Paediatric Regulation

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Objectives of the Regulation entered into force 26 January 2007

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

Timelines of Obligations

- **Immediate**
  - Free EMEA “paediatric” scientific advice
- **6 months from entry into force (July 2007)**
  - Paediatric Committee to be set up
- **18 months from entry into force (July 2008)**
  - Applications for MA (new products) should contain results of studies conducted in compliance with agreed PIP unless waiver or deferral
- **24 months from entry into force (January 2009)**
  - Application for new indication, new route of administration or new pharmaceutical for should contain results of studies in compliance with agreed PIP unless waiver or deferral
- **No deadline for Paediatric Use Marketing Authorisation (PUMA)** but need to results of studies in compliance with agreed PIP

Rewards

For currently unauthorised product and for patent-protected authorised product

- Results reported in Summary of Product Characteristics (SmPC)
- Authorisation in all EU Member States

Reward: 6-month extension of the Supplementary Protection Certificate

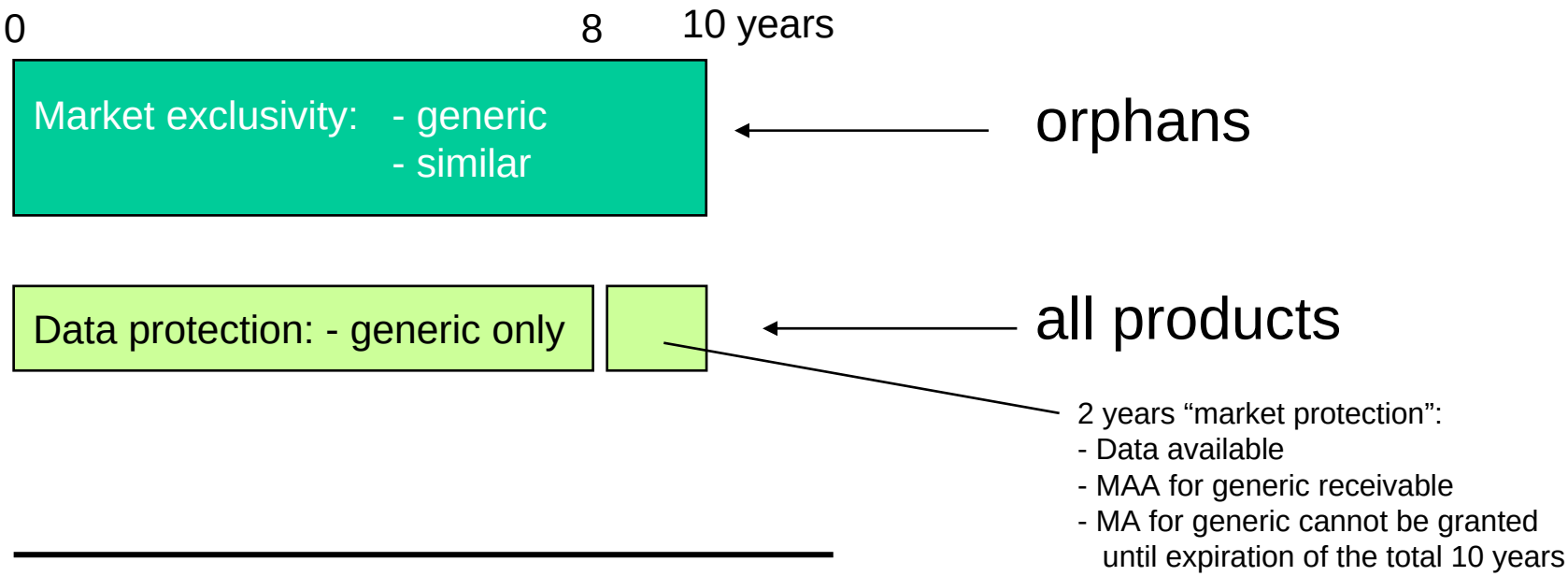
For orphan

Reward: 2 years of market exclusivity added to existing 10 years

PUMA

- Marketing authorisation in some or all Member States
- Brand name may be retained
- 10 years of data protection: (8+2)

