SUBMISSION OF PAEDIATRIC STUDIES ACCORDING TO ARTICLES 45 & 46 OF THE REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL (EC) No 1901/2006, AS AMENDED (Paediatric Regulation) AND OTHER PAEDIATRIC INFORMATION

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Question 1

Do Articles 45 and 46 apply to medicinal products irrespective of the route of authorisation?

Yes. Articles 45 and 46 apply to medicinal products irrespective of the route of authorisation, i.e. centralised procedure, mutual recognition procedure, decentralised procedure and purely national procedure.

Question 2

Do the obligations laid down in Articles 45 and 46 apply also to generics, well-established use products, authorised homeopathic medicinal products and traditional herbal products?

The requirement laid down in Articles 45 and 46 relate to all authorised medicinal products without exception.

Question 3

Should all completed paediatric studies (regardless of their place of conduct) be submitted to each competent Authority or does it apply only to studies conducted on the territory of the MS concerned?

The submission of all completed paediatric studies is regardless of their place of conduct of the trial. They should be submitted to each competent Authority where the product is authorised. The assessment however will be carried out through the work sharing-exercise for medicinal products authorised through mutual recognition/decentralised procedure and purely national procedure and by the CHMP for the centrally authorised products.

Question 4

For the purpose of this Regulation, shall paediatric studies mean only studies conducted in paediatric population (under Art. 2) or also studies conducted simultaneously in paediatric and adult population (e.g. enrolment criteria for subjects 12 to 65 years of age)?

Paediatric studies means any studies including patients aged < 18 years, including those with both adult and paediatric patients.

Question 5

According to Article 45, the Marketing Authorisation Holder shall submit to the competent Authority all paediatric studies completed by 26 January 2007. Does the competent Authority means the Authority which has authorised the product in question? I.e. in the case of centrally authorised products the EMEA and for MRP/DCP and purely national authorisations the competent Authority(ies) of the relevant Member State(s)?

Competent Authority means the Authority which has authorised the product in question, i.e. in the case of centrally authorised products the EMEA, for MRP/DCP the RMS and CMS and for purely national authorisations the National Competent Authority of the relevant MS.

Question 6

For the purpose of this Regulation, shall paediatric studies mean also studies performed by other sponsors than MAH, e.g. scientific associations?

Article 45 refers to any studies for an authorised product, whereas article 46 refers to marketing authorisation holder-sponsored studies only.

Question 7

How should Marketing Authorisation Holders comply with the requirements of Article 45 of the Paediatric Regulation?

Please refer to the Procedural guidance concerning submission of information about medicinal products, pursuant to the Paediatric Regulation, produced jointly by the CMD(h) and the EMEA, which can be found on the CMD(h) and EMEA websites.

Marketing Authorisation Holders should identify the potential regulatory consequences and include proposals to amend the product information with the submission of the paediatric studies, if appropriate.
A short critical expert overview should be added, clarifying the context of the data.

Question 8

In the procedural guidance concerning submission of information about medicinal products, pursuant to the Paediatric Regulation, Marketing Authorisation Holders are requested to submit the line listings together with a declaration (Annex I) and, for medicinal products with paediatric use, the respective wording of sections 4.1 and/or 4.2 of the SmPC (Annex II).
Does the deadline of 26 January 2008 also apply to the submission of the Annex II?

The line listing together with the declaration (Annex I) has to be submitted to the respective Competent Authority(ies) by 26 January 2008.
The CMD(h) and the EMEA would welcome to receive also the wording of the SmPC (4.1 and/or 4.2) for medicinal products with paediatric use (Annex II), as a one-off exercise by 26 January 2008.

However, the CMD(h) and the EMEA agreed with the request from Interested Parties to extend the deadline for submission of information on the wording of the SmPC (4.1 and/or 4.2) (Annex II) for medicinal products with paediatric use by a period of 3 months, i.e. until 26 April 2008.

Question 9

How should Marketing Authorisation Holders comply with the requirements of Article 46 of the Paediatric Regulation?

- Within 6 months of completion of the study, any marketing authorisation holder-sponsored trial involving the use in the paediatric population of a medicinal product covered by a marketing authorisation, should be submitted to the Competent Authority(ies), i.e. NCA(s) or EMEA (see question 5).
- Marketing Authorisation Holders do not need to resubmit safety data (as opposed to studies), submitted as part of Periodic Safety Update Reports (PSURs).
- The procedure described in the amended CMD(h) Best Practice Guide - EU work sharing procedure in the assessment of Paediatric data by National Competent Authorities will be followed with regard to timelines for the assessment of the paediatric studies submitted according to Article 46 of the Paediatric Regulation. In this procedure it is foreseen to work with a single rapporteur.

Question 10

According to Article 46, marketing authorisation holder-sponsored studies involving the use in the paediatric population of a medicinal product covered by a marketing authorisation should be submitted to the competent authority within 6 months of completion of the study.
In case a variation is intended to be submitted, e.g. to extend the indication of the product based on the results of the study, is it still necessary to submit the study according to Article 46?
If yes, will the assessment of the study be done at the time of the submission of the variation?

Marketing authorisation holder-sponsored studies which involve the use in the paediatric population of a medicinal product covered by a marketing authorisation have to be submitted to the competent authority within 6 months of completion of the study, regardless of the intention to submit a variation.
However, in the situation described above, Marketing Authorisation Holders are advised to clearly indicate their intention to submit a variation and whether it covers exactly the same set of data as the one being submitted.
Marketing Authorisation Holders should identify the potential regulatory consequences and include proposals to amend the product information with the submission of the paediatric studies, if appropriate.
A short critical expert overview should be added, clarifying the context of the data.

Question 11

Which data are to be submitted?

Studies or trials mean here those not yet submitted to Competent Authorities, involving the paediatric use of medicinal products authorised in the Community. Article 45 refers to any studies for an authorised product, whereas article 46 refers to marketing authorisation holder-sponsored studies only (Please refer to Q&A 6).

- Clinical studies and trials (phase I to IV)
- Non clinical studies (e.g. juvenile toxicology studies) not previously submitted, and relevant to the benefit/risk assessment of the paediatric studies submitted.
- Completed or discontinued studies;
- Published or not;
- Trials should be submitted regardless of the region where they were performed, the aim, outcome, population studied and indication.
- For paediatric trials, information on the pharmaceutical formulation(s) used in the trials, the existence of a formulation suitable for paediatric use, or on conditions for extemporaneous preparations should be submitted, if available.

Question 12

Which format should the Marketing Authorisation Holders use?

Study reports should preferably follow the CTD format and be submitted either as Word or PDF documents.
Electronic submission of information via CD-ROM is acceptable. In the case of older studies it may be necessary to submit an extended synopsis instead of a clinical study report when this is not available.
For studies not in English, an English extended synopsis will be acceptable, to accompany the report in original language.

Question 13

What else should the Marketing Authorisation Holders submit?

If the **medicinal product** is authorised **for paediatric use** [i.e. with either an indication in children (0 to 17 years inclusive) in 4.1, *OR* dosing information in children in 4.2 of the SmPC], the adequate information has to be stated in the line listing and the relevant wording as stated in the SmPC 4.1

and/or 4.2 has to be given in Annex II (see Best practice guide) in the relevant national language (for nationally authorised medicinal products) or in English for medicinal products authorised via MRP/DCP or centralised procedure (Please refer to Q&A 8).