Basic information

2004/0217(COD) COD - Ordinary legislative procedure (ex-codecision procedure) Regulation	Procedure completed
Medicinal products for paediatric use Amending Directive 2001/20/EC 1997/0197(COD) Amending Directive 2001/83/EC 1999/0134(COD) Amending Regulation (EC) No 726/2004 2001/0252(COD) Amended by 2006/0207(COD) Amended by 2014/0256(COD) **Subject** 4.20.02.06 Clinical practice and experiments 4.20.04 Pharmaceutical products and industry	

Key players

European Parliament

Committee responsible	Rapporteur	Appointed
ENVI Environment, Public Health and Food Safety	GROSSETÊTE Françoise (PPE-DE)	20/01/2005

Former committee responsible	Former rapporteur	Appointed
ENVI Environment, Public Health and Food Safety	GROSSETÊTE Françoise (PPE-DE)	20/01/2005

Former committee for opinion	Former rapporteur for opinion	Appointed
ITRE Industry, Research and Energy	TOIA Patrizia (ALDE)	27/01/2005
IMCO Internal Market and Consumer Protection	The committee decided not to give an opinion.	

Council of the European Union

Council configuration	Meetings	Date
Employment, Social Policy, Health and Consumer Affairs	2663	2005-06-02
Employment, Social Policy, Health and Consumer Affairs	2733	2006-06-01
Employment, Social Policy, Health and Consumer Affairs	2714	2006-03-10
Employment, Social Policy, Health and Consumer Affairs	2699	2005-12-08
Employment, Social Policy, Health and Consumer Affairs	2627	2004-12-06
Environment	2757	2006-10-23

European Commission	Commission DG	Commissioner
	Internal Market, Industry, Entrepreneurship and SMEs	VERHEUGEN Günter

Key events

Date	Event	Reference	Summary
29/09/2004	Legislative proposal published	COM(2004)0599	Summary
27/10/2004	Committee referral announced in Parliament, 1st reading		
06/12/2004	Debate in Council		
02/06/2005	Debate in Council		Summary
13/07/2005	Vote in committee, 1st reading		
20/07/2005	Committee report tabled for plenary, 1st reading	A6-0247/2005	
06/09/2005	Debate in Parliament		
07/09/2005	Decision by Parliament, 1st reading	T6-0331/2005	Summary
07/09/2005	Results of vote in Parliament		
10/11/2005	Modified legislative proposal published	COM(2005)0577	Summary
10/03/2006	Council position published	15763/3/2005	Summary
16/03/2006	Committee referral announced in Parliament, 2nd reading		
04/05/2006	Vote in committee, 2nd reading		Summary
08/05/2006	Committee recommendation tabled for plenary, 2nd reading	A6-0171/2006	
31/05/2006	Debate in Parliament		
01/06/2006	Decision by Parliament, 2nd reading	T6-0232/2006	Summary
01/06/2006	Results of vote in Parliament		
01/06/2006	Debate in Council		
23/10/2006	Act approved by Council, 2nd reading		
12/12/2006	Final act signed		
12/12/2006	End of procedure in Parliament		
27/12/2006	Final act published in Official Journal		

Technical information

Procedure reference	2004/0217(COD)
Procedure type	COD - Ordinary legislative procedure (ex-codecision procedure)
Procedure subtype	Legislation

Legislative instrument	Regulation
Amendments and repeals	Amending Directive 2001/20/EC 1997/0197(COD) Amending Directive 2001/83/EC 1999/0134(COD) Amending Regulation (EC) No 726/2004 2001/0252(COD) Amended by 2006/0207(COD) Amended by 2014/0256(COD)
Legal basis	EC Treaty (after Amsterdam) EC 095
Stage reached in procedure	Procedure completed
Committee dossier	ENVI/6/34376

Documentation gateway

European Parliament

Document type	Committee	Reference	Date	Summary
Amendments tabled in committee		PE357.553	25/05/2005	
Committee opinion	ITRE	PE353.602	26/05/2005	
Committee report tabled for plenary, 1st reading/single reading		A6-0247/2005	20/07/2005	
Text adopted by Parliament, 1st reading/single reading		T6-0331/2005 OJ C 193 17.08.2006, p. 0126-0224 E	07/09/2005	Summary
Committee draft report		PE370.187	10/03/2006	
Amendments tabled in committee		PE370.256	10/04/2006	
Committee recommendation tabled for plenary, 2nd reading		A6-0171/2006	08/05/2006	
Text adopted by Parliament, 2nd reading		T6-0232/2006	01/06/2006	Summary

Council of the EU

Document type	Reference	Date	Summary
Council statement on its position	06603/2006	27/02/2006	
Council position	15763/3/2005 OJ C 132 07.06.2006, p. 0001-0028 E	10/03/2006	Summary
Draft final act	03623/6/2006	12/12/2006	

European Commission

Document type	Reference	Date	Summary
Legislative proposal	COM(2004)0599	29/09/2004	Summary
Document attached to the procedure	SEC(2004)1144	29/09/2004	Summary
Modified legislative proposal	COM(2005)0577	10/11/2005	Summary

Commission communication on Council's position	COM(2006)0118	13/03/2006	Summary
Commission response to text adopted in plenary	SP(2006)2902	22/06/2006	
Commission opinion on Parliament's position at 2nd reading	COM(2006)0408	19/07/2006	Summary
Follow-up document	COM(2013)0443	24/06/2013	Summary
Follow-up document	COM(2017)0626	26/10/2017	Summary
Follow-up document	SWD(2020)0163	11/08/2020	
Follow-up document	SWD(2020)0164	11/08/2020	

National parliaments

Document type	Parliament /Chamber	Reference	Date	Summary
Contribution	PT_PARLIAMENT	COM(2013)0443	06/03/2014	

Other institutions and bodies

Institution/body	Document type	Reference	Date	Summary
EESC	Economic and Social Committee: opinion, report	CES0525/2005 OJ C 267 27.10.2005, p. 0001-0008	11/05/2005	

Additional information

Source	Document	Date
National parliaments	IPEX	
European Commission	EUR-Lex	

Final act

Regulation 2006/1901
OJ L 378 27.12.2006, p. 0001 Summary

Medicinal products for paediatric use

2004/0217(COD) - 26/10/2017 - Follow-up document

After a first report published in 2013, the Commission presented a **second report** on the impact of the paediatric Regulation (Regulation (EC) No 1901 /2006) ten years after its adoption.

The report provides an account of its achievements, both in public health and economic terms and an analysis on the extent to which its objectives have been met. It builds on a 10-year report prepared by the European Medicines Agency (EMA), a public consultation and discussions with Member States, the European Parliament and interested parties.

As a reminder, the Regulation is structured around **three main objectives**:

- to encourage and enable high-quality research into the development of medicines for children;
- to ensure, over time, that most medicines used by children are specifically authorised for such use with age-appropriate forms and formulations; and
- to increase the availability of high-quality information about medicines used by children.

