



EGA Position Paper

***EGA Comments
on the
Proposed Regulation on Incentives for the Development of
Medicines for Paediatric Use***

(in response to the second public consultation)

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The EGA represents over 500 companies in Europe
dedicated to the production and supply of affordable generic medicines.

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EGA Comments on The Proposed Regulation on Incentives for the Development of Medicines for Paediatric Use

1. Introductory remarks

The EGA welcomes the initiative to promote better medicines for children.

The objectives of improving the treatment of children with medicines must be achieved without delaying the authorisation of medicinal products for other populations – either the access of *new* medicines to the market for adult indications or the access of *generic* medicines to the market for adult indications.

Separate marketing authorisations must be granted for separate paediatric products (even where a company already holds a marketing authorisation for the product for adult indications), which shall not be substitutable by adult products.

Transparency must be a key aspect of the procedures laid out in the Regulation and any incentives offered must be proportionate to the costs incurred.

2. Incentives in the off-patent sector

A ten-year (or other) exclusivity period *could* serve as an incentive to encourage companies in the multi-source, off-patent market to perform studies and develop an independent paediatric product – particularly given that experience from the Orphan Regulation has shown this to be the case. However, this exclusivity should be

1. **Market exclusivity**, not *data* exclusivity, as is the Orphan Medicines precedent. This would be clearer and more effective as it would avoid an unnecessary division of a limited market by a number of very similar products. The period of exclusivity could also more easily be varied in function of the agreed incentive:cost relationship.
2. For a **separate marketing authorisation and paediatric product, clearly identifiable as such.**

Apart from the obvious issues of safer and more effective use of the medicine if a specific paediatric product is used for children, **it must be stipulated that the off-label prescription or dispensing of the existing adult product, where a child product is available, must not be permitted.** (The paediatric product will often have a new pharmaceutical form, formulation, dosage or method of delivery to the existing adult product, but this is especially important for cases where it does not.) Otherwise the incentives and the objectives they seek to achieve will be undermined.



And there should also be:

3. Free access to scientific advice;
4. Fee waivers for paediatric applications;
5. The possibility of assistance from the proposed paediatric development fund, for the performance of clinical trials and/or the development of a new pharmaceutical form, formulation, dosage or method of delivery.

3. Paediatric Development Fund

Given the key importance of the Fund to the achievement of the aims of this whole undertaking, we are concerned that priority is not being given to the setting up of the Fund and feel that it is imperative that this be an integral part of, if not the Regulation on paediatric incentives, at least the ‘package’ and discussed at the same time. It should also be mentioned in the Regulation and its administration listed as one of the tasks of the Paediatric Board in *Article 3.8*.

Since the majority of products used off-label for children are in the off-patent sector, it is also logical and in-line with public health priorities to give this funding priority availability for the off-patent sector. Moreover, this will give an essential tool to the Paediatric Board to help ensure the objectives of this legislative initiative are achieved.

4. Incentives in the on-patent sector

4.1 Proper Health Economic Impact Assessment

The ‘incentive’/reward for performing a paediatric study on a patented medicine currently being discussed is a 6-month SPC extension on the whole product.¹

It is essential that a valid economic impact assessment of such a measure be taken seriously into consideration and weighed against the costs of any trials and alternative means of achieving the established goals. This is particularly important as calculations show that relatively small investment by a patent holder will result in an excessively large reward and an unnecessarily high cost to the payers. Indeed there is currently no provision requiring transparency on the measures which have been benefited from – the trial may have been conducted with the support of a public research grant in the first place – meaning the public would end up paying for the information much more than twice over. Clearly **such transparency should be required by the Regulation so that it is possible to ensure the incentive/reward is proportionate to the cost.**

¹ It is not even made clear that this would not take effect until after the fulfilment of the deferred paediatric investigation plan, leaving open the possibility that companies would be rewarded before the reward is earned and thus reducing the power of the Paediatric Board to ensure the company does fulfil their Paediatric Investigation Plan requirements.



4.2 Costs

Annex 1 to this paper contains figures obtained from an independent commercial company performing paediatric studies. These are set-price tenders or quotes for full-service paediatric studies. They cover a range of therapeutic areas, which are understood to be fairly representative of the range of studies, which may be required.

We understand the prices also to be representative, as competition on the market causes a convergence of the prices charged by the various contract research organisations (CROs), although naturally studies performed by the relevant company itself or by academia may be cheaper as they would not include the commercial margins inherent here.

As can be seen, although the European-only studies have tended to include vaccines, which might be a little cheaper as a rule, of the 25 EU and US studies, only 2 of them exceeded €3 million, and those 2 with higher costs were in a large number of sites (and for respiratory complaints, which tend to have a fairly large market in children and are likely to generate a high return).

The average cost of these 25 full-service paediatric studies was €1.1 million. This figure should be compared with the cost to the EU's national healthcare systems of an extra 6 months of market exclusivity of the whole product. According to our calculations a **6-month patent extension would cost well over €60 million per medicine.**

The model proposed by the European Commission for on-patent products is therefore likely to be a very costly one for national health systems.

4.3. One Rule for All

The EGA proposes that there is no need to have different 'incentives' across the market.

If the 10-year (or other) period of market exclusivity on the paediatric product, is sufficient to *encourage* smaller generic companies to *choose* to develop paediatric products in the off-patent market – given that many of the priority products do lie in this sector and that here the incentive would be the only way to ensure that they are brought to market – surely the same incentive would also be sufficient *reward* for bringing the paediatric product to market for major companies under an obligation.

