

The Regulation of Paediatric Medicines in the EU

The EU has been provided with a Regulation that promotes and regulates paediatric medicines.

Its gestation and negotiation in the inter-institutional legal triangle are an exact reflection of the glories and miseries of European construction. It is frequently said that EU legislation is made behind the backs of its citizens and imposed by the bureaucrats of Brussels. This cliché is as false as it is common, as confirmed by the negotiations of the Regulation on Paediatric Medicines.

The initiation of the preparation of the Regulation was made in response to the widespread demand of the scientific community, the health authorities and even of public opinion. The reasons why medicinal products need to be studied in children are clear: more than 50% of the medicines used to treat the children of Europe have not been tested; the paediatric population is a vulnerable group with developmental, physiological and psychological differences from adults; there are differences in pharmacokinetics and dynamics; growth and maturation processes affect them. And there is a general lack of information and appropriate pharmaceutical formulations. To overcome this lack, clinical trials have to be carried out on children, which, in turn, create serious scientific, legal and ethical problems. Specific protection should be defined for research performed on children, at all stages and ages. In order to address the concerns about trials in children, the EU Directive on clinical trials lays down specific requirements to protect children who take part in clinical trials in the EU. The Commission is developing guidelines to implement this Directive.

Once more, the European Medicines Agency (EMA), in its function as the scientific organ of assessment and evaluation of medicinal products, prepared the scientific and technical foundations for the proposed legislation.

In 1997, the EMA organised a round table of experts to discuss paediatric medicines. In 1998, the Commission supported the need for international discussion on the performance of clinical trials in children. An ICH guideline was therefore agreed, which has been in force since July 2002. This international agreement has been very important and has reaffirmed the need for and the possibility of advancing toward a global legal statute for medicinal products.

On 29 September 2004, the EU Commission released the first proposal for a Regulation on Medicinal Products for Paediatric Use. The Council of Health Ministers reached political agreement on 9 December 2005, and the European Parliament agreed it in a second reading on 1 June 2006. Thus it is difficult to understand why its publication was so delayed, it being such a sensitive subject from the social and health point of view.

It must be remembered that the European Regulation has followed the US initiative of 1977 and its consolidation in the *Paediatric Research Equity Act of 2003*. As a consequence of the US initiatives the response has been extremely positive.

Key measure included in the EU Regulation is the creation of the Paediatric Committee, within the European Medicines Agency whose principal task is to agree a Paediatric Investigational Plan (PIP) which results must be submitted at the time of the Marketing Authorisation (MA) application of new products as well as of authorised products where new indications, new pharmaceutical forms and new routes of administration are sought.

The requirements will not apply to generics. For drugs not yet authorised or still covered by a patent, the Regulation establishes rewards and incentives that include an extension (six months) of the patent. In case of Orphan Medicinal Products the incentive is represented by the extension of market exclusivity (12 years instead of 10).

In case of authorised products no longer covered by patent whose sponsor voluntarily apply for a MA in children, the Regulation provides a new type of marketing authorisation, the Paediatric Use Marketing Authorisation (PUMA) providing data protection for a ten-year period. To generate studies on off-patent products the Regulation includes the opportunity of accessing 'ad hoc' European funds for the research and development through the EU Research Framework Programmes.

Moreover, free scientific advice provided by the Agency is envisaged as an incentive to sponsors developing medicines for children. Likewise, one of the objectives of this proposal is to increase the information available on the use of medicines for children.

Paediatric patients deserve to have the same access as adults to effective medicines. Parents must be given sufficient information to give informed consent for their child to participate in pharmaceutical research. In the coming years we will observe more pre-clinical and clinical research, and a comparable debate has also started in Japan, Canada, Australia and other countries.

With this Regulation the EU has a solid regulatory framework for paediatric drug development that can promote a strong academic infrastructure for clinical research, and a greater competitiveness in the pharmaceutical industry. The subsidies established, although modest, will have the effect of providing legal certainty and a vision of European society and its institutions that will create a favourable climate for companies to foster pharmaceutical innovation in paediatric medicines and will permit an open and trustful dialogue between the key stakeholders for paediatric health care needs.

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