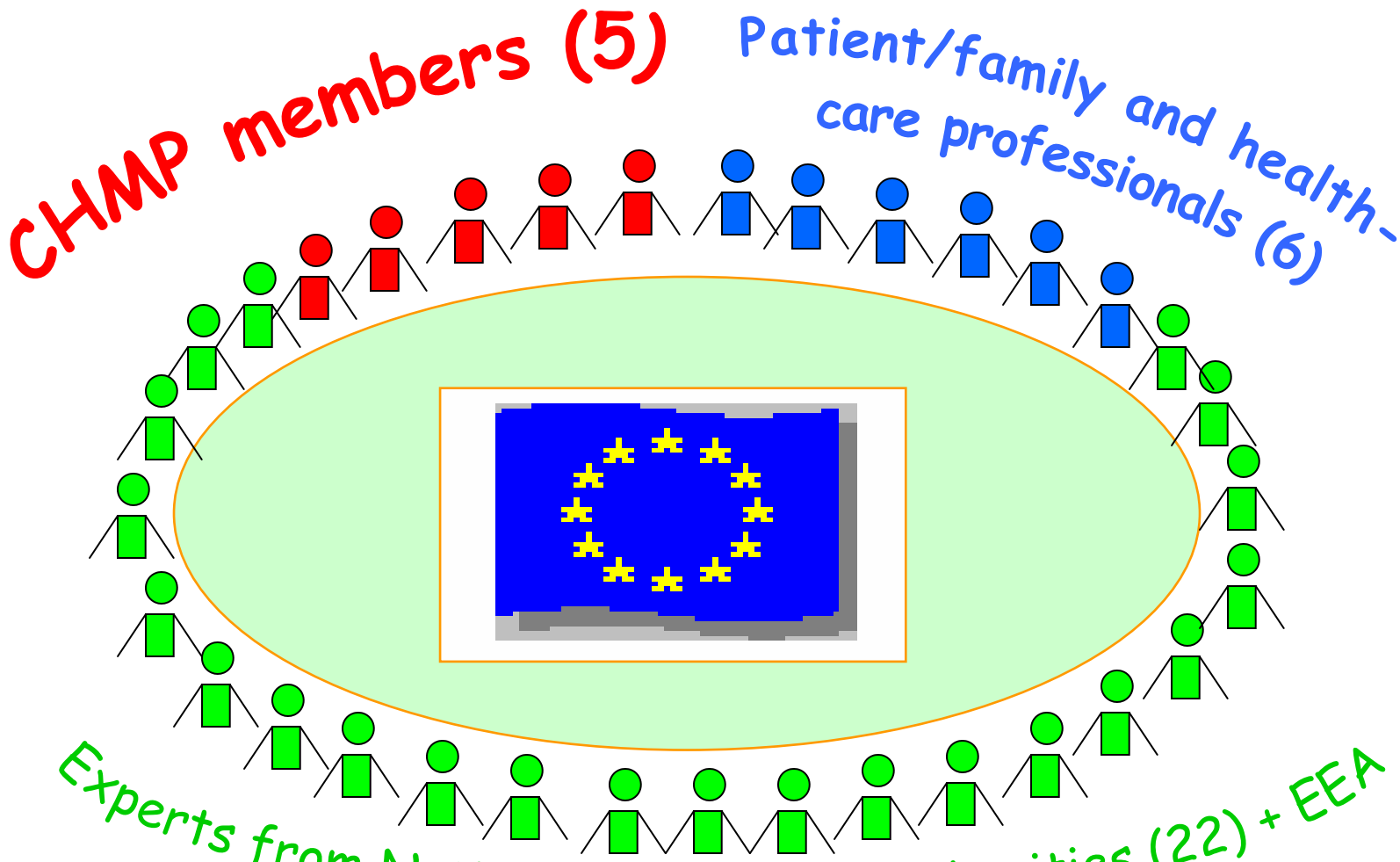
Data protection vs. reward



Paediatric reward:

There has to be a SPC (SPC is prolonged, not patent

Paediatric Committee (PDCO)

