Consultation in relation to the Paediatric Report

Ref. PCPM/16 – Paediatric Report

1. PART I - GENERAL INFORMATION ABOUT RESPONDENTS

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- o An industry association

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- o EU
- o Global (as a member of the IGBA)

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?

We agree with the Commission assessment that the Paediatric Regulation clearly helped to stimulate research and authorization of paediatric medicines.
However, looking at the developments of the legal framework, we believe that regulating medicines development separately for specific categories (i.e. paediatrics, orphan) should not become a future trend of population/product specific and fragmented legislation (i.e. for geriatric medicines etc.).

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?

Paediatric Regulation is an important enabler of increasing paediatric use, but practice has shown that the regulation does more to encourage paediatric research in existing adult indications/ use than

in driving dedicated paediatric specific R&D. The current framework does not differentiate between important unmet paediatric needs and less essential indications.

We agree with the analysis presented in point 2.2. that there is a disproportion between the development of paediatric specific indications and paediatric indications being a follow-on adult indication.
Frequently the dosage in adults is extrapolated to children (e.g. by body weight-based dosing); or the intended use of a medicine for treatment of adults is partially extended to include children "close" to adults, e.g. children of > 12 years or > 40 kg, etc. It could be emphasized that the range of children is wide, from newborns to adolescents, and it is a challenge to perform full paediatric studies for each "subgroup" of children. There is also a risk of overlapping with the orphan medicines regulation in view of the small patient populations.

Regarding the question: "*To what extent and in which therapeutic areas has the Regulation contributed to the availability of important new treatment options?"*, we are of the opinion that there has been a successful increase of paediatric medicines use for many indications: autoimmune diseases (juvenile rheumatoid arthritis, Crohns, psoriasis), transplantation, infectious diseases (vaccines, anti-viral treatment), oncology, haematology (blood coagulation), endocrinology (insulins, growth hormones). It should be mentioned that paediatric medicines use almost always requires a specific product form due to smaller volumes or lower drug concentrations to be administered in children, or due to another mode of dosage (e.g. body weight-dependent dosing instead of a fixed dose).

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?

We support the regulation with a view to ensuring that, once a paediatric investigation plan is completed and the paediatric medicine is authorised, the product should be placed on the market and available in the entire EU to be eligible for a reward. We believe this approach should be maintained.

Regarding the question: "Have existing treatments been replaced by new licensed treatments?", we do not have much visibility on the scale of the changing prescribing habits to newly authorized products, but the general impression is that doctors do continue off- label prescribing despite a new, appropriately tested product being available.
This is obviously contradictory to the objective of the Paediatric Regulation.
The reasons for the continuation of off- label prescribing should be studied in order to understand the main obstacles (education of prescribers? costs?). This could also partially provide the answer to an unsuccessful PUMA system, as the risk of off- label use is quoted as one of the reasons for not investing in PUMA.

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?

The statement indicating that costs of paediatric studies result in only a limited increase in the total costs of medicine development is probably correct in the case of the development of originator products/ NCE. However in the case of the development of generic/ biosimilar medicines, this statement is incorrect as 20m EUR constitutes a significant R&D investment. (This is one of reasons leading to low investment in PUMA for off-patent molecules). For this reason and other reasons as discussed in point 2.11, the requirements for PIP should not be applied to biosimilars. For the development of "value added medicines" (medicines with a well-known molecule with an additional value element in comparison to the originator products), costs of completing a PIP may be prohibitive for developing products (even for adults) if there is no chance of recognition by RP authorities (i.e. no price premium; "pure" generic price level").

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?

