



European Childhood Cancer Organisations' Recommendations following the European Commission's Evaluation of the Legislation for Medicines for Rare Diseases and Children and the launch of the Pharmaceutical Strategy for Europe

Executive Summary

The European Commission published a comprehensive evaluation of the legislation for medicines for rare diseases and children by assessing the strengths and weaknesses of the Orphan and Paediatric Medicine Regulation.

The lack of sufficient investment and the slow pace of innovation has stalled the progress in curing paediatric cancers, which remains the first cause of death by disease in children older than one year of age in Europe. Neither regulation served the urgent needs of children and adolescents with cancer, and those who are fortunate to survive their cancers must also cope with acute and persisting adverse long-term side effects caused by older medicines. Furthermore, there are still inequalities in access to new and essential medicines for children and adolescents with cancer across Europe.

Pan-European childhood cancer organisations welcome recognition of these unmet needs within the evaluation and further revision of legislations by putting forward **6 Key Recommendations for Paediatric Cancers**, which also have relevance to other Paediatric Life-Threatening Rare Diseases. More broadly these recommendations apply to what the childhood cancer community would like to see addressed within the Pharmaceutical Strategy for Europe.

Recommendation 1: Align the Regulations with Science and Unmet Needs of Children

Recommendation 2: Ensure Child Specific and First-In-Child Innovation

Recommendation 3: Implement Multi-Stakeholder Cooperation and Prioritisation as a Standard

Recommendation 4: Allocate Public Investment in Medicine Development for Children

Recommendation 5: Align Global Regulatory Environment

Recommendation 6: Ensure Equal Access to Essential and Novel Anticancer Medicines and to Supportive Care Medicines

For more information, please refer to the full paper below.

Because all children and adolescents deserve a carefree childhood and equal rights.

END OF EXECUTIVE SUMMARY



EUROPEAN CHILDHOOD CANCER ORGANISATIONS STATEMENT

European Childhood Cancer Organisations

SIOP Europe and CCI Europe: the European organisations representing childhood cancer professionals and parent and patient groups respectively welcome the recognition in the European Commission's Report that rare childhood diseases and paediatric cancers specifically have not been addressed sufficiently by the current medicine legislation [1-3].

Urgent action is required to revise the regulatory environment in line with a set of evidence-based proposals for development of innovative medicines for children and adolescents with cancer, and to improve access to new and essential medicines for these patients.

Paediatric Cancers in Europe

All individually rare, together **paediatric cancers are the leading cause of death** by disease in children over one year of age in Europe and contribute to life-long morbidity in survivors:

- More than **35,000 cases** are diagnosed annually;
- Over than **6,000 young patients** die each year;
- Up to **60% of the 500,000 survivors** experience long-term adverse side-effects.

Childhood cancers are a major burden that severely affects Europe's most vulnerable group – children, with serious repercussions on families and society at large.

Lack of Innovation as a Principal Culprit

Due to their individual rarity, **paediatric cancers have seen limited market innovation.**

Progress in cure rates has relied on academic-driven efforts using available medicines, originally meant for adults.

Today, stagnating survival in several hard-to-treat childhood malignancies still causes high mortality in these disease areas.

Whereas the use of established medicines has improved survival, this is consistently associated with acute and long-term adverse side effects that need to be addressed with new innovative treatments.

Overall, there is a lack of sufficient investment and enabling policies to boost innovation for children and adolescents with cancer in Europe.

Unequal Access to New and Essential Medicines

As shown by the findings of a survey in the Joint Action on Rare Cancers (2016-2019), EU Health Programme [4], there are important issues in access to medicines routinely used for the standard treatment of paediatric malignancies across Europe. Only 44% of the medicines were reported as always available in more than 90% of the surveyed countries. Shortages were a principal driver of non-availability, while financial barriers applied mainly in lower income countries and for newly approved expensive medicines.

Regulatory Environment for Innovation in Europe

The EU Paediatric (Medicines) Regulation (EC No 1901/2006) was launched in 2007 with the aim of meeting the specific therapeutic needs of children with better evaluated and authorised medicines. Unfortunately, more than ten years since the implementation of the EU Paediatric Regulation, **only 12 anti-cancer medicines have been authorised for a specific paediatric cancer indication, in contrast to over 150 for adult cancers.**

For its part, the Orphan Regulation also failed to address unmet needs of paediatric cancer patients. Between 2000 and 2016, 18/26 (70%) of anticancer medicines authorised for an orphan indication in adults with relevance to children were licensed, but there was no information about the drugs' use in children. Seven years later, additional paediatric-relevant information was added to the license for only one of these drugs [5].

This slow pace of innovation cannot serve paediatric cancer patients appropriately across the full range of specific malignancies that affect this population.