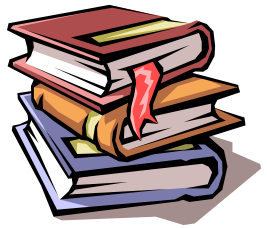


+ alternates

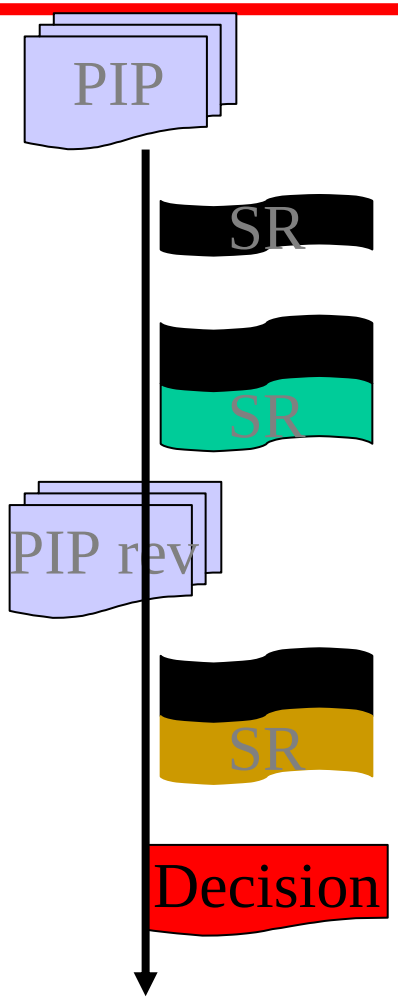
Paediatric Investigation Plans

- Details of timing and measures proposed (i.e studies, trials and pharmaceutical development) necessary to obtain a paediatric indication with an age appropriate formulation in all paediatric subsets affected by the condition
  - Quality
  - Safety
  - Efficacy

Marketing Authorisation criteria



What happens?



- Company (or Academic) prepares a Plan (PIP)
- EMEA writes Summary Report for Paediatric Committee
- Paediatric Committee (Rapporteurs) reviews the PIP and may request modifications (60 days)
- PIP modified by Company
- Re-discussed by Committee (90 days)
- Opinion adopted by PDCO at D120
- Opinion is transformed into EMEA Decision is binding on Company
- Plan is implemented (studies performed)
- **Compliance is checked!**

PRODUCT-SPECIFIC WAIVERS

- **Two types:**
  - **"total waiver" for all conditions/indications for a product**
  - **"partial waiver":** *one and more subset(s), indication(s),* **but there is a PIP**!
- **Legal grounds:**

- *Lack of efficacy and safety*
- *Disease or condition occurring only in adults population*
- *Lack of significant therapeutic benefit*

(+list of **class waivers** published by EMEA)

Significant therapeutic benefit

e.g

- expected improved efficacy?
- substantial improvement in safety?
- improved dosing scheme/method of administration?
- new clinically relevant age-appropriate formulation?
- new clinically relevant and therapeutic knowledge?
- new mechanism of action?

If early in development, likely based on assumptions

➡ *To be decided by the PDCO*

Deferrals

- A deferral is an agreement to have at least one study/measure initiated or completed after the regulatory procedure is started for adults
- A deferral does NOT:
  - Exempt the applicant from proposing a PIP
  - Necessarily allow the applicant to defer all measures

Other provisions of the Paediatric Regulation

Paediatric Therapeutic needs

- Inventory made public by Paediatric Working Party (2001-2007) published on EMEA website
- Survey on all existing uses of medicinal products in children by Member States *(answers from few MS)*
- After consultation of EC, Member States and interested parties, Paediatric Committee will update inventory of therapeutic needs
- Regular updates

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

Please refer to 'EMEA/PEG procedure for identifying paediatric needs' (EMEA/175192/2004/rev2) before reviewing any of the documents in the table below.

