



# EUROPEAN UNION

THE EUROPEAN PARLIAMENT

THE COUNCIL

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**REGULATION 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**

**REGULATION (EC) No .../2006 OF THE EUROPEAN PARLIAMENT  
AND OF THE COUNCIL**

**of 12 December 2006**

**on medicinal products for paediatric use and  
amending Regulation (EEC) No 1768/92,  
Directive 2001/20/EC, Directive 2001/83/EC  
and Regulation (EC) No 726/2004**

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 95 thereof,

Having regard to the proposal from the Commission,

Having regard to the Opinion of the European Economic and Social Committee<sup>1</sup>,

Having consulted the Committee of the Regions,

Acting in accordance with the procedure referred to in Article 251 of the Treaty<sup>2</sup>,

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<sup>1</sup> OJ C 267, 27.10.2005, p. 1.

<sup>2</sup> Opinion of the European Parliament of 7 September 2005 (OJ C 193 E, 17.8.2006, p. 225), Council Common Position of 10 March 2006 (OJ C 132 E, 7.6.2006, p. 1) and Position of the European Parliament of 1 June 2006 (not yet published in the Official Journal). Council Decision of 23 October 2006.

Whereas:

- (1) Before a medicinal product for human use is placed on the market in one or more Member States, it generally has to have undergone extensive studies, including pre-clinical tests and clinical trials, to ensure that it is safe, of high quality and effective for use in the target population.
- (2) Such studies may not have been undertaken for use in the paediatric population and many of the medicinal products currently used to treat the paediatric population have not been studied or authorised for such use. Market forces alone have proven insufficient to stimulate adequate research into, and the development and authorisation of, medicinal products for the paediatric population.
- (3) Problems resulting from the absence of suitably adapted medicinal products for the paediatric population include inadequate dosage information which leads to increased risks of adverse reactions including death, ineffective treatment through under-dosage, non-availability to the paediatric population of therapeutic advances, suitable formulations and routes of administration, as well as use of magistral or officinal formulations to treat the paediatric population which may be of poor quality.
- (4) This Regulation aims to facilitate the development and accessibility of medicinal products for use in the paediatric population, to ensure that medicinal products used to treat the paediatric population are subject to ethical research of high quality and are appropriately authorised for use in the paediatric population, and to improve the information available on the use of medicinal products in the various paediatric populations. These objectives should be achieved without subjecting the paediatric population to unnecessary clinical trials and without delaying the authorisation of medicinal products for other age populations.

- (5) While taking into account the fact that the regulation of medicinal products must be fundamentally aimed at safeguarding public health, this aim must be achieved by means that do not impede the free movement of safe medicinal products within the Community. The differences between the national legislative, regulatory and administrative provisions on medicinal products tend to hinder intra-Community trade and therefore directly affect the operation of the internal market. 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.
- (6) The establishment of a system of both obligations and rewards and incentives has proved necessary to achieve these objectives. The precise nature of these obligations and rewards and incentives should take account of the status of the particular medicinal product concerned. This Regulation should apply to all the medicinal products required for paediatric use and therefore its scope should cover products under development and yet-to-be authorised, authorised products covered by intellectual property rights and authorised products no longer covered by intellectual property rights.

- (7) Any concerns about conducting trials in the paediatric population should be balanced by the ethical concerns about giving medicinal products to a population in which they have not been appropriately tested. Public health threats from the use of untested medicinal products in the paediatric population can be safely addressed through the study of medicinal products for the paediatric population, which should be carefully controlled and monitored through the specific requirements for the protection of the paediatric population who take part in clinical trials in the Community laid down in Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use<sup>1</sup>.

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<sup>1</sup> OJ L 121, 1.5.2001, p. 34.

- (8) It is appropriate to create a scientific committee, the Paediatric Committee, within the European Medicines Agency, hereinafter "the Agency", with expertise and competence in the development and assessment of all aspects of medicinal products to treat paediatric populations. The rules on scientific committees of the Agency, as laid down in Regulation (EC) No 726/2004<sup>1</sup>, should apply to the Paediatric Committee. Members of the Paediatric Committee should therefore 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. The Paediatric Committee should be primarily responsible for the scientific assessment and agreement of paediatric investigation plans and for the system of waivers and deferrals thereof; it should also be central to various support measures contained in this Regulation. In its work, the Paediatric Committee should consider the potential significant therapeutic benefits for the paediatric patients involved in the studies or the paediatric population at large including the need to avoid unnecessary studies. The Paediatric Committee should follow existing Community requirements, including Directive 2001/20/EC, as well as International Conference on Harmonisation (ICH) guideline E11 on the development of medicinal products for the paediatric population, and it should avoid any delay in the authorisation of medicinal products for other populations deriving from the requirements for studies in the paediatric population.

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<sup>1</sup> Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1).

- (9) Procedures should be established for the Agency to agree and modify a paediatric investigation plan, which is the document upon which the development and authorisation of medicinal products for the paediatric population should be based. The paediatric investigation plan should include details of the timing and the measures proposed to demonstrate the quality, safety and efficacy of the medicinal product in the paediatric population. Since the paediatric population is in fact composed of a number of population subsets, the paediatric investigation plan should specify which population subsets need to be studied, by what means and by when.
- (10) The introduction of the paediatric investigation plan in the legal framework concerning medicinal products for human use aims at ensuring that the development of medicinal products that are potentially to be used for the paediatric population becomes an integral part of the development of medicinal products, integrated into the development programme for adults. Thus, paediatric investigation plans should be submitted early during product development, in time for studies to be conducted in the paediatric population, where appropriate, before marketing authorisation applications are submitted. It is appropriate to set a deadline for the submission of a paediatric investigation plan in order to ensure early dialogue between the sponsor and the Paediatric Committee. Furthermore, early submission of a paediatric investigation plan, combined with the submission of a deferral request as described below, will avoid delaying the authorisation for other populations. As the development of medicinal products is a dynamic process dependent on the result of ongoing studies, provision should be made for modifying an agreed plan where necessary.

- (11) It is necessary to introduce a requirement for new medicinal products and for authorised medicinal products covered by a patent or a supplementary protection certificate to present either the results of studies in the paediatric population in accordance with an agreed paediatric investigation plan or proof of having obtained a waiver or deferral, at the time of filing a marketing authorisation application or an application for a new indication, new pharmaceutical form or new route of administration. The paediatric investigation plan should be the basis upon which compliance with that requirement is judged. However, that requirement should not apply to generics or similar biological medicinal products and medicinal products authorised through the well-established medicinal use procedure, nor to homeopathic medicinal products and traditional herbal medicinal products authorised through the simplified registration procedures of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use<sup>1</sup>.
- (12) Provision should be made for research into the paediatric use of medicinal products which are not protected by a patent or supplementary protection certificate to be financed under Community research programmes.
- (13) In order to ensure that research in the paediatric population is only conducted to meet their therapeutic needs, there is a need to establish procedures for the Agency to waive the requirement referred to in Recital (11) for specific products or for classes or part of classes of medicinal products, these waivers being then made public by the Agency. As knowledge of science and medicine evolves over time, provision should be made for the lists of waivers to be amended. However, if a waiver is revoked, that requirement should not apply for a given period in order to allow time for at least a paediatric investigation plan to be agreed and studies in the paediatric population to be initiated before an application for marketing authorisation is submitted.

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<sup>1</sup> OJ L 311, 28.11.2001, p. 67. Directive as last amended by Directive 2004/27/EC (OJ L 136, 30.4.2004, p. 34).

