

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

□ 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

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

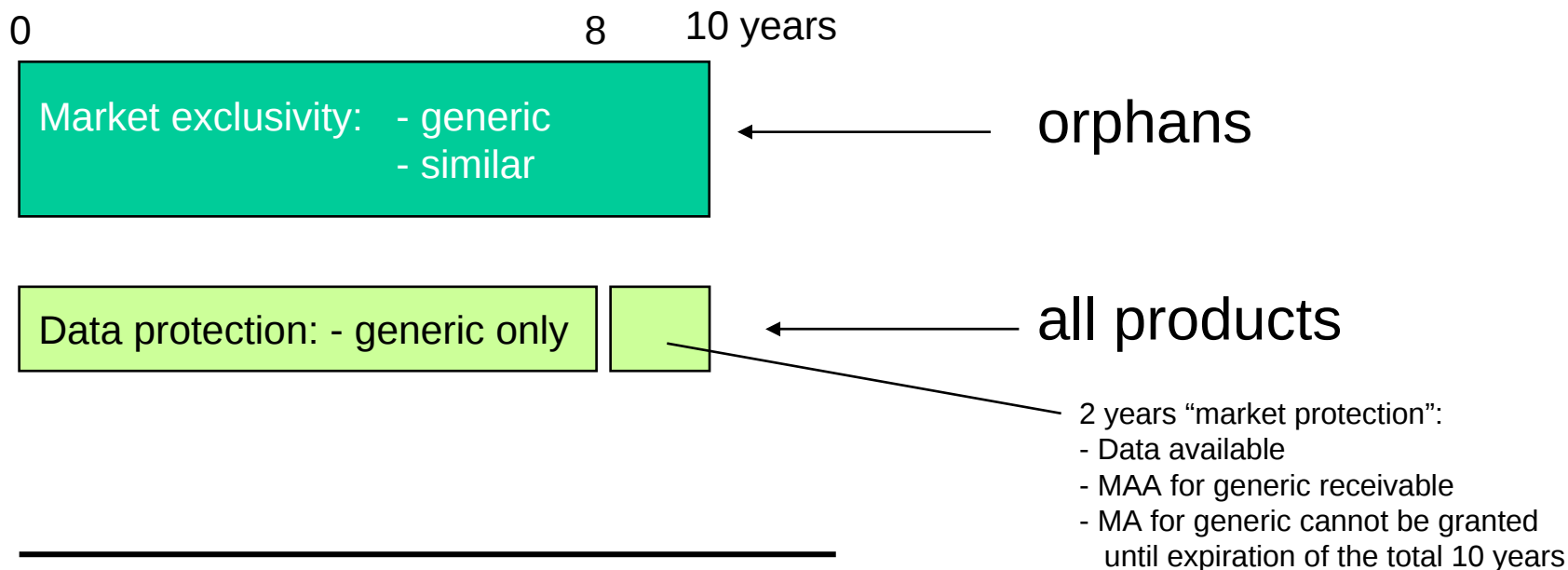
For orphan

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



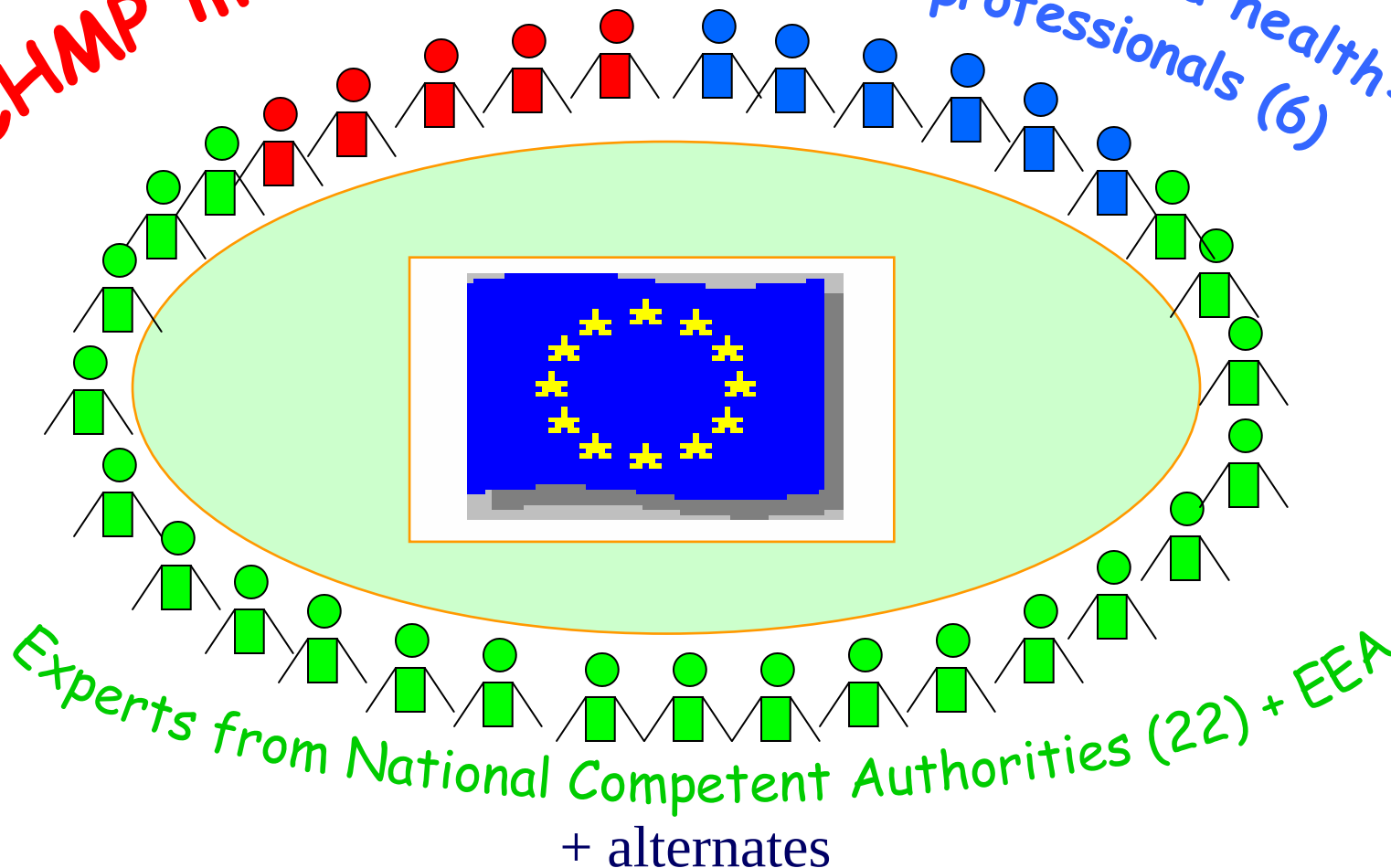
Paediatric reward:



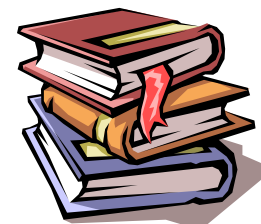
There has to be a SPC (SPC is prolonged, not patent)

CHMP members (5)

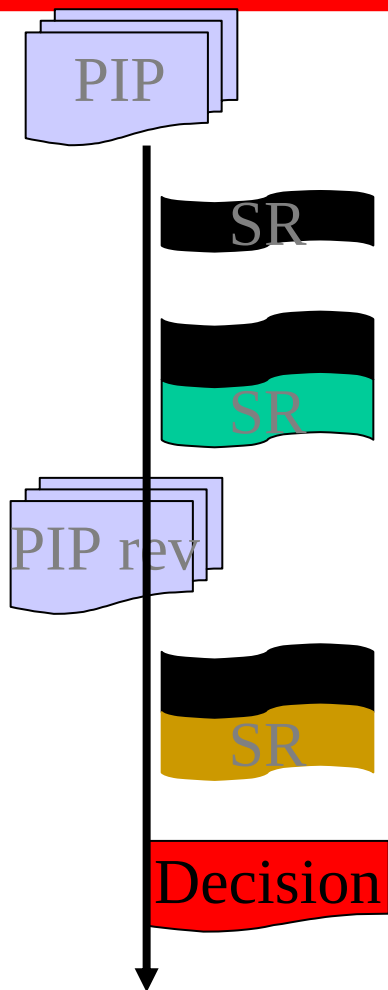
Patient/family and health-care professionals (6)



- 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!**

- **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)

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*

- 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

- 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 'EMA/PEG procedure for identifying paediatric needs' ([EMA/175192/2004/rev2](#)) before reviewing any of the documents in the table below.

