ICR The Institute of Cancer Research

Concept Paper submitted for Public Consultation on Commission Guidelines on the format and content of applications for paediatric investigation plans

Response from The Institute of Cancer Research, London

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Introduction

The Institute of Cancer Research, London welcomes the opportunity to comment on this concept paper on paediatric investigation plans, a topic of great interest to us.

The Institute of Cancer Research (ICR) would like to see an expansion of early-stage paediatric clinical trials in order to accelerate development of safe, effective, innovative treatments for children. An insufficient number of paediatric cancer trials restricts or delays access for children to the latest drugs, some of which could be of significant benefit to them.

The ICR is supportive of the EU Paediatric Medicine Regulation, which has been a significant step forward in increasing numbers of clinical trials for children, but believes the PIP process should be revised to deliver further benefits.

Do you have any comments on the format and content of applications for agreement on or modification of a paediatric investigation plan and request for waivers or deferrals?

We believe the system of paediatric investigational plans (PIPs) needs to be revised to ensure cancer drugs developed for adults are tested in children whenever their mechanism of action suggests they could be effective.

Pharmaceutical companies are given waivers from testing potentially important cancer drugs in children because the drugs are being registered for adult cancers that do not occur in children – even though the drugs may work in a way that could be effective against paediatric cancers and the drug target may exist in a childhood malignancy.

Modern cancer treatments are often targeted at genetic features of an individual's tumour, and this may be common to a number of cancers, rather than being designed for a single tumour type. This makes the mechanism of action of new treatments a more important factor than

tumour type for the majority of children's cancers, particularly those which have no adult equivalent.

The EMA's five year report to the European Commission[1] specifically highlights paediatric oncology as a neglected therapeutic area in need of improvement. It states that 'further steps are considered necessary to achieve the main objectives of the Paediatric Regulation for paediatric therapeutic areas such as paediatric oncology where little progress has been made'. The EMA suggests that in paediatric oncology, it is now necessary to take into account the mechanism of action of the treatment and the drug target when looking at the scope of PIPs and waivers.

We strongly support this recommendation. Revising this process would reduce the number of granted waivers and increase the number of trials that would proceed through the PIP mechanism.

An analysis published in 2013 [2] investigated whether the Paediatric Medicine Regulation is working for children and adolescents with cancer. The authors report that of 28 new oncology drugs authorised at the time of writing, 26 had a mechanism of action potentially relevant for paediatric malignancies. Yet of these 28 drugs, 14 were waived because the adult condition does not occur in children.

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.

[1] European Medical Agency. 5-year Report to the European Commission. General report on the experience acquired as a result of the application of the Paediatric Regulation. http://ec.europa.eu/health/fi les/paediatrics/2012-09_pediatric_report-annex1-2_en.pdf

[2] Vassal G, Geoerger B, Morland B. Is the European pediatric medicine regulation working for children and adolescents with cancer? *Clin Cancer Res* 2013; **19:** 1315–25. http://clincancerres.aacrjournals.org/content/early/2013/01/17/1078-0432.CCR-12-2551.full.pdf

Please feel free to raise any other issues or make any comments which have not been addressed in the consultation items above.

We believe that reforming the PIP process is particularly important because other routes available for evaluating and developing childhood medicines are not proving effective.

In the report 'Better Medicines for Children – From Concept to Reality'[3], the Commission points to other mechanisms to encourage the development of new drugs specifically for childhood cancers, such as the Orphan Regulation, which it suggests would be appropriate since all paediatric cancers are classed as rare diseases.

The ICR believes that orphan drug designation has not proved effective at providing incentives for companies to develop drugs solely for paediatric cancers. Data analysis by the ICR and others shows that as of June 2013, 25 approved orphan medicinal products were oncology drugs, representing a third of all approved orphan drugs. However, none of these drugs were registered for children in a different indication to adults, indicating that companies are not using this route for developing new drugs solely for paediatric cancers.

We feel that the Orphan Drug Regulation does not adequately meet the needs of children with cancer, further highlighting the need to revise the PIP process to ensure an increase of early-stage paediatric clinical trials.

[3] Commission to the European Parliament and Council. Better Medicines for Children — From Concept to Reality. General Report on experience acquired as a result of the application of Regulation (EC) No 1901/2006 on medicinal products for paediatric use.

http://ec.europa.eu/health/fi les/paediatrics/2013_com443/paediatric_report-com(2013)443_en.pdf