- (14) In certain cases, the Agency should defer the initiation or completion of some or all of the measures contained in a paediatric investigation plan, with a view to ensuring that research is conducted only when safe and ethical and that the requirement for study data in the paediatric population does not block or delay the authorisation of medicinal products for other populations.
- (15) Free scientific advice should be provided by the Agency as an incentive to sponsors developing medicinal products for the paediatric population. To ensure scientific consistency, the Agency should manage the interface between the Paediatric Committee and the Scientific Advice Working Group of the Committee for Medicinal Products for Human Use, as well as the interaction between the Paediatric Committee and the other Community committees and working groups concerning medicinal products.
- (16) The existing procedures for the marketing authorisation of medicinal products for human use should not be changed. However, from the requirement referred to in Recital (11) it follows that competent authorities should check compliance with the agreed paediatric investigation plan and any waivers and deferrals at the existing validation step for marketing authorisation applications. The assessment of quality, safety and efficacy of medicinal products for the paediatric population and the granting of marketing authorisations should remain the remit of the competent authorities. Provision should be made for the Paediatric Committee to be asked for its opinion on compliance and on the quality, safety and efficacy of a medicinal product in the paediatric population.

- (17) To provide healthcare professionals and patients with information on the safe and effective use of medicinal products in the paediatric population and as a transparency measure, information on the results of studies in the paediatric population, as well as on the status of the paediatric investigation plans, waivers and deferrals, should be included in product information. When all the measures in the paediatric investigation plan have been complied with, that fact should be recorded in the marketing authorisation, and should then be the basis upon which companies can obtain the rewards for compliance.
- (18) In order to identify medicinal products authorised for use in the paediatric population and enable their prescription, provision should be made for the labels of medicinal products granted an indication for use in the paediatric population to display a symbol which will be selected by the Commission on a recommendation by the Paediatric Committee.
- (19) In order to establish incentives for authorised products no longer covered by intellectual property rights, it is necessary to establish a new type of marketing authorisation, the Paediatric Use Marketing Authorisation. A Paediatric Use Marketing Authorisation should be granted through existing marketing authorisation procedures but should apply specifically for medicinal products developed exclusively for use in the paediatric population. It should be possible for the name of the medicinal product that has been granted a Paediatric Use Marketing Authorisation to retain the existing brand name of the corresponding product authorised for adults, in order to capitalise on existing brand recognition, while benefiting from the data exclusivity associated with a new marketing authorisation.

- (20) An application for a Paediatric Use Marketing Authorisation should include the submission of data concerning use of the product in the paediatric population, collected in accordance with an agreed paediatric investigation plan. These data may be derived from the published literature or from new studies. An application for a Paediatric Use Marketing Authorisation should also be able to refer to data contained in the dossier of a medicinal product which is or has been authorised in the Community. This is intended to provide an additional incentive to encourage small and medium-sized enterprises, including generic companies, to develop off-patent medicinal products for the paediatric population.
- (21) This Regulation should include measures to maximise access by the Community population to new medicinal products tested and adapted for paediatric use, and to minimise the chance of Community-wide rewards and incentives being granted without sections of the Community paediatric population benefiting from the availability of a newly authorised medicine. An application for a marketing authorisation, including an application for a Paediatric Use Marketing Authorisation, which contains the results of studies conducted in compliance with an agreed paediatric investigation plan should be eligible for the Community centralised procedure set out in Articles 5 to 15 of Regulation (EC) No 726/2004.
- (22) When an agreed paediatric investigation plan has led to the authorisation of a paediatric indication for a product already marketed for other indications, the marketing authorisation holder should be obliged to place the product on the market, taking into account the paediatric information, within two years of the date of approval of the indication. That requirement should relate only to products already authorised, but not to medicinal products authorised via a Paediatric Use Marketing Authorisation.

- (23) An optional procedure should be established to make it possible to obtain a single Community-wide opinion for a nationally authorised medicinal product when data on the paediatric population following an agreed paediatric investigation plan form part of the marketing authorisation application. To achieve this, the procedure set out in Articles 32, 33 and 34 of Directive 2001/83/EC could be used. This will allow the adoption of a Community harmonised Decision on use of that medicinal product in the paediatric population and its inclusion in all national product information.
- (24) It is essential to ensure that pharmacovigilance mechanisms are adapted to meet the specific challenges of collecting safety data in the paediatric population, including data on possible long-term effects. Efficacy in the paediatric population may also need additional study following authorisation. Therefore, an additional requirement for applying for a marketing authorisation that includes the results of studies conducted in compliance with an agreed paediatric investigation plan should be an obligation for the applicant to indicate how he proposes to ensure the long-term follow-up of possible adverse reactions to the use of the medicinal product and efficacy in the paediatric population. Additionally, where there is a particular cause for concern, the applicant should submit and implement a risk management system and/or perform specific post-marketing studies as a condition for the granting of the marketing authorisation.
- (25) It is necessary in the interests of public health to ensure the continuing availability of safe and effective medicinal products authorised for paediatric indications developed as a result of this Regulation. If a marketing authorisation holder intends to withdraw such a medicinal product from the market then arrangements should be in place so that the paediatric population can continue to have access to the medicinal product in question. In order to help achieve this, the Agency should be informed in good time of any such intention and should make that intention public.

- (26) For products falling within the scope of the requirement to submit paediatric data, if all the measures included in the agreed 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 product information, a reward should be granted in the form of a 6-month extension of the supplementary protection certificate created by Council Regulation (EEC) No 1768/92<sup>1</sup>. Any decisions by Member States' authorities as regards the setting of prices for medicinal products or their inclusion in the scope of national health insurance schemes have no bearing on the granting of this reward.
- (27) An application for an extension of the duration of the certificate pursuant to this Regulation should only be admissible where a certificate is granted pursuant to Regulation (EEC) No 1768/92.
- (28) Because the reward is for conducting studies in the paediatric population and not for demonstrating that a product is safe and effective in the paediatric population, the reward should be granted even when a paediatric indication is not authorised. However, to improve the information available on the use of medicinal products in the paediatric population, relevant information on use in paediatric populations should be included in authorised product information.

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<sup>1</sup> OJ L 182, 2.7.1992, p. 1. Regulation as last amended by the 2003 Act of Accession.

- (29) Under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products<sup>1</sup>, medicinal products designated as orphan medicinal products gain ten years of market exclusivity on the granting of a marketing authorisation for the orphan indication. As such products are frequently not patent-protected, the reward of supplementary protection certificate extension cannot be applied; when they are patent-protected, such an extension would provide a double incentive. Therefore, for orphan medicinal products, instead of an extension of the supplementary protection certificate, the ten-year period of orphan market exclusivity should be extended to twelve years if the requirement for data on use in the paediatric population is fully met.
- (30) The measures provided for in this Regulation should not preclude the operation of other incentives or rewards. To ensure transparency on the different measures available at Community and Member State levels, the Commission should draw up a detailed list of all the incentives available, on the basis of information provided by the Member States. The measures set out in this Regulation, including the agreement of paediatric investigation plans, should not be grounds for obtaining any other Community incentives to support research, such as the funding of research projects under the multi-annual Community Framework Programmes for Research, Technological Development and Demonstration Activities.

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<sup>1</sup> OJ L 18, 22.1.2000, p. 1.

- (31) In order to increase the availability of information on the use of medicinal products in the paediatric population, and to avoid unnecessary repetition of studies in the paediatric population which do not add to the collective knowledge, the European database provided for in Article 11 of Directive 2001/20/EC should include a European register of clinical trials of medicinal products for paediatric use comprising all ongoing, prematurely terminated, and completed paediatric studies conducted both in the Community and in third countries. Part of the information concerning paediatric clinical trials entered into the database, as well as details of the results of all paediatric clinical trials submitted to the competent authorities, should be made public by the Agency.
- (32) An inventory of the therapeutic needs of the paediatric population should be established by the Paediatric Committee after consultation with the Commission, the Member States and interested parties, and should be regularly updated. The inventory should identify the existing medicinal products used by the paediatric population and highlight the therapeutic needs of that population and the priorities for research and development. In this way, companies should be able easily to identify opportunities for business development; the Paediatric Committee should be able better to judge the need for medicinal products and studies when assessing draft paediatric investigation plans, waivers and deferrals; and healthcare professionals and patients should have an information source available to support their decisions as to which medicinal products to choose.