The assessment of the reward system shall be carried out from various perspectives:

1**. Benefit for the company due to the 6-month SPC extension**

In our opinion, the 6-months SPC extension as an incentive is sufficient as a reward and should not be increased. The balance between incentives for originators and follow-on generic/ biosilimilar medicines reached during the legislative process should be kept.
The 6-month SPC extension is used and is beneficial for originator companies. The last annual EMA report on the implementation of the paediatrics regulation which was published in May 2016 shows the regular and increased use of the SPC extension as a reward- "*A significantly higher number of active substances benefited from the six-month extension of the supplementary protection certificate (over 50% increase compared to 2014).Extensions of the Supplementary Protection Certificate are granted by National Patent Offices). In 2015, 28 active substances benefited from the six-month extension compared 13 in 2014"*

We do not fully agree with the assessment that a request to extend SPC is complicated due to the necessity of dealing with national patent offices. It was probably the case at the start of implementation. However, as mentioned in the consultation document, the number of SPC prolongations granted in the last ten years (nearly 500) shows that companies regularly receive the reward from the national patent office to which they apply.

2. **Time of request for a SPC extension – from generic/ biosimilar company perspective**
From the perspective of a generic/ biosimilar medicines company, the predictability and visibility of a granted reward is crucial for planning the product development, authorization and launch.
It would be beneficial for generic/ biosimilar companies to have clarity on SPC extensions sooner than the present 2 years. However, the fact that both sides of the industry experience some challenges, completing PIP 2 years before SPC expiry, as in the current legislation, seems to be a fair compromise between different needs.

3. Accumulation of rewards
The practice shows usage of both rewards (peadiatrics and orphan) for the same product which, we believe, was not the intention of the Regulators.
We are of the opinion that it should not be permissible to benefit from both rewards by using loopholes in the existing legal framework and this should be properly addressed.

Either the reward is an orphan exclusivity or an SPC extension.
See more comments under point 2.6 (orphan)

4. Recoup of clinical trial investments versus the benefit of a 6 month SPC extension for the entire product, including an adult form

With regard to the 6-month SPC extension for on-patent medicines, 6 months of paediatric extensions for originator products amount to a certain loss of savings for the EU healthcare systems. The question of whether the returns for originators are proportional or disposable remains to be assessed by the payers and health policy makers.
This issue has already been recognised by ECORIS in its Report to the Dutch Ministry of Health 2015 "How well does regulation work? The cases of paediatric medicines, orphan drugs and advanced therapies"[1]
"The main societal costs are related to the additional six month of SPC-protection, which delays the access of generic products and a price decrease. We estimate that the overall costs of protection are approximately € 18 million per year. A more detailed explanation for this estimation is provided in Annex A (under A4)"

The SPC extension for originator products amounts to millions of euros in annual sales for "mid – range" products and even more hundreds of millions of euros for "blockbusters", as is the case for Lipitor[2]. Pfizer's chewable, grape flavored form of Lipitor was granted a 6 month SPC extension, although there was no significant change in the recommended use of the medicine, which was already authorised for those aged 10 years old or over. Such a potential windfall in the case of blockbuster products could be seen as disproportionate for what is essentially compliance with new mandatory paediatric rules.
The risk might be that the SPC extension results in an increase of paediatric research in areas/ products that are financially attractive for originator companies, rather than focusing on areas of highest unmet medical needs for children.

The SPC paediatric extension is not granted according to a priority list of highest paediatric medical need as is the case for PUMA, which depends on the EMA's priority list, supporting studies into off-patent paediatric medicinal products.

Some examples of the economic impact and the loss of savings for some healthcare systems calculated by the UK, Belgian, and Dutch Generic Medicines Associations were already shared with the EC in the submission in 2012[3].

Examples of very profitable SPC extensions for blockbuster products shown against less profitable cases help to balance all paediatric development costs at the end. A 6-month SPC extension for an entire product (including adult presentations) seems to be a balanced reward and it should be seen as the maximum reward to be granted.

5. Some issues identified around the legal interpretation and application of the SPC extension - Combination products

[1] http://www.ecorys.nl/sites/default/files/NL%202310-30193%20EU-Regulations_Final_report_def-091115.pdf

[2] The 6 month SPC extension of Lipitor is worth 770 million Dollars, "Pfizer gets$800m boost for Lipitor" Financial Times, July 2011, http://www.ft.com/intl/cms/s/0/6892b926-aae3-11e0-b4d8-00144feabdc0.html#axzz2B5LiaEC1

[3] http://ec.europa.eu/health//sites/health/files/files/paediatrics/2013_pc_paediatrics/34-ega.pdf

We want to draw your attention to the fact that a SPC extension may be granted even when paediatric studies are not carried out. This is particularly applicable in case of mono/ combination products. The originator can benefit from a 6-month extension for a drug without any paediatric study being carried out. This is made possible due to the current SPC Regulation, not the Paediatric Regulation.
It is not our intention to insist on a requirement to perform another paediatric study in such a case as it would be unethical. However, we want to highlight the practical consequences of linking SPC rewards from the Paediatric Regulation with the SPC regulation itself.

