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EDITORIAL

A European Clinical Trials Registry for Children

The inadequate position of children with regard to optimal drug therapy is well recognised[1, 2]. One reason is the lack of clinical trials in children. Paediatric clinical studies are more difficult than studies in adults because of ethical, practical and economic considerations[3, 4]. Obtaining "informed" consent from young patients is difficult and must therefore involve the parents instead of the patient[5, 6]. The significant differences in pharmacokinetic and pharmacodynamic properties in the different age ranges require series of trials to be performed in various age groups. The paediatric drug market is also commercially difficult due to the relatively limited use of most drugs in children.

Attempts to improve the situation in Europe were initiated in 1997 when the Committee for Proprietary Medicinal Products (CPMP), part of the European Agency for the Evaluation of Medicinal Products (EMEA), published the "Note for guidance on clinical investigation of medicinal products in children"[7]. This guidance describes how and when drugs should be tested in children. Studies carried out between 1999 and 2002, however, found no significant improvement in the situation, with only a slight increase in the number of drugs with paediatric indications approved by the EMEA[8-10].

In 2000, the European Commission (EC) took a more proactive approach by proposing new regulatory actions to address the lack of suitably adapted paediatric medicinal products in a document entitled "Better Medicines for Children"[11]. This consultation document presented six main objectives: increasing the availability of authorised medicinal products that are suitably adapted to the needs of children of different age groups; ensuring that pharmacovigilance mechanisms are adapted to meet the challenges of possible long-term effects in specific cases; avoiding unnecessary studies through the publication of details of clinical trials already initiated; establishing a list of priorities for research; developing European excellence in the field of research, development, and assessment of clinical trials for paediatric medicinal products through the creation of a specific and dedicated committee or expert group; ensuring that the highest ethical criteria are met in carrying out the studies.

Another achievement was reached in 2001 when the International Conference on Harmonisation Guideline on the Clinical Investigation of Medicinal Products in the Paediatric Population came into effect in the United States, Europe, and Japan. A Directive on Good Clinical Practice was adopted in April 2001, which also addresses issues involving the inclusion of children in clinical trials and describes criteria for their protection. Following the proposal for the creation of a dedicated expert group in the EC's "Better Medicines for Children" document, the CPMP set up a Paediatric Expert Group in 2001, which is currently working to have a draft regulation promoting the development of medicinal products in children implemented. The strategies taken by the EC so far have shown a commitment to improving drug therapy for children.

Despite the various initiatives mentioned above, the situation remains inadequate and additional strategies are needed in Europe to promote the evidence based use of drugs in children. Clinical trials have a fundamental role in achieving this, since they are the key to distinguishing effective from non-effective or

harmful treatments. However, it is often difficult to identify the few paediatric studies carried out and to thus implement the knowledge derived from them. Most trials become public knowledge only once the results are published. However, studies that are stopped prematurely or with insignificant or negative results often remain unpublished[12, 13], leading to duplication of effort by other researchers or to concealment of potentially significant risks related to the use of certain substances. Another issue related to the inadequacy of paediatric drug information is the duplication of effort and resources in carrying out clinical studies on drugs and conditions on which ample knowledge already exists, instead of addressing those that lack information[14].

The development of a clinical trials registry specific to the paediatric field would therefore be valuable. Despite the remarkable efforts made to create numerous, diverse databases addressing the needs of the biomedical research community in the past few years, none have involved such a registry[15]. A registry of completed and ongoing clinical trials in children would be a useful resource for planning new studies, promoting communication and collaboration among researchers, facilitating patient access and recruitment into trials, preventing trial duplication and inappropriate funding, and identifying the therapeutic needs of children that remain neglected. It would also allow for active monitoring of new or evolved knowledge of drug therapies.

At the conclusion of the Fifth Framework Programme in 2002, the European Community decided to fund the development of a European register of clinical trials in children, following through with the commitment shown in its consultation document "Better Medicines for Children"[11]. The aim of the DEC-net project[16, 17], and of the network involved in carrying it out, is the creation of a fully integrated, online register developed to handle essential data on paediatric clinical trials that can be expanded in the future to include data from all the European member states. The project began in January 2003 and involves members from four countries: Italy, France, the United Kingdom, and Spain. The different clinical backgrounds and research experiences of the network's members will facilitate the creation of the register, which will also act as a tool for both promoting and co-ordinating paediatric drug research throughout Europe and for identifying areas where research is needed. We are currently organising the initial phase of the project and will then begin to identify planned and ongoing trials through communication with ethical review boards, national associations of paediatricians and paediatric pharmacists, pharmaceutical companies, etc. Information on the outcome of the studies, i.e. the results, conclusions and publications, will also be collected. In the meantime, the database and its interface for the Internet will be created. A promotional phase is planned during which national health agencies, international associations, the public and others will be informed of the registry. Input of trial data will then begin and the registry will be activated. Access will be allowed to everyone after a free, one-time registration.

Many registries on clinical trials in humans, both general and field-specific, have been set up and made available on the Web[18], but none have focused specifically on the paediatric population. This initiative will hopefully aid in making therapies more suitable for children.

The goal of drug therapy is the achievement of defined therapeutic outcomes that improve a patient's quality of life while minimising patient risk. Children have the same rights as adults to receive safe and effective medicines. Legislation and clinical trial registries together have the capacity to make knowledge of paediatric drug therapies reach its maximum potential throughout the world. The two strategies complement each other and the information obtained as a result of both can be summed. While legislation works slowly but thoroughly to improve the future situation, a paediatric clinical trial registry has the potential to render data available immediately. The ultimate goal would be a perfect symbiosis of these two forces, with legislation that is successful internationally and a single register that provides data from trials throughout the world, so that all information is trapped in a knowledge base that is accessible to all.

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