GENERAL REPORT
ON EXPERIENCE ACQUIRED AS A RESULT OF THE APPLICATION OF THE PAEDIATRIC REGULATION
(ARTICLE 50(2) OF REGULATION (EC) NO 1901/2006)

'EXPERIENCE ACQUIRED' AND 'LESSONS LEARNT' SUBMITTED FOR PUBLIC CONSULTATION

Deadline for Public Consultation: 28 November 2012

Consultation item No 1: Do you agree that the Paediatric Regulation has paved the way for paediatric development, making it an integral part of the overall product development of medicines in the European Union?

As the Paediatric Regulation has rendered it compulsory for all companies to submit a PIP, then yes the regulation has paved the way for paediatric development.

However, some pharma companies are still reluctant to develop PIPs for paediatric indications and therefore maybe do not explore the paediatric possibilities of their products far enough.

While the Paediatric Regulation has led to a certain amount of new authorisations that include paediatric indications, the regulatory instrument is recent and the data does not provide a sufficient basis for a comprehensive review. It will probably take at least a decade before the regulation can be judged in terms of its output. That said, it will always be a challenge to establish appropriate benchmarks for comparing off-label use with and without the Paediatric Regulation.

Consultation item No 2: Do you agree with the above assessment?

The PDCO has certainly worked very hard since 2008, having approved nearly 500 PIPs and evaluated many more.

In terms of success with respect to comparing off-label use with and without the Regulation, our associations concerned with paediatric indications have stated that there are still too many children being treated off-label. From treatment to palliative measures, children are still receiving off-label products.

It is important to find a way of measuring the impact of the Paediatric Regulation on this specific aspect.

In terms of output, the PUMA concept is a disappointment.
Consultation item No 3: Do you share this view? Could you give specific reasons for the disappointing uptake of the PUMA concept? Is it likely that PUMA will become more attractive in the coming years?

The lack of response to the PUMA opportunity may be linked primarily to a lack of awareness. It is mentioned that neither industry nor academic networks have taken full advantage of the PUMA to carry out research in off-patent products authorised for adults, however we know from experience that academic networks have little need to understand the regulatory processes and some industry partners, primarily smaller companies do not have the staff support to be familiar with all regulatory aspects either.

Promotion of the PUMA would be needed along with emphasis of the importance of providing information on the galenic form and how this is processed in children compared with adults. It will be very important to emphasise the need for Pharmacovigilance results.

Consultation item No 4: Do you agree that, generally speaking, the paediatric obligations have no impact on timelines in adult development, as there is no evidence for delays in marketing authorisation applications for reasons of compliance with the paediatric obligation? If you feel that there is an impact, practical examples would be appreciated.

We personally have no experience as we are not directly involved in development of products however our contact with Industry has painted a different picture with respect to this consultation item. We are certain that industry members will reply more fully to this point.

It is not the purpose of the Paediatric Regulation to replace an established system of medicinal product development by a new regulatory system. It aims to ensure that every innovation and every new product is screened for its potential use in children so that over time there will be a significant increase in the number of products for which specific paediatric data is available.

Consultation item No 5: Do you have any comments on the above?

While certainly not replacing the established system, it can be agreed that the obligation certainly adds a burden on pharmaceutical companies.

Paediatric patients' associations are concerned by the fact that products tested in adults are then applied to children's indications (which is the concern addressed by the Regulation), however they call for more sharing of available information that is published but not necessarily accessible to patients' groups or certain healthcare professionals. A mechanism

needs to be put in place to ensure such sharing of information occurs in practise and not only theory.

There is potentially too long a delay between end of Phase I trials in adults and the start of Phase II in children.

Consultation item No 6: Do you agree with the above?

Once again the issue of the burden is addressed, demonstrating an awareness of the additional time and work required to fulfil the obligations of the PIP. There are incentives (such as with the Orphan Regulation).

One additional concern that has been brought to our attention has been the disconnect between the scientific advice provided by the PDCO and that provided by the working party of the CHMP – the Scientific Advice Working Party. In the case of the latter, the scientific advice is non-binding however in the case of scientific advice added to a PIP, it becomes a requirement to fulfil for PIP approval.