	Reference	Notes
Anaesthesiology		
Assessment of the paediatric needs - Anaesthesiology	EMA/405166/2006	
Anti-infectious therapy		
Assessment of the paediatric needs - Anti-infectious therapy with focus on antimycotics, antivirals (except HIV)	EMA/435350/06	
Cardiology		
Assessment of the paediatric needs - Cardiovascular products	EMA/436949/06	See also the comments received during consultation on this list: EMA/404310/06
Chemotherapy I (Cytotoxic therapies)		
Assessment of the paediatric needs - Chemotherapy products (Part I)	EMA/CHMP/384641/06	See also the comments received during consultation on this list: EMA/CHMP/384188/06
Chemotherapy II (Supportive therapy)		
Assessment of the paediatric needs - Chemotherapy Products (Part II)	EMA/CHMP/224696/06	
Diabetes (Types I and II)		
Assessment of the paediatric needs - Diabetes (Types I and II)	EMA/224688/06 rev 1	
Epilepsy		
Assessment of the paediatric needs - Epilepsy	EMA/CHMP/377147/06	See also the comments received during consultation on this list: EMA/CHMP/377231/06
Gastroenterology		
Assessment of the paediatric needs - Gastroenterology	EMA/527934/07	
Immunology		

- 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)

European Commission
CORDIS

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- Nanosciences, Nanotechnologies, Materials and new Production Technologies / 10 Open calls
- Energy / 5 Open calls
- Environment (including Climate Change) / 6 Open calls
- Transport (including Aeronautics) / 9 Open calls
- Socio-economic sciences and Humanities / 5 Open calls
- Space / 1 Open call
- Security / 1 Open call
- General Activities / 1 Open call

Health

Calls for proposals

Call Identifier	Call Title	Publication Date	Deadline
FP7-HEALTH-2010-Alternative-Testing	Alternative Testing Strategies	2009-07-30	2010-02-03
FP7-ERANET-2010-RTD	ERA-NET Call 2010	2009-07-30	2010-01-19
FP7-AFRICA-2010	FP7-AFRICA-2010	2009-07-30	2010-01-14
FP7-HEALTH-2010-single-stage	HEALTH-2010-single-stage	2009-07-30	2009-11-19
FP7-HEALTH-2010-two-stage	HEALTH-2010-two-stage	2009-07-30	2009-10-29
FP7-INFLUENZA-2010	INFLUENZA-2010	2009-07-30	2009-10-29

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)



The screenshot shows the EudraCT website interface. At the top, there is a header with the European Clinical Trials Database logo and navigation links for Help and FAQ. Below the header, the main content area is titled 'Welcome to the Community Clinical Trial System Public Home Page'. It provides an overview of EudraCT as a database of clinical trials and explains that the site is the sponsor interface. A list of actions for sponsors is provided: getting a EudraCT number and completing the application form. A section for 'EudraCT Version 8 Release Update' states that the new version will be available in 2010. An 'Access to EudraCT Application' section explains that users must save XML and PDF files to their own computer. A 'New Features in EudraCT v7.0' section lists two new features: 'Validate XML' and 'Compare XML'.

European Clinical Trials Database

EudraCT

Welcome to the Community Clinical Trial System Public Home Page

EudraCT is a database of all clinical trials commencing in the Community from 1 May 2004 onwards. It has been established in accordance with Directive 2001/20/EC.

This site is the sponsor interface which gives the sponsor access to the EudraCT application in order to:

- Get a EudraCT number
- Complete, save as a .xml file on your computer and print a pdf version of the clinical trial application form

EudraCT Version 8 Release Update

The new version of EudraCT (Version 8), previously foreseen for the end of 2009, will now be available in 2010.

More detailed information will be published as it becomes available.

Access to EudraCT Application

You must save the xml files and the pdf files of your Clinical Trial Application Form to your own computer.

You are unable to save xml and pdf files to the EudraCT system.

Only the Member State Competent Authorities are able to do this when you send them your xml file.

