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European Commission
Health and Food Safety Directorate-General
Unit SANTE B/5
B-1049 Brussels

Reference: **PCPM/16 – Paediatric Report**

Subject: **Response to the European Commission's consultation document in preparation of the report on the Paediatric Regulation**

The European Haemophilia Consortium (EHC), registered in the EU Transparency Register under identification number 786550013705-85, welcomes the opportunity to comment on the consultation on the European Commission report on the Paediatric Regulation.

EHC is an umbrella patient organisation, representing 45 patient organisations in Europe for people with haemophilia and other rare bleeding disorders. These are rare, chronic and congenital conditions with various degrees of severity and they affect individuals throughout their entire life-span. As such, the Paediatric Regulation is of importance to EHC members, as they rely on replacement therapies from early childhood.

EHC response to the consultation	
Consultation item	Response
1	Yes
2	In our opinion, the Regulation has contributed to the availability of new treatment options. However, there are still therapeutic areas in which medicines for children are either lacking or children have only access to older generation of therapies, despite novel treatments being widely available for adults. This is because there is a lack of evidence due to little research in the paediatric population. This is, for example, the case for some important adjuncts used for the management of people with haemophilia A. It is also the case in haemostasis, where adult patients have access to new direct oral

	anticoagulant medicines, while the paediatric population still relies on 'older' medicines, such as warfarin.
3	No, to both questions.
4	It seems reasonable that manufacturers can recuperate additional costs incurred due to the Paediatric Regulation.
5	The reward system generally functions well, and early and strategic planning will ensure companies receive rewards. However, we also note that some products, in particular those developed for very rare bleeding disorders, such as factor X and factor XIII deficiencies, fail to reach patients. This is because Member States are either unwilling or unable to pay for prices demanded by the manufacturer to recuperate medicines' development costs. This can result in ethical dilemmas for those who were on the trial and may then be denied access upon marketing authorisation of the novel treatment. This can also lead to a more troubling situation in which individuals, that may have originally been unwilling to take part in clinical research, feel pressured to take part in clinical trials because they perceive it as the only opportunity to access treatment until authorisation and reimbursement are granted in their Member State.
6	It is likely that the orphan reward is more advantageous for companies developing products aimed to treat rare diseases.
7	Yes
8	When companies decide to conduct voluntary clinical paediatric research despite of an issued waiver, it will be up to individual ethical committees of hospitals and universities to decide whether these research projects can proceed. This should give us a certain level of confidence that unnecessary clinical trials will not be conducted in children. Nonetheless, to facilitate the work of these ethics committee, there should be a system in place whereby companies have to inform ethics committees if a product has received a waiver when submitting applications for research projects. As noted in the response to consultation item 2, we note a number of areas in which novel treatments are available for adults but cannot be prescribed to paediatric populations.
9	Yes
10	As outlined in the consultation document, the current Paediatric Regulation offers the possibility for companies receiving a waiver to nonetheless carry out a voluntary paediatric investigation plan (PIP) and benefit from rewards offered by the Regulation. We believe this situation should remain unchanged.
11	The rule of transfer, as outlined in the consultation document, is reasonable and should be maintained to ensure continued access to

	paediatric medicines.
12	We agree that the concept of PUMA is a disappointment. However, it seems likely that, thanks to pressures from the medical community, the number of PUMA applications may increase in the coming years.
13	The EHC supports paediatric research and agrees that it should be conducted in a timely manner. However, as expressed in previous exchanges with the European Medicines Agency, the EHC still believes that completion of full PIP, particularly in rarer conditions, such as haemophilia B, can significantly slow the completion of clinical trials and hinder access to novel treatments for adult populations. Hence, we question whether it is really necessary to conduct paediatric research in all clinical trials for coagulation factor concentrates. Furthermore, one important issue in haemophilia and other rare bleeding disorders is the long-term safety of products, in particular with regard to inhibitor development and thromboembolic events. In fact, we note that data submitted for marketing authorisation is limited and does not fully reflect the immunogenic profile of a new substance used on a regular basis over a lifespan. As an alternative or an addition to paediatric research, we would suggest to require a full post-marketing registry and data collection of real-world evidence. This could be accompanied with the threat of product removal if the metrics are not met. Not only would this speed up the products approval and availability, but it would also allow for a better observation of any undiscovered issues in these selected populations.
14	There should not be additional costs for review of PIP. In fact, sharing reviews, data and opinions with other regulatory agencies could contain regulatory costs in the long-term. Furthermore, any additional cost incurred by companies in developing novel treatment is likely to influence their pricing and will ultimately be borne by national payers.
15	We note that the Paediatric Regulation does not affect academic research per se; however, it does offer an incentive for companies to further invest in research in paediatric population.
16	With regard to our therapeutic area, we foresee an increase in the number of therapies becoming available using novel technologies. Additionally, we also see an increase in research and development of gene therapy using viral vectors. For this therapy, in particular, we foresee many discussions on the age at which patients will be able to access this potential cure. In fact, an early cure will remove burden of disease and maintain joints health, however there should be certain guarantees with regard to the safety of these treatments and the potential impact that they may have on children's physical development.
17	The implementation of the regulation does reflect our original understanding of the legislation.

	There are no further comments to be raised.

The EHC consents to the publication of all information in this contribution in whole, including the name of the organisation, and we declare that nothing within our response is unlawful or would infringe the rights of any third party in a manner that would prevent publication.

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