- Zero or negative term SPCs
The issue of calculating the extension was raised in the case of the term of the SPC being nil or negative and whether the national industrial property office still has to grant an SPC if, with the paediatric extension of six months, the ultimate term would become positive. Also, what would be the basis on which the total term would have to be calculated? If calculated on the basis of article 13, paragraphs 1 and 2 of the SPC Regulation resulting in a negative term, would the six month extension of paragraph 3 then have to be added to this negative term, ultimately resulting in an extension of less than six months? or does one then have to take zero term as a starting point, as a consequence of which each paediatric SPC extension will have a fixed effective term of 6 months?

These questions have come up before various national industrial property offices in respect of Merck's application for an SPC for a product with the generic name sitagliptin phosphate monohydrate (Januvia®). Calculated on the basis of article 13, paragraphs 1 and 2 SPC Regulation, the term of supplementary protection would be negative (minus 3 months and 14 days). However, with the six month paediatric extension, the ultimate term would turn positive.

On 8 December 2011, the Court of Justice of the European Union ("CJ") delivered its decision on another SPC matter that has caused disharmony in Europe: the possibility of granting zero and/or negative term SPCs.
The CJ concluded that it is possible to obtain a negative or zero term SPC. It also ruled that a negative term SPC cannot be rounded up to zero and that a paediatric extension should commence on the date determined in accordance with the (negative) term calculated according to Article 13)1) (i.e. prior to patent expiry). In the present case the SPC has a protection period of minus three months and 14 days. With a paediatric extension, Merck can benefit from additional protection during the two months and 16 days following the expiry of the patent.

The CJ concluded that it is possible to obtain a negative or zero term SPC, although the intention of the legislator was different
"During the Third meeting of national Supplementary Protection Certificate (SPC) experts held on 26 September 2008 at EMEA (Record, page 14/18), the European Commission has expressed "*that no paediatric extension should be granted for zero or negative term SPCs", and – notably - that "[t]herefore, the Commission may not support any teleological approach aiming to justify the grant of paediatric extension when there was no SPC granted with a positive term.*"
http://www.olswang.com/media/48497023/record_of_the_third_meeting.pdf

Legal aspects of SPC paediatric extension has a clear economic impact on healthcare budgets and the launch of the first generic and biosimilar products.

To ensure a fairer legal process in Europe, Medicines for Europe would like to propose the following:

1) One SPC 6 month extension to be only awarded once for one SPC
It should be ensured that the incentive provided by the six month extension of the certificate should be awarded only to the market authorization holder and only once for one SPC. It has to be strictly excluded that certificates which are granted to third parties will receive the extensions too. Reference

by third parties to already performed studies should not be allowed. Making this incentive exclusive to the company who sponsors the pediatric studies and is responsible for compliance with the PIP is in full accordance with the compensation concept of the pediatric regulation provision.

2) To impede negative term SPC extensions
It would be recommended to remove the possibility of "negative term SPCs". The SPC regulation should govern whether or not an applicant is able to obtain SPC protection. This was set five years from the date of filing the patent application. By permitting the granting of negative term SPCs, the Court of Justice of the EU has now reduced this time frame to four years and 6 months from the filing of a patent before SPC protection becomes a possibility. If this is to be enabled, one can present a forceful argument that this should be possible only through amendment of the SPC regulation (e.g. by amending Article 13, Regulation 469/2009) and not by the provision of an additional incentive in a different legislative regime.

