The Paediatric Working Group of EUCROF: Activities and Perspectives

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The European CRO Federation, EUCROF, was founded in October 2005 by national CRO associations of France, the Netherlands, Germany, UK, Italy, the Czech Republic and Spain with the clear aim to promote high quality research in Europe. EUCROF represents the interests of CROs based in Europe and maintains close relationships with regulatory bodies, pharmaceutical and biotech industry, and medical research communities. Currently, EUCROF has nine full members, i.e. CRO associations from Belgium, France, UK, Italy, the Netherlands, Germany, the Czech Republic, Spain and Turkey, and four associate members (individual CROs) from Portugal, Poland, Greece and Ireland. Over 260 small-to-medium and large CROs belong to EUCROF, totalling more than 11,000 professionals.

Various activities are promoted by EUCROF through specific working groups, one of them being the Paediatric Working Group (PWG), founded in 2007. Currently, the PWG consists of eleven members, based in the Czech Republic, France, Germany, Italy, Spain and the Netherlands. The PWG is currently focusing on clinical research methodology and ethics in paediatric clinical trials, with the aim of improving awareness of the need for clinical studies in children.

Clinical studies in children of different ages require special attention, knowledge and sensitivity as regards the peculiar characteristics of the paediatric population in terms of biology, pharmacology, therapy and need for appropriate psychological approach. This is also reflected in Chapter 4, ‘Clinical trials on minors’, of the EU Clinical Trials Directive 2001/20/EC to safeguard the rights and wellbeing of children participating in clinical research.

Children (a term used in the present article in a broad sense, encompassing all paediatric sub-populations from birth to the legal age of adulthood) are subject to many of the same diseases as adults and, consequently, are often treated with the same drugs. However, a large proportion of medicines administered to children are unlicensed for the specific age group and are prescribed off-label, which can place children at risk of under- or overdosing and of acute or long-term adverse effects. Data needed for effective and safe treatment of children cannot be linearly abstracted from adult data, thus specific research in children is necessary. In addition, there are diseases specific to children.

The difficulties in carrying out studies in children, due to ethical and practical constraints, and the costs of such research in children for pharmaceutical companies, in a relatively restricted market, are some of the reasons for the low percentage (about 30 per cent) of drugs which are specifically licensed in Europe for use in children. In order to improve the regulatory environment and give impulse to paediatric research, the European Parliament and the Council published the Paediatric Regulation (EC Regulation No. 1901/2006 as amended), which entered into force on 27th January 2007. As per the Paediatric Regulation, any new drug to be marketed in the EU, as well as any addition of indication, or new pharmaceutical for approved drugs in the EU, must have a Paediatric Investigation Plan (PIP) agreed with the European Medicines Agency. Incentives are provided to companies developing medicinal products for the paediatric population, such as free scientific advice for the PIP and a six-month extension of the patent protection. For products out of patent, an optional new marketing authorisation, Paediatric Use Marketing Authorisation (PUMA), is available when a paediatric indication is developed. The incentive for the latter is a ten-year data protection.

These new requirements and the new attitude towards paediatric clinical research represent the basis of the PWG’s objectives, which are the improvement of knowledge and application of the methodology specific to paediatric studies. The PWG’s activities and projects interface with the pharmaceutical industry, regulatory authorities, paediatricians and paediatric networks involved in clinical research in children. Major collaborations and cooperation have been established with the following organisations:

● EMA (European Medicines Agency): PWG was invited to the Second Workshop of the European Paediatric Network in March 2010 and to the launch of the European Network of Paediatric Research at the EMA (Enpr-EMA) in March 2011 as well as to the ‘Ethical issues in Clinical Trials’ workshop in November 2011.

● TEDDY (Task-force in Europe for Drug Development for the Young – www.teddyoung.org): a Network of
Excellence funded under the 6th EU Framework Programme. Support was given by PWG in 2010 to collect information from the ethics committees of 22 European countries on their awareness and knowledge of the current existing regulatory framework on paediatrics, and its impact on their workload.

- **EFGCP** (European Forum for Good Clinical Practice – www.efgcp.be): Joint organisation of an international congress on ‘Ethical challenges in clinical research at both ends of life’ to debate common lessons to be learnt on clinical research in the elderly and paediatric populations (Antwerp, 2010).

Several articles were recently published by the PWG on subjects related to the Paediatric Regulation and the activity of ethics committees in relation to paediatric studies. From the joint TEDDY/PWG survey mentioned above, it has become evident that a lack of knowledge, understanding and awareness of the current European paediatric regulatory framework exists, and that there is a need for training and education.

The PWG contribution to the improvement of the information available on the use of medicinal products in the paediatric population will help industry to improve their capacity in successfully managing this special sector of clinical development.

Since its establishment in July 2007, the Paediatric Committee (PDCO) at the EMA has received over a thousand PIPs/waiver applications, the majority of which (73 per cent) are for products not yet authorised. This translates into more than 1,500 indications covered by these applications.

Because of the increasing number and complexity of studies in children, as well as the high costs and extended time to conduct such clinical studies, it is evident that the acquisition of specific experience by CROs in paediatrics may be challenging. However, it also represents an opportunity to develop experience and knowledge of topics that have received little attention so far. These include new epidemiological, pharmacological, clinical and statistical aspects, new ethical approaches such as informed consent/assent, new approaches for recruitment and retention, and investigator-patient relationships.

By following the strategy set by the EMA for the establishment of a European Network of Paediatric Research and improving technical and administrative competence in the performance of paediatric clinical trials, CRO members of EUCROF will be able to partner effectively with the pharmaceutical industry and fully meet requirements.

A modern view of the CRO’s role in clinical development should include the capacity to provide counselling on the most efficient and cost-sensitive approach to clinical research in children. EUCROF members can also offer their experience to academic research groups developing non-sponsored clinical trials in children.

The next steps of PWG will be to consolidate the experience developed so far and to identify critical aspects that are worth further initiatives to foster clinical research in paediatrics. One such possibility is the development of a European template for informed consent/assent for paediatric studies.

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**References**


