



Ethical considerations for paediatric trials - how can Ethics Committees (ECs) in the European Member States and the Paediatric Committee (PDCO) at the European Medicines Agency work together?





## Ethical considerations for paediatric trials - how can Ethics Committees (ECs) in the European Member States and the Paediatric Committee (PDCO) at the European Medicines Agency work together?

#	Time	Agenda	Speaker	Min
--	09:00-09:05	Welcome		5
1	09:05-09:20	Role of the PDCO in the European regulatory system	Daniel Brasseur	15
2	09:20-09:35	Legal-regulatory framework for the assessment of paediatric trials in Europe and feed back on EMA meeting on third country clinical trials	Agnès Saint Raymond	15
3	09:35-09:45	Discussion		10





EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Role of the PDCO in the EU Regulatory System

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**Daniel Brasseur**  
PDCO Chair  
European Medicines Agency





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*(Acts whose publication is obligatory)*

**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**



# Accès aux Médicaments



6

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Official Jour

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REGULATION (EC) No 1901/2006 OF THE

of 1

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

(Text with EEA relevance)



## Key objectives of the Regulation

- To improve the health of the children of Europe, by:

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  - increasing high quality research for medicinal products for children
  - promoting the development and authorization of such medicines at the EU level
  - improving the information on medicines designed for children
- While *avoiding unnecessary studies* in children and not delaying the authorization of medicines for adults



## Key objectives of the Regulation



– To improve the health of the children

- increasing **high quality research** for medicinal products for children
- promoting the development and authorization of such medicines at the EU level
- improving the information on medicines designed for children

– While *avoiding unnecessary studies* in children and not delaying the authorization of medicines for adults



# Key Tools of the Regulation



- **Mandatory paediatric development for *new* products according to a PIP agreed upon by the PDCO (possible deferrals or waivers)**
- **Mandatory submission of paediatric data when filing new applications unless waiver or deferral approved by the PDCO**
- **New Marketing Authorisation Procedure for off-patent products (PUMA)**





## 3 Key Pillars of the Regulation



- **Obligation : Paediatric Investigation Plan [PIP]  
(agreed and compliant in its conduct)**
- **Reward [incentives] for studies conducted  
(6 months patent extension, only once)**
- **Paediatric Committee [PDCO] at the EMEA  
(advisory body to EMEA in its executive role)**



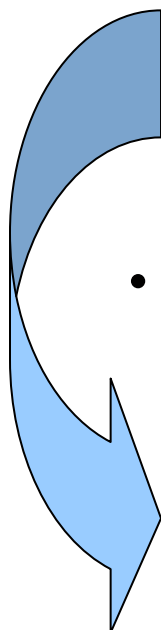
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Discovery  
(2-10 years)

Preclinical Testing  
(lab and animal testing)

Phase I  
(20-30 healthy volunteers used to check for safety and dosage)

Phase II  
(100-300 patient volunteers used to check for efficacy and side effects)

Phase III  
(1,000-3,000 patient volunteers used to monitor reactions to long-term drug use)

**PIP... is a plan**

including formulations, preclinical safety, clinical efficacy, and some pharmacovigilance

