reproductive and Urologic Products)	14	6
DSPTP (Division of Special Pathogen and Transplant Products)	20	15
TOTAL	**541**	**356**

FDA Iniziatives Effects

Drugs to Which FDA has Granted Pediatric Exclusivity for Pediatric Studies under Section 505A of the Federal Food, Drug, and Cosmetic Act (updated 2008)

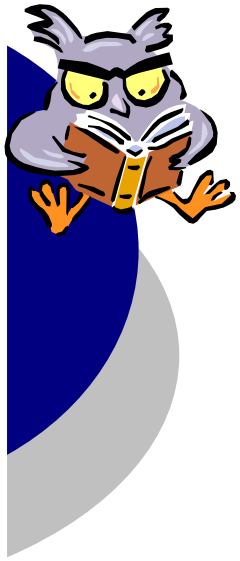
- **Total Exclusivity Determinations = 158**
- **Total Approved Active Moieties Granted Exclusivity = 139**
- **Total Approved Drugs Granted Exclusivity = 144**

→ ***Despite the trends towards globalization the measures taken in the US has brought little benefit to the children of Europe.***

→ ***International companies do not appear to be willing to voluntarily submit data collected in the US to support the authorisation of paediatric indications in the EU.***

European Initiatives

- EMEA - EC Round Table (Dec 1997)
- ICH Guideline E11 (2000)
- French Memorandum (July 2000)
- Council Resolution in (Dec 2000)
- Consultation with MS from Nov 2001 to Jan 2004
- Consultation Paper (Feb 2002)
- Reflection Paper (Nov 2002)
- Draft of Draft Regulation for Consultation by Member States (early 2003)
- Adoption of the Council common position 15763/3/2005 – C6-0087/2006 (Mar 2006)
- EP 2nd read approval (June 2006)
- Formal approval by the Council
- Entry into force January 1° 2007



The EU legislative process

- Regulation (EC) No 1901/2006 (OJ L 378, 27-12-2006)
- Regulation (EC) No 1902/2006 (OJ L 378, 27-12-2006)

REGULATION OF THE EUROPEAN PARLIAMENT & COUNCIL ON MEDICINAL PRODUCTS FOR PAEDIATRIC USE

This Regulation lays down rules concerning the development of medicinal products for human use in order to meet the specific therapeutic needs of the paediatric population, without subjecting children to unnecessary clinical or other trials and in compliance with Dir. 2001/20/EC (art.1)

Goals & Definitions

"Paediatric population" means that part of the population aged between birth-18 yrs

- **Pretermini : sotto le 36 settimane**
- **Neonati : dalla nascita ad 1 mese di vita**
- **Lattanti : da 1 mese a 2 anni**
- **Bambini : da 2 anni a 11 anni**
- **Adolescenti : da 12 a 17 anni**

Mandatory system for new products and variations

Voluntary system for old products

MEDICINAL PRODUCTS FOR PAEDIATRIC USE

"Medicinal product authorised for a paediatric indication":

medicinal product which is authorised for use in part or all of the paediatric population and in respect of which the details are specified in the SmPC drawn up in accordance with art 11 of Dir. 2001/83/EC.

- **Drugs for which a specific paediatric indication exists (4.1)**
- **Drugs for which a specific paediatric indication exists in some paediatric ages (4.1)**
- **Drugs for which an approved dosage by age exists (4.2)**

REGULATION OF THE EUROPEAN PARLIAMENT & COUNCIL- MAJOR INNOVATIONS

- **Paediatric Committee and PIP**
- **Inventory of therapeutic needs** (research priorities)
- ***European CT database*** (data from third countries too)
- **Ad hoc pharmacovigilance studies** (long term follow-up)

- **Inventory of all medicinal products authorised for paediatric use**
- **European Network for Paediatric Research**
- **Incentives and Research Founds** (provided by the E.C. and Member States)

26 July 2008

in development and to be authorised

- **New products**
- **Modifications of products still covered by patent**

26 January 2009

Authorised products no longer covered by patent OLD PRODUCTS

Which products ?

26 July 2007

in development and to be authorised

- **New products**
- **Modifications of products still covered by patent**

OBLIGATION:

Paediatric Investigation Plan (PIP)

(or **waiver** or **deferral**)

before a MA application for:

- new (including paediatric) indications
- new route of administration
- new pharmaceutical form (dosage form)

New Products obligations

Currently unauthorised products

26 July 2008

- Obligation to submit results of agreed Paediatric Investigation Plan **(PIP)** at time of marketing authorisation application, or Waiver/Deferral

  ➔ **OR INVALID APPLICATION**

Already authorised patented products

- Obligation to submit results of agreed Paediatric Investigation Plan **(PIP)** at time of application for new indication, new route of administration, new formulation, or Waiver/Deferral

  ➔ **OR INVALID APPLICATION**

26 January 2009

Paediatric Investigation Plan (PIP)

- A research and development program
- Ensure availability of paediatric data & and results ➔ basis for evaluation of the MA application
- Specify timelines, including Deferrals
- Reference to ICH E11

Paediatric Investigation Plan (PIP)

The Commission Guideline (Draft version Jan2007) is under preparation:

It includes modalities on

- *PIP requests*
- *Waiver requests*
- *Deferrals requests*
- *Key elements for PIP Decision*
- *Proposal for Significant Studies*
- *Compliance check*

Version January 2007

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

PIP Waivers/Deferrals

- Waiver of class, or indications or specific product
- Deferral, of initiation of studies and/or completion

