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Frequently asked questions on regulatory aspects of Regulation (EC) No 1901/2006 (Paediatric Regulation) amended by Regulation (EC) No 1902/2006
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This information addresses some questions relating to the Paediatric Regulation that are frequently asked by companies submitting applications to the European Medicines Agency (EMEA). It assumes that readers already have a fairly good understanding of the legislative provisions detailed in the Paediatric Regulation itself. Information of a more general nature will be made available via the EMEA website in due course.

The information contained in this document will be updated regularly.

1) When did the Paediatric Regulation enter into force?

The Paediatric Regulation entered into force on 26 January 2007, i.e. 30 days after publication in the *Official Journal of the European Union*.

2) What are the new obligations for pharmaceutical companies?

The Paediatric Regulation foresees a staggered entry into force of obligations relating to the development of medicinal products for use in children, depending on the type of medicinal product concerned, as outlined below:

a) For medicinal products not yet authorised by 26 July 2008

According to article 7 of the regulation, there is an obligation to include either the results of studies (conducted in compliance with a paediatric investigation plan (PIP)) or an EMEA decision on a waiver or on a deferred PIP in applications for marketing authorisation. This is requested for the validation of new application for marketing authorisation. This obligation applies as of 26 July 2008.

Applications for a PIP, including a deferral if relevant, and/or for a waiver should be submitted no later than the completion of the relevant human pharmacokinetic studies in adults, unless justified. If a product is already developed beyond such studies (i.e. beyond the end of phase I), this legal deadline for the submission of the application is not applicable. Nonetheless an application for a paediatric investigation plan (PIP), including a deferral if relevant and/or for a waiver should be submitted without delay to prevent any problems at the time of validation on the application for marketing authorisation.

b) For authorised products protected by a supplementary protection certificate, or by a patent eligible for a supplementary protection certificate

According to article 8 of the regulation, there is an obligation to include either the results of studies (conducted in compliance with a paediatric investigation plan) or an EMEA decision on a waiver or on a deferred PIP in applications for variation or extension (of an existing marketing authorisation) concerning a new indication, pharmaceutical form or route of

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administration. Article 8 will apply as well to stand-alone applications for an authorised patented product in the framework of a Global Marketing Authorisation. This is requested for the validation of such applications for variation or extension. This obligation applies 24 months after entry into force of the Paediatric Regulation, i.e. as of 26 January 2009.

c) For a Paediatric Use Marketing Authorisation (PUMA)

The application for a Paediatric Use Marketing Authorisation is voluntary. This provision is applicable since 26 July 2007. However, an application for a PUMA would have to contain the results of studies conducted in compliance with a paediatric investigation plan.

3) When can we submit a request for a paediatric investigation plan (PIP) or a waiver?

With reference to the obligations mentioned in question 2, it is up to applicants to determine for themselves when would be the best time to submit a request for a paediatric investigation plan, or for a waiver, for their medicinal product.

Information on timelines for notification of intent to file and for submission are published on this website.

4) When was the Paediatric Committee (PDCO) established?

According to the Paediatric Regulation, the Paediatric Committee was established within the EMEA by 26 July 2007.

The Paediatric Committee is composed of:

- 5 members (with their alternates) of the Committee for Medicinal Products for Human Use (CHMP), appointed by the CHMP itself;
- 1 member (and an alternate) appointed by each of the Member States whose national competent authority is not represented through the Paediatric Committee members appointed by the CHMP;
- 3 members (and their alternates) representing health professionals, appointed by the European Commission;
- 3 members (and their alternates) representing patients' associations appointed by the European Commission.

The PDCO has been operational with 27 members, even before finalisation of the appointment by the European Commission of the further 6 members representing healthcare professionals and patients' associations.

5) Can my application already contain the results of studies conducted in compliance with an agreed paediatric investigation plan before the obligations referred to in question 2 apply?

An applicant may voluntarily include the results of studies conducted in compliance with an agreed paediatric investigation plan as part of a new marketing authorisation application or of an application for a new indication, pharmaceutical form or route of administration before the obligations referred to in question 2 apply.

6) What are the requirements for format/content for paediatric investigation plan applications and waiver or deferral requests?

In accordance with the Paediatric Regulation, the European Commission is responsible for drawing up a document setting out the detailed arrangements for paediatric investigation plan applications and waiver or deferral requests, to cover:

- The format and content of applications for agreement or modification of paediatric investigation plans and of requests for waivers or deferrals;

- Operation of the compliance check;
- Proposed criteria for assessing significant studies.

This guidance document has been released by the European Commission. In addition, applicants should consult the procedural advice document published on the EMEA paediatric webpage.

7) Which medicinal products are exempt from the obligations referred to in question 2?

The following medicinal products are exempt from the obligation to submit paediatric investigation plans:

- Medicinal products authorised under Article 10 and 10(a) of Directive 2001/83/EC, as amended, i.e. generics, hybrid medicinal products, biosimilars and medicinal products containing one or more active substances of well-established medicinal use;
- Medicinal products authorised under Articles 13 to 16 of Directive 2001/83/EC, as amended, i.e. homeopathic and (traditional) herbal medicinal products.

8) Are there any incentives or rewards for products if paediatric development is already ongoing?

The Paediatric Regulation contains a provision allowing incentives or rewards to be obtained if:

- The studies are in compliance with the agreed paediatric investigation plan; and
- Some of the studies contained in the agreed paediatric investigation plan are completed after the entry into force of the Paediatric Regulation, i.e. after 26 January 2007;
- These studies are considered "significant".
- In addition, information on the results of the paediatric investigation plan should be included in the product information and a statement on compliance should be included in the marketing authorisation.
- An authorisation in all EU Member States, for the reward linked to articles 7 and 8.

Further information is provided in the guidance document from the European Commission.

9) Under which conditions will free scientific advice be provided in respect of paediatric products?

The provision of the Paediatric Regulation relating to free scientific advice provided by the EMEA is applicable from the date of the Regulation's entry into force, i.e. as of 26 January 2007.

Free scientific advice is not limited to questions relating to the content of a paediatric investigation plan. The fee exemption for scientific advice covers any part (i.e. quality, safety and/or efficacy) of a request, but is limited to aspects of paediatric development. If the request covers both, adult and paediatric development, the appropriate fee level will be determined by the questions relating to adult development.

10) Do we need to request scientific advice before submitting a paediatric investigation plan?

Requesting scientific advice is not mandatory and the advice given is not binding on the Paediatric Committee.

Scientific advice may be requested from the EMEA at any stage in the development of a product. Therefore, applicants may choose to request scientific advice first, to help in the preparation of a paediatric investigation plan, or to submit a paediatric investigation plan directly and follow it up with a request for scientific advice on, for example, combined adult and paediatric development in light of the paediatric investigation plan requirements.

Scientific advice is given by the Committee for Medicinal Products for Human Use, through its Scientific Advice Working Party.