April 27th, 2023

European Childhood Cancer Community Calls for a Swift Negotiation of the Revised EU Pharmaceutical Legislation to Cure more Children with Cancer

The European Society for Paediatric Oncology (SIOP Europe), the single united European organisation representing healthcare and research professionals in paediatric oncology, and Childhood Cancer International – Europe (CCI Europe), the only European patient organisation in paediatric cancer, have been involved in the **review, analysis and proposing of recommendations to improve the EU Paediatric Regulation and the EU Orphan Regulation since 2012**.

Yesterday, the European Commission published the long-awaited proposal for the revision of the EU Pharmaceutical legislation, which also includes provisions on medicines for rare diseases and children. The proposal follows the evaluation of the current General Pharmaceutical Legislation (Directive 2001/83, Regulation 726/2004) and the Paediatric (1901/2006) and Orphan Regulations (141/2000).

Neither the Paediatric nor the Orphan Regulations have succeeded in significantly improving young cancer patients' chance of survival. Indeed, over the last ten years, only 16 anticancer medicines have been authorised for a specific paediatric cancer indication, in contrast to over 150 for adult cancers[1]. Moreover, half of the anticancer medicines were authorised for the treatment of malignancies responsible for only 5·4% of all European childhood cancer deaths. In this light, **SIOP Europe and CCI Europe warmly welcome the proposal by the European Commission** which addresses several areas of concern previously identified by our community.

Now it is absolutely crucial to take a decisive step forward for the benefit of children with cancer with a swift negotiation and adoption of the European Commission's proposal and move towards its prompt implementation to accelerate innovation for children with cancer without further delay. The assessment process of the EU Paediatric Regulation started in 2012 and we are impatient to reap the benefits of a regulatory framework that will meet the need of young patients with cancer dying of cancer across Europe today.

SIOPE and CCI-E have analysed the European Commission's proposal and would like to underline the areas that we believe should be upheld during the negotiation process **as well as those where amendments can further strengthen the reform and ultimately, the fate of patients with unmet medical needs such as young cancer patients**.

SIOPE & CCI-E EVALUATION OF THE EUROPEAN COMMISSION'S PROPOSAL FOR REVISION OF THE EU PHARMACEUTICAL LEGISLATION

1. Science Based Paediatric Medicine Development

Uphold:

Under the current EU Paediatric Regulation, there is no obligation for a medicine developer to submit a Paediatric Investigation Plan (PIP) if the medicine originally developed for an adult cancer does not exist in children, even when the medicine has a relevant mechanism of action for a given type of paediatric cancer from a biological/molecular perspective. We are extremely pleased with the proposed introduction of paediatric medicine development based on the molecular target of a new medicine, as we have been calling for this modification since 2012. In addition, the use of the concept of "molecular target" is aligned

[1] Vassal et al. Impact of the EU Paediatric Medicine Regulation on New Anticancer Medicines for the Treatment of Children and Adolescents. The Lancet Child & Adolescent Health. 2023.

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with the United States' FDA Race for Children's Act and therefore meets our expectation to harmonise the global regulatory environment.

2. 'Unmet Medical Need' and 'High Unmet Medical Need'

Amend:

We welcome the introduction of important concepts of Unmet Medical Need (UMN) and High Unmet Medical Need (HUMN), but we believe that definition of these concepts requires clarification. We strongly advocate the creation of a flexible regulatory framework to define both concepts through a multistakeholder discussion process that would involve academia and reflect patients' needs, including their quality of life.

3. Multistakeholder Cooperation and Prioritisation

Uphold:

We endorse the introduction of multistakeholder involvement and medicine prioritisation, and we are enthusiastic to be meaningfully engaged in this process. A successful example would be the ACCELERATE Platform, which has demonstrated great value and impact of the multistakeholder collaboration in the field of paediatric cancer medicine development since 2012.

Amend:

We also plead for an adequate financial compensation for the time invested by academia and patient representatives and foresee Union budget for research and development in paediatric medicines in the areas of Unmet Medical Needs.

4. Improved Access to Novel Anticancer Medicines

Uphold:

Currently, newly approved medicines are not introduced into clinical practice in all Member States. We regard the provision of a specific additional data protection (24 months) for the introduction of a new medicine in all Member States as a great step towards more equality across Europe.

5. Improved Access to Essential Anticancer Medicines

Uphold:

We are delighted to see a dedicated chapter on the shortages of medicine and the long-awaited Union List of Critical Medicinal Products, and we are eager to collaborate on the implementation of these important initiatives.

6. Academic Drug Development and Repositioning of Medicines

Uphold:

We support the proposal to facilitate the repositioning of medicines, shelved or developed for other conditions, for the treatment of paediatric diseases. We also support the envisioned role of non-for-profit entities (academia) in generating data for repurposed medicines through fit-for-filing (a dataset that meets the expectations for inclusion in a regulatory package) trials.

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Amend:

This measure will require adequate resources for academic-led research and increased capacity within the EMA to improve access without delay to lifesaving medicines for patients who must otherwise resort to medicines prescribed off-label. Furthermore, to that end, we believe a mechanism will be necessary to ensure that industry provides academia with novel medicines and funding for the trials.

7. Early Start for the Development of Paediatric Medicines

Uphold:

We commend the introduction of the initial Paediatric Investigation Plan which aims to accelerate and simplify paediatric medicine development, foster evidence generation to inform life cycle PIP considerations, and support developments based on needs and robust science. Furthermore, we support the cap applied to the PIP deferral to the extent that the total duration of the deferral, including any prolongation granted, may not exceed 5 years.

Amend:

We recommend the reinforcement of the clear obligation to submit PIPs at the end of phase I clinical trials in adults.

8. First-in-Child Innovation

Amend:

The current proposal does not include specific incentives for first-in-child development and first-in-child marketing authorisation of medicines. We strongly recommend to include such incentives as this would be expected to increase commercial interest in the development of medicines specific to paediatric cancers (and paediatric rare diseases). Besides, we call for programmes allocating public funds to research projects addressing Unmet Medical Needs in paediatric indications.

In conclusion, we welcome and support the European Commissions' proposal for revision of the EU Pharmaceutical legislation for a more patient centric regulation. We believe the new legislation has the potential to facilitate the involvement of academia and patients in medicines development and ensure that patients' needs are meaningfully considered, but we highlight important areas for clarification and improvements as well as the urgent need to move forward with the negotiations and adoption of the proposal.

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ABOUT EUROPEAN CHILDHOOD CANCER ORGANISATIONS

Childhood Cancer International - Europe (CCI-E, or CCI Europe) represents childhood cancer parent and survivor groups as well as other childhood cancer organisations in Europe: 67 organisations in 34 European countries are members of CCI-E. CCI Europe works together with all relevant stakeholders for the same aim: help children and adolescents with cancer to be cured, with no - or as few as possible - long term health problems/late effects. **(www.ccieurope.eu)**

The European Society for Paediatric Oncology (SIOPE, or SIOP Europe) is the single united European organisation representing all professionals working in the field of childhood cancers. With more than 2,500 members across 35 countries, SIOP Europe is leading the way to ensure the best possible care and outcomes for all children and adolescents with cancer in Europe. **(www.siope.eu)**