- On initiative from applicant or PDCO
- For all or part of PIP
- Annual report to monitor deferred studies

Waivers

- specific medicinal product or class of medicinal products likely to be **ineffective** or **unsafe** in children
- disease or condition occurs **only in adults**
- the medicinal product does **not represent a significant therapeutic benefit** over existing treatments for paediatric patients

EUROPEAN MEDICINES AGENCY DECISION

of 3 December 2007

on a class waiver on conditions in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use as amended and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency formulated of its own motion on 23 November 2007 in accordance with Article 12 of Regulation (EC) No 1901/2006 as amended,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

Article 1

A waiver for

- Treatment of oropharyngeal epithelial carcinoma (excluding nasopharyngeal carcinoma)
- Treatment of lung carcinoma (small cell and non-small cell carcinoma)
- Treatment of breast carcinoma
- Treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours)
- Treatment of endometrial carcinoma
- Treatment of prostate carcinoma (excluding rhabdomyosarcoma)
- Treatment of hairy cell leukaemia
- Treatment of multiple myeloma
- Treatment of Alzheimer's Disease
- Treatment of vascular dementia and vascular cognitive disorder/impairment
- Treatment of organic amnesic syndrome (excluding amnesic syndrome caused by alcohol and other psychoactive substances)
- Treatment of amyotrophic lateral sclerosis
- Treatment of Parkinson's Disease (non-juvenile)
- Treatment of age-related macular degeneration
- Treatment of menopausal and other perimenopausal disorders
- Treatment of Chronic Obstructive Pulmonary Disease (COPD) (excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after (bone-marrow) transplantation),

the details of which are set out in the Opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 2

This decision is applicable to all

Deferrals

- request submitted at PIP time
- scientific and technical justification
- granted when:
  - it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population
  - studies in the paediatric population will take longer to conduct than studies in adults
- submitting an annual report to EMEA providing an update on progress with paediatric studies

per ottenere una deroga occorre farne richiesta all'EMEA

Entro 60 gg dal ricevimento domanda il Paediatric Board

Adotta un parere

la lista può essere rivista e emendata dal **PB** in qualsiasi momento

EMEA mantiene un elenco di tutte le deroghe concesse e ne pubblica l'elenco sul proprio sito web

In caso di revoca di una deroga, le richieste di AIC non si applicano per un periodo di 36 mesi a decorrere dalla data di rimozione dall'elenco.

Paediatric Committee (PDCO)