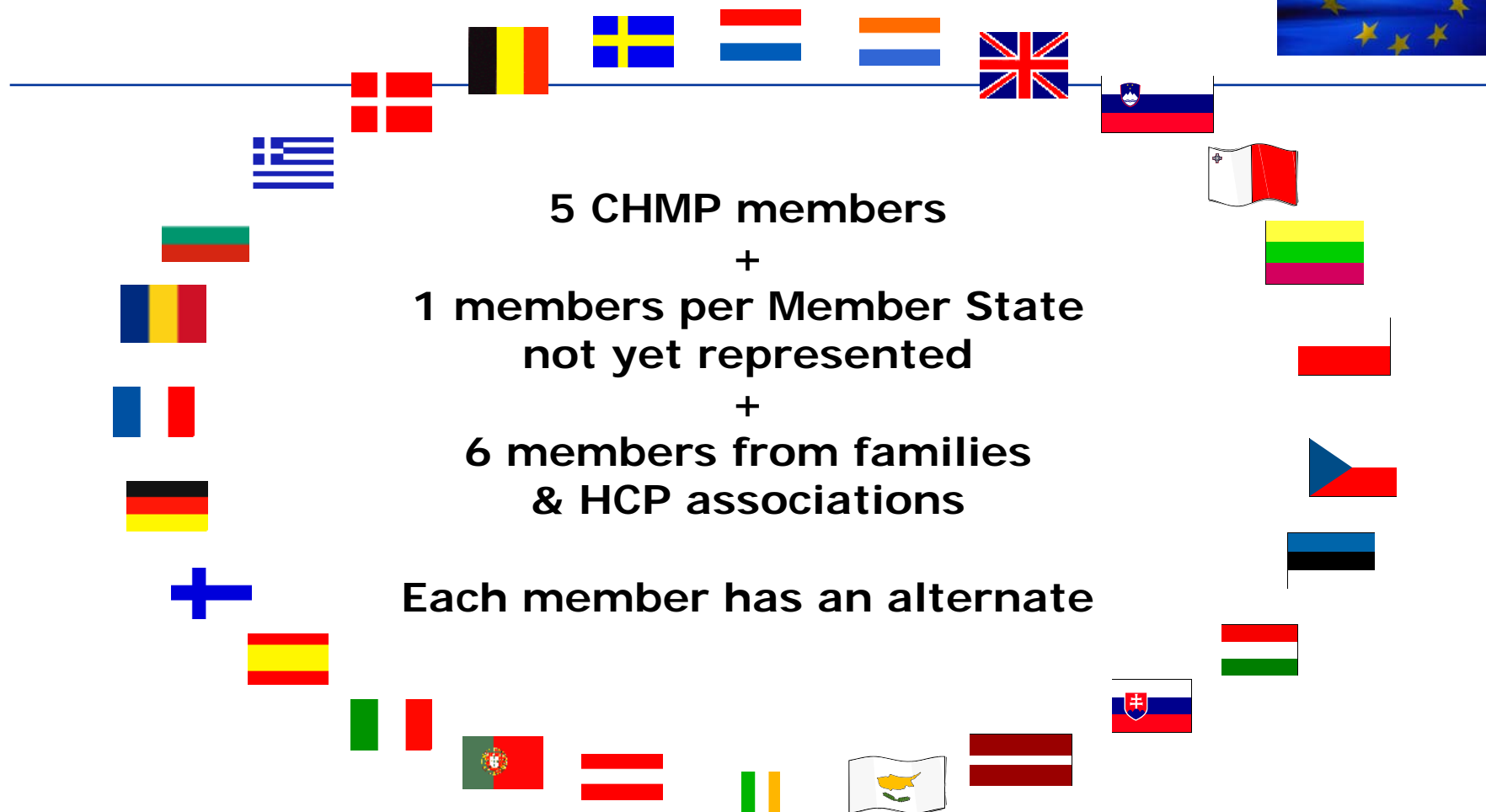
describing the drug development

-Timing of studies: start, duration and end, with respect to submission of Marketing Authorisation applications

-Population (age groups) to be studied



# PDCO





## *Article 6*

1. The tasks of the Paediatric Committee shall include the following:
  - (a) to assess the content of any paediatric investigation plan for a medicinal product submitted to it in accordance with this Regulation and formulate an opinion thereon;
  - (b) to assess waivers and deferrals and formulate an opinion thereon;



# Roles pertaining to fulfilling the needs

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## *Article 17*

1. Following receipt of a proposed paediatric investigation plan which is valid in accordance with the provisions of Article 15(2), the Paediatric Committee shall appoint a rapporteur and shall within 60 days adopt an opinion as to whether or not the proposed studies will ensure the generation of the necessary data determining the conditions in which the medicinal product may be used to treat the paediatric population or subsets thereof, and as to whether or not the expected therapeutic benefits justify the studies proposed. When adopting its opinion, the Committee shall consider whether or not the measures proposed to adapt the formulation of the medicinal product for use in different subsets of the paediatric population are appropriate.