The European Commission Report

Since 2016, paediatric cancer stakeholders in Europe have been working to convey the evidence of major unmet needs and multi-stakeholder-elaborated solutions to address the lack of innovative therapies for children and adolescents with cancer. The proclamation of several conclusions in the European Commission evaluation report [6] is a positive sign that needs to be followed by rapid action that can effectively address the identified issues:

“Neither regulation has proven effective in boosting the development of innovative medicines for children with rare diseases”

“Neither regulation offers specific incentives to promote the successful development of innovative medicines for use exclusively in children”

“The (Paediatric) Regulation does not necessarily address the greatest therapeutic needs of children (such as treatments of children's cancers and for new-borns)”

“Publicly funded research is important”



6 Key Recommendations for Paediatric Cancers

In light of the evaluation report of the European Commission and launched Pharmaceutical Strategy for Europe [7], **SIOP Europe** and **CCI Europe** put forward the following action areas and recommendations for further EU action.

Recommendation 1: Align the Regulations with Science and Unmet Needs of Children

- Implement an approach to paediatric medicine development driven by mechanism of drug action, disease biology and patient needs: this, includes suppression of article 11b of the paediatric medicine regulation.
- Reduce delays in starting the development of paediatric medicines.
- Better tailored incentives to ensure early start of paediatric development.

Recommendation 2: Ensure Child Specific and First-In-Child Innovation

- Facilitate repositioning of medicines failing in adults for the treatment of paediatric diseases, when there is a scientific and preclinical rationale.
- Incentivise the 'First-in-Child' development and marketed authorisation of medicines against specific paediatric biological targets for the treatment of children with life-threatening and debilitating rare diseases, such as paediatric cancers.

Recommendation 3: Implement Multi-Stakeholder Cooperation and Prioritisation as a Standard

- Pursue multi-stakeholder dialogue and cooperation to improve the implementation of the legislations for children and set up a mechanism to prioritise the best potential medicine candidates tailored to the unmet needs of children.

Recommendation 4: Allocate Public Investment in Medicine Development for Children

- Allocate and integrate sustainable new public investment into specific areas of orphan and paediatric medicines, linking with the Cancer Mission and other Horizon Europe funding streams [8]. Progress requires solid support for dedicated international academic research platforms, crosslinked to and informed by adult cancer and industry-driven research.
- Enable academic collaborations to collate and use Big Data and develop novel applications in Artificial Intelligence to foster ground-breaking discoveries across the research and care continuum. Overcoming the current limitations related to data silos inherent in current research (infra) structures, will allow full exploration of integrated datasets with great potential to gain new insights in paediatric cancer genesis, development and cure [9].



Recommendation 5: Align Global Regulatory Environment

- Align global drug development in paediatric oncology in relation to the RACE for Children Act [10].
- Organise the dialogue between FDA, EMA and regulatory networks in other jurisdictions to ensure rapid, safe and efficient development of paediatric anticancer medicines.

Recommendation 6: Ensure Equal Access to Essential and Novel Anticancer Medicines and to Supportive Care Medicines

- Ensure that essential medicines and supportive care medicines used to treat children and adolescents with cancer are accessible and affordable for all patients across Europe at all times, including measures to counter shortages, in line with the Essential Medicines List for children elaborated by the WHO and ongoing SIOP Europe Project on the Essential Medicines.
- Ensure equal, timely and affordable access to newly approved medicines for all patients across Europe, ensure alignment of Health Technology Assessment (HTA) evaluation and address siloed approaches between EMA and HTA evaluation, in regard to paediatric medicine development [11].

In addition, we emphasise the need for harmonised environment for cross-border clinical research including in relation to accelerating the implementation of the EU Clinical Trials Regulation.

The European Childhood Cancer Community Contribution

The European childhood cancer community has a long-track record of multi-stakeholder engagement and collaboration to boost innovation and stands ready to support the EU's further efforts in this area. Relevant initiatives include but are not limited to:

1. **MULTI-STAKEHOLDER ENVIRONMENT:** Multi-stakeholder **ACCELERATE Paediatric Strategy Forums** [12] to define unmet medical needs and prioritise for drug development.
2. **EXPERTISE IN PAEDIATRIC ONCOLOGY:** **Rapid access to expertise** in the field of paediatric oncology, biology, new drug development and regulatory science through ACCELERATE, ITCC and SIOP Europe.
3. **PATIENTS AT THE CENTRE:** Facilitated **participation and engagement of patients and parent representatives** through Childhood Cancer International – Europe.
4. **ESTABLISHED CLINICAL RESEARCH NETWORK:** The EU basic, translation and clinical research network, in particular **SIOP Europe Clinical Research Council**.

Our networks and expertise are committed to supporting the EU's further efforts to improve access to innovation for children and adolescents still dying of cancer in Europe and survivors who experience life-hindering late effects.



ABOUT EUROPEAN CHILDHOOD CANCER ORGANISATIONS

- **SIOPE Europe (www.siope.eu)** – The European Society for Paediatric Oncology (SIOPE Europe, or SIOPE) is the single, united European organisation of academia and healthcare professionals dedicated to childhood and teenage cancer, working in close partnership with patient, parent and childhood cancer survivor groups across Europe.
- **CCI Europe (www.ccieurope.eu)** – Childhood Cancer International - Europe (CCI Europe) represents childhood cancer parent and survivor groups as well as other childhood cancer organisations in Europe. 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.