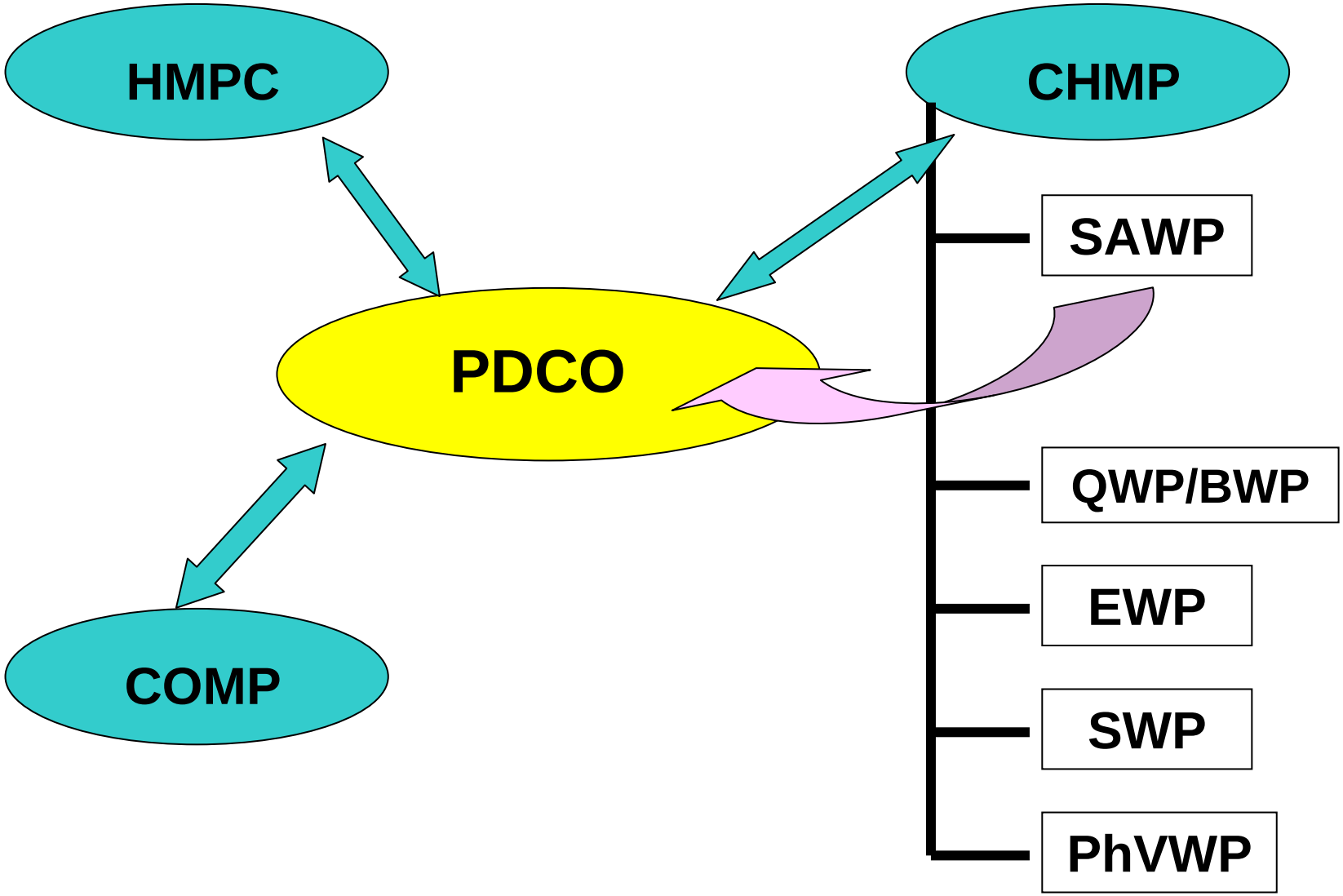
set up on July 2007

- **Expertise and competence** in medicines for paediatrics
- **No financial or other interests** in the pharmaceutical industry
- Primarily **responsible** for the assessment and agreement of **PIP**
- Primarily **responsible** for the system of **waivers** and **deferrals**
- Responsible in evaluating **potential significant therapeutic benefits**
- **Responsible** in order to avoid unnecessary studies
- **Responsible** in order to avoid **any delay** in MA (other populations) as a result of the requirements for studies in children

Paediatric Committee

- **5 members** of the CHMP;
- **1** person appointed by each MS whose national competent authority is not represented through the members appointed by the CHMP;
- **6 members** appointed by Commission, after consulting the EP (public call for expressions of interest) representing:
  - **healthcare professionals (3)**
  - **patient associations (3)**

PDCO & other groups



Orphan Drugs:
10-year period of market exclusivity extended to
12 years

- **New products**
- **Modifications of products still covered by patent**

REWARDS

Patent or Supplementary Protection Certificate:
extension of 6 months
in the MS where is authorised or authorisation is in progress

OBLIGATION:
Paediatric Investigation Plan (PIP) ….

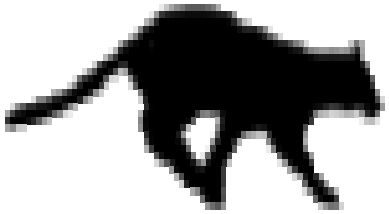
information in SmPC and authorisation in all MS
also for failure in leading to the authorisation of a paediatric indication, but the results of the studies conducted in SPC and/or PL

Authorised products no longer covered by patent
OLD PRODUCTS

PUMA

(Paediatric Use Marketing Authorisation)
covering exclusively therapeutic indications, appropriate strength, pharmaceutical form or route of administration which are relevant for use in the **paediatric population**

26 July 2007



Data Protection
for research, development and authorisation

Authorised products no longer covered by patent
OLD PRODUCTS

REWARDS

Incentives provided by Community (Framework Programs) or by MS

OPTIONAL:
Paediatric Use Marketing Authorisation (PUMA)

Brand name can be retained

Community 7th Framework Program Cooperation-Health

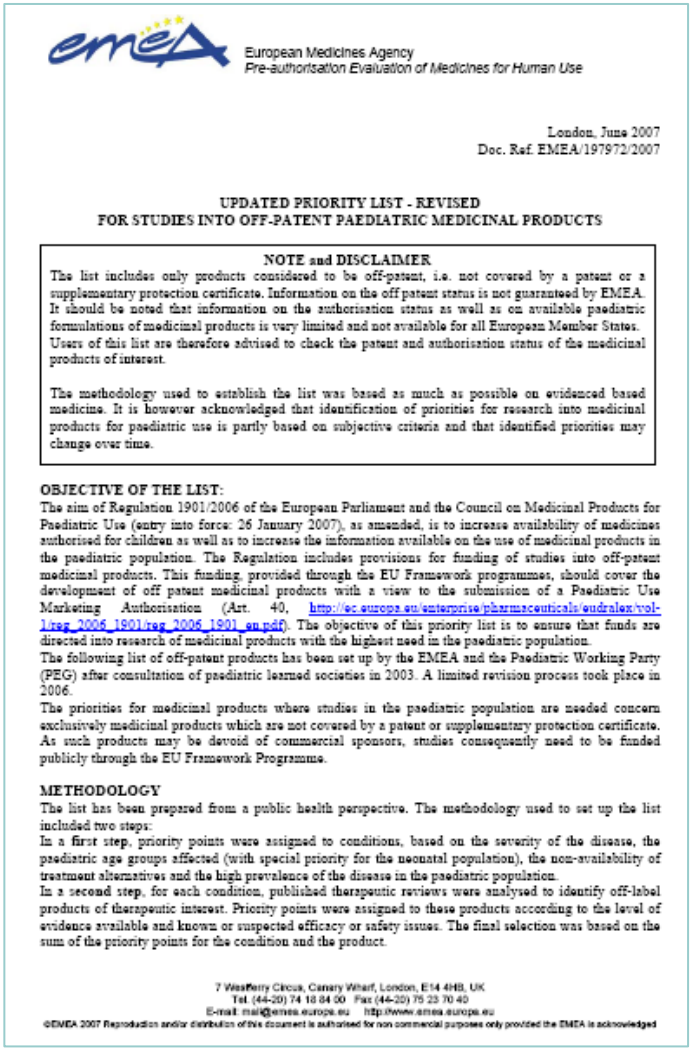
Paediatric medicinal products

HEALTH-2007-4.2-1: Adapting off-patent medicines to the specific needs of paediatric populations

(deadline: September 2007)

Support given to studies dedicated to provide evidence for specific paediatric use of off-patent medicinal products as included in the **EMEA-PEG priority list of Off-Patent Medicinal Products**

(> 100 drugs)



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, June 2007
Doc. Ref. EMEA/197972/2007

UPDATED PRIORITY LIST - REVISED
FOR STUDIES INTO OFF-PATENT PAEDIATRIC MEDICINAL PRODUCTS

NOTE and DISCLAIMER
The list includes only products considered to be off-patent, i.e. not covered by a patent or a supplementary protection certificate. Information on the off patent status is not guaranteed by EMEA. It should be noted that information on the authorisation status as well as on available paediatric formulations of medicinal products is very limited and not available for all European Member States. Users of this list are therefore advised to check the patent and authorisation status of the medicinal products of interest.