- (33) Clinical trials in the paediatric population may require specific expertise, specific methodology and, in some cases, specific facilities and should be carried out by appropriately trained investigators. A network, which links existing national and Community initiatives and study centres in order to build up the necessary competences at Community level, and which takes account of Community and third country data, would help facilitate cooperation and avoid unnecessary duplication of studies. This network should contribute to the work of strengthening the foundations of the European Research Area in the context of Community Framework Programmes for Research, Technological Development and Demonstration Activities, benefit the paediatric population and provide a source of information and expertise for industry.
- (34) For certain authorised products, pharmaceutical companies may already hold data on safety or efficacy in the paediatric population. To improve the information available on the use of medicinal products in the paediatric populations, companies holding such data should be required to submit them to all competent authorities where the product is authorised. In this way the data could be assessed and, if appropriate, information should be included in the authorised product information aimed at healthcare professionals and patients.
- (35) Community funding should be provided to cover all aspects of the work of the Paediatric Committee and of the Agency resulting from the implementation of this Regulation, such as the assessment of paediatric investigation plans, fee waivers for scientific advice, and information and transparency measures, including the database of paediatric studies and the network.

- (36) The measures necessary for the implementation of this Regulation should be adopted in accordance with Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission<sup>1</sup>.
- (37) Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 should therefore be amended accordingly.
- (38) Since the objective of this Regulation, namely improving availability of medicinal products tested for paediatric use, cannot be sufficiently achieved by the Member States and can therefore be better achieved at Community level, given that this will make it possible to take advantage of the widest possible market and avoid the dispersion of limited resources, the Community may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty. In accordance with the principle of proportionality, as set out in that Article, this Regulation does not go beyond what is necessary in order to achieve this objective,

HAVE ADOPTED THIS REGULATION:

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<sup>1</sup> OJ L 184, 17.7.1999, p. 23. Decision as amended by Decision 2006/512/EC (OJ L 200, 22.7.2006, p. 11).

**TITLE I**  
**Introductory provisions**

**CHAPTER 1**  
**SUBJECT MATTER AND DEFINITIONS**

*Article 1*

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

*Article 2*

In addition to the definitions laid down in Article 1 of Directive 2001/83/EC, the following definitions shall apply for the purposes of this Regulation:

- 1) "paediatric population" means that part of the population aged between birth and 18 years;
- 2) "paediatric investigation plan" means a research and development programme aimed at ensuring that the necessary data are generated determining the conditions in which a medicinal product may be authorised to treat the paediatric population;

- 3) "medicinal product authorised for a paediatric indication" means a medicinal product which is authorised for use in part or all of the paediatric population and in respect of which the details of the authorised indication are specified in the summary of the product characteristics drawn up in accordance with Article 11 of Directive 2001/83/EC;
- 4) "paediatric use marketing authorisation" means a marketing authorisation granted in respect of a medicinal product for human use which is not protected by a supplementary protection certificate under Regulation (EEC) No 1768/92 or by a patent which qualifies for the granting of the supplementary protection certificate, covering exclusively therapeutic indications which are relevant for use in the paediatric population, or subsets thereof, including the appropriate strength, pharmaceutical form or route of administration for that product.

## **CHAPTER 2**

### **PAEDIATRIC COMMITTEE**

#### *Article 3*

1. By ...\*, a Paediatric Committee shall be established within the European Medicines Agency set up under Regulation (EC) No 726/2004, hereinafter "the Agency". The Paediatric Committee shall be considered as established once the members referred to in Article 4(1)(a) and (b) have been appointed.

The Agency shall fulfil the secretariat functions for the Paediatric Committee and shall provide it with technical and scientific support.

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\* Six months from the entry into force of this Regulation.

2. Save where otherwise provided for in this Regulation, Regulation (EC) No 726/2004 shall apply to the Paediatric Committee, including the provisions on the independence and impartiality of its members.
3. The Executive Director of the Agency shall ensure appropriate coordination between the Paediatric Committee and the Committee for Medicinal Products for Human Use, the Committee for Orphan Medicinal Products, their working parties and any other scientific advisory groups.

The Agency shall draw up specific procedures for possible consultations between them.

#### *Article 4*

1. The Paediatric Committee shall be composed of the following members:
  - (a) five members, with their alternates, of the Committee for Medicinal Products for Human Use, having been appointed to that Committee in accordance with Article 61(1) of Regulation (EC) No 726/2004. These five members with their alternates shall be appointed to the Paediatric Committee by the Committee for Medicinal Products for Human Use;
  - (b) one member and one alternate appointed by each Member State whose national competent authority is not represented through the members appointed by the Committee for Medicinal Products for Human Use;
  - (c) three members and three alternates appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament, in order to represent health professionals;
  - (d) three members and three alternates appointed by the Commission, on the basis of a public call for expressions of interest, after consulting the European Parliament, in order to represent patient associations.

The alternates shall represent and vote for the members in their absence.

For the purposes of points (a) and (b), Member States shall cooperate, under the coordination of the Executive Director of the Agency, in order to ensure that the final composition of the Paediatric Committee, including members and alternates, covers the scientific areas relevant to paediatric medicinal products, and including at least: pharmaceutical development, paediatric medicine, general practitioners, paediatric pharmacy, paediatric pharmacology, paediatric research, pharmacovigilance, ethics and public health.

For the purposes of points (c) and (d), the Commission shall take into account the expertise provided by the members appointed under points (a) and (b).

2. The members of the Paediatric Committee shall be appointed for a renewable period of three years. At meetings of the Paediatric Committee, they may be accompanied by experts.
3. The Paediatric Committee shall elect its Chairman from among its members for a term of three years, renewable once.
4. The names and qualifications of the members shall be made public by the Agency.

#### *Article 5*

1. When preparing its opinions, the Paediatric Committee shall use its best endeavours to reach a scientific consensus. If such a consensus cannot be reached, the Paediatric Committee shall adopt an opinion consisting of the position of the majority of the members. The opinion shall mention the divergent positions, with the grounds on which they are based. This opinion shall be made accessible to the public pursuant to Article 25(5) and (7).

2. The Paediatric Committee shall draw up its rules of procedure for the implementation of its tasks. The rules of procedure shall enter into force after receiving a favourable opinion from the Management Board of the Agency and, subsequently, from the Commission.
3. All meetings of the Paediatric Committee may be attended by representatives of the Commission, the Executive Director of the Agency or his representatives.

#### *Article 6*

1. The tasks of the Paediatric Committee shall include the following:
  - (a) to assess the content of any paediatric investigation plan for a medicinal product submitted to it in accordance with this Regulation and formulate an opinion thereon;
  - (b) to assess waivers and deferrals and formulate an opinion thereon;
  - (c) at the request of the Committee for Medicinal Products for Human Use, a competent authority or the applicant, to assess compliance of the application for a Marketing Authorisation with the agreed paediatric investigation plan concerned and formulate an opinion thereon;
  - (d) at the request of the Committee for Medicinal Products for Human Use or a competent authority, to assess any data generated in accordance with an agreed paediatric investigation plan and formulate an opinion on the quality, safety or efficacy of the medicinal product for use in the paediatric population;

- (e) to advise on the content and format of data to be collected for the survey referred to in Article 42;
- (f) to support and advise the Agency on establishing the European network referred to in Article 44;
- (g) to assist scientifically in the elaboration of any documents related to the fulfilment of the objectives of this Regulation;
- (h) to provide advice on any question related to medicinal products for use in the paediatric population, at the request of the Executive Director of the Agency or the Commission;
- (i) to establish a specific inventory of paediatric medicinal product needs and update it on a regular basis, as referred to in Article 43;
- (j) to advise the Agency and the Commission regarding the communication of arrangements available for conducting research into medicinal products for use in the paediatric population;
- (k) to make a recommendation to the Commission on the symbol referred to in Article 32(2).

2. When carrying out its tasks, the Paediatric Committee shall consider whether or not any proposed studies can be expected to be of significant therapeutic benefit to and/or fulfil a therapeutic need of the paediatric population. The Paediatric Committee shall take into account any information available to it, including any opinions, decisions or advice given by the competent authorities of third countries.