3) A more transparent system
The application for an extension of the duration of a SPC already granted shall be lodged not later than two years before the expiry of the certificate (since January 26, 2012), which improves the planning of a product launch. To aim for a more transparent system, a database with statistics on PIPs, indicating whether they were successful or not, should be made publicly available. Incomplete documents or missing data of PIP applications should not be tolerated. One example of incomplete documents for an authorised paediatric extension is the case of Du Pont. The company was granted a paediatric extension for Losartan which failed to meet all requirements for a complete file.

To conclude, to aim for a fairer legal process, we would like to ensure that one SPC of 6 months' extension is only awarded once for one SPC, the possibility of a negative term SPC extension is removed and a more transparent system with a database on PIPs, indicating whether successful or not, is made publicly available.

2.6. The orphan reward

Consultation item No 6: How do you judge the importance of the orphan reward compared to the SPC reward?

The practice shows use of both rewards (paediatrics and orphan) for the same product which, we believe, was not the intention of the Regulators.
As mentioned in the EC consultation paper, in several instances, companies waived the product's orphan status in order to make the product eligible for the SPC reward rather than the orphan reward, as the former is often considered to be economically more attractive (as it covers the entire product, including the adult one). There are cases where companies have already benefited from the exclusivity offered due to orphan status and withdrawn the orphan status just before the end of the 10 year reward to be able to get another reward of 6 months' SPC extension for an entire product. The issue of benefiting from both rewards is currently a subject of the court judgment[4].

We are of the opinion that it should not be permissible to benefit from both rewards by using loopholes in the existing legal framework and this should be appropriately addressed.
Either the reward of an orphan exclusivity or an SPC extension shall be granted. It has to be

[4] The decision of the Provisions Judge of the District Court of The Hague of 30 March 2016- The Hague Court confirms paediatric extension of SPC for former EU orphan drug imatinib

emphasized that the sponsor has additional possibilities for extending the monopoly and getting additional rewards. Since most paediatric dosing schemes or product forms are different to the existing product forms for adults, the sponsors frequently apply for patents claiming the use of the product in children. This normally will create a very long protection period for the paediatric indication.

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?

For Medicines for Europe it is difficult to comment, as this question is geared more towards originator development. However, we believe that participating in early dialogue with Authorities during the development phase should be beneficial in reducing the number of further modifications. This dialogue should be open to all companies, regardless of the type of products (on-patent or off-patent).

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?

The concept of waivers and class waivers looks good for us, although we do not have extensive experience with submission of PIP as generic and biosimilar medicines are exempt from paediatric studies (with a view to avoiding unethical and unnecessary exposure of children to clinical studies) .

2.9. Deferrals

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

Yes, we fully agree with the assessment under 2.9. Deferrals are needed but should not delay availability of the product for adults. On the other hand, paediatric use trials should not be delayed intentionally. Again, it is more difficult for Medicines for Europe to comment, as this question is geared more towards originator development.
The concept of deferrals is important and necessary, to only be able to start studies on children once they are safe and ethical.

2.10. Voluntary paediatric investigation plans

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

Voluntary paediatric investigation is acceptable, but should be considered in the context of our earlier response about needing to better identify high unmet needs for paediatric R&D vs unnecessary indications.

As is shown in some other cases outside the paediatric medicines framework, "copy-pasting" of the US system to the European regulatory and legal framework does not fit into the EU system and EU specificity.

However, it should not exclude the option to submit the PIP on a voluntary basis whenever it can support the developments of paediatric medicines (incl. off-patent medicines).

2.11. Biosimilars

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

The question on development of specific age-appropriate paediatric formulations was raised in the context of biosimilar medicines. The lack of a full range of formulations for biosimilars (particularly the lack of paediatric formulations) may lead to products entering the market without being adapted to paediatric use. This could potentially exclude children from benefitting from these products. At the same time, in the case of biosimilars, it is likely that the originator product will remain on the market despite direct competition from biosimilars. A product that is adapted for use in children will therefore remain available.