The methodology used to establish the list was based as much as possible on evidenced based medicine. It is however acknowledged that identification of priorities for research into medicinal products for paediatric use is partly based on subjective criteria and that identified priorities may change over time.

OBJECTIVE OF THE LIST:
The aim of Regulation 1901/2006 of the European Parliament and the Council on Medicinal Products for Paediatric Use (entry into force: 26 January 2007), as amended, is to increase availability of medicines authorised for children as well as to increase the information available on the use of medicinal products in the paediatric population. The Regulation includes provisions for funding of studies into off-patent medicinal products. This funding, provided through the EU Framework programmes, should cover the development of off patent medicinal products with a view to the submission of a Paediatric Use Marketing Authorisation (Art. 40, http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2006_1901/reg_2006_1901_en.pdf). The objective of this priority list is to ensure that funds are directed into research of medicinal products with the highest need in the paediatric population.
The following list of off-patent products has been set up by the EMEA and the Paediatric Working Party (PEG) after consultation of paediatric learned societies in 2003. A limited revision process took place in 2006.
The priorities for medicinal products where studies in the paediatric population are needed concern exclusively medicinal products which are not covered by a patent or supplementary protection certificate. As such products may be devoid of commercial sponsors, studies consequently need to be funded publicly through the EU Framework Programme.

METHODOLOGY
The list has been prepared from a public health perspective. The methodology used to set up the list included two steps:
In a first step, priority points were assigned to conditions, based on the severity of the disease, the paediatric age groups affected (with special priority for the neonatal population), the non-availability of treatment alternatives and the high prevalence of the disease in the paediatric population.
In a second step, for each condition, published therapeutic reviews were analysed to identify off-label products of therapeutic interest. Priority points were assigned to these products according to the level of evidence available and known or suspected efficacy or safety issues. The final selection was based on the sum of the priority points for the condition and the product.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

Priority List Priority Points identification in Europe

Second step (to the products):

- off-label used,
- level of evidence available,
- known efficacy,
- suspected safety issues

Final step (2006)

The therapeutic need was included as defined by the PEG/Experts Groups

EMEA-PEG PRIORITY-LIST OF OFF-PATENT DRUGS FOR PAEDIATRIC STUDIES

Condition	Drugs/Class (n)	Specific needs
Migraine	3	Efficacy, Safety, Formulation
Seizures - epilepsy	1	PK, Efficacy, Safety Form(<3y9)
Solid tumours and other cancers	**27**	**Formulation, PK, Efficacy, safety**
Gastroesophageal reflux Oesophagitis Peptic ulcers	2 classes	Neonates and infants
Atopic dermatitis	1 class	Long term safety

Condition	Drugs /Class (n)	Specific needs
Obstructive lung D.	2 class	Efficacy, Safety (long-term), Formulation
BPD- Asthma	2 class	Long term safety
Tubulopathies	2	Efficacy Long-term safety
Sedation	4	All age groups
Pain (acute and chronic)	9	Formulation, Efficacy, Safety
Hypertension (chronic)	8	All age groups

EMEA-PEG PRIORITY-LIST OF OFF-PATENT DRUGS FOR PAEDIATRIC STUDIES

Condition	Drugs (n)	Specific needs
Hypertension (acute)	3	All age groups
Heart failure (acute and chronic)	12	Safety, Efficacy
Arrhythmias	3	All age groups
Hypercholesterolaemia	1 class	Familial and at-risk patients
Infections	2	Antibioresistance (Premature newborns)

Condition	Drugs (n)	Specific needs
Meningitis	1	ns
Tuberculosis	Not listed	Formulations of old products
Herpes virus (Systemic infections, encephalitis)	1	ns
HIV infection	1 class	more paediatric Formulations
Psychosis	1	Efficacy
Glaucoma-IOP	1	

Other incentives

Medicines for paediatrics be eligible for incentives provided by the **Community** or by the **Member States** to support R & D and availability

By **26 January 2008**, **Member States** shall communicate to the Commission details of taken measures

An **inventory of all incentives** updated regularly by the Commission and accessible to the public (by **26 July 2008**)

Inventories

Art. 42

MemberStates shall collect available data on **all existing uses** of medicinal products in the paediatric population and shall communicate these data to the Agency by **26 January 2009**

Art.43

The Paediatric Committee shall establish an inventory of therapeutic needs, with a view to identifying **research priorities**.