## **TITLE II**

### **Marketing authorisation requirements**

#### **CHAPTER 1**

#### **GENERAL AUTHORISATION REQUIREMENTS**

##### *Article 7*

1. An application for marketing authorisation under Article 6 of Directive 2001/83/EC in respect of a medicinal product for human use which is not authorised in the Community at the time of entry into force of this Regulation shall be regarded as valid only if it includes, in addition to the particulars and documents referred to in Article 8(3) of Directive 2001/83/EC, one of the following:
  - (a) the results of all studies performed and details of all information collected in compliance with an agreed paediatric investigation plan;
  - (b) a decision of the Agency granting a product-specific waiver;
  - (c) a decision of the Agency granting a class waiver pursuant to Article 11;
  - (d) a decision of the Agency granting a deferral.

For the purposes of point (a), the decision of the Agency agreeing the paediatric investigation plan concerned shall also be included in the application.

2. The documents submitted pursuant to paragraph 1 shall, cumulatively, cover all subsets of the paediatric population.

#### *Article 8*

In the case of authorised medicinal products which are protected either by a supplementary protection certificate under Regulation (EEC) No 1768/92, or by a patent which qualifies for the granting of the supplementary protection certificate, Article 7 of this Regulation shall apply to applications for authorisation of new indications, including paediatric indications, new pharmaceutical forms and new routes of administration.

For the purposes of the first subparagraph, the documents referred to in Article 7(1) shall cover both the existing and the new indications, pharmaceutical forms and routes of administration.

#### *Article 9*

Articles 7 and 8 shall not apply to products authorised under Articles 10, 10a, 13 to 16 or 16a to 16i of Directive 2001/83/EC.

#### *Article 10*

In consultation with the Member States, the Agency and other interested parties, the Commission shall draw up the detailed arrangements concerning the format and content which applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals must follow in order to be considered valid and concerning the operation of the compliance check referred to in Articles 23 and 28(3).

## CHAPTER 2

### WAIVERS

#### *Article 11*

1. Production of the information referred to in point (a) of Article 7(1) shall be waived for specific medicinal products or for classes of medicinal products, if there is evidence showing any of the following:
  - (a) that the specific medicinal product or class of medicinal products is likely to be ineffective or unsafe in part or all of the paediatric population;
  - (b) that the disease or condition for which the specific medicinal product or class is intended occurs only in adult populations;
  - (c) that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.
2. The waiver provided for in paragraph 1 may be issued with reference either to one or more specified subsets of the paediatric population, or to one or more specified therapeutic indications, or to a combination of both.

#### *Article 12*

The Paediatric Committee may of its own motion adopt an opinion, on the grounds set out in Article 11(1), to the effect that a class or a product-specific waiver, as referred to in Article 11(1), should be granted.

As soon as the Paediatric Committee adopts an opinion, the procedure laid down in Article 25 shall apply. In the case of a class waiver, only paragraphs 6 and 7 of Article 25 shall apply.

### *Article 13*

1. The applicant may, on the grounds set out in Article 11(1), apply to the Agency for a product-specific waiver.
2. Following receipt of the application, the Paediatric Committee shall appoint a rapporteur and shall within 60 days adopt an opinion as to whether or not a product-specific waiver should be granted.

Either the applicant or the Paediatric Committee may request a meeting during that 60-day period.

Whenever appropriate, the Paediatric Committee may request the applicant to supplement the particulars and documents submitted. Where the Paediatric Committee avails itself of this option, the 60-day time-limit shall be suspended until such time as the supplementary information requested has been provided.

3. As soon as the Paediatric Committee adopts an opinion, the procedure laid down in Article 25 shall apply.

### *Article 14*

1. The Agency shall maintain a list of all waivers. The list shall be regularly updated (at least every year) and made available to the public.

2. The Paediatric Committee may, at any time, adopt an opinion advocating the review of a granted waiver.

In the case of a change affecting a product-specific waiver, the procedure laid down in Article 25 shall apply.

In the case of a change affecting a class waiver, paragraphs 6 and 7 of Article 25 shall apply.

3. If a particular product-specific or class waiver is revoked, the requirement set out in Articles 7 and 8 shall not apply for 36 months from the date of the removal from the list of waivers.

## **CHAPTER 3**

### **PAEDIATRIC INVESTIGATION PLAN**

#### **SECTION 1**

#### **REQUESTS FOR AGREEMENT**

##### *Article 15*

1. Where the intention is to apply for a marketing authorisation in accordance with Article 7(1)(a) or (d), Article 8 or Article 30, a paediatric investigation plan shall be drawn up and submitted to the Agency with a request for agreement.

2. The paediatric investigation plan shall specify the timing and the measures proposed to assess the quality, safety and efficacy of the medicinal product in all subsets of the paediatric population that may be concerned. In addition, it shall describe any measures to adapt the formulation of the medicinal product so as to make its use more acceptable, easier, safer or more effective for different subsets of the paediatric population.

#### *Article 16*

1. In the case of the applications for marketing authorisation referred to in Articles 7 and 8 or the applications for waiver referred to in Articles 11 and 12, the paediatric investigation plan or the application for waiver shall be submitted with a request for agreement, except in duly justified cases, not later than upon completion of the human pharmacokinetic studies in adults specified in Section 5.2.3 of Part I of Annex I to Directive 2001/83/EC, so as to ensure that an opinion on use in the paediatric population of the medicinal product concerned can be given at the time of the assessment of the marketing authorisation or other application concerned.
2. Within 30 days following receipt of the request referred to in paragraph 1 and in Article 15(1), the Agency shall verify the validity of the request and prepare a summary report for the Paediatric Committee.
3. Whenever appropriate, the Agency may ask the applicant to submit additional particulars and documents, in which case the time-limit of 30 days shall be suspended until such time as the supplementary information requested has been provided.

### *Article 17*

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

Within the same period, either the applicant or the Paediatric Committee may request a meeting.

2. Within the 60-day period referred to in paragraph 1, the Paediatric Committee may request the applicant to propose modifications to the plan, in which case the time-limit referred to in paragraph 1 for the adoption of the final opinion shall be extended for a maximum of 60 days. In such cases, the applicant or the Paediatric Committee may request an additional meeting during this period. The time-limit shall be suspended until such time as the supplementary information requested has been provided.

### *Article 18*

As soon as the Paediatric Committee adopts an opinion, whether positive or negative, the procedure laid down in Article 25 shall apply.

### *Article 19*

If, having considered a paediatric investigation plan, the Paediatric Committee concludes that Article 11(1)(a), (b) or (c) applies to the medicinal product concerned, it shall adopt a negative opinion under Article 17(1).

In such cases, the Paediatric Committee shall adopt an opinion in favour of a waiver under Article 12, whereupon the procedure laid down in Article 25 shall apply.

## **SECTION 2 DEFERRALS**

### *Article 20*

1. At the same time as the paediatric investigation plan is submitted under Article 16(1), a request may be made for deferral of the initiation or completion of some or all of the measures set out in that plan. Such deferral shall be justified on scientific and technical grounds or on grounds related to public health.

In any event, a deferral shall be granted when it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population or when studies in the paediatric population will take longer to conduct than studies in adults.

2. On the basis of the experience acquired as a result of the operation of this Article, the Commission may adopt provisions in accordance with the procedure referred to in Article 51(2) to define further the grounds for granting a deferral.

*Article 21*

1. At the same time as the Paediatric Committee adopts a positive opinion under Article 17(1), it shall, of its own motion or following a request submitted by the applicant under Article 20, adopt an opinion, if the conditions specified in Article 20 are met, in favour of deferring the initiation or completion of some or all of the measures in the paediatric investigation plan.

An opinion in favour of a deferral shall specify the time-limits for initiating or completing the measures concerned.

2. As soon as the Paediatric Committee adopts an opinion in favour of deferral, as referred to in paragraph 1, the procedure laid down in Article 25 shall apply.