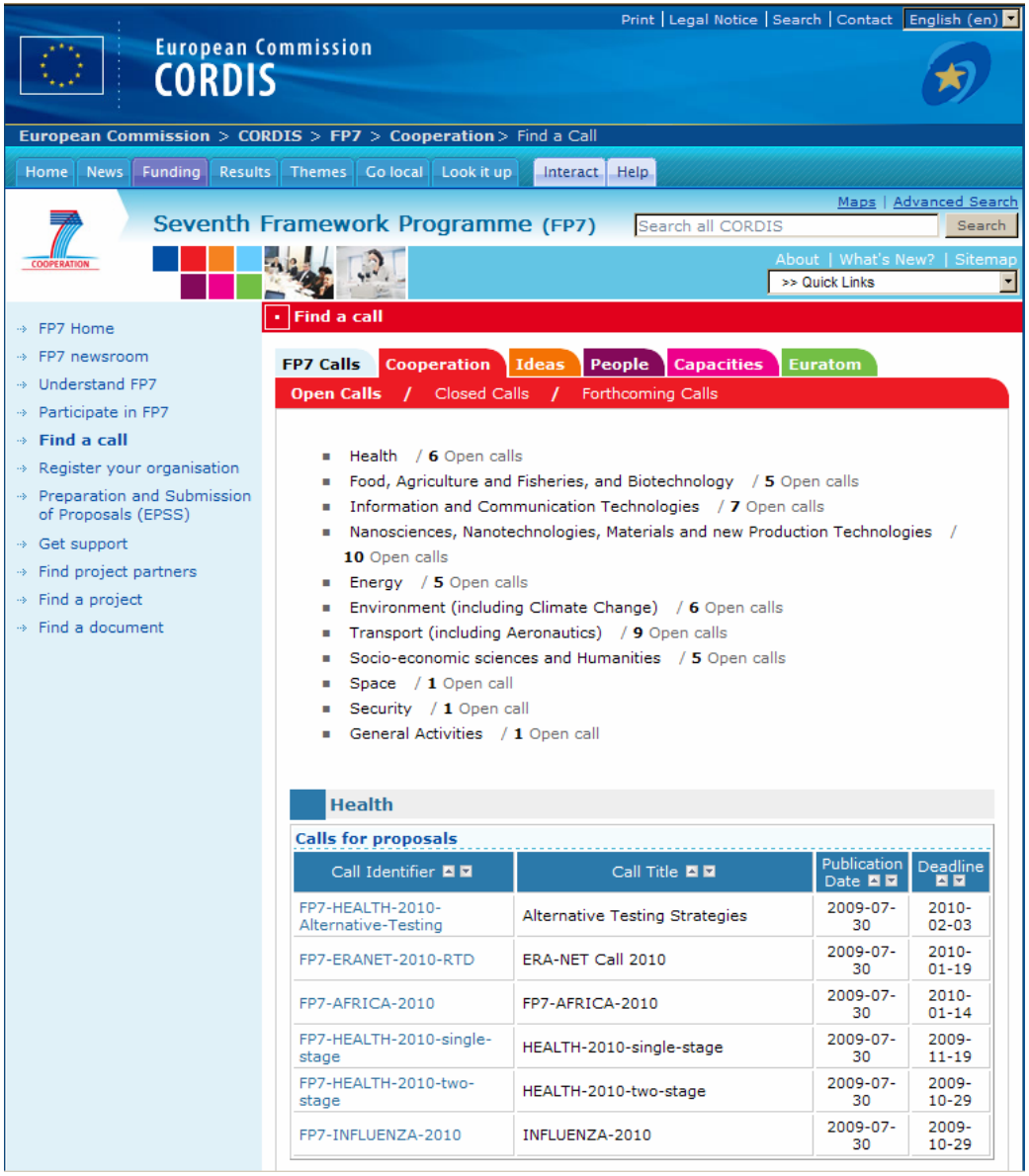
	Reference	Notes
Anaesthesiology		
Assessment of the paediatric needs - Anaesthesiology	EMEA/405166/2006	
Anti-infectious therapy		
Assessment of the paediatric needs - Anti-infectious therapy with focus on antimycotics, antivirals (except HIV)	EMEA/435350/06	
Cardiology		
Assessment of the paediatric 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	
Diabetes (Types I and II)		
Assessment of the paediatric needs - Diabetes (Types I and II)	EMEA/224688/06 rev 1	
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		

Funding of studies for off-patent medicines for children

- EU funding
- Liaison with EC (DG Research) for calls for proposals under the 7th framework programme

- Priority list of off-patent medicinal products for paediatric studies

  (revised version published in September 2009)

