PCPD/12/01 — Public Consultation on Paediatric Report

Experience acquired/lessons learnt

Response from the Swedish Medical Products Agency (MPA)

1. A CHANGE OF CULTURE: NOWADAYS PAEDIATRIC DEVELOPMENT IS AN INTEGRAL PART OF PRODUCT DEVELOPMENT

MPA Comment:

In Sweden, medicines for children have been highlighted in a new national strategy for use of medicines outlined by the Swedish Government (2011). As a result, MPA has received a government commission to "improve the knowledge of paediatric medicines and their utilization" which means working in close collaboration with health care professionals across paediatrics. So far, a number of areas within paediatric medicine and paediatric psychiatry have been highlighted and are currently being subject to inventories, in-depth studies, educational activities, development of therapeutic guidelines etc. Some examples of such paediatric areas that the MPA is currently working with are: antibiotics in neonatal sepsis, procedural pain in children, sleep medicines to children and adolescents, use of neuroleptic medicines in paediatrics, maternal medicines during breastfeeding, medicines used in paediatric anaesthesia and intensive care etc.

2. HAS THE REGULATION DELIVERED IN TERMS OF OUTPUT? TOO EARLY TO JUDGE.

MPA Comment:

Yes, it is too early to judge as development of medicines takes very long. It could be added that, although few new medicines have yet been authorized with paediatric indications, there has been a massive work dedicated to producing and/or updating a number of regulatory and scientific guidelines to provide assistance to pharmaceutical companies as well as to assessing competent authorities in the development and review process of medicines for children.

3. THE PUMA CONCEPT: A DISAPPOINTMENT

MPA Comment:

There is a great need for more paediatric medicines, including medicines with a paediatric indication and appropriate paediatric formulations and forms for all the medicines that are currently used off-label in children through extemporaneous preparations of inadequate quality.

One reason for the disappointing results with regard to the PUMA concept may be that the Regulation still requires quite extensive development, for example in all relevant paediatric age groups. For example, a pharmaceutical company would like to develop a medicinal product with a special child friendly formulation that might suit children from 2 – 6 years of age, but be less suitable for younger children and not relevant to older. If this medicine also may be used by younger and older children, according to the Regulation, the medicine also has to be developed to suit those age groups. This could be perceived by the company as too heavy a commitment in relation to the potential profit and as the PUMA concept is voluntary, the company decision may well be not to develop at all, and, hence, a much wanted paediatric formulation for 2-6 year olds is not developed.

Pharmaceutical companies do not seem to be willing to invest in PUMAs, where substitution with generic adult pharmaceutical forms is the rule, and where this type of innovation is not rewarded by payers. In addition, academic health care may not be willing to invest in research on old medicines because they are probably convinced that most of the current off label use relies on sufficient data.

The PUMA might become more effective if requirements were less extensive (which may have to also reflect the reward).

4. WAITING QUEUES? NO EVIDENCE OF DELAYS IN ADULT APPLICATIONS

MPA Comment:

We have had little indication that the Regulation has caused delays in applications. There have been occasional cases where the company has submitted a PIP very late and incorrectly assumed that a waiver would be accepted, but the situation has been solved.

5. MISSING THE POINT? PAEDIATRIC DEVELOPMENT IS DEPENDENT ON ADULT DEVELOPMENT, NOT PAEDIATRIC NEEDS

MPA Comment:

Although it is true that paediatric development is dependent on pharmaceutical companies wishing to develop for the adult population where there is a potentially profitable market, the Regulation has made it possible for the Paediatric Committee to encourage companies in directions where there are specific paediatric unmet needs. The Paediatric Committee, by using the known or presumed mechanism of action of a drug intended for a specific adult condition, may propose to match the drug with a specific paediatric condition where there is an unmet need. Whether this will result in further paediatric development remains to be demonstrated.

6. THE BURDEN/REWARD RATIO —A BALANCED APPROACH?

MPA Comment:

This will have to be evaluated at a later point. We have nothing to add.

7. ARTICLES 45/46: THE HIDDEN GEM OF THE PAEDIATRIC REGULATION

MPA Comment:

Articles 45/46 have placed a very heavy work load on competent authorities and, to establish whether this work has been worth the effort and proved an effective tool to increase the knowledge on paediatric drug use as well as efficacy and safety of paediatric drugs in terms of added text into the SmPC, a further evaluation involving all the work-sharing competent authorities is needed.

Whether competent authorities have been able to assess old paediatric studies, which often do not meet modern requirements for scientific data, in the context of well established use of the medicine in question, is another issue. If a medicine has been used in the paediatric population for 30 – 40 years without a paediatric mention in the SmPC, the submitted old studies should, together with the well established use, support updating of the SmPC with paediatric information. This issue should be discussed among the work-sharing competent authorities.

8. **LOST IN INFORMATION: HEALTHCARE PROFESSIONALS NOT AS RECEPTIVE AS EXPECTED**

MPA Comment:

Healthcare professionals may not always be as receptive to new scientific information on the use of particular products in children as might be expected. Moreover, they are probably convinced that most of the current off label use relies on sufficient data.

This problem has to be addressed primarily at national level. For this reason, special efforts are being made in Sweden (see q1) in order to further involve healthcare professionals in improving utilization of medicines in all areas of paediatric medicine.

9. CLINICAL TRIALS WITH CHILDREN: NO SPECIFIC PROBLEMS DETECTED

MPA Comment:

Nothing to add.

10. UNNECESSARY EFFORTS? NON-COMPLETED PAEDIATRIC INVESTIGATION PLANS

MPA Comment:

Ideally, a PIP that is submitted early (end of phase 1) should have few key binding elements (as important parts of the development cannot be appropriately identified at an early stage) but the company should be requested to resubmit the PIP for a modification at each phase of development. Whether this situation is being achieved in the work with PIPs is not entirely clear. It is our impression that the PDCO is working with this as an aim.

11. SOPHISTICATED FRAMEWORK OF EXPERTISE ACHIEVED

MPA Comment:

It is our opinion that the Paediatric Regulation is contributing to the establishment of a comprehensive framework of paediatric expertise in the European Union, mainly through the work of expert delegates and EMA staff of the paediatric committee as spin-off effects of their work with paediatric investigation plans for new medicines, guidelines and inventories of unmet needs etc and through Enpr-EMA.

12. ANY OTHER ISSUE?

MPA Comment:

One remaining concern is that those responsible for development (pharmaceutical companies) and critical assessment (competent authorities) of paediatric medicines and the pricing bodies do not communicate. This could potentially lead to a situation where the health care professionals, who may be convinced that most of the current off label use relies on sufficient data, choose to continue to utilize inexpensive off label medicines for children instead of selecting those medicines that are especially developed for the paediatric population and, therefore, probably more expensive. This is an important national issue, as more and more specific paediatric medicines become available. The MPA has no legal influence on the issue but could flag such issues as efficacy, safety and age appropriate formulations of drugs used by the paediatric population.