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: Finnish Medicines Agency

Transparency Register ID number (for organisations): n/a

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- o A public authority

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Please indicate the level at which your organisation is active:

- o National (National competent authority)
- o EU (part of the EU regulatory network)

2. PART II – CONSULTATION ITEMS

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

2.1. 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?
Yes – it is agreed that specific legislation is needed to support development of high quality evidence based paediatric medicines. This fact is clearly brought to light in the EMA 10-year report, the conclusions of which are supported.

2.2. 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?
The progress provided by the Paediatric Regulation can now clearly be seen. However, it is agreed that it does not equally address all paediatric needs in particularly for conditions that are paediatric specific and where development would be separate from a preceding adult development. This is typical for e.g. a large number of paediatric cancers or conditions specific to neonates. The problems in relation to paediatric-only development and in neonatology have rightly so been highlighted in the EMA-report, as well as the efforts undertaken so far to alleviate the situation.

2.3. 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 Have existing treatments been replaced by new licensed treatments?
As summarised in sections 1 and 2. in the EMA report, the paediatric regulation has improved access to new authorised medicines and the access to information on paediatric medicines (also on 'old' off-patent medicines through articles 45 and 46). However, on a member state level, the overall access to medicines authorised in children is likely to vary, due to the fact that even though a product is authorised it may not factually be on the market. This would especially apply to paediatric specific formulations (for the youngest subsets) or the lowest strengths of a particular pharmaceutical form, and for off-patent products. This is more likely to occur in countries that represent a small market. Additionally, for nationally authorised off-patent products, paediatric specific products may be available only in some countries (with a bigger market). Whether or not the new therapies have reached the patient is also likely to depend on the policy making and the reimbursement system of each country.

2.4. 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?
It is not considered possible to comment on this point without further data on the cost estimates (industry, academia), the return of investment and the public health (cost) impact of the prolonged protection of the products having benefited of the reward.

2.5. 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 further comments on this point.

2.6. The orphan reward

Consultation item No 6: How do you judge the importance of the orphan reward compared to the SPC reward?
No further comments to this point.

2.7. 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?
Agreed that activities have been improved and streamlined from EMA/PDCO perspective. There is still room for improvement, as highlighted in the report under section 6. Lessons learned.

2.8. 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 'mechanism of action' approach is principle supported, but it is agreed that this would need some additional measures to provide a framework for the approach, both for regulators and industry.

2.9. Deferrals

Consultation item No 9: Do you agree with the above assessment of deferrals?
Yes. In addition, by deferring paediatric trials (or certain subsets), the main force of the regulation in blocking the marketing authorisation application (in adults) is lost and thereby also the incentive to do the (remaining) paediatric trials.

2.10. Voluntary paediatric investigation plans

Consultation item No 10: Do you have any comments on the above?
Voluntary submissions for paediatric development are scarce, despite the fact that paediatric needs in additional/alternative conditions are often pointed out during assessment of waivers.

2.11. Biosimilars

Consultation item No 11: Do you have any comments on the above?
The fact that biosimilars are not obliged to support the paediatric indications and paediatric specific formulations/presentation may present a public health problem. The lack of a paediatric specific, age appropriate formulation or presentation increases the risk of medication (dosing) errors. The fact that the originator with an appropriate formulation/presentation is (in principle) available, may not be sufficient to prevent off-label use, as cost considerations may well be dominant. The obligation for the originator to transfer marketing authorization to third party is considered extremely relevant also in this context.

2.12. 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?
While the concept of the PUMA is still very valid, the problem statement presented in the consultation paper is supported. All steps of the chain from medicine development to availability to the end-user would need to be addressed, including policy making related to reimbursement, in order to observe significant changes to the development of (and true availability to) paediatric specific products of off-patent medicines.

2.13. 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?

It is agreed that paediatric trials pose particular problems. Recruitment problems and feasibility issues are often given as the reason when e.g. timelines need to be prolonged or studies are proposed to be changed or removed from PIPs.
In order to support the conduct of paediatric trials, a better infrastructure is needed, as stated also in the EMA report (6. Lessons learned). Additional interactions between researchers running clinical trials, ethics committees, patient representatives (including young people's advisory groups) and regulators are needed to increase understanding and remove obstacles for clinical trials.
For areas of great therapeutic interest, a system for prioritisation would need to be developed. An increased and systematic interaction with academia and health-care professionals would be needed to achieve a better understanding of positioning drugs and define paediatric needs and a rational for preferences between products under development.

2.14. 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?

The exemption of reimbursement to the national authorities for assessment of paediatric investigation plans does clearly limit the use of resources for these activities within our agency. Some kind of reimbursement system (either through fees to industry and/or redistribution of other fees) would be beneficial for the national agencies in order to improve work distribution and prioritisation of paediatric assessments.

2.15. 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 summary presented in the consultation paper is endorsed. Infrastructure needs to be developed to support paediatric research and clinical trials. Basic research both related to the paediatric specific (aspects of) diseases as well as paediatric pharmacology, developmental aspects of physiology / pharmacokinetics / pharmacodynamics and paediatric/age appropriate formulations is needed, which, when available, would enable more informed and thereby faster development of individual medicines.

2.16. "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?

Highly individualised medicines are being developed, targeting small subsections of a particular disease population expected to be amenable to the particular treatment. This applies both to advanced/biological and chemical therapies. As previously stated above under item 15, directing more efforts to basic research would be essential to support paediatric drug development.

2.17. 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 Regulation has made a clear difference, more medicines are developed for children and more studies are being conducted. In this respect implementation does reflect initial expectations. However the need for medicines specific for children (diseases in children) cannot be emphasised enough. Some therapeutic areas have seen progress, while for others the availability of new therapies are still limited and further work is needed.

As an addition to discussions on deferrals in point 9:
Late submissions relative to timelines of submitting an adult and/or paediatric marketing authorisation application are problematic. This is particularly problematic, when they concern paediatric only (orphan) products, where most of the intended paediatric studies have been completed or are already ongoing. The decision making is hampered in these situations as there is the pressure not to delay submission of marketing authorisation, although the starting point of late submission has been created by the applicant.

In order not to delay the planned application (for authorisation in adults), the expectation is that the paediatric trials are all deferred. For paediatric only development, the situation becomes a delicate balancing act between not delaying potential access (to age subsets already studied) and trying to improve the studies by requesting new or revised trials (which need to be deferred), as the studies may have been performed in a less than optimal way.

Additionally, the clinical trials approval process is separate from the PIP procedure, which is not helpful for intercepting initiation of paediatric trials that as of yet have not been discussed at the EMA or do, as of yet, not have an agreed PIP. The disconnection between trial approvals and the PIP process is also not helpful where the applicant has decided to deviate from the agreed PIP (for diverse reasons), and will apply for a modification only after initiating or having completed the trial(s).