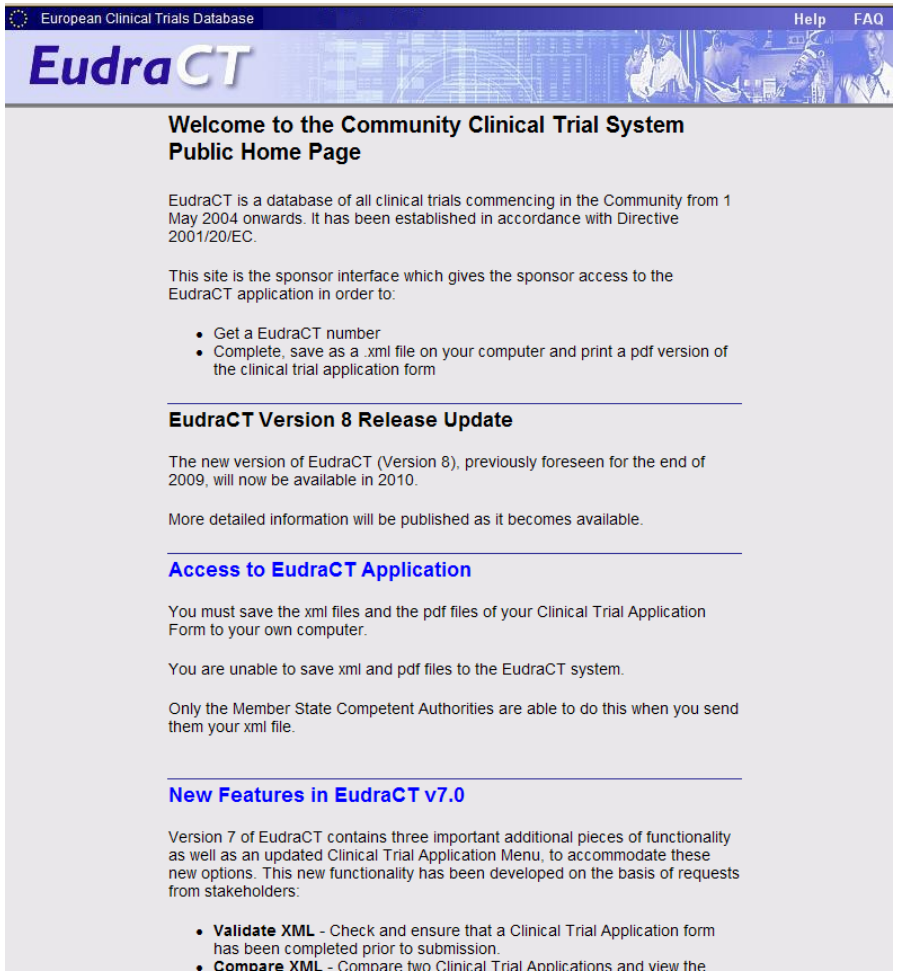


Provision of Information

Paediatric clinical trials in EUDRACT:

- To include third countries trials linked to a PIP
- To include results of all trials and of other trials 'submitted to competent authorities'
- Paediatric information to be made public
- Expected to be implemented: Q2 2010

Public access to paediatric information for authorised products (EudraPharm)



European Paediatric Research Network

- To link together 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

+ Consultation of European Commission/Member States/Interested parties
+ Adopted by Management Board
+ 1st workshop at EMEA: February 2009
+ 2 working groups:

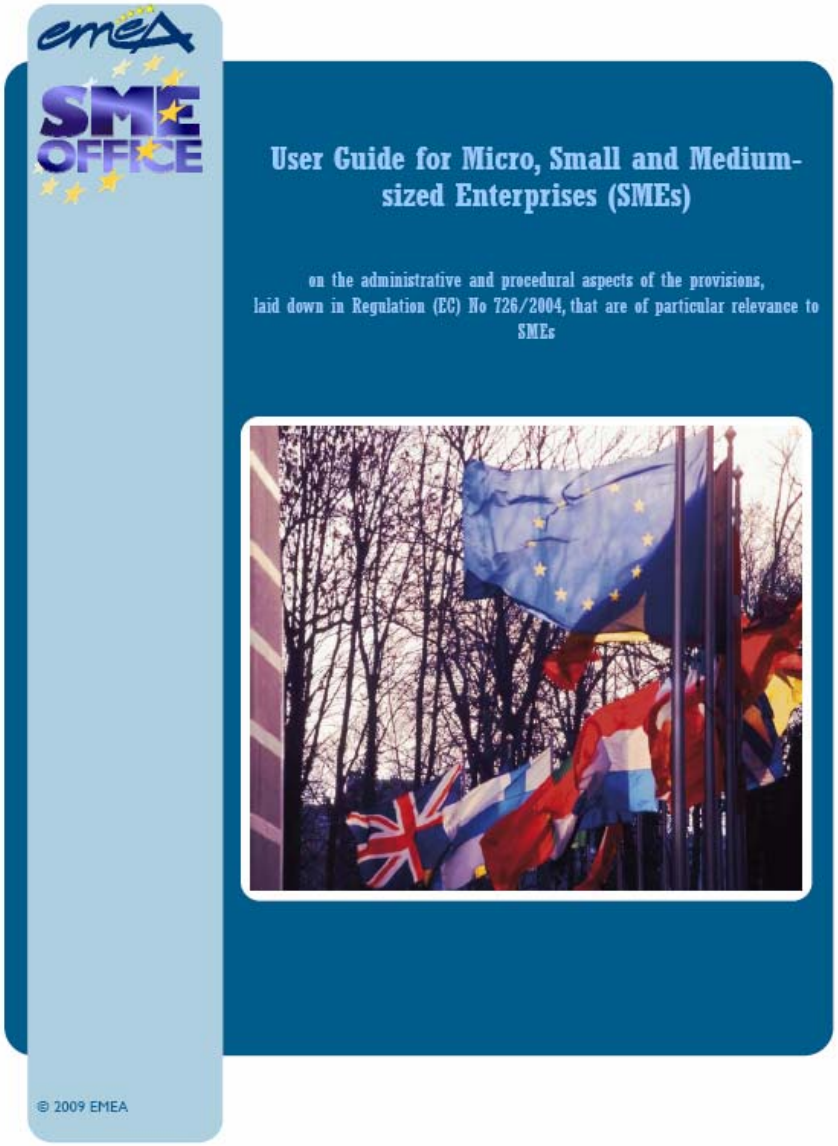
  Working Group 1: "Paediatric network implementation"
  Working Group 2: "Recognistion criteria and quality standards for self-assessment"

Art. 45 and 46

- Art. 45: all existing paediatric studies on authorised medicinal product to be comunicated to EMEA/CA (deadline 26/1/2008)
- Art. 46: all new studies, sponsored by applicant, on authorised products to be submitted to EMEA/CA within 6 months of completion, whether part of a PIP or not.

Where to find information?

General introduction to regulatory issues



http://www.emea.europa.eu/pdfs/SME/43039908en.pdf

EMEA Paediatrics website:
http://www.emea.europa.eu/htms/human/paediatrics/introduction.htm

EU Commission Guideline on Format and Content of applications for PIPs/waivers/deferrals

http://www.emea.europa.eu/pdfs/human/paediatrics/Guideline_2008_C243_01.pdf

24.9.2008 EN Official Journal of the European Union C 243/1

II

(Information)

INFORMATION FROM EUROPEAN UNION INSTITUTIONS AND BODIES

COMMISSION

Communication from the 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

(2008/C 243/01)

I need more help!

EMEA procedural advice

European Medicines Agency - Human Medicines - Medicines for children - Paediatric investigation - Microsoft Internet Explorer

File Edit View Favorites Tools Help | Address http://www.emea.europa.eu/htms/human/paediatrics/pips_procedural.htm | Go

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Introduction
The EU Paediatric Regulation
Paediatric Committee
Guidance for applicants
Scientific advice
Paediatric investigation plans (PIPs), waivers and modifications
Paediatric-use marketing authorisations (PUMAs)
Compliance
Submission of paediatric studies
Opinions and decisions on PIP applications
Background
Class waivers
Product-specific decisions
Paediatric-related information
Paediatric needs
Paediatric clinical trials
Priority list of off-patent medicines
Scientific guidance
Paediatric formulations
Presentations
EU paediatric network
Global cooperation
Member States
International
Workshops
Related links

Medicines for children — A brighter future for child health

Guidance for applicants

Paediatric investigation plans (PIPs), waivers and modifications - Procedural Advice

This procedural advice addresses a number of questions which applicants may have before submitting an application. The information provided - under the form of Questions and Answers - will be expanded or reviewed progressively, and will be marked by NEW! or "Rev." upon publication.

