EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Health systems, medical products and innovation
Medicines: policy, authorisation and monitoring

PAED 003

PAEDIATRICS – Meeting with Member States and the European Medicines Agency

19 September 2016

RECORD

On 19 September 2016 a paediatric expert group meeting took place in Brussels, chaired by Unit B5 - *Medicines: policy, authorisation and monitoring* of Directorate General Health and Food Safety. Representatives from 22 Member States and the European Medicines Agency and its Paediatric Committee participated at the meeting.

1. ADOPTION OF THE AGENDA

The agenda (PAED 001) was adopted without changes.

2. SETTING THE SCENE – THE PAEDIATRIC REPORT

Under the terms of the Paediatric Regulation, the Commission has to present in 2017 a second report to the European Parliament and the Council regarding the experience acquired with the Regulation (Article 50(3) of Regulation (EC) No 1901/2006).

The Commission services outlined the context of this 2nd report, which is currently being prepared, as well as its context. Following a progress report published by the Commission in 2013, this second report will provide a more in-depth analysis of the experience with the Regulation, both with regard to public health goals and with regard to the economic rewards provided.

The report will be informed by several projects and data sources, currently assembled by the Commission with the support of external bodies and partners. This includes data collected by the European Medicines Agency (EMA) together with its Paediatric Committee (PDCO) regarding the key health related outputs. Additionally, a study has been commissioned analysing the economic impact of the Regulation.

While the report is a legal obligation, which follows directly from the Regulation, it also has to be seen in the context of the recent conclusion of the Council on strengthening the balance in the EU pharmaceutical systems, as well as in the context of the planned evaluation of the EU system on supplementary protection certificates.

The Chair noted that the purpose of the expert meeting is the following:

- To update on the state of play of preparatory work for the 2nd report;
- To debrief Member States on preliminary results from the EMA data gathering and the economic study;
- To exchange views with Member States regarding their experience with the Regulation;
- To inform about next steps including the public consultation.

3. THE ECONOMIC IMPACT OF THE PAEDIATRIC REGULATION

The contractor selected by the Commission for the economic study presented preliminary results from the study, including on regulatory costs, the rewards and incentives provided by the regulation and on direct and indirect benefits. The contractor also outlined the data sources used, which consisted of a detailed literature research, surveys with industry, databases and a Delphi expert panel. Additionally, challenges were highlighted as some of the study questions were exploratory and the ability to build on previous research was limited.

The contractor is confident that once completed, the study will provide thought-provoking insights in the economic impact of the regulation.

The subsequent discussion allowed delegations present at the meeting to request clarifications and to comment on results. The following points were covered: the costs of paediatric trials compared to other trials, the costs of trials of a paediatric-only development compared to a development that builds on an adult product, the contribution of (academic) networks and the funding provided through public bodies, which may alleviate trial costs of commercial undertakings.

Delegations were additionally interested whether the contractor analysed specifically the PUMA (paediatric use marketing authorisation) reward and the results he had obtained.

4. EXPERIENCE WITH THE PAEDIATRIC REGULATION FROM A PUBLIC HEALTH PERSPECTIVE

Together with the Paediatric Committee, the EMA had analysed public health related output benchmarks of the Regulation. For the purpose of the meeting, EMA representatives summarised the data collected. This included output figures with regard to agreed and completed paediatric investigation plans, as well as a quantitative and qualitative analysis of new authorised medicines/indications for children over the last ten years. Additionally, data on other aspects were provided, such as clinical trials, impact on (academic) research networks and high-quality research in general. The information was complemented with some reflections on lessons learnt.

The subsequent discussion focussed on the lessons learnt. Many delegations highlighted the positive impact of the Regulation, but also mentioned that due to the specific mechanisms of the legislation, many paediatric research projects are rather driven by adult developments than by paediatric needs. By way of example, reference was made to the many pending type II diabetes paediatric investigation plans (PIPs), which result from a wave of new adult medicines that are currently developed for this disease. While the

disease also exists in children, the current disease burden for children in Europe is still rather low and would not require massive research investment in this area. The PDCO chair and EMA reported that efforts have been made to convince stakeholders to engage in collaborative paediatric research for type-II diabetes to reduce the number of necessary trials, but experience shows that companies are hesitant to answer those calls, as they seem not used to collaborative projects for new developments, which may reach blockbuster status in adults.

Additionally, some delegations considered that more efforts are needed in areas where there is a specific need, especially in paediatric-only diseases (e.g. paediatric oncology). It was observed that most companies would focus on complying with the obligations set by the Regulation and would refrain from additional voluntary research, if that is not mandated. It may therefore appropriate to consider restricting the scope of the waivers (derogations) provided by the Regulation.

Other points of discussion related to the timing of the PIP discussion and the experience with deferrals and with the PUMA reward for off-patent medicines. There was general agreement that the number of three authorised PUMAs after ten years is disappointing.