# Roles pertaining to fulfilling the needs

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**PDCO**  
**PIPlan**



# Roles pertaining to fulfilling the needs

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**PDCO**  
**PI Plan**

**SAWP**  
**R&D**





# Roles pertaining to fulfilling the needs

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**PDCO  
PIPlan**

**EC  
CT advice**

**SAWP  
R&D**

**NCA  
CT auth**



# Roles pertaining to fulfilling the needs

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**PDCO  
PIPlan**

**EC  
CT advice**

**Academia  
CT conduct**

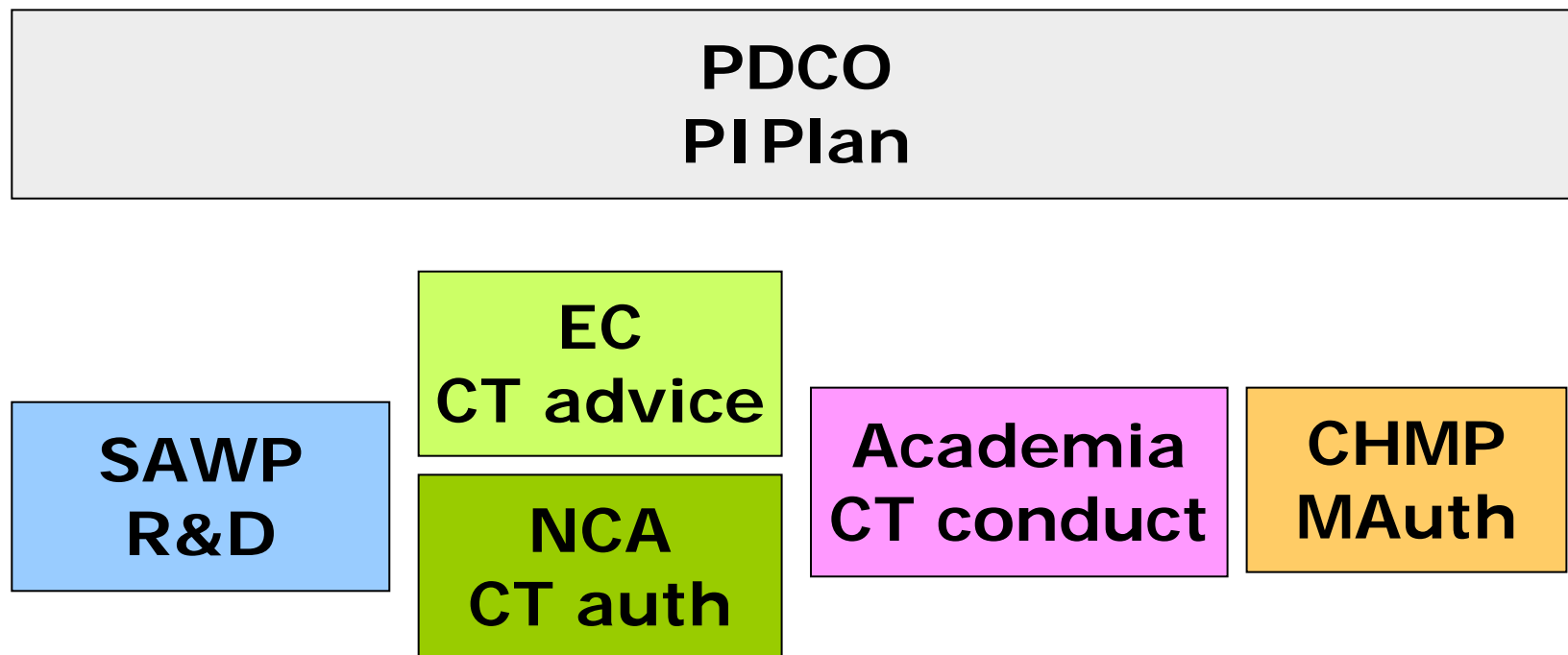
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R&D**

