Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 (Text with EEA relevance)

REGULATION (EC) No 1901/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 12 December 2006

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

(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[(1)],

Having consulted the Committee of the Regions,

Acting in accordance with the procedure referred to in Article 251 of the Treaty[(2)],

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

Changes to legislation: *There are outstanding changes not yet made to Regulation (EC) No 1901/2006 of the European Parliament and of the Council. Any changes that have already been made to the legislation appear in the content and are referenced with annotations. (See end of Document for details) View outstanding changes*

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[(3)].

(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[(4)], 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

***Changes to legislation:** There are outstanding changes not yet made to Regulation (EC) No 1901/2006 of the European Parliament and of the Council. Any changes that have already been made to the legislation appear in the content and are referenced with annotations. (See end of Document for details) View outstanding changes*

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.

(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

Changes to legislation: *There are outstanding changes not yet made to Regulation (EC) No 1901/2006 of the European Parliament and of the Council. Any changes that have already been made to the legislation appear in the content and are referenced with annotations. (See end of Document for details) View outstanding changes*

6 November 2001 on the Community code relating to medicinal products for human use[(5)].

(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.

(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.

***Changes to legislation:** There are outstanding changes not yet made to Regulation (EC) No 1901/2006 of the European Parliament and of the Council. Any changes that have already been made to the legislation appear in the content and are referenced with annotations. (See end of Document for details) View outstanding changes*

(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