The main findings of the report are as follows:

More medicines for children: the figures show that the Regulation has had a **significant impact** on the development of paediatric medicines in the Union. Pharmaceutical companies now view this development as integral to the overall development of medicinal products.

Between 2007 and 2016, **more than 260 new paediatric medicines were authorised**. In addition, the number of agreed paediatric investigation plans (PIPs) has increased significantly. This result, which would not have been achieved without specific legislation, underlines that the Regulation remains relevant. In addition, the measures taken to improve its application have gradually increased its effectiveness.

Better medicines: the last 10 years have seen some considerable progress in the **availability** of medicines for children in certain therapeutic fields because of the Regulation. Rheumatology or infectious diseases are often referred to as prime examples.

The increase in paediatric research and the number of new products with specific paediatric indications is encouraging. Those positive results do however not evenly spread among all therapeutic areas, but concentrate in some, often linked to research priorities in adults rather than children. **This shows that the Regulation works best in areas where the needs of adult and paediatric patients overlap**.

The report notes that especially, in diseases that are **rare and/or unique to children** and which in many cases are equally supported through the orphan legislation, major therapeutic advances often failed to materialise.

It seems difficult to understand why companies refrain from taking advantage of the Orphan Drug Regulation for pediatric cancers as they do for adult cancers. A huge number of new adult cancer products are thriving thanks to the Orphan Drug Regulation, but this is not the case for childhood cancer, although all are considered rare within the meaning of the Regulation.

Therefore and before proposing any amendments, the Commission intends to **take a closer look at the combined effects of the Orphan and Paediatric Regulation** through a joined evaluation of those two legal instruments aimed at supporting medicine development in subpopulations of particular need.

Reward system: the Regulation places an additional burden on pharmaceutical companies by asking them to carry out paediatric research, which they might not have undertaken otherwise. The Regulation however, links this obligation with a reward system in order to allow companies to recuperate the additional upfront costs incurred as a result of it through prolonged protection period.

Still the use of rewards was limited to **55 % of the completed PIPs and there are instances of over- or under compensation** pointing to certain limitations of the current system. Additionally, the paediatric use marketing authorisation (**PUMA**) concept with its specific reward has failed to deliver.

Next steps: this report marks not the end, but an essential intermediate step in the debate on a joint vision about the future parameters for paediatric and orphan medicines. The further evaluation supporting this process aims at providing results **by 2019** so to allow the next Commission to take informed decision about possible policy options.

In the meantime, the Commission is committed to a **positive agenda of concrete actions** in order to streamline the current application and implementation together with EMA wherever needed. This includes:

- providing additional **transparency** of new products authorised with paediatric indications;
- analysing the experience with use of deferrals and consider changes in practice to ensure **speedier completion of PIPs**;
- revisiting processes and expectations in the context of handling of applications for PIPs and if necessary adapt the corresponding Commission guideline;
- exploring opportunities to discuss **paediatric needs** in an open and transparent dialogue involving all relevant stakeholders like academia, health care providers, patients/care givers, paediatric clinical trial networks, industry and regulators; delivering **regular updates** about development and trends of the paediatric medicines landscape in the EU;
- fostering international cooperation and harmonisation.

Additionally, it will further support high-quality healthcare and research for children through projects such as the **European Reference Networks**, which connect health care providers and centres of expertise. Those networks have the potential of significantly improving access to diagnosis and treatment in the short term and to make a difference in terms of child health.

Medicinal products for paediatric use

2004/0217(COD) - 19/07/2006 - Commission opinion on Parliament's position at 2nd reading

The Commission has accepted all of the amendments adopted by the European Parliament, which are the result of a compromise package agreed between the European Parliament and the Council with a view to adopting the Regulation in second reading. The Commission notes that the amendments are in line with the objectives set out in the Commission's initial proposal. The amendments to the Common Position refer to:

- "reward" provisions in the form of a six-month extension of the supplementary protection certificate;
- the introduction of a five-year transition period, following the entry into force of the Regulation, which allows for an extended deadline regarding "supplementary protection certificate" applications;
- a clarification of certain rules and provisions concerning, amongst other things: the independence and impartiality of the Paediatric Committee; publication of the Committee's opinion; pharmacovigilance and risk management; early dialogue between companies developing medicinal products and the Paediatric Committee on whether a product should be developed for children; and preventing delays for the authorisation of medicinal products.

Agreement between the institutions has been facilitated by a Commission declaration made during the June 2006 Plenary session, which states that the Commission will request the "Committee for Medicinal Products for Human Use", to draw up an opinion on the use of carcinogens, mutagens and substances toxic to reproduction as excipients of medicinal products for human use. The Commission will transmit the Committee's Opinion to the European Parliament and the Council. Within six months of the Opinion being finalised the Commission will decide whether or not to take any further action.

Medicinal products for paediatric use

2004/0217(COD) - 07/09/2005 - Text adopted by Parliament, 1st reading/single reading

The European Parliament adopted a resolution drafted by Françoise GROSSETÊTE (EPP-ED, FR) and made several amendments to the Commission' s proposal. The main point of debate involved the best way to give incentives to pharmaceutical companies to invest more money in paediatric medicine. The Commission proposed that companies should have an extra six months of protection under existing patents. A number of Members wanted to have a shorter additional period or one which depended on the size of the company. The rapporteur was firmly in favour of a fixed period. Some member states had argued for a shorter extension, in order to support their generic drug manufacturers. A review clause states that this point should be reassessed six years after the Regulation enters into force.

The remaining amendments mostly relate to the following:

-many amendments aim to shorten procedures and administrative delays, to improve transparency and the exchange of information to prevent unnecessary clinical trials;

-Parliament felt that a specific inventory of paediatric medicinal product needs must be adopted by the Paediatric Committee set up under the Regulation after consultation with the Commission, the Member States and interested parties, and regularly updated. The inventory should identify the existing medicines used by children and highlight the therapeutic needs of children and the priorities for research and development. In this way, companies should be able to identify easily opportunities for business development; the Paediatric Committee should be able to better judge the need for medicines and studies when assessing draft paediatric investigation plans, waivers and deferrals; and healthcare professionals and patients should have a reliable information source available to support their decisions as to which medicines to choose.

-A new Chapter 1a on identification of needs is inserted. The Agency must publish the inventory within two years of the entry into force of the Regulation and update it regularly, including the data from trials carried out in third countries. This inventory will also be aimed at establishing research priorities.

-Within one year of the entry into force of the Regulation, the Management Board of the Agency will adopt an implementing strategy for the launching and operation of the European network. This network must be compatible with the work of strengthening the foundations of the European Research Area in the context of the Community Framework Programmes for Research, Technological Development and Demonstration Activities.

-the Paediatric Committee must be independent of the pharmaceutical industry and be composed of members with recognised and documented international-level experience and knowledge of that industry.

-In view of the fact that 50% of medicinal products for paediatric use have not been tested, provision is made for funding for research on medicines for paediatric use which are not patent-protected or do not have supplementary protection certification to be financed under Community research programmes. Parliament wished to establish a Community programme for research into medicinal products for children (Medicines Investigation for the Children of Europe - MICE).