**NCA  
CT auth**



# Roles pertaining to fulfilling the needs

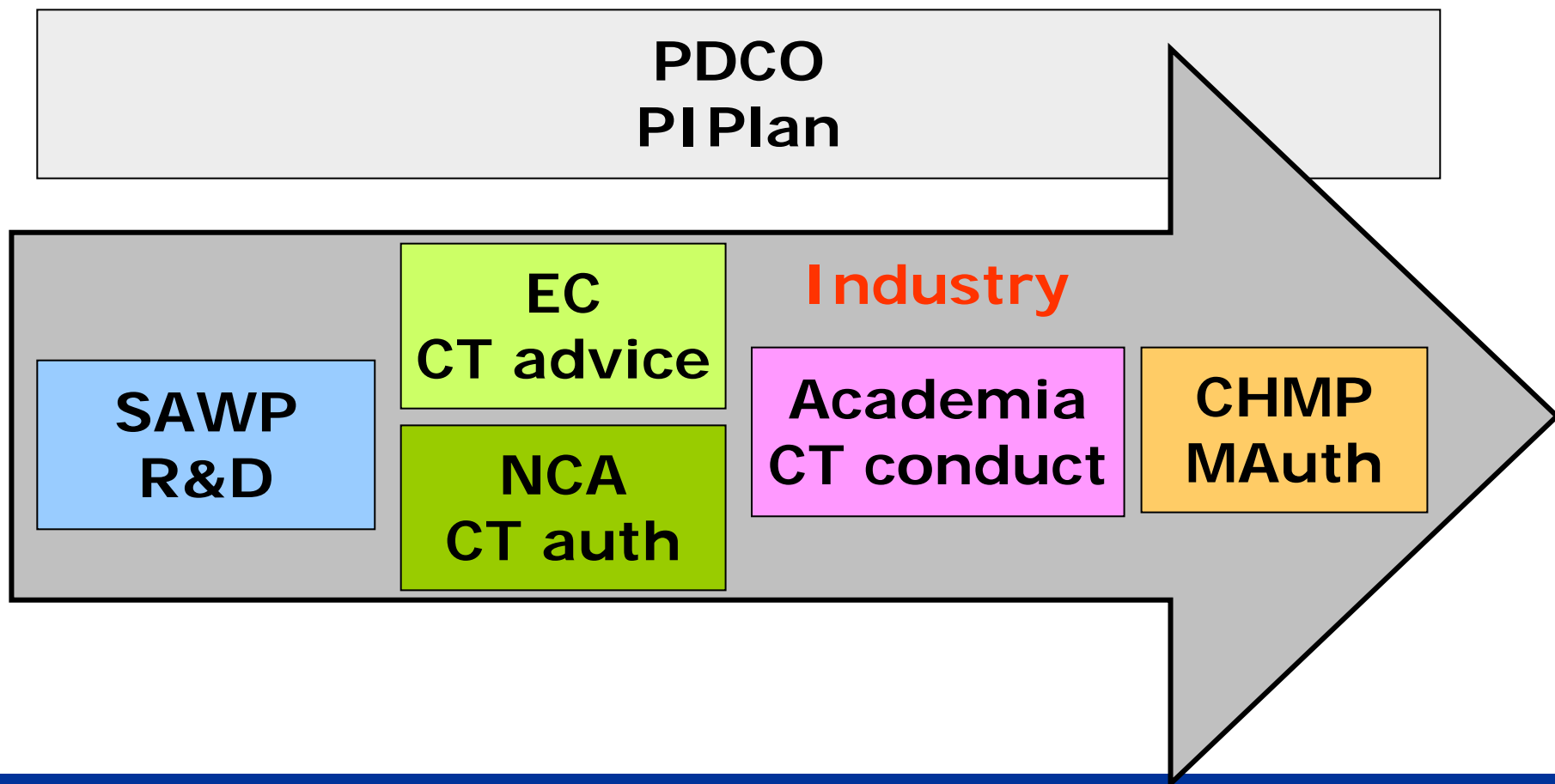
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# Roles pertaining to fulfilling the needs

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# Roles pertaining to fulfilling the needs

- (c) at the request of the Committee for Medicinal Products for Human Use, a competent authority or the applicant, to assess compliance of the application for a Marketing Authorisation with the agreed paediatric investigation plan concerned and formulate an opinion thereon;
- (d) at the request of the Committee for Medicinal Products for Human Use or a competent authority, to assess any data generated in accordance with an agreed paediatric investigation plan and formulate an opinion on the quality, safety or efficacy of the medicinal product for use in the paediatric population;
- (f) to support and advise the Agency on establishing the European network referred to in Article 44;
- (g) to assist scientifically in the elaboration of any documents related to the fulfilment of the objectives of this Regulation;





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**PENET** was established in 1991 as a collaboration between paediatric HIV centres in Europe. This was principally funded by the European Union through BIONED II, by governmental bodies in a number of European countries and by support from the pharmaceutical industry.

