European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

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Report on Paediatric development and Juvenile Animal Studies Assessors meeting
3 July 2009
EMEA

The paediatric EU Regulation (EC) No 1901/2006 requires that any marketing authorisation (MA) application for a new medicinal product should include either the results of studies conducted in compliance with an agreed paediatric investigation plan (PIP), or an EMEA decision on a waiver or on a deferred PIP. As a result, earlier inclusion of children in clinical trials may lead to adjustments of the non-clinical development plans through dedicated studies addressing developing organ systems. Studies in juvenile animals as models for paediatric development need to be discussed in this context.

On 3 July 2009, a one day workshop was organised at the EMEA, sponsored by the Paediatric Committee and the CHMP Safety Working Party, putting together non-clinical and clinical assessors involved in Paediatric Investigation Plans (PIP) evaluations, and focusing on juvenile animal testing.

In the morning session, several presentations were given on the format and content of PIPs, on the CHMP/SWP guideline on non-clinical testing in juvenile animals (Guideline on the Need for Non-Clinical Testing in Juvenile Animals of Pharmaceuticals for Paediatric Indications, EMEA/CHMP/SWP/169215/2005), and on the Paediatric Committee Non-clinical Working Group that has been established to support PIP evaluations and has held monthly meetings since November 2008. A literature review on the comparison of organ development in various animal species was also presented as a basis for further discussions.

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After the scene-setting presentations of the morning sessions, break-out sessions were organised where small groups discussed the need, purpose and protocol design of juvenile animal studies in selected situations. Four cases had been selected to illustrate the most common and controversial situations and possible scenarios.

The cases addressed:
- An oncology product, with new-in-class pharmacology and with potential treatment of infants
- A product intended for preterm newborns/neonates
- A product where the molecular entity was not new in class and effects observed in animal studies mainly derived from exaggerated pharmacology, and
- A biotechnology product for a chronic non malignant disease.

The groups discussed the different cases and presented their evaluations in the plenary.

There was general consensus that case-by-case analysis is needed before requesting a juvenile animal study. If the need for a study is identified, various aspects of the protocol design that need to be carefully taken into consideration are species selection, animal age at start, study duration and endpoints to be monitored. Situations which might not require juvenile studies include those where adult experience reveals no particular concerns and the main safety aspects derive from exaggerated pharmacology. When deciding on the species and the age of the animals for study initiation, the developmental stage of the target organs of concern should be taken into consideration to allow for an extrapolation to the development in children. When the rat is shown to be a relevant species, its use should be preferred to non-rodents in the juvenile animal study.

In conclusion, the workshop was very interactive thanks to highly motivated and interested participants and was well received by the participants During the discussions, significant experience was exchanged and the bases for a common understanding on the interpretation and application of the guideline on non-clinical testing in juvenile animals were set up.