



How will EU Paediatric Legislation stimulate Paediatric Research?

Narrowing the Gap between the Perspectives of Public Health, Paediatric Research and Pharmaceutical Products

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On 20 October 2005, the European Forum of Good Clinical Practice (EFGCP) held a one-day workshop in Brussels to elaborate ways to stimulate paediatric research in Europe in light of the ongoing legislative debate on the proposed EU Paediatric Regulation. With the active participation of high-profile representatives (regulators, industry, clinicians, patients and academia), a highly constructive debate took place which resulted in a number of conclusions on effective research programmes and communication strategies.

As far as paediatric medicines are concerned, Europe has arrived at a crossroads: Although the proposed EU Paediatrics legislation is well on the way to legislative adoption (foreseen for mid-2006), participants agreed that its success will largely depend on its capability to “**serve children and make medicines more efficacious and safe for them**”, as Prof. Hannsjörg W. Seyberth, Zentrum für Kinder-

und Jugendmedizin der Philipps Universität Marburg, Germany pointed out. In certain disease areas, such as infectious diseases, rheumatology, cardiac diseases, diabetes and asthma, the development of special paediatric medicines is particularly important and specific clinical trials in children are needed and regulators need to demand specific paediatric studies in these therapy areas. Here, the **off-label use of medicines**, — i.e. their prescription for other than the intended indications—is particularly prominent and potentially dangerous, as **proper treatment and control cannot be ensured**.

One of the workshop’s central conclusions was that although the funding provisions (e.g. MICE¹) foreseen in the draft regulation will surely serve to stimulate paediatric research, **networking and concerted actions of all the different parties** involved will be needed to ensure the sustainable

development of better medicines for children in Europe.

Several speakers underlined that a simple, but often neglected observation should act as guideline for further actions: **children are not small adults. Their medical treatment needs differ from those of adults.** This has to be taken into account by doctors when defining choice of medication, dosage and intake mode. Whereas the treatment of adults can rely on a amount of data resulting from clinical trials relating to safety, efficacy and responder rate, paediatric data in Europe is available to a far lesser extent.

Medicines Investigation for the Children of Europe (MICE). MICE should be seen as additional tool for promoting high quality, ethical research leading to the development and authorisation of medicines for children through the provision of funding for studies, including clinical trials, into the paediatric use of medicines not covered by a patent or supplementary protection certificate.



Clinical trials for paediatric medicines require a remarkably **different set-up** from clinical trials for 'adult' drugs. The number of participants will be smaller; the formulation of the drug has a much larger role to play and should be adapted to children's needs. Special attention has to be given not only to the patients themselves, but also to their parents. Their needs have to be met, so they are put in a position to make an **informed and free choice** about their treatment. This includes the need for parents to have access to information on the treatment options available from all relevant sources, including the pharmaceutical industry.

In this context, it is vital that **joint efforts are made to facilitate the performance of clinical trials**: i.e. procedures should be coordinated or harmonized, new methodologies will have to be developed to ensure the least burden and risk from medicines actually making the condition worse in the child or causing other adverse events.

All bodies—from Regulators to the public—needs to be convinced of the immediate need and future possibilities when generating paediatric data. In this context, appropriate teaching and training programmes for the different groups involved (regulators, researchers, nurses,

etc) have to be established. Child-specific ethical standards should be set jointly, resulting, for example, in the redesign of informed consent forms in a way which is suitable for children.

Industry, clinicians and academia will have to cooperate on this through **public-private partnerships**. The authorities should support these efforts through the establishment of a European register for paediatric trials.

It is important to note that Europe will not have to start from scratch in these efforts. **Networks and centres of excellence** exist at both national (e.g. Paed-Net: Germany, BPDN: Belgium, RIPS: France) and EU (e.g. 7th Framework Programme/ Teddy, Medichildren) levels. The European Medicines Agency (EMA) will have a key role to play in **their integration and supervision to avoid duplication of research** and unnecessary tests on children.

Patient safety is key. Therefore it is important not only to encourage a paediatric-specific authorisation of drugs, but also to closely monitor possible side-effects of authorised drugs. The EMA is aware of this and has consequently launched a public consultation to develop **guidelines for pharmacovigilance of medicines used in children**. Comments of all parties are highly recommended in this context.

Clearly, industry has a crucial part to play in the development

of better medicines for children. Therefore, the **competitiveness of the pharmaceutical industry needs to be ensured through adequate incentives**, when promoting Europe as the most attractive place for pharmaceutical R&D with a view to enhancing access to paediatric medicines.

The proposed EU regulation on medicines for children has been largely welcomed by all stakeholders concerned. To ensure its success after its entry into force in late 2006, in a way which can directly be measured in terms of improved children's health, it is important that these stakeholders already begin to work together on the development of effective research programmes and communication strategies. This workshop has laid the groundwork for the definition of some of the prerequisites for collaboration.

In September 2004, the European Commission published a proposal for a regulation aimed at promoting medicines for children. The need for such a proposal results from the fact that more than 50% of medicines used by children are not tested or authorised and may consequently lead to ineffective or even harmful treatment. Market forces are insufficient to remedy this situation, as the market is small and studies in children judged to be too complex.

The proposal therefore seeks to improve children's health in the EU by

- increasing high quality research into paediatric medicines;
- promoting their development and authorisation, without delaying the authorisation of medicines for adults and duplicating studies unnecessarily;
- improving the information on paediatric medicines.