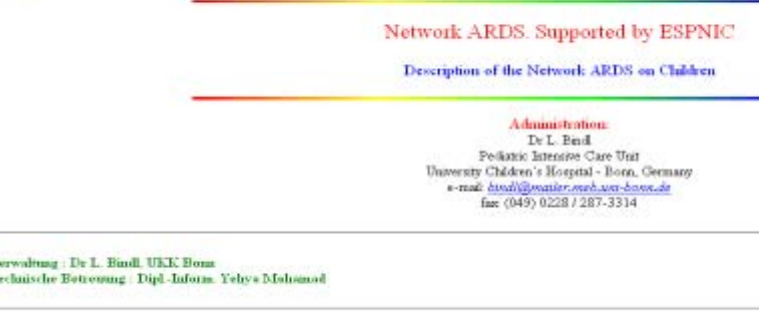
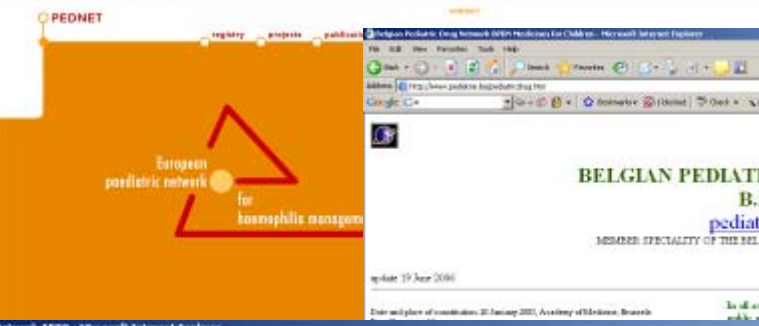
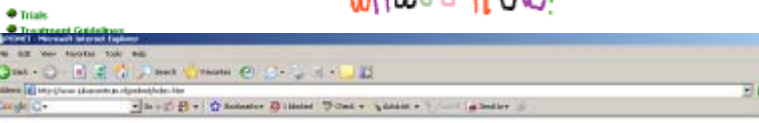
The PENET foundation for the treatment and care of children with HIV serves as an umbrella for the PENET clinical trials network as well as for future work in training and cohort collaborations.

Many questions about treatment for HIV can be answered in adults but it is unnecessary to repeat all trials in children. However, the natural history of vertical HIV infection differs from that in adults in some important ways and the tolerance of drugs in children may also be different.



European Medicines Agency

## What's new?



**Paediatric Network ARDS: Hypoxic Respiratory Failure**

**Description**

Hypoxic respiratory failure in children is a rare condition, the incidence being incidence below 1/100 000. It undergoes continuous changes in origin and treatment strategies. Treatment requires a high input of resources. The outcome depends on the underlying disease as well as on high quality intensive care.

Due to the diversity of underlying conditions and the low incidence controlled trials to evaluate these strategies are extremely difficult or nearly impossible. "Registries, that carefully compile patients treated by a given therapy may be a reasonable, and immediately available, alternative to randomized studies that protect the access of children to life-saving technologies" (Boveldt 1997).

The continuous and compiled observation of many cases from different institutions in some kind of network may allow to identify changes in etiology over time, changes in outcome over time, variation in outcome of patients with similar etiology and severity of ARDS in different institutions, variation in outcome of patients with similar etiology and severity of ARDS in relation to certain treatment strategies, identification of risk factors.

The knowledge of these factors may allow the definition of quality standards (average and optimal outcome for defined subgroups), elimination of risk factors, better planning of collaborative trials.

The data base may facilitate the contact between institutions and institutions caring for similar subgroups of patients with the possibility to do investigations for those subgroups and to exchange experiences.

London, 15 January 2008

Doc. Ref. EMEA/MB/543523/2007

# The Network of Paediatric Networks at the EMEA Implementing Strategy

PAED-Net  
Tafeliches Netzwerk

Willkommen auf der Homepage des PAED-Net

PAED-Net  
Aktivitäten  
Fortbildungen  
Klinische Studien  
Kooperationen

International Trials Organization - Microsoft Internet Explorer

http://www.internationaltrials.org/Description.html

PRINTO  
Paediatric Rheumatology International Trials Organization

SITE MENU

**ABOUT PRINTO**  
Home  
What is PRINTO  
Objectives  
Membership  
Structure

**RESEARCH PROJECTS**  
Ongoing projects  
Past projects

**PUBLICATIONS**  
Abstracts  
Reports  
Presentations

**CONTACT**  
Contact PRINTO  
Apply for membership  
Help center

MEMBER AREA

Use ID:

Password:

FOR FAN

**Paediatric Rheumatology International Trials Organisation (PRINTO)**

The Paediatric Rheumatology International Trials Organisation (PRINTO) is a pan-governmental international network founded by eleven Member and Observer Nations in 1998, and initially included 19 European countries. Now more than 50 and more than 200 member countries, with the goal to foster, facilitate and coordinate the development, conduct, analysis, and reporting of multi-centre, international clinical trials and/or outcome standardisation studies in children with paediatric rheumatic diseases (PRD).