With regard to the prevalence of off-label use in the paediatric population and the impact of the Regulation to reduce those uses, some delegations pointed out that for neonates off-label use is still rather common. The same would be true for old, established compounds, for which additional paediatric research is often not commercially attractive. Some experts took the view that off-label use should not be perceived as negative, when significant clinical experience exists with some old, commonly used medicines, which might be the only available treatment alternative. However, there is a need to replace off-label use by authorised medicines in order to improve children's health outcomes. In this context, it was also mentioned that recruitment for paediatric studies becomes more difficult, once a product is approved for adults and it is widely used off-label, as in such situation parents often fail to see the added-value of agreeing that their child participates in clinical research.

5. OPEN FLOOR – EXCHANGE OF VIEWS WITH MEMBER STATES REGARDING THEIR EXPERIENCE

During this session, delegates reported their experience with the Regulation from a national perspective. Specific consideration was given to the following topics: availability, clinical trials with children, impact on national resources and future pressure points.

With regard to availability, some delegations reported that new paediatric medicines may not be immediately available in their country and that pricing could be a problem. Moreover, it was stressed that the current exemption of 'biosimilars' from the paediatric obligations could pose problems, as it may lead to those products entering the market without the paediatric formulations or dosage forms. In view of the upswing of the biosimilar market in recent years, this could potentially exclude children from benefitting directly from this category of medicines.

As far as paediatric clinical research is concerned, it was highlighted that the Regulation led to a considerable increase in clinical trials. Some Member States used the entry into force of the Regulation as an opportunity to establish or upgrade national research networks. However, some delegations pointed out that paediatric trials need the full support from clinicians and hospitals, which are sometimes put off by 'bureaucratic' procedures. Several experts referred to the beneficial factor of including networks in the running of clinical trials and the useful impact of the Enpr-EMA network, but also

stressed the need to continue to financially support basic research. The Commission services stressed that additional efforts are considered and that a public-private partnership to create a trans-European paediatric network under IMI ('Innovative Medicines Initiative') is about to be launched later this year.

The complementary benefit of academic trials was also mentioned, as well as the benefit of involving academic networks and children early in the design of a trial to improve its quality and feasibility or regarding the appropriate wording of information that is passed on to children.

Some experts also suggested that there is a need for improving the collection of data about the off-label use (of older compounds) with a view to consider to what extent such data could be harvested for the purpose of additional paediatric indications. Reference was made to some national schemes in which public money/grants were used to support such research or which are aimed at ensuring that off-label use is transformed into an authorised use. It was also mentioned that there may be need for additional training to inform healthcare professionals about new paediatric medicines and risk of off-label use/misuse in hospitals and ambulant care settings.

As far as recruitment difficulties are concerned, it was recognised that paediatric trials are typically more challenging than adult trials. Again, the beneficial factor of networks and the early involvement of patients in the design of a trial were mentioned, as they could help to address those challenges.

Concerning the impact of the Regulation on national resources, it was stressed that the legislation presupposes an important investment (of resources) by Member States, e.g. through appointing members to the Paediatric Committee and by contributing to the assessment of paediatric investigation plans.

As the assessment of those plans does not attract any fee, national experts are not reimbursed by the European Medicines Agency for performing these activities. The proper functioning of the mechanism is therefore not only relying on EMA resources, it is also relying on national in-kind contributions.

Many delegates highlighted the difficulty for national competent authorities following from the no-fee model. Some agencies pay external assessors for the PIP evaluation and this has to be financed through the general budget of an agency. Moreover, some competent authorities report that in the wake of budgetary constraints they are increasingly faced with difficulties to maintain staff levels with regard to paediatric expertise. In the long term this could have an impact on the sustainability of the system.

Finally, with regard to potential pressure points, delegates mentioned the long duration of paediatric trials, long deferrals or the discontinuation of PIPs, as well as the need to better reflect paediatric needs, e.g. through focussing on the mechanism of action of a compound instead of the adult condition as a starting point for discussing the paediatric development programme. Some delegates also mentioned the need to better support voluntary research, especially in areas where a specific disease/condition exists in children only.

6. PREVIEW OF THE PUBLIC CONSULTATION

The Commission services explained the purpose and timing of the public consultation. Such consultations are an essential element of the Commission's working methods and aim at making the EU more transparent and accountable, but also more effective, as those affected by laws understand best the impact those rules have, and can provide the evidence need.

In this case the consultation aims at receiving additional input on the experience with the Regulation especially from patients, academia and industry.

The consultation is planned to start in November 2016 and should last 3 months. The feedback received will be published and will feed into the final report.

7. NEXT STEPS

The Commission services were grateful for the input and comments received during the meeting. It is intended to inform the Pharmaceutical Committee at its next meeting in October about the results of this meeting.

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