New Features in EudraCT v7.0

Version 7 of EudraCT contains three important additional pieces of functionality as well as an updated Clinical Trial Application Menu, to accommodate these new options. This new functionality has been developed on the basis of requests from stakeholders:

- **Validate XML** - Check and ensure that a Clinical Trial Application form has been completed prior to submission.
- **Compare XML** - Compare two Clinical Trial Applications and view the



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 EMA: February 2009
 - + 2 working groups:
 - Working Group 1: "Paediatric network implementation"
 - Working Group 2: "Recognition criteria and quality standards for self-assessment"

- Art. 45: all existing paediatric studies on authorised medicinal product to be communicated 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?



User Guide for Micro, Small and Medium-sized Enterprises (SMEs)

on the administrative and procedural aspects of the provisions,
laid down in Regulation (EC) No 726/2004, that are of particular relevance to
SMEs



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

EMA Paediatrics website:

<http://www.emea.europa.eu/htms/human/paediatrics/introduction.htm>



European Medicines Agency - Human Medicines - Medicines for children - Introduction - Microsoft Internet Explorer

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Medicines for children A brighter future for child health

Introduction

New legislation governing the development and authorisation of medicines for use in children aged 0 to 17 years was introduced in the European Union in January 2007.

The new piece of legislation — Regulation (EC) No 1901/2006 as amended (the 'Paediatric Regulation') — introduces sweeping changes into the regulatory environment for paediatric medicines, designed to better protect the health of children in the EU.

The Paediatric Regulation also brings in many new tasks and responsibilities for the European Medicines Agency, chief of which is the creation and operation of a Paediatric Committee within the Agency to provide objective scientific opinions on any development plan for medicines for use in children.

This new section of the EMEA website has been created to provide convenient access to all information relating to the Agency's work in the area of paediatric medicines, and will be updated regularly as new information becomes available.

More information

Questions relating specifically to the authorisation of paediatric medicines may be submitted to: paediatrics@emea.europa.eu

[PDCO Press Releases](#)

EMA INFORMATION FOR YOU

The EMEA is committed to the provision of clear and comprehensive information to the public about all aspects of its work. Your views on this new web section, its contents and functionality are welcome, and may be submitted to our webmaster using this e-mail address: [EMA Webservices](#).

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Local intranet

EMA procedural advice



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

Address: http://www.emea.europa.eu/hums/paediatrics/pips_procedural.htm

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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 EMA 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!

EMA 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: EMA/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 EMA 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 EMA 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 EMA 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?

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)

EMA procedural advice

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



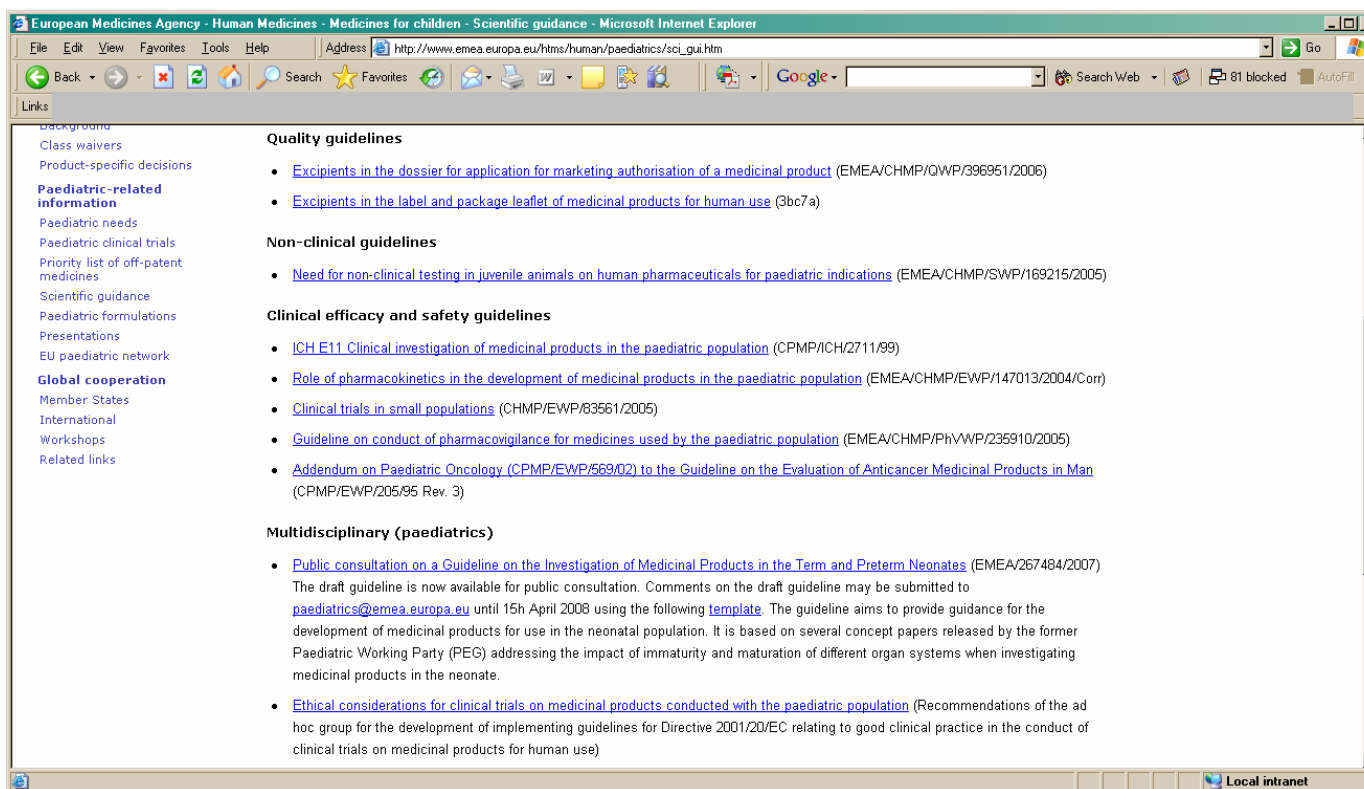
Frequently asked questions on regulatory aspects of Regulation (EC) No 1901/2006