To learn more about PRINTO click here

**IN THE SPOTLIGHT**

**10 FEBRUARY 2007**  
Quality of life in 116-year-old patients

**15 FEBRUARY 2007**  
11th EORTC meeting

**25 FEBRUARY 2007**  
PRINTO/INTOUSA membership registry just started

If you are already member of PRINTO please login to submit the data received to members.

**ATTENTION!**  
For technical support or question about the website contact [printo-ask-help@expatriate-paedi.eu](mailto:printo-ask-help@expatriate-paedi.eu)





# Roles pertaining to fulfilling the needs

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The screenshot shows the European Medicines Agency website. The main heading is 'Scientific Guidelines for Human Medicinal Products'. Below this, there is a section for 'Multidisciplinary Guidelines'. A legend indicates: C = Concept Paper, D = Draft Guideline, A = Adopted Guideline, O = Overview of Comments. A table lists various guidelines, with the 'Adopted' column highlighted in red.

Title	C	D	A	O	Reference Number	Publication Date
<b>Paediatrics</b>						
Investigation of medicinal products in the term and preterm neonate		♦	♦	♦	EMA/536810/08	July 2009
Conduct of Pharmacovigilance for medicines used by the paediatric population	♦	♦	♦	♦	EMA/CHMP/235910/05	June 2006
Reflection Paper: Formulations of Choice for the Paediatric Population	♦				EMA/CHMP/PEG/194810/2005	
Note of Explanation to accompany publication of Reflection Paper on Formulations of Choice for the Paediatric Population (EMA/CHMP/PEG/194810/2005)	♦				EMA/196218/05	Jun 2005
Impact of Brain Immaturity when investigating medicinal products intended for Neonatal use	♦				EMA/181377/06	Release for consultation Jun 2006
Impact of Lung and heart Immaturity when investigating medicinal products intended for	♦				EMA/CHMP/PEG/114218/06	Release for consultation Mar 2006



# Roles pertaining to establishing needs

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10 December 2010  
EMA/794083/2009  
Human Medicines Development and Evaluation

(e) to advise on the content and format of data to be collected for the survey referred to in Article 42;

(i) to establish a specific inventory of paediatric medicinal product needs and update it on a regular basis, as referred to in Article 43;

(j) to advise the Agency and the Commission regarding the communication of arrangements available for conducting research into medicinal products for use in the paediatric population;

Report on the survey of all paediatric uses of medicinal products in Europe

Established according to article 42-43 of Regulation (EC) No 1901/2006 of the European Parliament and of the Council on medicinal products for Paediatric use



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European Medicines Agency  
*Evaluation of Medicines for Human Use*

London, 04 July 2008  
Doc. Ref. EMEA/224688/2006/rev1

**ASSESSMENT OF THE PAEDIATRIC NEEDS  
DIABETES TYPE I AND II**



# Roles pertaining to establishing needs

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EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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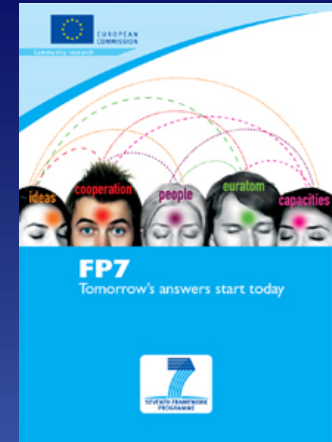
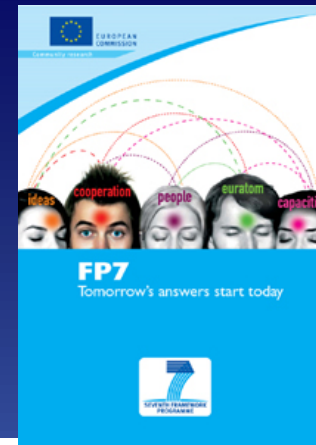
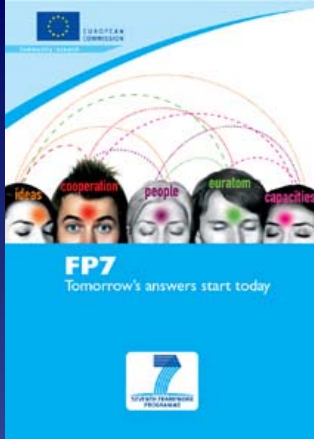
26 July 2010\*  
EMA/480197/2010  
Human Medicines Development and Evaluation