-Details of the results of all completed studies conducted in accordance with an agreed paediatric investigation plan, whether terminated prematurely or not, as well as details of the results of all studies funded by the Community and the Member States to support research into and the development and availability of medicinal products for paediatric use, including any studies funded by the MICE programme, will be published by the Agency with, whenever applicable, all relevant conclusions for medicinal products in the same therapeutic class that cover the same proposed paediatric use.

-There should be a European register of clinical trials of medicinal products for paediatric use. Such studies should also be entered in the databases of clinical investigations currently in operation at national level. Studies in children already performed in third countries should not be repeated. However, if unavoidable, control studies should be possible.

-There are some additional clauses on pharmacovigilance matters;

-An application for an extension of the duration of a certificate must be lodged not later than six months before the expiry of the certificate, rather than two years.

-If a medicinal product is authorised for a paediatric indication and the marketing authorisation holder has benefited from the incentive provisions in the Regulation, if the marketing authorisation holder discontinues placing the medicinal product on the market, the holder must allow a third party to use the pharmaceutical, pre-clinical and clinical documentation contained in the file on the medicinal product.

-The Commission must carry out an analysis of the incentive and reward operations under Articles 36 and 37, with a financial assessment relating to the research costs and profits resulting from such incentives. Should the analysis show the mechanism to be ill-suited to the results sought or achieved, an amendment of the articles will be proposed.

Medicinal products for paediatric use

2004/0217(COD) - 02/06/2005

Pending receipt of the European Parliament's opinion, the Council held a policy debate on the proposal for a Regulation on medicinal products for paediatric use with a view to further examination of the text.

The debate focused on the following two questions:

– extension of the validity of the supplementary protection certificate, as a way of encouraging investment in pharmaceutical products for paediatric use;

– allowing public access to data on paediatric clinical trials in order to avoid unnecessary paediatric clinical trials.

During the debate, particular emphasis was placed on the importance of encouraging research in this field and improving access to paediatric medicines, in view of the need to produce medicines adapted to the specific physical and psychological characteristics of children.

The delegations recognised the incentive value of a measure extending the protection certificate. Some of them, however, wanted to discuss the proposal further, in particular the length of the extension1 and the date on which the impact of the mechanism would be reviewed, given the less positive effects that such a measure might also produce (e.g. delay in the placing on the market of generic medicines).

Delegations were generally in favour of making the results of clinical trials more widely available, as this would help to avoid unnecessary clinical trials, but further discussion was needed to establish, in particular, how widely available this would mean.

Medicinal products for paediatric use

2004/0217(COD) - 10/03/2006 - Council position

The common position has been adopted by the Council by qualified majority. The European Parliament adopted 69 amendments to the proposal. 42 of these have been incorporated, either in full, in part or in principle into the Council’s common position corresponding to around two thirds of the proposed amendments. 27 amendments have not been accepted. The common position incorporates most of the amendments proposed by the European Parliament accepted or accepted in principle by the Commission in its amended proposal.

The following amendments were amongst those that were **accepted** by the Council:

- the Paediatric Committee will be established within 6 months after the entry into force of the Regulation;

- the Paediatric Committee should appoint a rapporteur as part of the preparation of decisions on product specific waivers;

- the Council agrees to the amendments on updating and public availability of the list of waivers;

- the Council supports the principle of avoiding double rewards gained on the basis of the same research in the following particular situation. Directive 2001/83/EC as amended by Directive 2004/27/EC, provides that the period of market protection shall be extended by one year if the marketing authorisation holder obtains an authorisation for a new indication which is judged to bring significant clinical benefit in comparison with existing therapies. In the case of a new paediatric indication, this additional year of market protection should not be granted together with the six-month extension when based on the same research. To avoid this cumulative reward, the Council has introduced a new paragraph in the relevant Article.

The Council also accepted the following amendments in full, part or in principle;

- transparency of clinical trials in children;

- on the role of the Paediatric Committee in compliance and in assessing safety, quality and efficacy of a medicine;

- provisions in the event of discontinuation of medicines;

- funding for studies;

- labelling of medicines provisions;

- provisions on clearer timelines for procedures;

- deadlines for the implementation of the regulation, and on review of the paediatric regulation;

- on the use of the data on the clinical trials database to avoid unnecessary studies;

- on taking account of international data;

- on the composition of the Paediatric Committee and providing for the consultation of the European Parliament;

- on opinions of the Paediatric Committee and their publication,

- on a list of waivers on modifying the Paediatric Investigation Plan;

- on product information, on a European logo, on which medicines should be labelled with the European logo, on a register of marketing deadlines;

- on public access to details of trials in the European database;

- on publication of the names of those infringing the regulation;

- on the review of the operation of the Regulation and of the system of rewards and incentives.

European Parliament amendments **not incorporated** in the common position:

- the Council did not consider the Paediatric Committee to be primarily responsible for the ethical assessment of the Paediatric Investigation Plan. Ethical assessment of proposals for clinical trials is the primary responsibility of the Ethics Committees. The Council does not consider that members of the Paediatric Committee must have international-level experience and knowledge of the pharmaceutical industry.

- the Council decided to delete the amendment on independence and impartiality of the members of the Paediatric Committee, since detailed provisions on such requirements are already set out in Regulation 726/2004, to which explicit reference is made;

- the Council supports the principle that the Committee should advise on communication about the conduct of clinical trials in children, but does not consider it appropriate for the Paediatric Committee to have a self-promoting function;

- the Council considers that the amendment opening a possibility to provide information on ongoing paediatric studies, is not necessary. The Commission proposal does not require the completion of all paediatric studies at the time of application for marketing authorisation. The “deferral” provision allows for delay in the initiation of paediatric clinical studies so as to ensure that the studies are only done when it is safe and ethical to do so. The Commission proposal also provides for the deferral decision to contain a timetable to complete the studies. The Council agrees with the Commission proposal in these respects;

- the Council agrees with the Commission proposal that provides for the summary report to be prepared by the Agency. This is consistent with the operating methods of the Committee on Orphan Medicinal Products. Ten days are inadequate for the preparation of the summary report by the Agency;

- the Council considers that it would be confusing for the patient and carer if some, but not all, products authorised for paediatric use were identified by a Community symbol on the label. The symbol, therefore, should apply to all medicinal products with a paediatric indication. In addition, the meaning of the symbol should be explained in the patient information leaflet and a deadline should be introduced for the application of the symbol;

- with regard to post-authorisation requirements, the Council supports the text of the Commission proposal which makes it clear that the legal obligation is to market within two years. In addition, existing EC pharmaceutical legislation sets out clear deadlines both for the granting of a marketing authorisation and for national decisions concerning the pricing and reimbursement for medicinal products. The Council considers that it is inappropriate, therefore, to provide for derogations in the application of this provision in cases where competent authorities are unable to meet such deadlines;

- with risk management systems when the competent authority has cause for concern, the European Parliament proposed to make such a system compulsory. The Council recalls that the EC pharmaceutical legislation has recently been amended and now contains strengthened and new pharmacovigilance measures, including risk management systems. The proposed Regulation contains a provision for the competent authority, whenever it has cause for concern, to require a risk management system to be put in place. The Council does not find it appropriate to make this provision compulsory, as there may be occasions when such a requirement would add an unnecessary burden and may present a barrier to access to appropriate medicines.