(<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”



The screenshot shows a Microsoft Internet Explorer browser window displaying the EMEA website. The address bar shows the URL: http://www.emea.europa.eu/htms/human/paediatrics/sci_gui.htm. The page content is organized into a sidebar with navigation links and a main content area with a list of guidelines.

European Medicines Agency - Human Medicines - Medicines for children - Scientific guidance - Microsoft Internet Explorer

Address: http://www.emea.europa.eu/htms/human/paediatrics/sci_gui.htm

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Quality guidelines

- [Excipients in the dossier for application for marketing authorisation of a medicinal product](#) (EMEA/CHMP/QWP/396951/2006)
- [Excipients in the label and package leaflet of medicinal products for human use](#) (3bc7a)

Non-clinical guidelines

- [Need for non-clinical testing in juvenile animals on human pharmaceuticals for paediatric indications](#) (EMEA/CHMP/SWP/169215/2005)

Clinical efficacy and safety guidelines

- [ICH E11 Clinical investigation of medicinal products in the paediatric population](#) (CPMP/ICH/2711/99)
- [Role of pharmacokinetics in the development of medicinal products in the paediatric population](#) (EMEA/CHMP/EWP/147013/2004/Corr)
- [Clinical trials in small populations](#) (CHMP/EWP/83561/2005)
- [Guideline on conduct of pharmacovigilance for medicines used by the paediatric population](#) (EMEA/CHMP/PhVWP/235910/2005)
- [Addendum on Paediatric Oncology \(CPMP/EWP/569/02\) to the Guideline on the Evaluation of Anticancer Medicinal Products in Man](#) (CPMP/EWP/205/95 Rev. 3)

Multidisciplinary (paediatrics)

- [Public consultation on a Guideline on the Investigation of Medicinal Products in the Term and Preterm Neonates](#) (EMEA/267484/2007)
The draft guideline is now available for public consultation. Comments on the draft guideline may be submitted to paediatrics@emea.europa.eu until 15h April 2008 using the following [template](#). The guideline aims to provide guidance for the development of medicinal products for use in the neonatal population. It is based on several concept papers released by the former Paediatric Working Party (PEG) addressing the impact of immaturity and maturation of different organ systems when investigating medicinal products in the neonate.
- [Ethical considerations for clinical trials on medicinal products conducted with the paediatric population](#) (Recommendations of the ad hoc group for the development of implementing guidelines for Directive 2001/20/EC relating to good clinical practice in the conduct of clinical trials on medicinal products for human use)

Local intranet

- **EMA:**

- 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



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?



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?



- 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