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New EU Regulation on medicinal products for paediatric use in force since January 26, 2007

On January 26, 2007 the new EU regulation on medicinal products for paediatric use, as amended, came into force. This new legislation significantly changes the requirements for drug development and licensing of medicinal products in the EU/EEA – not only for new, but also for existing active substances. As a regulation, it is directly binding and does not require any additional legislative acts on a Member State basis.

One of the key measures of the regulation requires the EMEA to set up a new scientific committee, the paediatric committee (PDCO), which will consist of 5 members of the Committee for Human Medicinal Products (CHMP) including their alternates and one representative each of the remaining 22 Member States, again including their alternates. In addition, the European Commission is to appoint three members each to represent patient associations and health care professionals and their alternates. The regulation requires that the PDCO will have to be operational by July 26, 2007. The expertise represented by the PDCO should cover the scientific areas relevant to paediatric medicinal products and should include at minimum pharmaceutical development, paediatric medicine, general practitioners, paediatric pharmacy, paediatric pharmacology, paediatric research, pharmacovigilance, ethics and public health.

Of greatest significance for the pharmaceutical industry is the new requirement that as of July 26, 2008, only those new applications for a marketing authorisation will be valid that contain an agreed paediatric investigation plan (PIP), including the results of all studies performed and details of all information collected in compliance with the PIP, unless a waiver or deferral has been granted by the EMEA. The PIP will need to specify the timing and measures proposed to assess the quality, safety and efficacy of the medicinal product in all subsets of the paediatric population that may be concerned. In addition, it has to describe any measures to adapt the formulation of the medicinal product to make its use more acceptable, easier, safer or more effective for different subsets of the paediatric population. It will be the task of the PDCO, amongst others, to assess PIPs and applications for a waiver or a deferral. The ultimate decision whether to agree to a PIP or to grant a waiver or a deferral, however, will be made by the EMEA, based on the PDCO's recommendation. The PIP or an application for a waiver or a deferral will normally have to be submitted at the time that human pharmacokinetic studies in adults will have been completed. Neither a PIP, a waiver or a deferral, however, will be cast in stone. The regulation foresees the possibility for a modification of the PIP, which will have to be agreed upon by the PDCO. Also, both waivers and deferrals will be reviewed on a routine basis. Reasons for granting a waiver may be that the medicinal product or class of products is likely to be ineffective or unsafe in part or all of the paediatric population, that the disease or condition for which the product is intended does not occur in the paediatric population or that the specific product does not represent a significant therapeutic benefit over existing treatments. A deferral may be applicable when, e.g. it is appropriate to conduct studies in adults prior to initiating studies in the paediatric population or when studies in the paediatric population will take longer than studies in adults.

The requirement to submit a PIP including the respective study results, or an agreed waiver or deferral, however, does not only apply to new active substances, it is equally applicable to existing active substances. It applies regardless of the licensing procedure selected, i.e. it is equally applicable to national, centralised, decentralised applications or applications in the mutual recognition procedure. The only exemptions the regulation provides for are bibliographic, generic and hybrid applications as well as traditional and homeopathic medicinal products. A PIP and the result of studies in the paediatric population also have to be submitted for a repeat use application in order to make it valid. Thus, the coming into force of this new regulation has a dramatic impact on companies' launch strategies and product portfolios! In order to ensure future successful drug developments, it is a clear MUST for the industry to carefully assess the impact of the new requirements on their business activities. As outlined above, there is no way a marketing authorisation application for a medicinal product for human use – other than the exemptions listed - will be accepted by anyone of the EU/EEA competent authorities without an agreed PIP including the respective study results, an agreed waiver or deferral. However, as any paediatric indication now paves the way to the centralised procedure – regardless of whether the product contains a new or existing active substance – companies are presented with more options and more flexibility in their filing strategy.

Thus, the regulation does not only define new requirements, it also provides possible rewards and incentives. For a new medicinal product covered by a patent or a supplementary protection certificate, for example, an extension of the protection period by six months is offered if the marketing authorisation application includes the results of all studies conducted in compliance with the PIP and the product is authorised in all EU/EEA Member States. For medicinal products no longer covered by data protection, the regulation introduces a new type of marketing authorisation, the paediatric use marketing authorisation (PUMA), covered by ten years of data protection. An application for a PUMA has to include all data to establish quality, safety and efficacy in the paediatric population, including any specific data needed to support an appropriate strength, pharmaceutical form or route of administration in accordance with an agreed PIP. A PUMA will be a separate authorisation for a product for use in the paediatric population. However, it may retain the name of any medicinal product of the same company which contains the same active substance, i.e. it can benefit from an established brand name.

At present, EMEA and the European Commission have published a list of action items for the timely implementation of the different requirements of the new regulation. The Commission has also published a draft guideline on the format and content of the PIP for comments until March 30, 2007. Make sure you keep informed on the latest developments in this changing environment!

Susanne Keitel, March 10, 2007