The Council also **rejected** the following amendments:

- on the removal of the requirement for a medicinal product to be authorised in all Member States;

- a European competition to design a logo to be used to label medicines for children,

- the exclusion of the extension of the supplementary protection certificate for products which have received a patent covering the same paediatric use in the EU,

- on the number of extensions of the supplementary protection certificate;

- on a simplified marketing authorisation procedure for orphan drugs;

- on the harmonisation of national measures enacting penalties;

- on the deadline for submission of an application for an extension of the supplementary protection certificate;

- on transitional measures for paediatric investigation plans

- on the date of introduction of the requirements.

The Council introduced **other modifications introduced by the Council** common position compared with the amended proposal.

- A recital was modified to delete the explicit reference to Article 95 of the Treaty.

- The Council states that, in analogy to what is the case for the Committee for Human Medicinal Products, it will introduce alternates for the members and specify the procedure for their appointment. In view of the introduction of alternates, the Council considers that six members are sufficient to represent the interests of healthcare professionals and patient associations. However, the Council considers that it should be made clear that three members should represent healthcare professionals and three members should represent patient associations. The list of disciplines represented on the Committee applies to the Committee as a whole and should be incorporated in the list of disciplines set out in the Regulation. The Commission did not object to these changes as it believes that the relevant expertise and balance of representation will be maintained.

An additional task of the Paediatric Committee is to recommend a symbol for the labelling of medicines indicated for children. The Paediatric Committee shall consider whether or not proposed studies can be expected to be of significant therapeutic benefit or fulfil a therapeutic need of the paediatric population.

The Council clarified that the requirements for the results of studies in children or an Agency decision on a waiver or deferral shall cover both existing and the new indications, pharmaceutical forms and routes of administration.

A modification states that 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.

The Council clarified that when the applications are submitted in accordance with the procedure set out in Directive 2001/83/EC, the verification of compliance, including, as appropriate, requesting an opinion of the Paediatric Committee, shall be conducted by the reference Member State.

Incentives provided for would also not be granted in the event of non compliance detected during the scientific assessment.

The Agency will have ten days to transmit the opinion of the Paediatric Committee to the applicant.

It is the Marketing Authorisation Holder that should submit any paediatric studies already completed, to clarify the competent authorities' role in updating product information.

Finally, the Council clarified: the procedures when Supplementary Protection Certificate applications are pending; the contents of an application for an Supplementary Protection Certificate extension and how to submit such an application; extensions may be revoked if granted contrary to the provisions of the paediatric regulation and how this will occur; the appeals system.

Medicinal products for paediatric use

2004/0217(COD) - 13/03/2006 - Commission communication on Council's position

The Commission states that it supports the common position. To a very large degree the common position is in line with the Commission's amended proposal. In addition it introduces a small number of changes to the Commission's amended proposal which improve the text while maintaining the initial objectives of the Commission. Many of these modifications concern improvements in the layout of the text or constitute editorial improvements which do not change the meaning or practical application of the Regulation.

Key amendments proposed by the European Parliament in the first reading, such as transparency and membership of the Paediatric Committee, transparency of clinical trials in children, provisions in the event of discontinuation of medicines, funding for studies, labelling of medicines, clearer timelines for procedures, deadlines for the implementation of the regulation, avoiding double rewards and clarifying in what circumstances rewards will be granted, and on review of the paediatric regulation are present in the common position, sometimes with drafting changes to ensure the legal consistency of the text and technical workability of the measures and procedures put in place.

Medicinal products for paediatric use

2004/0217(COD) - 12/12/2006 - Final act

PURPOSE: to lay down rules concerning the development of medicinal products for human use in order to meet the specific therapeutic needs of the paediatric population.

LEGISLATIVE ACT: Regulation (EC) No 1901/2006 of the European Parliament and of the Council 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.

CONTENT: The Council adopted this Regulation on medicinal products for paediatric use and approved all the amendments passed by the European Parliament at second reading. The Regulation is aimed to address the current situation in Europe, whereby more than 50% of the medicines used to treat children have not been tested and are not authorised for use on children. The health and therefore quality of life of the children of Europe may suffer from a lack of testing and authorisation of medicines for their use.

The Regulation aims to improve child health, by increasing the availability throughout the Community of medicinal products that have been appropriately tested and authorised for paediatric use, while removing obstacles to intra-Community trade in paediatric medicinal products. The Regulation aims in particular to meet the following objectives:

- to ensure that medicinal products used to treat children have been the subject of ethical high-quality research and appropriate clinical trials;

- to ensure that those medicinal products are duly authorised;

- to improve information on the use of medicinal products intended specifically for children and transparency on paediatric clinical trials, while avoiding unnecessary clinical trials on children and delays on the authorisation of medicinal products for other age populations.

To that end, the Regulation contains a combination of obligations and incentives.

The main obligation created by the Regulation is that either the results of clinical studies obtained in accordance with a paediatric investigation plan, or proof of having obtained a waiver for medicines that are of no paediatric use, must be submitted as part of the procedure for obtaining marketing authorisation. For medicines protected by a patent or an SPC, incentives are provided through the extension of exclusive rights. The regulation also aims to certify a safe use of off-patent medicinal products for the treatment of children, through the introduction of a new type of marketing authorisation for off-patent medicines that have been appropriately tested for paediatric use, the PUMA, as well as through provisions on funding of research into the appropriate use of off-patent medicinal products for paediatric treatment.

A scientific committee, the Paediatric Committee, is created within the European Medicines Agency, with expertise and competence in the development and assessment of all aspects of medicinal products to treat paediatric populations.

The proposed system covers medicinal products for human use within the meaning of the directive on the Community code relating to medicinal products for human use and is in full compliance with the EU clinical trials directive.

In order to fulfil its objectives, the new Regulation also introduces some amendments to the regulation that created a supplementary protection certificate for medicinal products, the directive on the Community code relating to medicinal products for human use, the regulation laying down procedures for the authorisation and supervision of medicinal products and the EU clinical trials directive.

In a Declaration, the Commission states that, in view of the risks of carcinogens, mutagens and substances toxic to reproduction, it will request the Committee for Medicinal Products for Human Use of the European Medicines Agency to draw up an opinion on the use of these categories of substances as excipients of medicinal products for human use, on the basis of Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

The Commission will transmit the opinion of the Committee for Medicinal Products for Human Use to the European Parliament and the Council. Within six-months of the opinion of the Committee for Medicinal Products for Human Use, the Commission will inform the European Parliament and the Council of any necessary action it intends to take to follow-up on this opinion.