In view of biosimilar development and the whole concept of follow-on, off patent products (generic or biosimilar), the exemption shall be maintained as the relevant knowledge for using the active substance in children, such as the dosage information for the paediatric population, was already obtained through clinical research with the originator product (at least, for those products which were authorised after the Regulation entered into application). It is therefore not justified to repeat paediatric trials for these product categories (even less so as it would have to be done repetitively by every biosimilar applicant and thereby also question the feasibility) and going into the PIPs concept for biosimilars is not justified scientifically. To establish any formal obligations for biosimilar sponsors to investigate paediatric use in a routine way is against the regulation of the development of biosimilars and the widely accepted general concept of biosimilars.

In addition, the paediatric regulation is a system of obligations, rewards and incentives. However, for biosimilars the rewards and incentives would effectively not be possible as currently seen with the example of the PUMA where market exclusivity does not work (the SPC extension is not applicable for biosimilars). Likewise the concept would be difficult to implement in the case of biosimilars.

To conclude:

- Biosimilars (and generic, hybrid medicines) should continue to be exempt from the obligations of the Paediatric Regulation based on the justification that it is scientifically and ethically not justified to conduct or repeat paediatric studies with biosimilar medicines:

a) Based on the overall biosimilarity demonstrated between the biosimilar and the reference product, an approved biosimilar is allowed to refer to the safety and efficacy data established for the reference product. The same scientific principle should apply for the paediatric information from the reference product.

b) The Paediatric Regulation aims to ensure that medicines for use in children are made available without subjecting children to unnecessary trials or delaying the authorisation of medicines for use in

adults. The reference product was subject to, or likely has completed, a paediatric investigation plan and therefore relevant information is available on the use of the medicine for children. Moreover, a PIP may delay availability of the biosimilar product for use in adults due to additional development efforts.
c) The concept of extrapolation of indications used for an adult product shall also be fully applicable to paediatric indications and the alignment with the SmPC of the reference product should be possible based on the same principles as for adults.
d) Feasibility of paediatric studies with biosimilars is very limited as the reference medicinal product is available for the paediatric patient group, and parents would be hesitant to enroll their children. It is also very questionable ethically.

• Biosimilar developers may deviate from the reference product with regard to strength, pharmaceutical form, formulation, excipients or presentation - if justified (CHMP/437/04 Rev 1); this includes specific paediatric formulations and presentations and should be maintained:
e) There is no need to enforce the development of paediatric forms since this will likely be regulated by the market. If biosimilar developers choose to "drop" the development of paediatric forms, they will also not be eligible to claim the associated paediatric indication. In particular, in tender businesses, those biosimilar sponsors following the "carve-out" approach will face a competitive disadvantage since the restricted label may limit their ability to cover all patient groups and therefore the opportunity to supply an entire hospital/country etc.. In fact, the innovator company may even benefit, should biosimilar companies restrict themselves to adult indications.
f) Due to the competitive environment, it is likely that biosimilar developers will develop a product formulation suitable for paediatrics, however this is likely as a second step. A "step by step" approach starting with the development of the adult form first, and the development of the product formulation suitable for paediatrics as a second step should be acceptable; in particular since innovator companies usually follow a similar approach.
g) A formal request to develop and market all (paediatric) presentations at initial approval may delay the availability of the biosimilar.

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?

The fact that PUMA has been granted only few times shows that, despite expectations, the PUMA concept itself is not sufficient to promote the research in off patent paediatric indications. Considering the pricing pressure that the generic medicines industry is under, the investment in clinical trials for paediatric use is practically impossible in view of the high cost of the studies and the very low and unpredictable return on investment for new paediatric medicinal products. There is no clear willingness from the payers to recognize the value of "off-patent" paediatric medicines. Data exclusivity (even if very long for PUMA) is not an appropriate incentive as long as there is no commitment/ understanding from the payers to reward the investment in off- patent paediatric research (it could be called "paediatric bonus"). The newly developed PUMA paediatric medicines will enter automatically in the "generic price" category, already very low due to prices established on "adult" products that have already been on the market for some time. This makes investment in paediatric clinical trials not economically viable.

In addition, due to the risk of off-label use as the product is off-patent and other generics already in the market, the PUMA concept is even less attractive.