### **SECTION 3**

## **MODIFICATION OF A PAEDIATRIC INVESTIGATION PLAN**

#### *Article 22*

If, following the decision agreeing the paediatric investigation plan, the applicant encounters such difficulties with its implementation as to render the plan unworkable or no longer appropriate, the applicant may propose changes or request a deferral or a waiver, based on detailed grounds, to the Paediatric Committee. Within 60 days, the Paediatric Committee shall review these changes or the request for a deferral or a waiver and adopt an opinion proposing their refusal or acceptance. As soon as the Paediatric Committee adopts an opinion, whether positive or negative, the procedure laid down in Article 25 shall apply.

### **SECTION 4**

## **COMPLIANCE WITH THE PAEDIATRIC INVESTIGATION PLAN**

#### *Article 23*

1. The competent authority responsible for granting marketing authorisation shall verify whether an application for marketing authorisation or variation complies with the requirements laid down in Articles 7 and 8 and whether an application submitted pursuant to Article 30 complies with the agreed paediatric investigation plan.

Where the application is submitted in accordance with the procedure set out in Articles 27 to 39 of Directive 2001/83/EC, the verification of compliance, including, as appropriate, requesting an opinion of the Paediatric Committee in accordance with paragraph 2(b) and (c) of this Article, shall be conducted by the reference Member State.

2. The Paediatric Committee may, in the following cases, be requested to give its opinion as to whether studies conducted by the applicant are in compliance with the agreed paediatric investigation plan:
  - (a) by the applicant, prior to submitting an application for marketing authorisation or variation as referred to in Articles 7, 8 and 30, respectively;
  - (b) by the Agency, or the national competent authority, when validating an application, as referred to in point (a), which does not include an opinion concerning compliance adopted following a request under point (a);
  - (c) by the Committee for Medicinal Products for Human Use, or the national competent authority, when assessing an application, as referred to in point (a), where there is doubt concerning compliance and an opinion has not been already given following a request under points (a) or (b).

In the case of point (a), the applicant shall not submit its application until the Paediatric Committee has adopted its opinion, and a copy thereof shall be annexed to the application.

3. If the Paediatric Committee is requested to give an opinion under paragraph 2, it shall do so within 60 days of receiving the request.

Member States shall take account of such an opinion.

#### *Article 24*

If, when conducting the scientific assessment of a valid application for Marketing Authorisation, the competent authority concludes that the studies are not in conformity with the agreed paediatric investigation plan, the product shall not be eligible for the rewards and incentives provided for in Articles 36, 37 and 38.

## **CHAPTER 4 PROCEDURE**

#### *Article 25*

1. Within ten days of its receipt, the Agency shall transmit the opinion of the Paediatric Committee to the applicant.
2. Within 30 days following receipt of the opinion of the Paediatric Committee, the applicant may submit to the Agency a written request, citing detailed grounds, for a re-examination of the opinion.

3. Within 30 days following receipt of a request for re-examination pursuant to paragraph 2, the Paediatric Committee, having appointed a new rapporteur, shall issue a new opinion confirming or revising its previous opinion. The rapporteur shall be able to question the applicant directly. The applicant may also offer to be questioned. The rapporteur shall inform the Paediatric Committee without delay in writing about details of contacts with the applicant. The opinion shall be duly reasoned and a statement of reasons for the conclusion reached shall be annexed to the new opinion, which shall become definitive.
4. If, within the 30-day period referred to in paragraph 2, the applicant does not request re-examination, the opinion of the Paediatric Committee shall become definitive.
5. The Agency shall adopt a decision within a period not exceeding 10 days following receipt of the Paediatric Committee's definitive opinion. This decision shall be communicated to the applicant in writing and shall annex the definitive opinion of the Paediatric Committee.
6. In the case of a class waiver as referred to in Article 12, the Agency shall adopt a decision within ten days following receipt of the opinion of the Paediatric Committee as referred to in Article 13(3). This decision shall annex the opinion of the Paediatric Committee.
7. Decisions of the Agency shall be made public after deletion of any information of a commercially confidential nature.

## **CHAPTER 5**

### **MISCELLANEOUS PROVISIONS**

#### *Article 26*

Any legal or natural person developing a medicinal product intended for paediatric use may, prior to the submission of a paediatric investigation plan and during its implementation, request advice from the Agency on the design and conduct of the various tests and studies necessary to demonstrate the quality, safety and efficacy of the medicinal product in the paediatric population in accordance with Article 57(1)(n) of Regulation (EC) No 726/2004.

In addition, this legal or natural person may request advice on the design and conduct of pharmacovigilance and risk management systems as referred to in Article 34.

The Agency shall provide advice under this Article free of charge.

### **TITLE III**

#### **Marketing authorisation procedures**

#### *Article 27*

Save where otherwise provided in this Title, marketing authorisation procedures for the marketing authorisations covered by this Title shall be governed by the provisions laid down in Regulation (EC) No 726/2004 or in Directive 2001/83/EC.

# CHAPTER 1

## MARKETING AUTHORISATION PROCEDURES FOR APPLICATIONS FALLING WITHIN THE SCOPE OF ARTICLES 7 AND 8

### *Article 28*

1. Applications may be submitted in accordance with the procedure laid down in Articles 5 to 15 of Regulation (EC) No 726/2004 for a marketing authorisation as referred to in Article 7(1) of this Regulation which includes one or more paediatric indications on the basis of studies conducted in compliance with an agreed paediatric investigation plan.

Where authorisation is granted, the results of all those studies shall be included in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product, provided that the competent authority deems the information to be of use to patients, whether or not all the paediatric indications concerned were approved by the competent authority.

2. Where a marketing authorisation is granted or varied, any waiver or deferral which has been granted pursuant to this Regulation shall be recorded in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product concerned.

3. If the application complies with all the measures contained in the agreed completed paediatric investigation plan and if the summary of product characteristics reflects the results of studies conducted in compliance with that agreed paediatric investigation plan, the competent authority shall include within the marketing authorisation a statement indicating compliance of the application with the agreed completed paediatric investigation plan. For the purpose of the application of Article 45(3), this statement shall also indicate whether significant studies contained in the agreed Paediatric Investigation Plan have been completed after the entry into force of this Regulation.

#### *Article 29*

In the case of medicinal products authorised under Directive 2001/83/EC, an application as referred to in Article 8 of this Regulation may be submitted, in accordance with the procedure laid down in Articles 32, 33 and 34 of Directive 2001/83/EC, for authorisation of a new indication, including the extension of an authorisation for use in the paediatric population, a new pharmaceutical form or a new route of administration.

That application shall comply with the requirement laid down in point (a) of Article 7(1).

The procedure shall be limited to the assessment of the specific sections of the summary of product characteristics to be varied.

## CHAPTER 2

### PAEDIATRIC USE MARKETING AUTHORISATION

#### *Article 30*

1. Submission of an application for a paediatric use marketing authorisation shall in no way preclude the right to apply for a marketing authorisation for other indications.
2. An application for a paediatric use marketing authorisation shall be accompanied by the particulars and documents necessary to establish quality, safety and efficacy in the paediatric population, including any specific data needed to support an appropriate strength, pharmaceutical form or route of administration for the product, in accordance with an agreed paediatric investigation plan.

The application shall also include the decision of the Agency agreeing the paediatric investigation plan concerned.

3. Where a medicinal product is or has been authorised in a Member State or in the Community, data contained in the dossier on that product may, where appropriate, be referred to, in accordance with Article 14(11) of Regulation (EC) No 726/2004 or Article 10 of Directive 2001/83/EC, in an application for a paediatric use marketing authorisation.

4. The medicinal product in respect of which a paediatric use marketing authorisation is granted may retain the name of any medicinal product which contains the same active substance and in respect of which the same holder has been granted authorisation for use in adults.

*Article 31*

Without prejudice to Article 3(2) of Regulation (EC) No 726/2004, an application for a paediatric use marketing authorisation may be made in accordance with the procedure laid down in Articles 5 to 15 of Regulation (EC) No 726/2004.

## **CHAPTER 3**

### **IDENTIFICATION**

*Article 32*

1. Where a medicinal product is granted a marketing authorisation for a paediatric indication, the label shall display the symbol agreed in accordance with paragraph 2. The package leaflet shall contain an explanation of the meaning of the symbol.
2. By ...,\* the Commission shall select a symbol following a recommendation of the Paediatric Committee. The Commission shall make the symbol public.