Please consult this procedural advice, the EC "PIP Guideline" (available online at http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2008:243:0001:0012:EN:PDF and the Frequently Asked Questions document (available online at http://www.emea.europa.eu/pdfs/human/paediatrics/52008506en.pdf), before sending a request for further information.

If you need further information on the content, please do not hesitate to contact the Paediatric Team at Paediatrics@emea.europa.eu.

When sections applying to the electronic submission of documents and the template form are amended, the modifications are expected to be reflected in submissions of applications/request for modifications/modifications of PIPs, starting from 3 months after the date of the amendments.

Click on the following questions to see the procedural advice, or alternatively the whole Q&A document can be visualized.

Questions addressed in the Q&A document:

#	Question	Applicable from	Date of last revision
1	How and when should I submit a PIP/waiver Letter of Intent?	current	March 2008
2	When should I submit the application for a PIP and /or Waiver?	current	October 2007
3	To whom should I submit the PIP/waiver application?	current	October 2007
4	How many copies should I submit for a PIP/waiver application?	current	March 2008
5	What information should be provided in the cover letter accompanying the application?	current	October 2007
6	What are the technical requirements for the electronic submission of PIP/waiver applications?	June 2008	March 2008
7	How do I use the electronic template for the PIP/ waiver application (part A)?	current	October 2007
8	What information should I include in the electronic template for PIP/waiver applications (Part A)?	current	October 2007
9	How should I present the scientific documentation (parts B to F)?	June 2008	March 2008
10	What shall I submit if my product falls in a condition listed in the EMEA decision on class waivers?	current	March 2008
11	Should I submit a separate PIP/waiver application in case of duplicate marketing authorisations/marketing authorisation applications?	current	March 2008

http://www.emea.europa.eu/home.htm — Local intranet

I need more help!

EMEA procedural advice (also available as single PDF file)

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

London 15 January 2009
Doc Ref: EMEA/651100/2008

Questions and answers on the preparation of applications for a PIP and/or waiver

1) How and when should I submit a PIP Letter of intent?

The EMEA Secretariat should be formally notified of the intent to submit an application for paediatric investigation plan, and/or a request for waiver or deferral, using the published Letter of Intent template.

The deadline for the Letter of Intent is normally 2 months before the planned submission date of the complete application.

The Letter of Intent should be sent to the following address: paediatrics@emea.europa.eu, using the EMEA secure email system, Eudralink. Should you not yet have a Eudralink account, please contact eudralink@emea.europa.eu in order to open an account. A referee contact person within EMEA is needed, when opening a Eudralink account. If you do not have a specific referee, please use "*paediatric*" as referee.

2) When should I submit the application for PIP and /or Waiver?

Two must-read documents:

Commission Guideline on Format and Content of applications for PIPs/waivers/deferrals

(http://www.emea.europa.eu/pdfs/human/paediatrics/Guideline_2008_C243_01.pdf)

EMEA procedural advice

(http://www.emea.europa.eu/pdfs/human/paediatrics/practical_aspects.pdf)