The Agency shall make the inventory public at the latest by **26 January 2010**

Therapeutic Needs- PEG Lists

	Reference	Notes
Anaesthesiology		
Assessment of the paediatric needs - Anaesthesiology	EMEA/405166/2006	
Anti-infectious therapy		
Assessment of the paediatric needs - Anti-infectious therapy with focus on antimycotics, antivirals (except HIV)	EMEA/435350/06	
Cardiology		
Assessment of the paediatric needs - Cardiovascular products	EMEA/436949/06	See also the comments received during consultation on this list: EMEA/404310/06
Chemotherapy I (Cytotoxic therapies)		
Assessment of the paediatric needs - Chemotherapy products (Part I)	EMEA/CHMP/384641/06	See also the comments received during consultation on this list: EMEA/CHMP/384188/06
Chemotherapy II (Supportive therapy)		
Assessment of the paediatric needs - Chemotherapy Products (Part II)	EMEA/CHMP/224696/06	

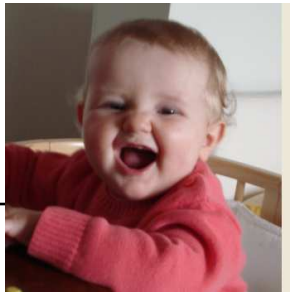
Therapeutic Needs- PEG Lists

Diabetes (Types I and II)		
Assessment of the paediatric needs - Diabetes (Types I and II)	EMEA/224688/06	
Epilepsy		
Assessment of the paediatric needs - Epilepsy	EMEA/CHMP/377147/06	See also the comments received during consultation on this list: EMEA/CHMP/377231/06
Gastroenterology		
Assessment of the paediatric needs - Gastroenterology	EMEA/527934/07	
Immunology		
Assessment of the paediatric needs - Immunology	EMEA/CHMP/381922/06	See also the comments received during consultation on this list: EMEA/CHMP/381452/06
Migraine		
Assessment of the paediatric needs - Migraine	EMEA/224515/06	

Therapeutic Needs- PEG Lists

Nephrology		
Assessment of the paediatric needs - Nephrology	EMEA/13306/07	
Obstructive lung disease		
Assessment of the paediatric needs - Asthma and other obstructive chronic lung diseases	EMEA/439727/06	
Pain		
Assessment of the paediatric needs - Pain	EMEA/CHMP/18922/05	
Psychiatry		
Assessment of the paediatric needs - Psychiatry	EMEA/288917/07	
Rheumatology		
Assessment of the paediatric needs - Rheumatology	EMEA/CHMP/234105/2005	See also the comments received during consultation on this list: EMEA/207562/06

Results -4- Therapeutic Needs Analysis



Results from Experts Group in different Therapeutic Area have been considered

EMEA PEG- Paediatric Expert Group

11 TEDDY Experts Therapeutic Groups

TEDDY- Paediatric Rare Diseases Expert Group

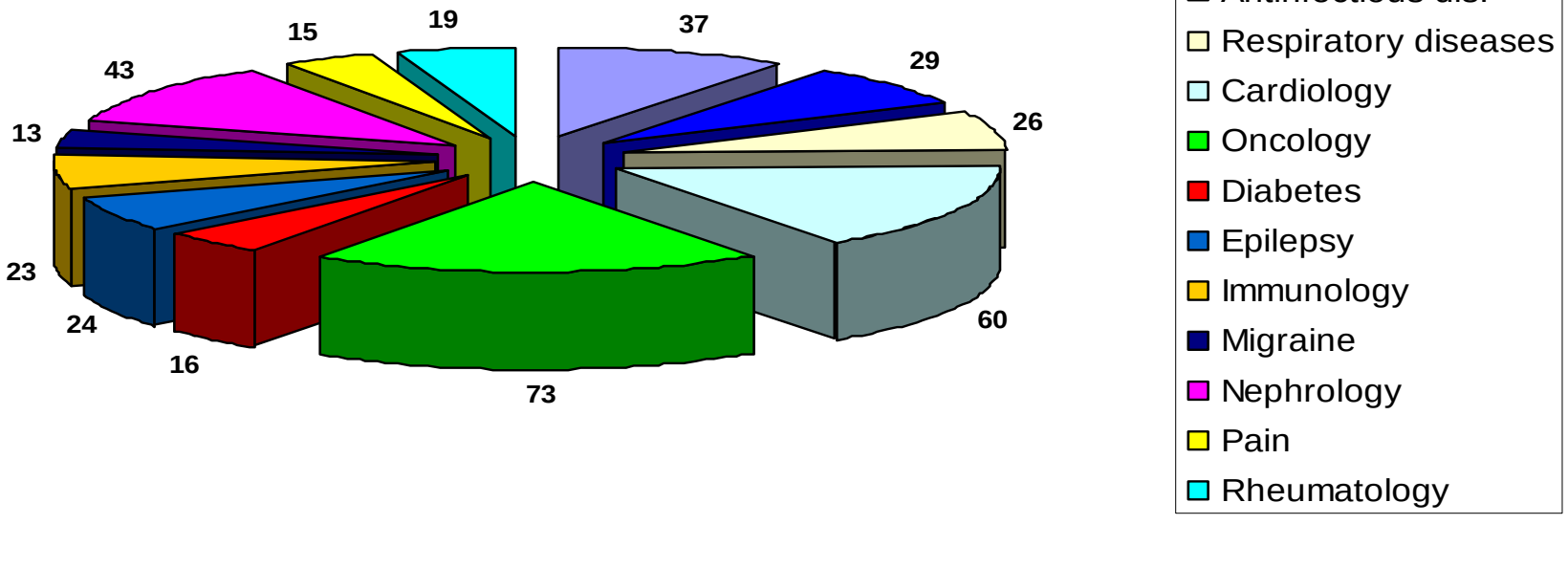
SIOP- International Society of Paediatric Oncology

