“Children are not small adults...”

Since the EU’s “Paediatric Regulation” came into effect in July 2007, applicants for marketing authorisations have become familiar with the requirements of paediatric investigation plans (PIPs) for the development of medicines in children. “Children are not small adults” is a term commonly used to explain that the pharmacokinetics, dose and other aspects of how a product affects children need to be investigated and cannot be extrapolated from adult data. The EMA’s Paediatric Committee (PDCO) and applicants alike have had interesting learning experiences over the past six or more years, and these are explored in depth in this edition’s two focus articles on the Paediatric Regulation.

In the first article, Dirk Mentzer, the chair of PDCO, discusses how the challenge for regulators, investigators and industry is to balance the current legislative requirements versus the financial burden of developing medicines for children as an extension of adult medicines’ development. Dr Mentzer – a paediatrician by training – notes that, given that most PIPs are deferred, it may be some time before the paediatric population feels the benefit of this initiative. He advocates early interaction between the applicant and the EMA, in line with the Paediatric Regulation’s Article 16(1). While many medicines in development may gain “class waivers”, PDCO has to consider the available pharmacological information and evidence on the mode of action of the candidate compound in relation to its potential paediatric use feeding into the a condition related to the proposed adult indication. Work is ongoing to simplify strategic PIP proposals, specifically in the therapeutic areas of oncology and asthma and is planned for paediatric type 2 diabetes.

In the second article on this topic, Dr Daniel Brasseur – a paediatrician who was one of the driving forces behind the Paediatric Regulation – says that the Regulation has been a success in terms of efforts made, quality of the guidance and advice given for the development of formulations, as well as the design of nonclinical studies and clinical trials. However, it is acknowledged that the implementation of a simple concept has become a highly complex system. Dr Brasseur provides examples of how industry has interpreted the Regulation over the past six years, and how this has led to misunderstandings between applicants and the EMA. He also makes proposals to improve and simplify the process in advance of 2017, when the Regulation is due to be revised.

Also in this edition we have an interview with Dr Tomas Salmonson from the Swedish Medicines Agency (MPA) on his role as chair of the Committee for Medicinal Products for Human Use (CHMP). He discusses the function of the EMA’s pharmacovigilance committee, the PRAC, and how rapporteurships are distributed. In addition, he comments on the EMA’s reorganisation into a horizontal body in order to give better scientific and regulatory support to the various committees, and the limited usage of conditional approvals and compassionate use programmes.

On a separate note, the voluntary harmonisation procedure (VHP) for clinical trial applications (CTAs), which was introduced in 2008 as a means of simplifying the often complex process of obtaining approval for multinational trials in the EU, is reviewed. The experiences of the past four and a half years of the VHP were discussed in a recent workshop, a report of which is published in this edition.

A further meeting report in this issue summarises the learnings of a recent workshop on parallel scientific advice between the EMA and health technology assessment (HTA) bodies. The workshop was oversubscribed, indicating the level of interest from industry in this area. HTA bodies or payers such as the UK’s NICE are increasingly looking for indicators of cost-effectiveness when assessing expensive new treatments, and they are increasingly involved in the scientific advice process when designing pivotal trials.

In the veterinary arena, the conduct and outcomes of inspections and audits is discussed in the second part of a two-part paper on veterinary pharmacovigilance. The authors offer their experiences in the preparation and conduct of such inspections and audits, with extensive discussion on findings from inspections.

As ever, the regulatory affairs arena is constantly changing, and some of these challenging processes are summarised in this edition of Regulatory Rapporteur.

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Since the Paediatric Regulation came into effect, the implementation of a simple concept has become a highly complex system, leading to many misunderstandings between industry and regulators.