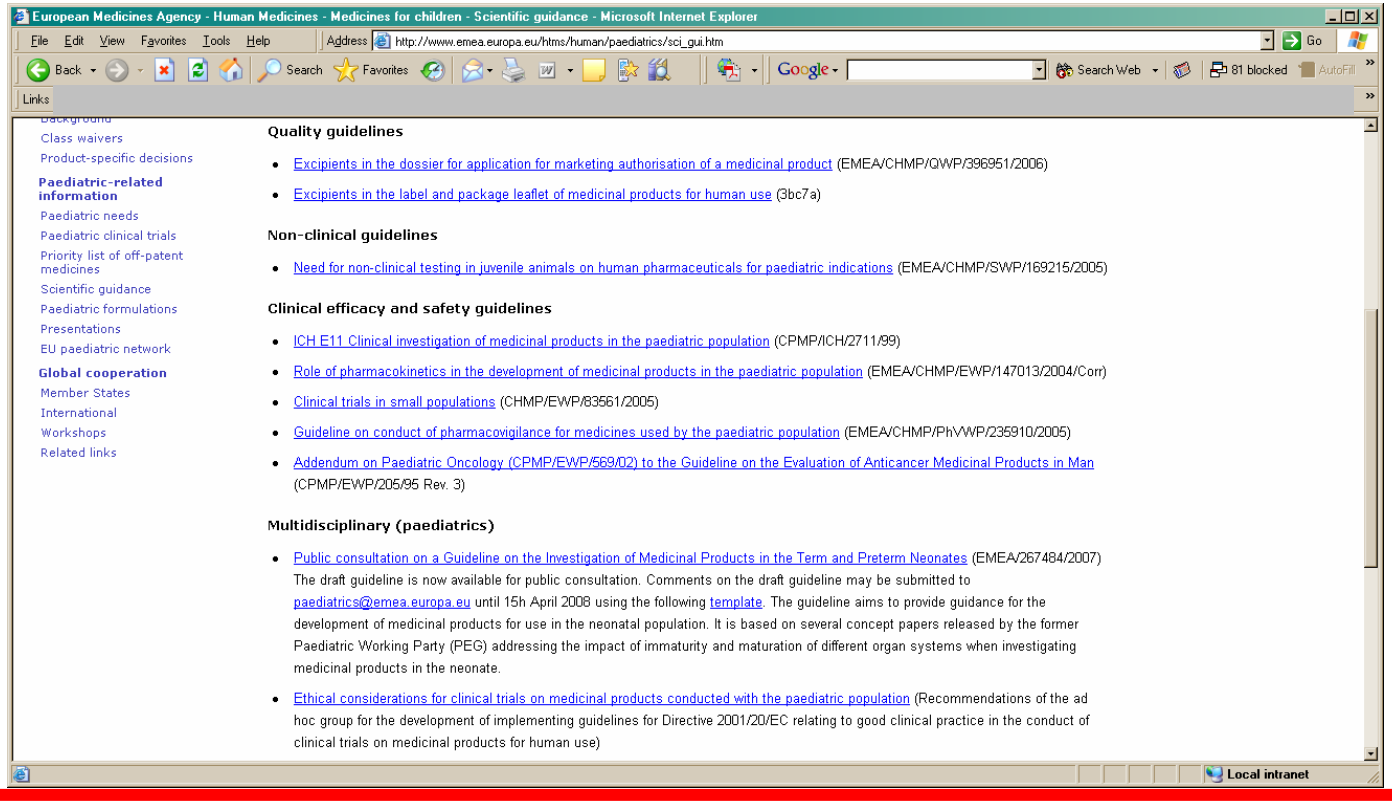
Additional reading:

Frequently asked questions on regulatory aspects of Regulation (EC) No 1901/2006

(http://www.emea.europa.eu/pdfs/human/paediatrics/52008506en.pdf) **- a bit outdated though**

Scientific guidelines of specific paediatric relevance

(http://www.emea.europa.eu/htms/human/paediatrics/sci_gui.htm)
including **ICH E11 "Clinical Investigation of Medicinal Products in the Paediatric Population"**



Websites

- **EMEA:**
  - **www.emea.europa.eu**
  - Go to “Medicines for Children” pages

- **European Commission**:
  - DG Enterprise website: **http://ec.europa.eu/enterprise/pharmaceuticals/**
  - DG Research: **Cordis.europa.eu**

Quiz!

1. A company develops an adult indication only, do they need a Paediatric Investigation Plan?
2. What are the ages that the plan must cover for a paediatric medicine?

Quiz!

3. A company wants to develop a designated orphan medicinal product. Do they need a PIP?
4. A company has added a new strength for an existing tablet formulation of an authorised product. Do they need a PIP?

Conclusions

- High expectations
- Diversity in tasks including new tasks for EMEA
- Paediatric studies become an integral part of the clinical development programme leading to increased demand for paediatric expertise & studies
- Requirement for suitable paediatric formulations
- Balance to be found between fulfilling objectives of the Regulation while avoiding unnecessary trials in children and delay in adult development
- Ensure flexible, pragmatic & collaborative implementation to facilitate its success
- Collaboration with other authorities to ensure global development