Reimbursement rules may not evaluate PUMA in a satisfactory manner and may attach little value to medicines with "old"/ off-patent active substances, giving them a low reimbursement price or no reimbursement, even if they include a new age-appropriate formulation. National authorities could consider encouraging the development and use of new paediatric medicines in the off patent sector through therapeutic guidelines and adaptation of reimbursement rules.

The fundamental difference between performing paediatric studies for off-patent and on- patent medicines is related to the decision making process, including access to financial support. To get EU financial support for paediatric clinical trials on off-patent medicine, the company must respond to the real unmet paediatric needs as published by the EMA in its priority list.
In the case where products are still under patent, investment in some paediatric studies and the choice of paediatric indication to benefit from 6 months SPC extension differ significantly from off-patent cases.

The off-patent medicines for the paediatric population have to be further supported and strengthened not only by the PUMA but also by therapeutic guidelines and adaptation of reimbursement rules at national level. With regard to the ongoing discussion on HTA at EU-level, the difficulties of market access for PUMA, mentioned above, could be a part of the dialogue with national authorities (with a view to opening P&R negotiations for the product that also provides PUMA)

What is the advantage of maintaining it? Could the development of off-patent medicines for paediatric use be further stimulated?
Perhaps the problem of off-label use should be first solved at the medical community level. The associations of paediatrics or other organisations (e.g. European Paediatric Association or European Academy of Paediatrics) may also contribute to proper testing of paediatric use in children (due to sponsored research programmes) and to publish guidelines afterwards (then to be followed by Marketing Authorization Holders by amending the SmPC). There are some examples already (ASCO guidelines for the treatment of cancer patients).

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?

Without incentives collaborative research in therapeutic areas between competing companies is likely to be difficult if not impossible to achieve. In specific disease areas, where there are lots of competing trials and some may not be necessary perhaps, there is more the Agency could do via transparency or providing information on what specific gaps need to be filled in therapeutic areas to avoid duplication of similar trials (e.g. similar to the list of therapeutic needs). Maybe there is a need to consider more options for class waivers in busy therapeutic areas where significant information has already been obtained, or by using extrapolation based approaches to avoid unnecessary trials.

The trials just must be "relevant" to address a well-defined need in the "subpopulation" children.

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?

We understand that the work done by the competent authorities supporting the developments of

paediatric medicines need to be remunerated. We assume that the current financing of the authorities' contribution is covered by the budget of each authority and constitutes a part of total costs. Somehow fees collected through other regulatory procedures cover this "paediatric gap".
The problem may appear at the time when the authorities calculate their fees (and the total income) based on allocation of time/resources per types of activities.

For societal benefit and for stimulation of research in paediatric indications, we would support fee exemption (especially when the company might not benefit from any reward for paediatric development). However, we also encourage the authorities to put in place some measures leading to optimisation of their internal processes by saving resources from administrative activities and reallocating to activities more beneficial from a societal/ public health perspective (i.e. paediatrics).

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?

We do not comment as we do not have a good overview of the effects on paediatric research. From an external perspective, the Regulation should have a strong impact and it should substantially promote paediatric research.

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?

We want to highlight another aspect of paediatric development and the tools available to be rewarded for a paediatric research. There is a trend of paediatric use being more and more protected by so called "use patent" claims. The expiry of these patents exceed the expiry of the SPC extension and the Orphan designation exclusivity, which then become less important.

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?

To conclude, the existing legislation is favorable for paediatric use of medicines. However it is important, that this legislation should by no means comprise generics and biosimilars.

- With regard to using both rewards (paediatrics and orphan) for the same product, we are of the opinion that it should not be permissible to benefit from both rewards by using loopholes in the existing legal framework and this should be properly addressed.
- "SPCs with a negative term" should not be granted
- Regarding biosimilar development and the whole concept of follow-on, off patent products

(generic or biosimilar), the exemption shall be maintained as the relevant knowledge for using the active substance in children, such as dosage information for the paediatric population, has already been obtained through clinical research with the originator product

- Data exclusivity (even if very long for PUMA) is not an appropriate incentive as long as there is no commitment/ understanding from the payers to reward the investment in off- patent paediatric research (it could be called “paediatric bonus”).