## Revised priority list for studies into off-patent paediatric medicinal products

for the 5<sup>th</sup> call 2011 of the 7<sup>th</sup> Framework Programme of the European Commission

**This priority list of off patent medicines is the basis only for the 5<sup>th</sup> Call 2011 of the 7<sup>th</sup> Framework Programme of the European Commission.**

**The 6<sup>th</sup> call 2012 will be based on a separate priority list.** Please refer to the [website](#) of the European Medicines Agency.



# Priority List

In accordance with the Paediatric Regulation, an inventory of the needs for medicines intended for children, as established by the Paediatric Committee, will be published shortly after 26 January 2009.

A similar exercise to establish paediatric needs was carried out between 2001 and 2007 by the Paediatric Working Party (PEG) — a temporary working party of the CHMP, established prior to implementation of the Paediatric Regulation. The lists of paediatric needs as adopted by the PEG will serve as a basis for the inventory of needs to be established by the Paediatric Committee.

### List of paediatric needs (as established by the Paediatric Working Party)

Please refer to 'EMA/PEG procedure for identifying paediatric needs' ([EMA/175192/2004/rev2](http://emea.europa.eu/pdfs/other/peg/peg_procedure_for_identifying_ped_needs.pdf)) before reviewing any of the documents in the table below.

# Framework Programme

EURATOM  
CAPACITIES  
IDEAS  
PEOPLE  
COOPERATION

## Moving lines of thinking



# Roles pertaining to establishing needs

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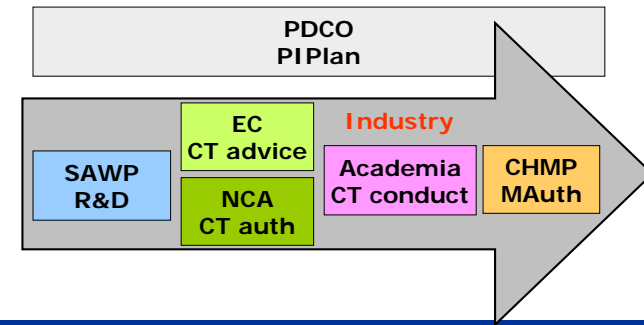
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# The EMA/PDCO regularly hold workshops on paediatrics-related topics

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[Expert Meeting on Clinical Investigation of New Drugs for the Treatment of Chronic Hepatitis C in the Paediatric Population](#), April 2011 [High grade glioma expert group](#), December 2010 [Expert Group Meeting on Paediatric Heart Failure](#), November 2010 [Paediatric Rheumatology Experts Group Meeting](#), November 2010 [Expert meeting on gastroenterology and rheumatology](#), June 2010 [Expert meeting on neonatal and paediatric sepsis](#), June 2010 [Expert meeting on specific immunotherapy](#), January 2010 [Workshop on paediatric formulations for assessors in national regulatory agencies](#), 2010 [Second workshop on European Paediatric Network](#), 2010 [Paediatric Rheumatology Experts Group Meeting](#), 2009 [Paediatric Epilepsy Experts Group Meeting](#), 2009 [Meeting of the Paediatric Diabetes Mellitus Experts Group](#), 2009 [Meeting of the Paediatric Human Immunodeficiency Virus \(HIV\) Experts Group](#) [First European Medicines Agency Workshop on European Paediatric Network](#), 2009 [European Medicines Agency workshop on modelling in paediatric medicines](#), 2008 [Workshop on FP7 and off-patent medicines developed for children](#), 2007 [Workshop on Neonates](#), 2006 [Workshop on Paediatric pain](#), 2004



## Conclusion

The role of PDCO is to foster/coordinate  
research  
in children  
on medicinal products  
allowing the conduct of sound programmes  
generating useful & Q information  
for a safe and easy use,  
placing such medicinal products on the market



A cartoon illustration of a man in a white shirt and black tie emerging from an open envelope. He has a wide, joyful smile and is holding a rectangular sign that says "Thank You!" in red, handwritten-style text. The envelope is open, and the man's head and shoulders are visible above the flap. The background is plain white.

Thank  
You!