The accountable number of authorised medicines Consultation in relation to the Paediatric Report

Ref. PCPM/16 – Paediatric Report

1. PART I - GENERAL INFORMATION ABOUT RESPONDENTS

Your name or name of the organisation/company: Paul-Ehrlich-Institut

Transparency Register ID number (for organisations): _____

Country: Germany

E-mail address: pei@pei.de

Received contributions may be published on the Commission's website, with the identity of the contributor. Please state your preference:

- ✓ My contribution may be published under the name indicated; I declare that none of it is subject to copyright restrictions that prevent publication
- o My contribution may be published but should be kept anonymous; I declare that none of it is subject to copyright restrictions that prevent publication
- o I do not agree that my contribution will be published at all

Please indicate whether you are replying as:

- o A citizen
- o A business
- o A non-governmental organisation (NGO)
- o An industry association
- o A patient group
- o A healthcare professional organisation
- o Academia or a research or educational institute
- ✓ A public authority
- o Other (please specify)

If you are a business, please indicate the size of your business

- o Self-employed
- o Micro-enterprise (under 10 employees)
- o Small enterprise (under 50 employees)
- o Medium-sized enterprise (under 250 employees)
- o Large company (250 employees or more)

Please indicate the level at which your organisation is active:

- o Local
- ✓ National
- o Across several countries
- ✓ EU

- Global
-

Part II – Consultation items

(You may choose not to reply to every consultation items)

1.1. More medicines for children

Consultation item No 1: Do you agree that specific legislation supporting the development of paediatric medicines is necessary to guarantee evidence-based paediatric medicines?
This is supported by the increased number of medicines authorised for the use in the paediatric population in the EU since implementation oft he Paediatric Regulation compared to regions with a likewise regulation undermines the need for a regulated system to overcome marked forces in the field of pharmaceutical development.

1.2. Mirroring paediatric needs

Consultation item No 2: Do you have any comments on the above? To what extent and in which therapeutic areas has the Regulation contributed to the availability of important new treatment options?
According to the landscape of conditions reflected in the PIP applications so fare the specific focus on therapeutic needs of the paediatric population have not been in the focus of the PIP application as the research and development of medicinal products is mainly driven by aim to address disease affecting large populations. However, for these diseases the Paediatric regulation has fulfilled it objective to secure the paediatric needs in the respective medicinal product development.

1.3. Availability of paediatric medicines in the EU

Consultation item No 3: In your experience, has the number of new paediatric medicines available in Member States substantially increased? Have existing treatments been replaced by new licensed treatments?
No Comments

1.4. Reasonable costs

Consultation item No 4: Do you have any comments on the costs for pharmaceutical companies to comply with an agreed paediatric investigation plan?
So far the financial impact on both systems like research and development as well as public health and insurance costs has not been disclosed. Therefore the solely presentation for the cost pharmaceutical companies to fulfil the obligation related to the PIP opinion does not allow any judgement.

1.5. Functioning reward system

Consultation item No 5: Do you agree that the reward system generally functions well and that early, strategic planning will usually ensure that a company receives a reward?

No comments

1.6. The orphan reward

Consultation item No 6: How do you judge the importance of the orphan reward compared to the SPC reward?

No comments

1.7. Improved implementation

Consultation item No 7: Do you agree that the Regulation's implementation has improved over time and that some early problems have been solved?

No comments

1.8. Waivers and the 'mechanism of action' principle

Consultation item No 8: Do you have any comments on the above? Can you quantify and qualify missed opportunities in specific therapeutic areas in the last ten years?

The revised approach to define and accept Class waiver published in July 2015 is appropriately reflection the scientific evidence available related to medical product development. The same approach should apply for all PIP applications to ensure that the paediatric needs are reflected according to the available scientific evidence. The Regulation has introduced the deferral to ensure, that the medicinal product development is not delayed by the obligation to fulfil the PIP.

1.9. Deferrals

Consultation item No 9: Do you agree with the above assessment of deferrals?

The deferral s implemented to avoid marketing authorisation of adult indications in case paediatric medicinal product development is expected to delay initial marketing authorisation application.
As reflected consultation item 1 and 2 the main driver for medicinal product development is still based on the objective to cover the medical need related to adult disease. Hence, the ground to grant a deferral as described in Art. 20 of the regulation applies and is therefore granted b the PDCO in the vast majority of PIP applications. However, accepting that the medical need to treat adults has public health priorities over the medical need to treat children will in future not significantly improve the timely authorisation of medicinal products for adults. In this respect the EC should review the Art 20 (2) and propose respective grounds to grant a deferral. This may be feasible by adding ground and scenarios for granting deferrals into the current EC guideline (*Guideline on the format and content of applications for agreement or modification of a paediatric investigation plan...*)

1.10. Voluntary paediatric investigation plans

Consultation item No 10: Do you have any comments on the above?

