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: F. Hoffmann-La Roche Ltd

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Please indicate whether you are replying as:

- o A citizen
- x 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
- o 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)
- x Large company (250 employees or more)

Please indicate the level at which your organisation is active:

- o Local
- o National
- o Across several countries
- o EU
- x Global

2. PART II – CONSULTATION ITEMS

Roche executive summary

The Paediatric Regulation has offered a major opportunity to improve child health in Europe by facilitating the development of drugs suitable for children and building up significant paediatric-specific expertise. Significant progress has been accomplished at this point and this should be reinforced and built on.

In line with the EFPIA's response, Roche agrees that the paediatric legislation has a major impact on paediatric drug development in EU and triggers cooperation between companies, health authorities, academia and patients.

Roche, while building on the EFPIA's position, complements the discussion with additional proposals, provided in the relevant comment boxes. These aim at facilitating the implementation of the current paediatric legislation, strengthening collaborations models across stakeholders and accelerating paediatric drug development.

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?

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?
Roche supports the EFPIA's position in relation to this item. Roche would like to strengthen that an identification and definition of unmet paediatric needs is necessary to ensure transparency to all stakeholders on the areas of need in which research is ongoing and if so, what type of research. It would further guide resources and paediatric development efforts to areas with the highest unmet need on the side of companies and the public sector (regulators/ HTA bodies). Once the needs are identified, the EMA and the pharmaceutical industry should join forces and create synergies to identify molecules from the same class or with the same mechanism of action and prioritise molecules entering paediatric drug development.

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?

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?

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?

2.6. The orphan reward

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

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?

Roche supports the EFPIA's position in relation to this item.
Roche would like to suggest some measures that would help to improve the efficiency in developing and executing paediatric investigational plans include:

- Earlier and more comprehensive scientific and regulatory dialogue: this should involve experts and patients or their representatives, to agree on an overall paediatric development plan and the timing of PIP submission. This would allow the creation, agreement on and conduct of the PIP to fit more naturally within the drug development process. At the same time it would improve the scientific robustness of the PIP and reduce the need for multiple modifications.

- Globally aligned programs in paediatric populations: while the FDA and the EMA/PDCO are already collaborating in paediatrics there should be additional opportunities with different agencies. In particular it would be important to have more systematic and early joint EMA-FDA discussions or scientific advice on the paediatric development programs.

- Master PIPs: a Master PIP used for all programs and in the same condition and including pre-agreed diseases, endpoints, go-no go decisions in order to avoid repeated discussions and review of individual PIPs and decrease the duration of the time needed to initiate paediatric clinical trials.

- Products developed for diseases with paediatric onset / initial marketing authorisation applications (MAA) covering paediatric population: considerations should be given on whether the current EU Paediatric Regulation is appropriate for products developed for diseases with paediatric onset/ products with initial MAA covering paediatric population (e.g. treatment of rare genetic neuromuscular disease such as Spinal Muscular Atrophy or Duchenne Muscular Dystrophy). In particular, considerations should be given to the fact that the requirement to have a PIP and key binding elements agreed with the PDCO during a lengthy review procedure likely followed by modifications procedures to ensure PIP compliance for MAA validation are high administrative efforts, potentially leading to a delay in development, MAA filing and access to new treatments in high medical need (rare) diseases with prevalence in both paediatric and adult population.

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?

2.9. Deferrals

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

2.10. Voluntary paediatric investigation plans

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

2.11. Biosimilars

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

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?

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?

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?

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?

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?

Roche believes that one of the emerging trends will be innovative approaches to paediatric-drug development and clinical trials design.

The oncology field is of particular importance and still represents an area of high unmet medical need as children with cancer need timely access to new and more effective therapeutic options in pace with the latest advances in science. One of the challenges faced by industry is the rarity of paediatric cancers leading to difficulties to design and conduct clinical trials as well as competition between companies to recruit patients for the paediatric studies. Thus, to enable earlier access to innovative molecules for children with cancer and to optimize early-stage data collection for confirmatory trial decision-making, Roche is proposing an evidence-based, targeted Master Trial approach in paediatric oncology: a new mechanism of action (MOA)-based phase 1 or 2 Master Trial platform is being developed to screen multiple agents across different paediatric tumour types. Multiple sponsors could use a single master trial platform to screen their agents and to identify the most promising molecules to advance into late-stage development.

This Master Trial has been discussed with the FDA and the EMA/PDCO and has received a Qualification Advice (Procedure No. EMEA/H/SAB/072/1/QO/2016/PED). Once the master trial is implemented, Roche would like to offer the possibility for other companies to use the Master Trial platform.

Roche has already initiated two independent, early-phase paediatric studies for atezolizumab (Tecentriq) and cobimetinib (Cotellic) that utilize a MOA-based approach.
For more information about the two clinical trials, please refer to the ClinicalTrials.gov identifiers: NCT02639546 and NCT02541604.

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?