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\* One year from the entry into force of this Regulation.

3. The provisions of this Article shall also apply to medicinal products authorised before the entry into force of this Regulation, and to medicinal products authorised after the entry into force of this Regulation but before the symbol has been made public, if they are authorised for paediatric indications.

In this case, the symbol and the explanation referred to in paragraph 1 shall be included in the labelling and package leaflet respectively of the medicinal products concerned not later than two years after the symbol has been made public.

## **TITLE IV**

### **Post-authorisation requirements**

#### *Article 33*

Where medicinal products are authorised for a paediatric indication following completion of an agreed paediatric investigation plan and those products have already been marketed with other indications, the marketing authorisation holder shall, within two years of the date on which the paediatric indication is authorised, place the product on the market taking into account the paediatric indication. A register, coordinated by the Agency, and made publicly available, shall mention these deadlines.

### *Article 34*

1. In the following cases, the applicant shall detail the measures to ensure the follow-up of efficacy and of possible adverse reactions to the paediatric use of the medicinal product:
  - (a) applications for a marketing authorisation that includes a paediatric indication;
  - (b) applications to include a paediatric indication in an existing marketing authorisation;
  - (c) applications for a paediatric use marketing authorisation.
  
2. 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. The risk management system shall comprise a set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicinal products, including the assessment of the effectiveness of those interventions.

Assessment of the effectiveness of any risk management system and the results of any studies performed shall be included in the periodic safety update reports referred to in Article 104(6) of Directive 2001/83/EC and Article 24(3) of Regulation (EC) No 726/2004.

In addition, the competent authority may request submission of additional reports assessing the effectiveness of any risk minimisation system and the results of any such studies performed.

3. In addition to paragraphs 1 and 2, the provisions on pharmacovigilance as laid down in Regulation (EC) No 726/2004 and in Directive 2001/83/EC shall apply to marketing authorisations for medicinal products which include a paediatric indication.
4. In the **case** of a deferral, the marketing authorisation holder shall submit an annual report to the Agency providing an update on progress with paediatric studies in accordance with the decision of the Agency agreeing the paediatric investigation plan and granting a deferral.

The Agency shall inform the competent authority if it is found that the marketing authorisation holder has failed to comply with the decision of the Agency agreeing the paediatric investigation plan and granting a deferral.

5. The Agency shall draw up guidelines relating to the application of this Article.

#### *Article 35*

If a medicinal product is authorised for a paediatric indication and the marketing authorisation holder has benefited from rewards or incentives under Article 36, 37 or 38, and these periods of protection have expired, and if the marketing authorisation holder intends to discontinue placing the medicinal product on the market, the marketing authorisation holder shall transfer the marketing authorisation or allow a third party, which has declared its intention to continue to place the medicinal product in question on the market, to use the pharmaceutical, pre-clinical and clinical documentation contained in the file of the medicinal product on the basis of Article 10c of Directive 2001/83/EC.

The marketing authorisation holder shall inform the Agency of its intention to discontinue the placing on the market of the product no less than six months before the discontinuation. The Agency shall make this fact public.

## **TITLE V**

### **Rewards and incentives**

#### *Article 36*

1. Where an application under Article 7 or 8 includes the results of all studies conducted in compliance with an agreed paediatric investigation plan, the holder of the patent or supplementary protection certificate shall be entitled to a six-month extension of the period referred to in Articles 13(1) and 13(2) of Regulation (EEC) No 1768/92.

The first subparagraph shall also apply where completion of the agreed paediatric investigation plan fails to lead to the authorisation of a paediatric indication, but the results of the studies conducted are reflected in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product concerned.

2. The inclusion in a marketing authorisation of the statement referred to in Article 28(3) shall be used for the purposes of applying paragraph 1 of this Article.

3. Where the procedures laid down in Directive 2001/83/EC have been used, the six-month extension of the period referred to in paragraph 1 shall be granted only if the product is authorised in all Member States.
4. Paragraphs 1, 2 and 3 shall apply to products that are protected by a supplementary protection certificate under Regulation (EEC) No 1768/92, or under a patent which qualifies for the granting of the supplementary protection certificate. They shall not apply to medicinal products designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000.
5. In the case of an application under Article 8 which leads to the authorisation of a new paediatric indication, paragraphs 1, 2 and 3 shall not apply if the applicant applies for, and obtains, a one-year extension of the period of marketing protection for the medicinal product concerned, on the grounds that this new paediatric indication brings a significant clinical benefit in comparison with existing therapies, in accordance with Article 14(11) of Regulation (EC) No 726/2004 or the fourth subparagraph of Article 10(1) of Directive 2001/83/EC.

#### *Article 37*

Where an application for a marketing authorisation is submitted in respect of a medicinal product designated as an orphan medicinal product pursuant to Regulation (EC) No 141/2000 and that application includes the results of all studies conducted in compliance with an agreed paediatric investigation plan, and the statement referred to in Article 28(3) of this Regulation is subsequently included in the marketing authorisation granted, the ten-year period referred to in Article 8(1) of Regulation (EC) No 141/2000 shall be extended to twelve years.

The first paragraph shall also apply where completion of the agreed paediatric investigation plan fails to lead to the authorisation of a paediatric indication, but the results of the studies conducted are reflected in the summary of product characteristics and, if appropriate, in the package leaflet of the medicinal product concerned.

#### *Article 38*

1. Where a paediatric use marketing authorisation is granted in accordance with Articles 5 to 15 of Regulation (EC) No 726/2004, the data and marketing protection periods referred to in Article 14(11) of that Regulation shall apply.
2. Where a paediatric use marketing authorisation is granted in accordance with the procedures laid down in Directive 2001/83/EC, the data and marketing protection periods referred to in Article 10(1) of that Directive shall apply.

#### *Article 39*

1. In addition to the rewards and incentives provided for in Articles 36, 37 and 38, medicinal products for paediatric use may be eligible for incentives provided by the Community or by the Member States to support research into, and the development and availability of, medicinal products for paediatric use.
2. By ...\*, the Member States shall communicate to the Commission detailed information concerning any measures they have enacted to support research into, and the development and availability of, medicinal products for paediatric use. This information shall be updated regularly at the request of the Commission.

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\* One year from the entry into force of this Regulation.

3. By ...\*, the Commission shall make publicly available a detailed inventory of all rewards and incentives provided by the Community and Member States to support research into, and the development and availability of, medicinal products for paediatric use. This inventory shall be updated regularly and the updates shall also be made publicly available.

*Article 40*

1. Funds for research into medicinal products for the paediatric population shall be provided for in the Community budget in order to support studies relating to medicinal products or active substances not covered by a patent or a supplementary protection certificate.
2. The Community funding referred to in paragraph 1 shall be delivered through the Community Framework Programmes for Research, Technological Development and Demonstration Activities or any other Community initiatives for the funding of research.

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\* 18 months from the entry into force of this Regulation.

## TITLE VI

### Communication and coordination

#### *Article 41*

1. The European database created by Article 11 of Directive 2001/20/EC shall include clinical trials carried out in third countries which are contained in an agreed paediatric investigation plan, in addition to the clinical trials referred to in Articles 1 and 2 of that Directive. In the case of such clinical trials carried out in third countries, the details listed in Article 11 of that Directive shall be entered into the database by the addressee of the Agency's decision on a paediatric investigation plan.

By way of derogation from the provisions of Article 11 of Directive 2001/20/EC, the Agency shall make public part of the information on paediatric clinical trials entered in the European database.

2. Details of the results of all the trials referred to in paragraph 1 and of any other trials submitted to competent authorities in compliance with Articles 45 and 46 shall be made public by the Agency, whether or not the trial was terminated prematurely. These results shall be submitted without delay to the Agency by the clinical trial sponsor, the addressee of the Agency's decision on a paediatric investigation plan, or by the marketing authorisation holder as appropriate.