The essence of the problem arises when there is conflicting advice from PDCO and SAWP.

This will hopefully be addressed in part by the EMA Executive Director's initiative of regular meetings with all Chairs of EMA scientific committees however this still needs to be addressed at the Committee level too.

Consultation item No 7: Do you agree that Articles 45/46 have proved to be an efficient and successful tool for gathering and compiling existing paediatric data and making it available to the competent authorities and subsequently, via databases, to the interested public?

It may very well be the case the Articles 45/46 have successfully gathered information on paediatric however the relevant stakeholders that would benefit most from this information need to be aware of it and have access to it. The stakeholders include the carers, parents and treating physicians as these are the people who have the most contact with the patient and in the case of healthcare professionals, they are those who make the decisions regarding the treatment regimen. Easy access to this information in a language that can be understood is also needed.

Consultation item No 8: Do you agree that healthcare professionals may not always be as receptive to new scientific information on the use of particular products in children as might be expected? Do you agree that this problem has to be addressed primarily at national level? How could healthcare professionals be more interested and engage in paediatric clinical research?

The problem could stem from the lack of information or awareness of the existence of this information. Healthcare professionals certainly have an obligation to inform themselves of the most up to date information relating to medicinal products and treatments, however in the case of paediatric diseases and rare diseases, the professional may only come across one or two cases (if that) in their professional career.

While the general impression from our members is that healthcare professionals are eager to learn they are still prescribing medicinal products off-label without necessarily even being aware that it is off-label.

Clear, simple and easily accessible information coming from the PDCO or EMA PDCO secretariat regarding scientific information would help to address this issue. This could be made available on the website but also needs wider dissemination, perhaps through the learned societies etc. It must be brought to their attention more closely to attract their interest and engagement

Consultation item No 9: Do you have any comments on developments in clinical trials with children following the adoption of the Regulation and in view of the above description?

Our paediatric patients' associations have responded that they would like to see greater collaboration between academics and industry in the organisation of paediatric clinical trials. Better organisation in general is requested in order not to duplicate trials. There is also a request to accept the data on trials that has been accepted by other national medicines agencies, such as EMA, FDA, Japan, etc..

For every successful authorised medicinal product there are many that fail to make the finishing line. In terms of output, this leads to some unnecessary efforts involving the compilation and screening of paediatric investigation plans. On the other hand, early submission of and agreement to the paediatric investigation programme is necessary for the paediatric development to fit smoothly into the overall product development.

Consultation item No 10: Do you have any comments on this point?

While it is certainly true that the Paediatric Regulation obliges an additional 'burden' to development of medicines, given that many medicines fail in early phase. The existence of a

regulation that is designed to protect children and ensure high-quality research is clearly welcome.

Paediatric studies should not be conducted thoughtlessly and without proper planning and consultation. The role of the experts at PDCO is to provide that advice in order for the approach to become more common and accepted and that with time it is no longer considered a burden.

Consultation item No 11: Do you agree that the Paediatric Regulation has contributed substantially to the establishment of a comprehensive framework of paediatric expertise in the European Union?

The creation of the PDCO, which includes patients' representatives and health care professionals in addition to regulatory experts from the various member states, is one such example of paediatric expertise.

The creation of the Enpr-EMA is another example of a comprehensive framework of paediatric expertise in the EU and a positive development, allowing paediatric groups to share knowledge, challenges and best practice in order to identify common solutions across several paediatric diseases..

Consultation item No 12: Overall, does the implementation of the Regulation reflect your initial understanding/expectations of this piece of legislation? If not, please precise your views. Are there any obvious gaps with an impact on paediatric public health needs?

Overall the Paediatric Regulation has been a very welcome and necessary advance in the path to address the important issue of medicines for children and in particular the overwhelming use of products off-label.

The PIP is considered to be long, complicated and represents a regulatory burden and industry is still reluctant to develop PIPs due to these facts.

As is frequently the case, more communication and consultation with the right (and all) stakeholder groups is important. We have recently learnt of endeavours by the PDCO to communicate more and this is applauded.

Patients, parents and carers look for information on medicines and frequently find non-validated information. The PDCO/EMA could play a better role in provide simple, clear and accessible information to all concerned stakeholders.