Consequently, we recommend that the Commission propose a limited period of market exclusivity be granted to the separate marketing authorisation of a separate paediatric product, instead of the proposed 6-month SPC extension on the whole product. It should be specified in the law that market authorisations benefiting from this provision are not entitled also to a data exclusivity period, particularly as the appropriate market exclusivity period may well be less than a data exclusivity period.



As in the case of the off-patent product, the on-patent paediatric product would have a separate marketing authorisation (and possibly different pharmaceutical form, formulation, dosage or method of delivery) than the adult medicine. It would also have its own packaging (blue “P” with star) and patient/parent information directed at paediatric use.

Patent holders would not only benefit from the extended market exclusivity for the paediatric medicine/formulation - which could extend beyond the patent - but would also benefit from the corresponding increase in market revenues generated by paediatric use of the product while under patent.

Studies having a negative outcome may result in changes to the summary of product characteristics of the adult product (which must be included – and be able to be included - for all similar products, generic included) but the adult marketing authorisation cannot receive additional exclusivity of any kind.

The same principle must apply as in the off-patent sector: in those borderline cases where the patent-holder might be obliged to perform paediatric studies but it is unlikely that the result will be a paediatric product from which to recoup the costs of the studies, the Paediatric Board could choose to subsidise the costs of the clinical trial from the proposed EU paediatric study fund.

Rewards should not be granted for the authorisation of a paediatric product that is obvious (sufficient data is already available regarding the appropriate use of the medicinal product in the relevant child population(s)).

5. Ethical measures

Provisions must be included to prevent the unnecessary repeat of studies in children, which would be unethical. Furthermore, all existing data must be collated as a high priority measure to prevent the performance of studies where enough published data, results of studies done, or experience of off-label use, for example, is available to simplify the trial design, limit the number of subjects needed for the clinical trial or even, possibly, avoid the need for one altogether. In this regard *Articles 25, 26, 28 and 29* are welcomed.

6. Paediatric Board

The PB, must be composed of independent experts and should draw on the knowledge, experience and skills of experts in the field of the products being assessed by being supported by an even larger list of independent experts – all of these should make a public declaration of interests. The points made in *Article 3.7* are key. (As mentioned under point 3 ‘Fund’ above) there should also be mention of their role in administering the proposed paediatric development fund and a cross-reference to this proposed piece of legislation included.



7. Other points

7.1 It must be possible to appeal decisions

Article 11 – The opinion of the Paediatric Board and related information shall be made public and it must be possible not only for the company concerned but also for other stakeholders to appeal this decision.

7.2 It must be possible for all relevant products to include SmPC changes

The Regulation must also specify that all changes to the summary of product characteristics, including those resulting from pre-existing or other studies (mentioned in *Articles 28* and *29*) may be applied to other relevant products on, or coming onto, the market – such as generics. This is important in the context of safety, harmonisation and competition.

8. Conclusions

The EGA welcomes the Commission proposals for improving medicines for children but is concerned that the draft proposal has not focused sufficiently on the off-patent sector and has created a model of rewards for on-patent products which would create an unnecessarily high cost burden on healthcare systems.

The EGA therefore recommends:

1. **The same incentives/reward model in both on-patent and off-patent sectors**, based on appropriate periods of *market* exclusivity covering the separate marketing authorisation for the separate paediatric medicinal product. Consequently, there would be no need for costly patent/SPC extension or any measure impacting on the adult product.
 - The objectives of improving the treatment of children with medicines must be achieved without delaying the authorisation of medicinal products for other populations – either the access of new medicines to the market for adult indications or the access of generic medicines to the market for adult indications.
 - Separate marketing authorisations must be granted for separate paediatric products (even where a company already holds a marketing authorisation for the product for adult indications), which shall not be substitutable by adult products.
 - Appeal against the granting of rewards/incentives must be possible
 - Any information included in the summary of product characteristics of the adult product must also be able to be included in that of all similar products on the market.



- Transparency must be a key aspect of the procedures laid out in the Regulation and any incentives offered must be proportionate to the costs incurred.
2. The **paediatric development fund** must be part of the legislative proposals, should be referred to in the Regulation and elaborated in detail at the same time. It must be targeted at use in the off-patent sector, where the major need for the development paediatric medicines has been identified and where the Paediatric Board will need additional tools to achieve the desired results.
 3. **Ethical measures** must be strongly incorporated into the proposals.
 4. The **Paediatric Board** must be independent of all parts of the industry (originators and generic) and its members must make comprehensive declarations of interests.



Annex 1 – paediatric study cost statistics

25 full service studies in paediatrics since 1998

Commercial bids made by independent Contract Research Organisation
(Number of sites acts as a surrogate for complexity)

average cost €1.1 million (@ US\$1 = €0.8)

THERAPEUTIC AREA	Number of Sites	US Dollars in Thousands
Vaccine: European	5	84
Vaccine: European	3	113
Vaccine: European	21	128
Neonatal: European	1	141
Vaccine: European	2	190
Vaccine: European	15	207
Neonatal: European	4	230
Vaccine: European	24	301
Respiratory	15	356
GI	5	360
GERD	10	629
GERD	20	667
Metabolic Disease	3	913
Burns	12	1,149
Neonatal	15	1,165
GERD	15	1,202
Haematology	16	1,303
Oncology	10	1,338
GERD	15	1,376
GI	24	1,602
GERD	31	1,887
Respiratory	43	2,051
Rheumatoid Arthritis	69	3,297
Respiratory	60	5,115
Respiratory	90	8,786