European Respiratory Society (Paediatric Area)

Results -4- Therapeutic Needs Analysis

13 Therapeutic areas - 378 drugs
Paediatric 170 – No Paediatric 208

ATC Distribution

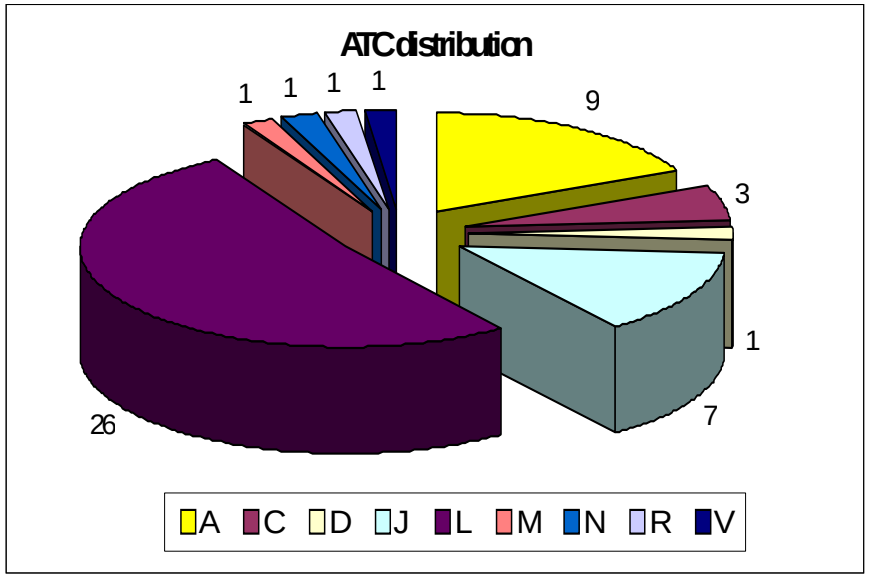


TEDDY

EMEA DRUGS (n: 50) FOR WHOM A PAEDIATRIC DEVELOPMENT IS REQUESTED

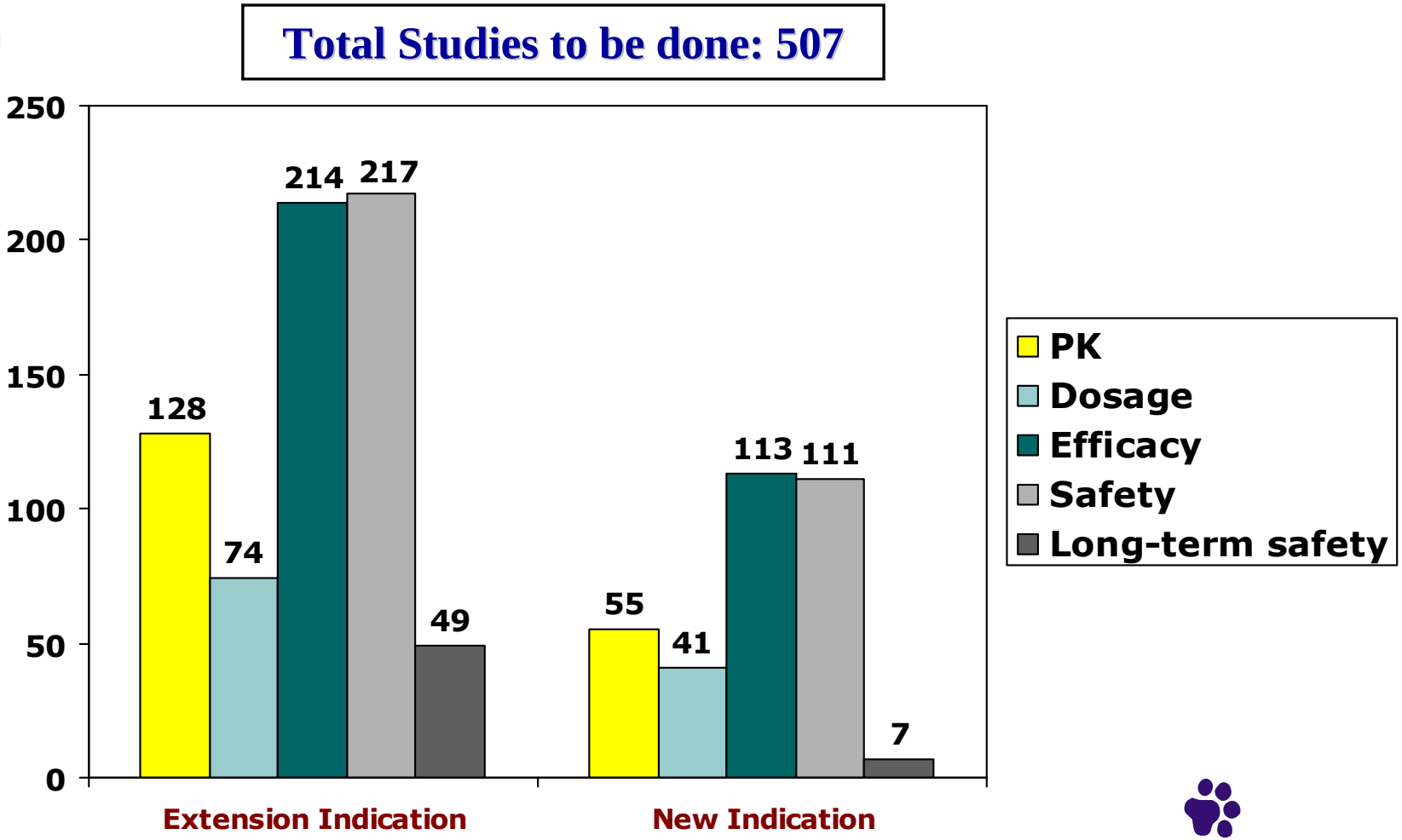
- 20 onco-immunological agents
- 8 monoclonal antibodies
- 6 Orphan drugs
- 22 extensions to paediatric age
- 7 new indications
- 11 extension by age/new indications

