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: Solving Kids’ Cancer

Transparency Register ID number (for organisations): 018086926003-18

Country: United Kingdom

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Received contributions may be published on the Commission’s website, with the identity of the contributor. Please state your preference:

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Please indicate whether you are replying as:

- A citizen
- A business
- **A non-governmental organisation (NGO)**
- An industry association
- A patient group
- A healthcare professional organisation
  - Academia or a research or educational institute
  - A public authority
- Other (please specify)

If you are a business, please indicate the size of your business

- Self-employed
- Micro-enterprise (under 10 employees)
- Small enterprise (under 50 employees)
- Medium-sized enterprise (under 250 employees)
- Large company (250 employees or more)

Please indicate the level at which your organisation is active:

- Local
- **National**
- Across several countries
- EU
- Global
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?

Investigating new agents in children and adolescents is particularly difficult as their numbers are few, studies are costly and outcomes are not guaranteed. This leads to long delays for companies who answer to shareholders, and so sadly a waiver to avoid having to test efficacy in children is the attractive option for many. Children are ultimately sidestepped in the drug development process because of financial challenges.

For diseases like childhood cancers, this means that the prognosis for many remains bleak, rates of relapse are high, and the children who do survive are forced to live with serious and life changing side effects of treatment.

In addition, without the availability of paediatric medicines - with paediatric formulations (e.g. liquid rather than tablet form) and safe and appropriate dosing instructions – off-label use of medicines developed for adult indications will continue to be a widespread practice, prescribed by clinicians at their own risk.

Off-label usage does not serve the research community or patients well, given that these medicines have not been confirmed as safe or efficacious in this population.

Solving Kids’ Cancer agrees that specific legislation is absolutely vital to the provision of more medicines for children, which could go towards improving and saving the lives of 35,000 children diagnosed with cancer in Europe each year.

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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?

Cancer remains the primary cause of death by disease of children and adolescents in Europe, yet investment in research into childhood cancers lags far behind that for adults. The Regulation has largely failed to improve the outlook in this area,
35,000 are children and young people are diagnosed with cancer in Europe each year, and 6,000 die. This is clear evidence that the medicinal needs of this population are not being met.

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?

There have been many incredible advances in the treatment of adult cancers in the past 10 years, but childhood cancer is losing out for many reasons, including the opportunity for industry to apply for waivers in the drug development process.

Investigating new agents in children and adolescents is particularly difficult as their numbers are few, studies are costly and outcomes are not guaranteed. This leads to long delays for companies who answer to shareholders, and so sadly a waiver to avoid having to test efficacy in children is the attractive option for many.

The inclusion of waivers (as in the existing legislation) means that the number of new paediatric medicines has not substantially increased. The bottom line is that children are often sidestepped in the drug development process because of financial challenges. Without addressing this loophole which has been exploited by industry, the needs of children and young people with cancer will continue to remain largely unaddressed.
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?

Solving Kids’ Cancer recognises that it is costly to run clinical research projects in the paediatric population, but these costs could be tolerated by large pharmaceuticals to achieve the goals of improving survival and reducing toxicity for children with cancer and other serious illnesses.

For smaller biotechs, improved incentives and financial rewards could go towards addressing this issue and ensure that it becomes an attractive area to operate.

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?

Solving Kids’ Cancer does not believe that the current reward system generally functions well. The development of specific paediatric medicines for children with cancer is an area which remains largely unaddressed, providing proof that the current reward system is unsatisfactory and does not stimulate significant activity in this area.
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 comment.

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?

No comment.
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?

Where drugs are being developed for a disease which does not exist in children (e.g. lung cancer), companies can apply to have the associated compulsory Paediatric Investigation Plan waived. This is despite the fact that the underlying molecular biology (or mechanism of action) is known to be active in a number of childhood cancers.

One example where this has been demonstrated is crizotinib. This drug is now authorised in Europe for the treatment of non-small cell lung cancer (NSCLC). Research on crizotinib began as recently as 2007, but its development in children was waived in 2010 on the grounds that “NSCLC does not exist in children”. However crizotinib has shown efficacy in the childhood cancer neuroblastoma - the mechanism of action is the same.

In the first five years of the Regulation, 26 adult drugs with a potential relevance to childhood cancers were developed, but over half of these had paediatric waivers (ITCC, 2012). In response, the Institute of Cancer Research made this statement in 2014:

“We strongly support replacing the class waiver system with one that looks at the mechanism of action of the drug, and feel that this would substantially increase the number of paediatric trials for potentially very important drugs for childhood cancers.”
2.9. Deferrals

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

No comment.

2.10. Voluntary paediatric investigation plans

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

Solving Kids’ Cancer believes that the investigation and development of new drugs in children should not be a voluntary action relying on the goodwill of industry. Cancer remains the number one cause of death by disease in children in Europe; this should make it an urgent priority for the European Commission to address through effective legislation which promotes activity in this area.
2.11. Biosimilars

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

No comment.

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?

No comment.
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?

In diseases like high-risk neuroblastoma, fewer than 1 in 2 children will survive. The only way to improve the outcome for children diagnosed with this childhood cancer is further clinical research, so that safe and effective treatments can be established for these children.

Clinical research involving children is an area of activity which raises many questions and concerns. The experience of Solving Kids’ Cancer has been that children (and their parents) are keen for the opportunity to participate in clinical trials, providing hope (even in early phase trials) where previously there has been none.

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?

No comment.
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?

Most children diagnosed with cancer are treated with chemotherapy drugs which are over 30 years old, originally developed for adults. The lack of innovative research in paediatric cancers has meant that survival rates for the most resistant cancers have remained unchanged, the prospect for cure at relapse remains low, and the toxicities (both acute and long-term) are significant.

The Regulation has not effectively changed this outlook over this past 10 years.

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?

Significant scientific progress has been made in recent years in the treatment of adult cancers. These advances have included the concept of personalised medicine and immunotherapies. These are two extremely costly areas of research and it is likely that both incentives to develop, and penalties for failure to develop, are required to stimulate research in the paediatric community. The only way to
ensure that the childhood cancer community are not left behind in these scientific advances is through developing effective legislation which protects this vulnerable population.

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 held great promise for children affected by cancer in Europe, as well as other diseases. However the promise has not been fulfilled, with the inclusion of a clear loophole in the form of class waivers which has been exploited by industry.

Cancer remains the first cause of death by disease for children in Europe. Many of the 35,000 diagnosed each year face toxic and life-changing therapy, life-limiting side effects, a poor prognosis, and ultimately premature death. The significant progress made in the treatment of adult cancers has not been reflected in the paediatric population. This is something which needs to be urgently addressed by the European Commission.