ENTRY INTO FORCE : 26/01/2007. Article 7 is applicable from 26/07/2008. Article 8 is applicable from 26/01/2009. Articles 30 and 31 are applicable from 26/07/2007.

Medicinal products for paediatric use

2004/0217(COD) - 29/09/2004 - Legislative proposal

PURPOSE: to improve the health of children in Europe by increasing the research, development and authorisation of medicines for use in children.

PROPOSED ACT: Regulation of the European Parliament and of the Council.

CONTENT: the European Commission is proposing this Regulation following a Council Resolution, which called on the Commission to make regulatory proposals ensuring that new medicinal products for children and medicinal products already on the market are fully adapted to the specific needs of children. In order to fulfil this task the Commission has set out a number of objectives, which the proposed Regulation should fulfil, namely:

- To ensure that medicines used to treat children are subject to high quality research;

- To ensure that medicines used to treat children are appropriately authorised for use in children;

- To improve the information available on the use of medicines in children and;

- To achieve these objective without subjecting children to unnecessary clinical trials and in full compliance with the EU Clinical Trials Directive.

Until now, more than 50% of the medicines used to treat children in Europe have not been tested and are not authorised for use in children. Reluctance to test medicines on children has been cited as the main reason for this huge gap in authorised medicines for the paediatric population. The Commission suggests that this problem can be addressed by using the EU Directive on clinical trials, which lays down specific requirement to protect children who take part in clinical trials across the EU. Some of the key measures being proposed include:

- The creation of a paediatric committee. This will be responsible primarily for the assessment and agreement of paediatric investigation plans and requests for waivers and deferrals. Further, it may assess compliance with paediatric investigation plans and be asked to assess the results of studies. It will assess whether or not studies are unnecessary. At the same time it will avoid any delay in the authrorisation of medicines for other populations as a result of the requirement for studies in children.

- Marketing authorisation requirements. One of the central elements of the proposed Regulation is the introduction of a paediatric investigation plan. When drawing up the plan two principles need to be applied. Firstly, studies should only be conducted if there is a potential therapeutic benefit to children. Duplication of studies should be avoided. Secondly, that the requirements for studies in children should not delay the authorisation of medicines for other populations. Thus, unless a waiver or deferral has been granted, a paediatric investigation plan needs to be submitted at the time of application.

- Waivers from the requirement. The Paediatric Committee will draw up a list of waivers of specific medicinal products and classes of medicinal products. This will apply mostly to medicines being developed for adults, which are not needed to treat children.

- Deferrals from the timing or completion of studies in children. This will apply to studies in cases where some initial experience of a product has already been applied to adults or on studies, which might take longer in children than in adults.

- Marketing authorisation procedures. The procedures set out in existing pharmaceutical legislation are not altered by the proposal. It is being proposed that an application for a marketing authorisation including at least one paediatric indication based on the results of an agreed paediatric investigation plan will have access to the centralised Community procedure.

- The Paediatric Use Marketing Authorisation (PUMA). PUMA is being proposed as an incentive for off-patent medicines. It is a new type of authorisation. It will utilise existing marketing authorisation procedures but is specifically designed for paediatric medicine. Companies with a PUMA authorisation may continue using the brand name of their product – but in order to make it identifiable as a paediatric medicine the brand name will be followed a subscript of the letter P.

- Extension of the duration of the supplementary protection certificate. This is designed for new medicines and for products covered by a patent or a Supplementary Protection Certificate (SPA). It will only apply if all the measures included in the paediatric investigation plan are complied with, if the product is authorised in all Member States and if relevant information on the results of studies is included in the product – in which case the SPA can be extended for six months.

- Extended market exclusivity for orphan medicinal products. This is included in order to extend the ten-year period of orphan market exclusivity to twelve-years if the requirements for data on use in children are fully met.

- Paediatric study programme: Medicines Investigation for the Children of Europe (MICE). This measure is being introduced in order to offer funding for studies into the paediatric use of medicines not covered by a patent or a supplementary protection certificate.

- Information on the use of medicines for children. The Commission proposes extending the EudraCT database, which is designed to serve the purposes of the Clinical Trials Directive, by expanding the database to include all ongoing and terminated paediatric studies conducted both in the Community and third countries. Further, the Paediatric Committee will establish an inventory of therapeutic needs of children. European networks and clinical trial centres will be linked in a bid to facilitate co-operation and to avoid duplication of studies.

- Lastly, under the title "Other Measures" it is being proposed that the Paediatric Committee will be managed by the EMEA. Free scientific advice from the EMEA to sponsors for the development of medicines for children is also being proposed. The Regulation will put an additional burden on the EMEA and it is, therefore, being proposed that the Community subsidy to the EMEA be increased.

FIANCIAL IMPLICATIONS:

- Budget lines and headings: 02.040201 – European Agency for the Evaluation of Medicinal Products - Subsidy under Titles 1 and 2 - 02.040202 – European Agency for the Evaluation of Medicinal Products - Subsidy under Title 3.

- Overall figures: Total allocation for action (Part B): EUR 21 282 million for commitment.

- Period of application: 2007 to 2012.

- Overall multi-annual expenditure – commitment appropriations/payment appropriations: A total of EUR 21,282 for commitment appropriations and a total of EUR 21,282 for payment appropriations.

- Overall financial impact of human resources and other administrative expenditure:

Staff will be need for the Secretariat of the Paediatric Committee, Paediatric Investigation Plan applications, the Paediatric Research Network, Funding of studies and Support staff. The total foreseen for 2007 are 3, extending to 26 by 2012 and beyond.

Medicinal products for paediatric use

2004/0217(COD) - 01/06/2006 - Text adopted by Parliament, 2nd reading

The European Parliament adopted a resolution drafted by Françoise **GROSSETÊTE** (EPP-ED, FR) on the new rules framing the marketing of medicines for children. A series of compromise clauses were negotiated with the Council and Commission. The law will cover medications currently in development and not yet authorised, authorised medications covered by patents as well as authorised products that are not covered by intellectual property rights. The Regulation will require pharmaceutical companies to draw up “paediatric investigation plans” (a research and development programme aiming at guaranteeing the necessary data for those who require paediatric treatment) before filing authorisation requests for new medicines intended for children. In exchange, the duration of supplementary protection certificates (an intellectual property right) will be extended by six months. The same reward, subject to the same conditions, will also be available for medicines already on the market and still covered by intellectual property rights.

The other main points of the compromise agreement are as follows:

Legal base: Parliament stated that any action to promote the development and authorisation of medicinal products for paediatric use is therefore justified with a view to preventing or eliminating these obstacles. Article 95 of the Treaty is therefore the proper legal basis.