ATC distribution (n: 50 drugs)



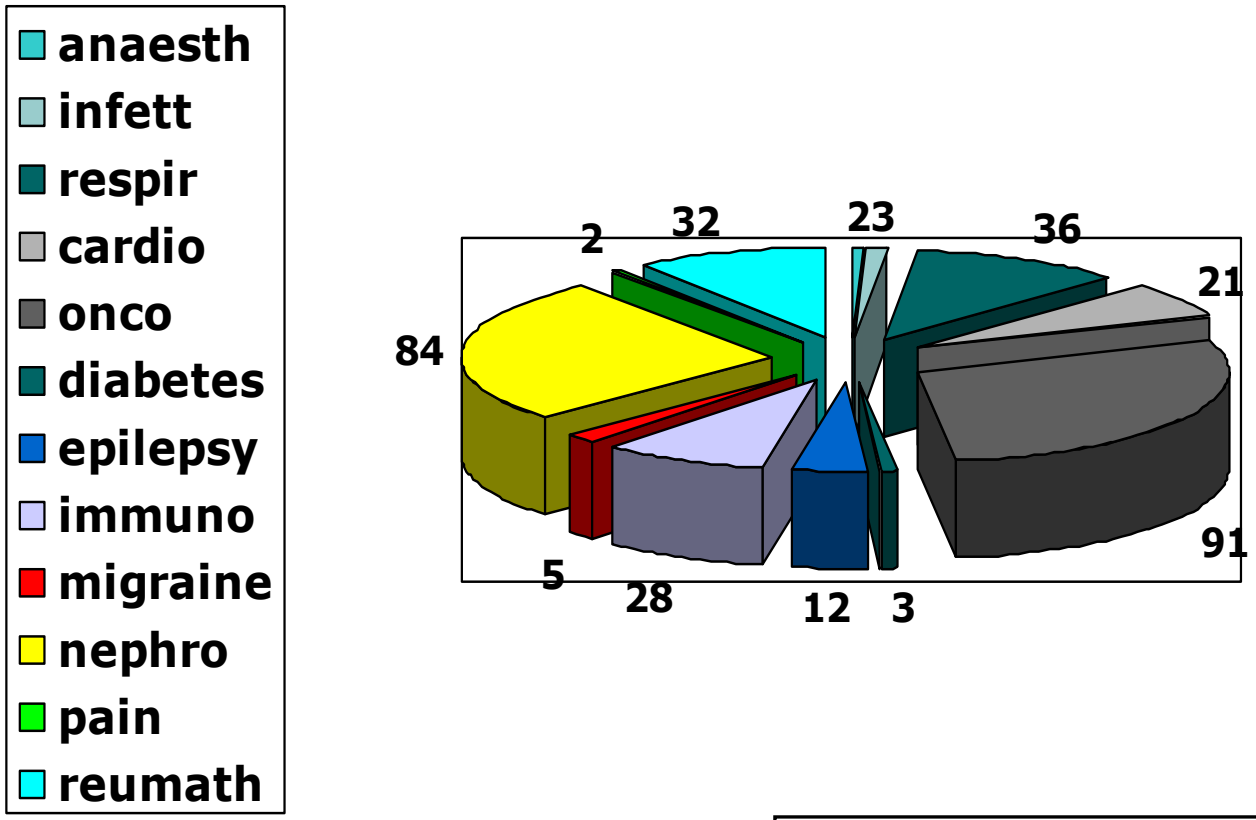
TEDDY

Results -4- New studies Needs



TEDDY

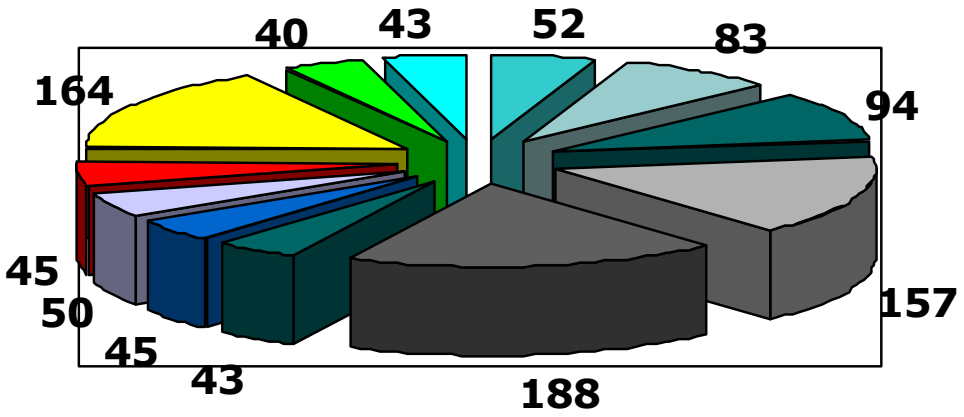
Results -4- New studies Needs



Studies for a new indication

TEDDY

Results -4- New studies Needs



Studies for paediatric exstension

TEDDY

The Future of Paediatric Medicines: Facts and Concerns

Are all these studies absolutely necessary?