3. In consultation with the Agency, Member States and interested parties, the Commission shall draw up guidance on the nature of the information referred to in paragraph 1 to be entered in the European database created by Article 11 of Directive 2001/20/EC, on which information shall be made accessible to the public in application of paragraph 1, on how clinical trial results shall be submitted and be made public in application of paragraph 2, and on the Agency's responsibilities and tasks in this regard.

#### *Article 42*

Member States shall collect available data on all existing uses of medicinal products in the paediatric population and shall communicate these data to the Agency by ...\*.

The Paediatric Committee shall provide guidance on the content and the format of the data to be collected by ...\*\*.

#### *Article 43*

1. On the basis of the information referred to in Article 42 and after consulting the Commission, the Member States and the interested parties, the Paediatric Committee shall establish an inventory of therapeutic needs, in particular with a view to identifying research priorities.

The Agency shall make the inventory public at the earliest by ...\* and at the latest by ...\*\*\* and shall update it regularly.

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\* Two years from the entry into force of this Regulation.  
\*\* Nine months from the entry into force of this Regulation.  
\*\*\* Three years from the entry into force of this Regulation.

2. In establishing the inventory of therapeutic needs, account shall be taken of the prevalence of the conditions in the paediatric population, the seriousness of the conditions to be treated, the availability and suitability of alternative treatments for the conditions in the paediatric population, including the efficacy and the adverse reaction profile of those treatments, including any unique paediatric safety issues, and any data resulting from studies in third countries.

*Article 44*

1. The Agency shall, with the scientific support of the Paediatric Committee, develop a European network of existing national and European networks, investigators and centres with specific expertise in the performance of studies in the paediatric population.
2. The objectives of the European network shall be, inter alia, to coordinate studies relating to paediatric medicinal products, to build up the necessary scientific and administrative competences at European level, and to avoid unnecessary duplication of studies and testing in the paediatric population.
3. By ...\*, the Management Board of the Agency shall, on a proposal from the Executive Director and following consultation with the Commission, the Member States and interested parties, adopt an implementing strategy for the launching and operation of the European network. This network must, where appropriate, 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.

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\* One year from the date of entry into force of this Regulation.

## *Article 45*

1. By ...<sup>\*</sup>, any paediatric studies already completed, by the date of entry into force, in respect of products authorised in the Community shall be submitted by the marketing authorisation holder for assessment to the competent authority.

The competent authority may update the summary of product characteristics and package leaflet, and may vary the marketing authorisation accordingly. Competent authorities shall exchange information regarding the studies submitted and, as appropriate, their implications for any marketing authorisations concerned.

The Agency shall coordinate the exchange of information.

2. All existing paediatric studies, as referred to in paragraph 1, and all paediatric studies initiated prior to the entry into force of this Regulation shall be eligible to be included in a paediatric investigation plan, and shall be taken into consideration by the Paediatric Committee when assessing applications for paediatric investigation plans, waivers and deferrals and by competent authorities when assessing applications submitted pursuant to Article 7, 8 or 30.
3. Without prejudice to the previous paragraph, the rewards and incentives of Articles 36, 37 and 38 shall only be granted provided that significant studies contained in an agreed Paediatric Investigation Plan are completed after the entry into force of this Regulation.

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<sup>\*</sup> One year from the date of entry into force of this Regulation.

4. In consultation with the Agency, the Commission shall draw up guidelines to establish assessment criteria for the significance of studies for the purposes of applying paragraph 3.

*Article 46*

1. Any other marketing authorisation holder-sponsored studies which involve the use in the paediatric population of a medicinal product covered by a marketing authorisation, whether or not they are conducted in compliance with an agreed paediatric investigation plan, shall be submitted to the competent authority within six months of completion of the studies concerned.
2. Paragraph 1 shall apply independent of whether or not the marketing authorisation holder intends to apply for a marketing authorisation of a paediatric indication.
3. The competent authority may update the summary of product characteristics and package leaflet, and may vary the marketing authorisation accordingly.
4. Competent authorities shall exchange information regarding the studies submitted and, as appropriate, their implications for any marketing authorisations concerned.
5. The Agency shall coordinate the exchange of information.

**TITLE VII**  
**General and final provisions**

**CHAPTER 1**  
**GENERAL PROVISIONS**

**SECTION 1**  
**FEES, COMMUNITY FUNDING, PENALTIES AND REPORTS**

*Article 47*

1. Where an application for a paediatric use marketing authorisation is submitted in accordance with the procedure laid down in Regulation (EC) No 726/2004, the amount of the reduced fees for the examination of the application and the maintenance of the marketing authorisation shall be fixed in accordance with Article 70 of Regulation (EC) No 726/2004.
2. Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Medicines Agency<sup>1</sup> shall apply.

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<sup>1</sup> OJ L 35, 15.2.1995, p. 1. Regulation as last amended by Regulation (EC) No 1905/2005 (OJ L 304, 23.11.2005, p. 1).

3. Assessments of the following by the Paediatric Committee shall be free of charge:
- (a) applications for waiver;
  - (b) applications for deferral;
  - (c) paediatric investigation plans;
  - (d) compliance with the agreed paediatric investigation plan.

*Article 48*

The Community contribution provided for in Article 67 of Regulation (EC) No 726/2004 shall cover the work of the Paediatric Committee, including scientific support provided by experts, and of the Agency, including the assessment of paediatric investigation plans, scientific advice and any fee waivers provided for in this Regulation, and shall support the Agency's activities under Articles 41 and 44 of this Regulation.

*Article 49*

1. Without prejudice to the Protocol on the Privileges and Immunities of the European Communities, each Member State shall determine the penalties to be applied for infringement of the provisions of this Regulation or the implementing measures adopted pursuant to it in relation to medicinal products authorised through the procedures laid down in Directive 2001/83/EC and shall take all measures necessary for their implementation. The penalties shall be effective, proportionate and dissuasive.

Member States shall inform the Commission of these provisions by ...\*. They shall notify any subsequent alterations as soon as possible.

2. Member States shall inform the Commission immediately of any litigation instituted for infringement of this Regulation.
3. At the Agency's request, the Commission may impose financial penalties for infringement of the provisions of this Regulation or the implementing measures adopted pursuant to it in relation to medicinal products authorised through the procedure laid down in Regulation (EC) No 726/2004. The maximum amounts as well as the conditions and methods for collection of these penalties shall be laid down in accordance with the procedure referred to in Article 51(2) of this Regulation.
4. The Commission shall make public the names of anyone infringing the provisions of this Regulation or of any implementing measures adopted pursuant to it and the amounts of, and reasons for, the financial penalties imposed.

#### *Article 50*

1. On the basis of a report from the Agency, and at least on an annual basis, the Commission shall make public a list of the companies and of the products that have benefited from any of the rewards and incentives in this Regulation and the companies that have failed to comply with any of the obligations in this Regulation. The Member States shall provide this information to the Agency.

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\* Nine months from the date of entry into force of this Regulation.

2. By ...<sup>\*</sup>, the Commission shall present to the European Parliament and the Council a general report on experience acquired as a result of the application of this Regulation. This shall include in particular a detailed inventory of all medicinal products authorised for paediatric use since its entry into force.
3. By ...<sup>\*\*</sup>, the Commission shall present a report to the European Parliament and the Council on the experience acquired as a result of the application of Articles 36, 37 and 38. The report shall include an analysis of the economic impact of the rewards and incentives, together with an analysis of the estimated consequences for public health of this Regulation, with a view to proposing any necessary amendments.
4. Provided that there are sufficient data available to allow robust analyses to be made, the provisions of paragraph 3 shall be fulfilled at the same time as the provisions of paragraph 2.

## **SECTION 2**

### **STANDING COMMITTEE**

#### *Article 51*

1. The Commission shall be assisted by the Standing Committee on Medicinal Products for Human Use set up by Article 121 of Directive 2001/83/EC, hereinafter referred to as "the Committee".

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<sup>\*</sup> Six years from the date of entry into force of this Regulation.

<sup>\*\*</sup> Ten years from the date of entry into force of this Regulation.

2. Where reference is made to this paragraph, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

The period laid down in Article 5(6) of Decision 1999/468/EC shall be set at three months.