Committee independence: In line with Parliament’s demands, the compromise enhances the independence of the Paediatric Committee. It therefore states that Members of the Paediatric Committee should) not have financial or other interests in the pharmaceutical industry which could affect their impartiality, should undertake to act in the public interest and in an independent manner, and should make an annual declaration of their financial interests. This Committee, established within

the European Medicines Agency (EMEA), will be responsible for assessing and approving the ‘paediatric investigation plans’ which should accompany requests for authorisation for the marketing of new drugs. The institutions have also agreed that the opinions of the Paediatric Committee should be made public. Between two and three years after entering into force the Paediatric Committee will draw up an inventory of therapeutic benefits in order to determine research priorities.

Substances that are carcinogenic, mutagenic or toxic for reproduction: A statement from the Commission indicates that, in view of the risks of carcinogens, mutagens and substances toxic to reproduction, the Commission will request the EMA to draw up an opinion on the use of these categories of substances as excipients of medicinal products for human use, on the basis of Articles 5(3) and 57(1)(p) of Regulation 726/2004/EC. The Commission will transmit the opinion of the Committee for Medicinal Products for Human Use to the European Parliament and the Council. Within six months of the opinion the Commission will inform the European Parliament and the Council of any necessary action it intends to take to follow up on this opinion.

Supplementary protection certificates: the Council text on the duration of the extension of supplementary protection certificates still stands. Parliament had proposed that extensions should only be granted from the time when a medicine has received authorisation for marketing in all the member states. The Council recommended the extension of SPCs immediately a product is authorised in all the member states and if relevant information on the results of studies is included in product information: this is the provision finally retained. The difference is significant since there is often a considerable gap between the moment when a medicine is authorised and the time it effectively reaches the market. Parliament approved a transitional clause which states that, for five years after the regulation enters into force, the application for an extension of the duration of a certificate already granted shall be lodged not later than six months before the expiryof a Supplementary Protection Certificate.

The risk management system: where there is particular cause for concern, the competent authority shall require, as a condition for granting marketing authorisation, that a risk management system be set up or that specific post-marketing studies be performed and submitted for review.

Medicinal products for paediatric use

2004/0217(COD) - 29/09/2004 - Document attached to the procedure

COMMISSION’S IMPACT ASSESSMENT

For further information regarding the context of this issue, please refer to the summary of the Commission’s initial proposal on medicinal products for paediatric use COM(2004)0599 dated 29/09/2004.

1- POLICY OPTIONS AND IMPACTS

1.1- Option 1 - No action: on the basis of the available evidence it is concluded that the current public health issue regarding medicines for children will not be resolved in the EU until a specific legislative system is put in place. The health and therefore quality of life and future of Europe’s children may suffer from a lack of testing and authorisation of medicines for their use.

1.2- Option 2 - Industry self-regulation: one potential option to increase the research, development and authorisation of medicines for children is to work with industry to develop a code of practice by which the industry could self-regulate. However, such a system would rely entirely on the goodwill of industry and industry has generally been unwilling to make the investment required to authorise medicines for children in the EU even when the data to support authorisation have already been generated as a result of the laws that exist in the US. Furthermore, self-regulation would place the entire burden of this public health issue on industry with no mechanisms for rewards. Also, government intervention is required to ensure the right studies are done for the benefit of children rather than studies being conducted only because the market returns are likely to be high.

1.3- Option 3 - Member State action: the public health issue is Community-wide and the regulation of medicines is Community-based. Nevertheless, the draft paediatric regulation does leave room for complementary Member State actions.

1.4- Option 4 - Requirements without rewards and incentives without requirements: providing an incentive in the form of Intellectual Property Rights (IPRs) would lead some companies to do the necessary research, development and authorisation of some medicines for children. However, the main driver for research would remain market forces i.e. the potential for industry to profit from the research conducted and the IPR awarded. This would mean that the therapeutic needs of children, which are the drivers of the research, development and authorisation of medicines in the draft paediatric legislations, might come second to consideration of profit.

1.5- Option 5 - New products: why not reward with data protection: data protection could be used to reward industry for meeting the requirements for new and patent-protected authorised products in the draft paediatric regulation. However, data protection is less valuable to the innovative industry than supplementary protection certificate (SPC) extension and the draft Regulation is already offering the innovative industry a shorter period of SPC extension than it is demanding.

1.6- Option 6 - New products: why not reward with administrative market exclusivity: Some have argued that a system of "administrative" market exclusivity, as is operated under the EU Orphan Regulation should be considered for new paediatric medicines. But orphan medicines are few in number and therefore the operation of a system of "administrative" market exclusivity is possible. Considering their number and the multiple competent authorities in Europe responsible for the authorisation of medicines, such a system would be administratively impossible for paediatric medicines.

1.7- Option 7 - Older products: why not use market exclusivity as the incentive? A system of "administrative" market exclusivity has also been considered by the Commission, for off-patent medicines for children. The central argument against such a system is that generics will already be on the market. Unless generic marketing authorisations for a particular active drug substance were revoked following authorisation of one off-patent product for children then market exclusivity is impossible in a multi-product environment. In contrast, a data protection scheme is practical for all off-patent drugs for children even if the incentive is less when no child-specific formulation is required.

Impacts:

In the short term, the workload of the EMEA and National Competent Authorities will increase and there will be a need to secure the services of additional experts to assess paediatric investigation plans and the data generated from studies in children. In the longer term, the costs of paediatric medication and paediatric health care may increase as the costs of testing are carried forward. The impact on revenues and profits of pharmaceutical companies will depend on the price elasticity of children's medicines and households' willingness-to-pay and insurance companies' willingness-to-reimburse. Healthcare professionals appear willing – and may even feel obliged – to switch to tested medicines. National governments may decide to negotiate or enforce price reductions.

The draft Regulation will create jobs for the innovative industry by requiring the development and authorisation of medicines for children. Across the entire innovative sector there will be an increase in the costs of phase III clinical trials of about 160 – 360 million Euros after the first year (an increase in total European expenditure on drug development of 1% - 2.5%). This amounts to about EUR 4 million per product. It is estimated that the six-month extension of the SPC will lead to the producers of generic medicines incurring a one-time loss of between EUR 86 million and EUR 342 million, which represents the value of market opportunities lost during the transitional period.

It is possible that the 6-month extension of the SPC may mean a small rise in costs for consumers and health insurers but the Commission states that the figures need to be treated with caution, as the prescribing of generics will bring down costs. There will be savings resulting from more effective treatment, fewer adverse drug reactions and lower wastage of medicines (currently, high-dose adult formulations are used with the excess being discarded).

The Commission feels that data-protection remains the best and most practical incentive for off-patent products. The Paediatric Use Marketing Authorisation (PUMA) is most likely to be effective where a child specific formulation or dosage form is required as this will likely lead to preferential prescribing over non child-adapted products. Also, the fact that the Paediatric Board is likely to block repeat testing in children unless a significant therapeutic benefit for children is foreseen means that the PUMA with its data-protection may, for some products, result in market exclusivity (although this cannot be guaranteed). It is acknowledged, however, that it will not, on its own, provide sufficient incentive to ensure that all the off-patent medicines needed by children are tested and authorised for children. To effectively deal with the off-patent market, other measures, including the Paediatric Study Programme, as well as, the inventory of paediatric therapeutic needs, will also need to be in place.