Are there enough children to include in the trials in the same therapeutic area?

Who should pay for this? In particular for drugs that are still in patent and needed for children?

TEDDY

Post-authorisation requirements Pharmacovigilance

Pharmacovigilance mechanisms adapted to meet the specific challenges of collecting **safety** data in children.

Obligation to include **long term follow up** of adverse drug reactions

Post marketing data – pharmacovigilance

- **Long term follow-up safety**
- **Risk management**
- **Risk minimisation**
- **Post-authorisation studies**
- **Need for evaluation of efficacy & success of such risk management systems**

Network for the performance of clinical studies for children

Clinical trials in the paediatric population require:

- specific expertise
- specific methodology
- specific facilities

- linking existing **National and European initiatives** and study centres for competences
- facilitating co-operation and conduct of studies
- avoiding duplication of studies
- contributing to strengthening the **European Research Area** in the context of Community Framework Programmes

The Network of Paediatric Networks at the EMEA Implementing Strategy

European Medicines Agency

London, 15 January 2008
Doc. Ref. EMEA/MB/543523/2007

The Network of Paediatric Networks at the EMEA Implementing Strategy

4. Existing paediatric networks

In parallel to the meetings held at the EMEA in 2005 and 2006, an informal inventory has identified that many different paediatric networks, investigators and centres with specific expertise*[1] exist in the Community, or are under construction. The relevant networks are those with an interest in the development of medicinal products. They can be identified as:

- national networks, generally benefiting from public funding (at present 7 national networks have been identified),
- European networks publicly funded, such as TEDDY (Task Force in Europe for Drug Development of the Young) which is funded through the 6th Framework Programme,
- paediatric 'sub-speciality' networks at European level and beyond, which group centres working in the same therapeutic area (e.g. HIV infection, rheumatology),
- age-related networks (e.g. neonatal networks),
- activity or structure-related networks (e.g. community-practitioners networks, hospital-based dedicated clinical-research centres linked by a common structure, pharmacovigilance networks)
- networks including paediatric centres but not dedicated solely to paediatric research.

The inventory will be expanded and developed.

Inventories

Art. 42

MemberStates shall collect available data on **all existing uses** of medicinal products in the paediatric population and shall communicate these data to the Agency by **26 January 2009**

Art.43

The Paediatric Committee shall establish an inventory of therapeutic needs, with a view to identifying **research priorities**.

The Agency shall make the inventory public at the latest by **26 January 2010**

Inventories

Art 45

MAH should submit to the competent authorities all paediatric studies completed by the date of entry into force of the legislation (26 January 2007). These studies must be submitted by 28 January 2008.

Art. 46

Any other marketing authorisation holder-sponsored studies which involve the use in the paediatric population of a medicinal product covered by a marketing authorisation, whether or not with an agreed PIP, shall be submitted (6 months)

The competent authority may update the summary of product characteristics and package leaflet,

and may vary the marketing authorization accordingly.

Inventories: Responsibilities of MAH

- Procedural Guidance concerning submission of information about medicinal products as requested by the Paediatric Regulation (54.62 kb) (version with correct link to Q&A, Dec 2007)
- Template for submission of Information on Paediatric Studies from MAH to NCAs - line listing (10.22 kb) editable version: .xls
- Annex I : MAH Declaration
  editable version: .doc

Identification

Where a medicinal product is granted a marketing authorisation for a paediatric indication based on the results of studies conducted in compliance with an agreed PIP,

the label shall display the symbol agreed. The package leaflet shall contain an explanation of the meaning of the symbol.

By January 26th 2008 the Commission shall select a symbol following a recommendation of the PDCO

Comparison of Paediatric Drug Regulation Europe vs. United States	US	Europe	Comment
Legislation	Pediatric Research Equity Act 2003	Paediatric Regulation	
Requirements	Pediatric Advisory Committee issues Written Requests For NDAs, a pediatric waiver or investigational plan must be submitted.	Pediatric Committee will review a Pediatric Investigational Plan (PIP)	PIP is mandatory in EU for approval of the adult product. Written Requests are not mandatory for an adult approval
Off patent products	No legislation	Pediatric Use Marketing Authorization (PUMA) giving 10 years data protection	Will the PUMA prove sufficiently attractive to generic companies?

Comparison of Paediatric Drug Regulation Europe vs. US	US	Europe	Comment
Legislation	Pediatric Research Equity Act 2003	Paediatric Regulation	
Carrot	6 month period of additional market provisions during which generic competitors can not be marketed	6 month period of additional market provisions during which generic competitors can not be marketed	EU proposal based on successful US experience.
Stick	Must meet pediatric assessment per Written Request	Must have PIP	No adult approval unless PIP agreed or waived in Europe
Support for pediatric medicinal research	Funding for NICHD	No funding in the Regulation but in the EU-RFPs	Funding of scientific endeavor at a European level has proved problematic

Impatto Regolatorio del Regolamento Pediatrico

'CRITICITA'

e

INNOVAZIONI'

Differenze USA-EUROPA possono influenzare i processi di globalizzazione

Il ruolo assunto dall'EMEA (PDCO) può creare conflitti verso le Agenzie Regolatorie Nazionali

Anche nelle Procedure Decentrata e MR viene inserito un momento centralizzato (PIP)

Aumenta il potere regolatorio diminuisce la discrezionalità delle Aziende