3. The Committee shall adopt its rules of procedure.

## **CHAPTER 2**

### **AMENDMENTS**

#### *Article 52*

Regulation (EEC) No 1768/92 is hereby amended as follows:

- 1) in Article 1, the following definition shall be added:

"(e) "Application for an extension of the duration" means an application for an extension of the duration of the certificate pursuant to Article 13(3) of this Regulation and of Article 36 of Regulation (EC) No .../...<sup>+</sup> of the European Parliament and of the Council of ... on medicinal products for paediatric use\*;

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\* OJ L ..., ..., p. ....";

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<sup>+</sup> Note to OJ: Please insert number and date of this Regulation.

2) in Article 7, the following paragraphs shall be added:

- "3. The application for an extension of the duration may be made when lodging the application for a certificate or when the application for the certificate is pending and the appropriate requirements of Articles 8(1)(d) or 8(1a), respectively, are fulfilled.
4. The application for an extension of the duration of a certificate already granted shall be lodged not later than two years before the expiry of the certificate.
5. Notwithstanding paragraph 4, for five years following the entry into force of Regulation (EC) No .../...<sup>+</sup>, the application for an extension of the duration of a certificate already granted shall be lodged not later than six months before the expiry of the certificate.";

3) Article 8 shall be amended as follows:

(a) in paragraph 1, the following point shall be added:

"(d) where the application for a certificate includes a request for an extension of the duration:

- (i) a copy of the statement indicating compliance with an agreed completed paediatric investigation plan as referred to in Article 36(1) of Regulation (EC) No .../...<sup>+</sup>;

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<sup>+</sup> Note to OJ: Please insert number of this Regulation.

- (ii) where necessary, in addition to the copy of the authorisations to place the product on the market as referred to in point (b), proof that it has authorisations to place the product on the market of all other Member States, as referred to in Article 36(3) of Regulation (EC) No .../...<sup>+</sup>.";

(b) the following paragraphs shall be inserted:

- "1a. Where an application for a certificate is pending, an application for an extended duration in accordance with Article 7(3) shall include the particulars referred to in paragraph 1(d) and a reference to the application for a certificate already filed.
- 1b. The application for an extension of the duration of a certificate already granted shall contain the particulars referred to in paragraph 1(d) and a copy of the certificate already granted.";

(c) paragraph 2 shall be replaced by the following:

- "2. Member States may provide that a fee is to be payable upon application for a certificate and upon application for the extension of the duration of a certificate.";

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<sup>+</sup> Note to OJ: Please insert number of this Regulation.

4) Article 9 shall be amended as follows:

(a) in paragraph 1, the following subparagraph shall be added:

"The application for an extension of the duration of a certificate shall be lodged with the competent authority of the Member State concerned.";

(b) in paragraph 2, the following point shall be added:

"(f) where applicable, an indication that the application includes an application for an extension of the duration.";

(c) the following paragraph shall be added:

"3. Paragraph 2 shall apply to the notification of the application for an extension of the duration of a certificate already granted or where an application for a certificate is pending. The notification shall additionally contain an indication of the application for an extended duration of the certificate.";

5) in Article 10, the following paragraph shall be added:

"6. Paragraphs 1 to 4 shall apply mutatis mutandis to the application for an extension of the duration.";

6) in Article 11, the following paragraph shall be added:

"3. Paragraphs 1 and 2 shall apply to the notification of the fact that an extension of the duration of a certificate has been granted or of the fact that the application for an extension has been rejected.";

7) in Article 13, the following paragraph shall be added:

"3. The periods laid down in paragraphs 1 and 2 shall be extended by six months in the case where Article 36 of Regulation (EC) No .../...<sup>+</sup> applies. In that case, the duration of the period laid down in paragraph 1 of this Article may be extended only once.";

8) the following Article shall be inserted:

"Article 15a

Revocation of an extension of the duration

1. The extension of the duration may be revoked if it was granted contrary to the provisions of Article 36 of Regulation (EC) No .../...<sup>+</sup>.
2. Any person may submit an application for revocation of the extension of the duration to the body responsible under national law for the revocation of the corresponding basic patent.";

9) Article 16 shall be amended as follows:

(a) the text of Article 16 becomes that Article's paragraph 1;

(b) the following paragraph shall be added:

"2. If the extension of the duration is revoked in accordance with Article 15a, notification thereof shall be published by the authority referred to in Article 9(1).";

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<sup>+</sup> Note to OJ: Please insert number of this Regulation.

10) Article 17 shall be replaced by the following:

"Article 17

Appeals

The decisions of the authority referred to in Article 9(1) or of the bodies referred to in Articles 15(2) and 15a(2) taken under this Regulation shall be open to the same appeals as those provided for in national law against similar decisions taken in respect of national patents."

### *Article 53*

In Article 11 of Directive 2001/20/EC, the following paragraph shall be added:

"4. By way of derogation from paragraph 1, the Agency shall make public part of the information on paediatric clinical trials entered in the European database in accordance with the provisions of Regulation (EC) No .../...<sup>+</sup> of the European Parliament and of the Council of ... on medicinal products for paediatric use\*.

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\* OJ L ..., ..., p. ...."

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<sup>+</sup> Note to OJ: Please insert number and date of this Regulation.

#### *Article 54*

In Article 6 of Directive 2001/83/EC, the first subparagraph of paragraph 1 shall be replaced by the following:

- "1. No medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive or unless an authorisation has been granted in accordance with Regulation (EC) No 726/2004, read in conjunction with Regulation (EC) No .../...<sup>+</sup> of the European Parliament and of the Council of ... on medicinal products for paediatric use\*.

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\* OJ L ..., ..., p. ....".

#### *Article 55*

Regulation (EC) No 726/2004 is hereby amended as follows:

- 1) Article 56(1) shall be replaced by the following:

"1. The Agency shall comprise:

- (a) the Committee for Medicinal Products for Human Use, which shall be responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for human use;

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<sup>+</sup> Note to OJ: Please insert number and date of this Regulation.

- (b) the Committee for Medicinal Products for Veterinary Use, which shall be responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for veterinary use;
- (c) the Committee on Orphan Medicinal Products;
- (d) the Committee on Herbal Medicinal Products;
- (e) the Paediatric Committee;
- (f) a Secretariat, which shall provide technical, scientific and administrative support for the committees and ensure appropriate coordination between them;
- (g) an Executive Director, who shall exercise the responsibilities set out in Article 64;
- (h) a Management Board, which shall exercise the responsibilities set out in Articles 65, 66 and 67.";

2) in Article 57(1), the following point shall be added:

"(t) taking decisions as referred to in Article 7(1) of Regulation (EC) No .../...<sup>+</sup> of the European Parliament and of the Council of ... on medicinal products for paediatric use\*.

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\* OJ L ..., ..., p. ....";

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<sup>+</sup> Note to OJ: Please insert number and date of this Regulation.

3) the following Article shall be inserted:

"Article 73a

Decisions taken by the Agency under Regulation (EC) No .../...<sup>+</sup> may form the subject of an action before the Court of Justice of the European Communities under the conditions laid down in Article 230 of the Treaty."

## **CHAPTER 3**

### **FINAL PROVISIONS**

#### *Article 56*

The requirement laid down in Article 7(1) shall not apply to valid applications pending at the time of entry into force of this Regulation.

#### *Article 57*

1. This Regulation shall enter into force on the thirtieth day following that of its publication in the Official Journal of the European Union.

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<sup>+</sup> Note to OJ: Please insert number of this Regulation.

2. Article 7 shall apply from ...<sup>\*</sup>.

Article 8 shall apply from ...<sup>\*\*</sup>.

Articles 30 and 31 shall apply from ...<sup>\*\*\*</sup>.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Strasbourg,

*For the European Parliament*

*The President*

*For the Council*

*The President*

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<sup>\*</sup> 18 months following the date of entry into force of this Regulation.  
<sup>\*\*</sup> 24 months following the date of entry into force of this Regulation.  
<sup>\*\*\*</sup> Six months following the date of entry into force of this Regulation.