In the short term, the impacts of the additional requirements (labelling, placing on the market, post-marketing requirements and submission of pre-existing studies) will mean that existing medicines, newly tested in children and authorised will be made available. Health care professionals will gain better knowledge of the safety of paediatric medicines and, as a result, children will receive safer treatment. If complied with adequately, the additional requirements will generate considerable benefits to European children and prevent the misallocation of resources at comparatively low marginal costs to pharmaceutical companies and government authorities. Both can build on currently existing (mandatory) systems for pharmacovigilance (specific estimates of these additional costs are not available).

Appropriate labelling of tested paediatric drugs will create a sharper definition of paediatric and other segments of the market for off-patent drugs. Health care professionals benefit from increased transparency in the choice between tested and untested off-patent medicines: it will be easier to see whether a drug is tested for use in children or not.

The post-marketing requirement will force companies to develop an improved understanding of the safety, efficacy and quality of their paediatric medicines, which may result in the development of better medicines for children. Children can be treated more effectively and there will most likely be fewer cases of adverse drug reaction or suboptimal treatment. The impact of this requirement can only really be fully ascertained at a later date, because the long-term effects of a medicine in children cannot necessarily be assessed until much later in a child's development.

The optional centralised assessment via the existing Community referral procedure provides a streamlined route to gain a harmonised EU-wide opinion on paediatric use of already authorised products. The centralised assessment will also facilitate access to more Member State markets.

In the long run free scientific advice, communication and coordination (and the study fund) will generate economies of scale and scope in pharmaceutical R&D and paediatric testing. Together, they are generally considered a highly valuable measure that will provide a strong stimulus to paediatric research in Europe. An EU paediatric study programme has the potential to stimulate research and development of off-patent medicines for children and could have a major beneficial impact on EU pharmaceutical companies, including SMEs, and a major impact on clinical trials conducted in the EU including strengthening pharmaceutical R&D in Europe.

Environmental impact: the development and manufacture of medicinal products requires natural resources and generates waste. In addition, households, GPs and hospitals regularly dispose of unused medicinal products. However, considering that at present, adult preparations of medicines are usually used to treat children with the clear wastage that that incurs (high dose preparations of adult medicines being opened, small quantities being used to treat children and the excess discarded), the draft paediatric regulation may actually reduce the environmental impact of use of medicines by children.

Equity within and between generations: Future generations of children are more likely to be enrolled in clinical trials, but in return they will be provided with better medicines, more effective and safer treatment, and a higher quality of life.

CONCLUSION: the Commission has opted to present its proposal for a Regulation on paediatric medicines for several reasons. The lack of tested, authorised medicines for children is a Europe-wide issue. Surveys of off-label and unlicensed use of medicines are available from many EU Member States and all show that children are denied innovation and children are being treated with medicines meant for adults and those medicines may not work in children and may present safety hazards. Secondly, the current system for the regulation of medicines is a Europe-wide system. Therefore, the most efficient and effective way to improve the availability of medicines for children across the Community is via the existing Community system of pharmaceutical legislation (including granting marketing

authorisations) and the Community system of supplementary protection certificates. Indeed, given the Community nature of the existing pharmaceutical legislation, the scope for unilateral action by individual Member States is limited.

2- FOLLOW-UP

The following measures are provided for in the draft Regulation: a database of paediatric studies; annual reports from the Member States to the Commission on problems encountered with the implementation of the Regulation; annual publication of lists of companies that have benefits from the rewards / incentives or companies that have failed to comply with the obligations, and; within six years of entry into force, a general report on experience acquired as a result of the application of the Regulation, including, in particular, a detailed inventory of all medicinal products authorised for paediatric use since it came into force.

Medicinal products for paediatric use

2004/0217(COD) - 10/11/2005 - Modified legislative proposal

Following the first reading of the proposed Regulation in Parliament, the Commission has given its opinion on the Parliamentary amendments and modified its initial proposal accordingly.

The Commission has accepted eighteen amendments in their entirety. In summary, they relate to:

- Amendments highlighting that the objective of the proposal is to promote the circulation of safe medicinal products and that not all testing on children may be appropriate. A further amendment, accepted by the Commission, clarifies that studies on children may not always be possible prior to granting marketing authorisations for adults and that the provision for medicines for children should not delay marketing authorisation applications for medicines in adults. An amendment highlighting the role of the Paediatric Committee in checking compliance with the paediatric investigation plan and in giving an opinion on the safety, quality and efficacy of medicine in children was also accepted by the Commission.

- The proposed amendment which seeks to avoid unnecessary studies on children through the use of data on the clinical trials database.

- Further amendments acknowledged by the Commission and incorporated into the modified proposal include those highlighting the importance of taking international data into account when establishing and operating a European clinical trial network, clarifying that children should not be subjected to any unnecessary trials, (be they clinical or other) and an amendment clarifying that the opinion of the Paediatric Committee will be adopted by a majority of members, with the divergent views being published for public scrutiny.

- Other amendments relating to the Paediatric Committee and adopted by the Commission refer to the appointment of a rapporteur for the Committee and an amendment ensuring that the list of waivers are regularly updated and made available to the public.

- Also accepted are amendments proposing the establishment of a European logo for paediatric medicines and that existing paediatric medicines authorised for children should be labelled with the that logo.

- An amendment establishing a publicly accessible register indicating the deadline for placing newly authorised products for children on the market.

- The last two amendments accepted by the Commission ensure that the scope of Commission guidance concerning the database of clinical trials includes what information should be made public and how the Agency should achieve this and clarifying that ongoing, as well as, completed studies should be taken into account by the Committee when assessing paediatric investigation plans, waivers and deferrals.

Those accepted by the Commission in part or in principle refer, *inter alia*, to amendments:

- Concerning the independence and requirements in terms of professional experience of the members of the Paediatric Committee and the need to ensure that any studies in children have potential significant therapeutic benefits for them. The Commission suggests that a rewording is necessary to clarify that the members of the Committee must have experience relevant to the work of the Committee – but that this experience may have been gained other than in the pharmaceutical industry. In addition, the Commission has changed the wording in order to clarify that, when the Paediatric Committee considers the potential significant therapeutic benefits of a medicine, these potential benefits relate to either the patients to be included in studies or the paediatric population at large.

- Intended to clarify that, in some circumstances, it is not appropriate to conduct studies in children in parallel with adult studies. The recital has been reworded to specify the mechanisms foreseen in the Regulation (waivers and deferral) to address such a situation.

- Providing for the establishment of a research programme into the paediatric use of medicinal products, which are not protected by a patent or supplementary protection certificate.

- Concerning the inventory of therapeutic needs. This has been partially reworded to provide for a longer deadline for publication. The survey will take two years to complete and the Paediatric Committee should be granted twelve months to carefully assess the data and adopt the inventory.

- Requiring the Paediatric Committee to be operational within six months from the date of entry into force of the Regulation. A reformulation of the amendment has been necessary to ensure that the deadline can be met.