References:

1. European Medicines Agency. Report on a multi-stakeholder workshop held at EMA on How to better apply the Paediatric Regulation to boost development of medicines for children. 2018.
https://www.ema.europa.eu/en/documents/report/how-better-apply-paediatric-legislation-boost-development-medicines-children-report-multi_en.pdf
2. European Commission. State of Paediatric Medicines in the EU 10 years of the EU Paediatric Regulation. 2017.
https://ec.europa.eu/health/sites/health/files/files/paediatrics/docs/2017_childrensmedicines_report_en.pdf
3. SIOPE Europe, Unite2Cure, CRUK. Paediatric Cancer Medicines-Urgent need to speed up life-saving innovation Position statement. 2016.
https://siope.eu/media/wp-content/uploads/2013/12/Multistakeholder_proposals_Paediatric_Regulation1.pdf
4. Joint Action on Rare Cancers; D9.1 Report summarising the result of the survey on accessibility of standard treatment and recommendations to Member States and Europe to overcome bottlenecks. 2019.
<https://jointactionrarecancers.eu/images/work-packages/wp9/D9.1%20Report%20summarising%20the%20results%20of%20the%20survey%20on%20accessibility%20of%20standard%20treatment%20and%20recommendations%20to%20Member%20States%20and%20Europe%20to%20overcome%20bottlenecks.pdf>
5. Vassal G, et al. Orphan Drug Regulation: A missed opportunity for children and adolescents with cancer. Eur J Cancer 2017; 84:149–58.
<http://www.ncbi.nlm.nih.gov/pubmed/28818704>
6. European Commissions' Evaluation of Evaluation of the Medicines for Rare Diseases and Children Legislation. 2020.
https://ec.europa.eu/health/human-use/paediatric-medicines/evaluation_en
7. European Commission. Pharmaceutical Strategy for Europe; 2020.
https://ec.europa.eu/commission/presscorner/detail/en/ip_20_2173



8. Kearns PR, et al. A European paediatric cancer mission: aspiration or reality? Vol. 20, The Lancet Oncology. 2019. p. 1200–2.
[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(19\)30487-5/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(19)30487-5/fulltext)
9. SIOP Europe. Artificial Intelligence and Big Data: Towards the next frontier in paediatric cancer research & innovation in Europe. 2020.
<https://siope.eu/news/iccd-2020-news-release-artificial-intelligence-and-big-data/>
10. 115th Congress 1st Session. A bill to amend the Federal Food, Drug, and Cosmetic Act to establish a program to increase the development of new drugs to treat pediatric cancers, and for other purposes. 2017.
<https://www.govinfo.gov/content/pkg/BILLS-115hr1231ih/pdf/BILLS-115hr1231ih.pdf>
11. Schoot R, et al. Market access to new anticancer medicines for children and adolescents with cancer in Europe. 2022.
<https://www.sciencedirect.com/science/article/pii/S0959804922000673>
12. Vassal G, et al. Creating a unique, multi-stakeholder Paediatric Oncology Platform to improve drug development for children and adolescents with cancer. Eur J Cancer 2015; 51(2):218–224.
[https://www.ejancer.com/article/S0959-8049\(14\)01065-X/pdf](https://www.ejancer.com/article/S0959-8049(14)01065-X/pdf)

Useful links:

- Vassal G, et al. SIOP Europe Strategic Plan: A European Cancer Plan for Children and Adolescents. 2015.
<https://siope.eu/european-strategic-plan/>
- Vassal G, et al. Access to Essential Anticancer Medicines for Children and Adolescents in Europe. 2020
[https://www.annalsofoncology.org/article/S0923-7534\(20\)43223-5/fulltext](https://www.annalsofoncology.org/article/S0923-7534(20)43223-5/fulltext)
- Kowalczyk JR, et al. European Standards of Care for Children with Cancer. 2013
<https://pubmed.ncbi.nlm.nih.gov/24300454/>
- European Elections Manifesto of the Paediatric Cancer Community:
<https://siope.eu/news/european-elections-2019-manifesto-paediatric-oncology-haematology-communit/>
- JARC – Joint Action on Rare Cancers. Rare Cancer Agenda 2030: Ten Recommendations from the EU Joint Action on Rare Cancers. Casali PG, Trama A, editors. Lecce: Youcanprint; 2019. 131 p.
https://jointactionrarecancers.eu/attachments/article/265/Rare_Cancer_Agenda_2030.pdf
- JARC – Joint Action on Rare Cancers. Report summarizing recommendations to facilitate referral of children to trial centers offering innovative medicines. 2019.
<https://jointactionrarecancers.eu/images/work-packages/wp9/D9.2%20Report%20summarizing%20recommendations%20to%20facilitate%20referral%20of%20children%20to%20trial%20centers%20offering%20innovative%20medicines.pdf>