The presented data do not support, in a return of investment driven medical product development

scenario, a voluntary medicinal product development for small populations unless appropriate incentive are provided, like incentives related to orphans designation which are also targeting small populations. The current rewarded incentive for fulfilling voluntary paediatric investigation plans (PUMA) is very much depending on the national health technology assessment system (HTA) and reimbursement regulations in each of the EU member states.
The reason of PDCO for agreeing on a medical product development plan with applicant also implies a significant therapeutic benefit over existing treatment in the paediatric population. Unfortunately, this is not stated explicitly in the Paediatric regulation like it is an named objective of the orhans designation. Therefore, a respective statement related to the justification of decisions taken by PDCO may be helpful to improve the promotion of voluntary paediatric investigation plansleading to a PUMA

1.11. Biosimilars

Consultation item No 11: Do you have any comments on the above?

Biosimilars are exempted for the obligation to apply for a PIP in parallel to an adult development for marketing authorisation application. In this respect the scenario is possible, that a biological medicinal product is specifically developed according the the requirement laid down in the paediatric regulation, but the Biosimilar will only cover the formulation and indication focussing on the treatment of the adult population. Assuming that the cost for treatment with Biosimilars is lower, the likelihood for off-label use is increasing. The solution could be, that in case the originator medicinal product is authorised based on the paediatric regulation, the authorised paediatric indication should be addressed in the label of the Biosimilar provided bioequivalence studies are conclusive.

1.12. PUMA — Paediatric-use marketing authorisation

Consultation item No 12: Do you share the view that the PUMA concept is a disappointment? What is the advantage of maintaining it? Could the development of off-patent medicines for paediatric use be further stimulated?

The PUMA concept it self is not a disappointment, as a respective number of pharmaceutical companies have submitted a PIP with the objective of a PUMA, however to bring the medicines to the bedside of children a collaboration of PDCO with national HTA and reimbursement systems is warranted. (see also Consultation item No 10)

1.13. Scientifically valid and ethically sound — Clinical trials with children

Consultation item No 13: Do you have any comments on developments in clinical trials with children following the adoption of the Regulation and in view of the above discussion?

Clinical trial approval is in the responsibility of national EU member states. As PDCO is defining the frame and the specific key binding elements for the paediatric development including the clinical trial a scientific cooperating between the responsible bodies is expected and should be supported, especially in view of the upcoming implementation of the EU Clinical trial Regulation. The obliged clinical trial in children from the PIP opinion should be in accordance with European laws to avoid difficulties with the national approval procedure of these clinical trials.

1.14. The question of financial sustainability

Consultation item No 14: Do you have any views on the above and the fact that the paediatric investigation plan process is currently exempt from the fee system?

It is appreciated, that waving the fees for any regulatory assessment related to a paediatric medicinal product development is a strong incentive to the applicants. However, without knowing the financial impact on the public health costs a definite comment is not possible.

1.15. Positive impact on paediatric research in Europe

Consultation item No 15: How do you judge the effects of the Paediatric Regulation on paediatric research?

The awareness to develop a systematic infrastructure to support high quality paediatric research is increasing. The most recent IMI (*Innovative Medicines Initiative*) is supporting a project to build a EU wide paediatric research network to facilitate paediatric research and feasibility of clinical trials in the paediatric population.

1.16. "Mirror, mirror on the wall" - Emerging trends and the future of paediatric medicines

Consultation item No 16: Are there any emerging trends that may have an impact on the development of paediatric medicines and the relevance of the Paediatric Regulation?

The PRIME concept of the EMA is an excellent example for incorporating all available regulatory and scientific competence of the EU regulatory network, how the dialog along the medicinal product development life-cycle can support the forthcoming clinical trial requirements for the later marketing authorisation application.

1.17. Other issues to be considered

Consultation item No 17: Overall, does the Regulation's implementation reflect your initial understanding/expectations of this piece of legislation? If not, please explain. Are there any other issues to be considered?

The assessment of the clinical trial and study data by the NCAs related to Art. 45 applications has improved in a respective number of medicinal products the information and knowledge of the respective SmPC. However, the workload related to the assessment is considerable high also for those cases where appropriate paediatric information is already available in the SmPC. Taking this into account it could be considered, that the assessment of applications related to medicinal products, like vaccines for example, could be suspended from further Art. 45 assessments. With respect to the assessments of Art 46 procedures a robust collaboration between CHMP and PDCO could secure the harmonisation of the information from the medicinal product life-cycle into the ongoing PIP assessment procedure.