- Broadening the composition of the Paediatric Committee and providing for the consultation of the European Parliament before the designation of the members appointed by the Commission. The Commission will be adding “general practitioners” to the list of those sitting on the Paediatric Committee.

- Concerning the Paediatric Committee’s task as regards the inventory of therapeutic needs.

- Stating that the Committee must take account of results and assessments performed in third countries.

- Introducing a deadline for the Agency to adopt a Decision. The Commission, however, proposes a ten day deadline.

- Providing that, in cases where a company stops commercialising a product then the company must allow another company access to marketing authorisation. The Commission has reworded the amendment so that the periods of protection granted by the reward or incentive should have expired for this provision to apply. The Commission also considers it appropriate that those holding a market authorisation should be allowed to transfer their authorisation rather than relying on Article 10c of Directive 2001/83.

- Excluding an extension of the supplementary protection certificate for products which have received any form of data or market exclusivity for the same paediatric use in the EU. This has been done to avoid cumulative rewards.

- On the review of the operation of the Regulation. The review will include a public health assessment alongside an economic assessment.

Amendments not accepted by the Commission include, *inter alia*,:

- Those proposing to move the recital dealing with the survey, inventory and network to a new Chapter 1a.

- Those, that task the Paediatric Committee with the ethical assessment of paediatric investigation plans. The primary responsibility of the Committee will be scientific.

- Those aimed at introducing a flexible deadline for placing existing medicinal products which have been newly authorised for children on the market

- Those that want to remove the requirement for a medicinal product to be authorised in all Member States as a prerequisite for the extension of the supplementary protection certificate.

- Those making specific mention, in the Regulation’s’ objectives, of medicinal products intended for the treatment of rare congenital conditions suffered by children given that the Regulation applies to all paediatric populations and to all diseases suffered by children.

- Those that request the Member States to collect available data on existing uses of medicinal products and the drawing up of an inventory of therapeutic needs within a year.

- Those amendments providing that applications for agreement on paediatric investigation plans should include a summary report, reducing the deadline for validation of such applications by the Agency from 30 to 10 days and removing the deadline for industry to submit and discuss its plans for paediatric studies with the Paediatric Committee.

- Those aimed at creating a European competition to design a logo for paediatric medicines. The choice of the logo will require the expertise of specialists in paediatric medicines. Hence the modified proposal states that the Paediatric Committee will choose a new logo within one year of the Regulation’s entry into force.

- Those that duplicate or amend some of the pharmacovigilance provisions contained in the Community pharmaceutical legislation.

- Those excluding an extension of the supplementary protection certificate for products whose active substance has already benefited from a patent covering the paediatric use or formulation, since this would run counter to the core objective of the proposed Regulation, namely stimulating research into paediatric medicines. However, and in line with the purpose of this amendment, the Commission does clarify that rewards associated with a completed Paediatric Investigation Plan should only be triggered by research completed after the Regulation has entered into force.

- Those reducing the deadline for submission of an application for an extension of the supplementary protection certificate since it takes approximately two years to conduct the necessary studies and to obtain a marketing authorisation for a generic product.

- Those introducing transitional measures relating to paediatric investigation plans. Applications submitted prior to the entry into force of the Regulation can not include findings from studies with agreed investigation plans since there will be no legal basis in pharmaceutical legislation or competent committee within the Agency to agree paediatric investigation plans in advance of the Regulation's entry into force.

- Those which seek to shorten the number of months from entry into force of the Regulation since they are considered unworkable.

Medicinal products for paediatric use

2004/0217(COD) - 24/06/2013 - Follow-up document

The Commission presents its General Report on experience acquired as a result of the application of Regulation (EC) No 1901/2006 on medicinal products for paediatric use five years after the Regulation's entry into force. The report concludes that despite more than five years of experience, the true impact of the Regulation on the health of children will only become apparent over time as experience is accumulated in the longer term. There are encouraging signs though.

- Better and safer research: before the Paediatric Regulation entered into force, many pharmaceutical companies considered the adult population their key market. Research into the potential use of an adult product in the paediatric population was often side-lined or not considered at all. With the obligations introduced by the Regulation, forcing companies to screen every new (adult) product for its potential paediatric use, the situation has been turned around.

By the end of 2012, the European Medicines Agency had agreed 600 paediatric investigation plans. Of these, 453 were for medicines that were not yet authorised in the EU, while the remainder related to new indications for patent-protected products or paediatric use marketing authorisations.

- More medicines available for children: over 12 years (from 1995 to 2006), 108 of all 317 indications of 262 centrally authorised medicines included the paediatric population. Since the Paediatric Regulation entered into force, 31 out of 152 new medicines have been authorised for paediatric use, 10 of which met the conditions of Article 7. This is no more than a 'snapshot' of the effects of the Regulation as this figure is likely to increase in the future, as a considerable number of the new, already authorised, medicines are subject to an investigation plan where completion was deferred to avoid delays in the authorisation of the adult product. It follows that in the years to come many more of those 152 new medicines are expected to be authorised for paediatric use.

- Increased information on medicines used by children: since 2008, more than 18 000 study reports on roughly 2200 medicinal products have been submitted, revealing the large amount of existing paediatric information available at company level.

Some **lessons** have been learnt in the last five years. Their impact on the overall performance of the Regulation has to be closely monitored. They include:

- Better access to treatment, since 2008, more than 600 paediatric investigation plans have been approved. However, only a minority of them has been completed to date; the vast majority are still on-going. This is due to the **long development cycles of medicinal products**, often lasting more than a decade and the near-systematic deferral of paediatric studies. The high number of deferrals may not have been initially expected, but are currently a reality, as for most of the medicinal products that have been authorised so far, the R&D programme started before the entering into force of the Regulation. Consequently, the paediatric requirements could not be taken into account from the beginning of the product development.

Criticism has been voiced that the Regulation **will fail to ensure a breakthrough** in areas of particular paediatric need, such as paediatric oncology. This argument is related to the fact that the starting point for the majority of paediatric investigation plans is an ongoing R&D programme for a medicinal product for adults. An intrinsic consequence of this approach is that these products primarily target adult conditions.

Moreover, the Regulation grants **waivers from its obligations** where the disease or condition for which the specific medicinal product is intended occurs only in adult populations. This legislative approach creates friction in the case of diseases that are specific and exclusive to children.

- PUMA: the Paediatric Regulation introduced a **new type of marketing authorisation** - the Paediatric Use Marketing Authorisation (PUMA). As an incentive to carry out research into the potential paediatric use of off-patent medicinal products that have been authorised for adults, this marketing authorisation offers 8 years of data and 10 years of market exclusivity to any new off-patent product developed exclusively for use in the paediatric population. To date, only one PUMA has been granted, with a few more projects currently in the pipeline. The EMA will in future accept paediatric investigation plans for a PUMA that cover only certain age groups and not the entire paediatric population. This may offset some of the reservations that currently hamper better endorsement of the PUMA concept.