



DATE: 19 September 2007

EXCO/ES07/CET/1501

WORKING DOCUMENT

MEETING : EXCO Meeting in *Seville, Spain*

DRAWN UP BY : Francesco Paolo Vatti, CET Group 5

SUBJECT: EU directive on paediatric drugs

PURPOSE: For information

TABLED TO: All Attendees



INTRODUCTION

Regulation EC 1901/2006 came into force on 26 January 2007, providing a new legal frame for the approval of drugs for paediatrics purposes. Before that, such an approval had not been based on trials carried out on paediatric patients, which sometimes resulted in under estimated doses or even in health damages.

STARTING POINTS

The Regulation has been released on the bases of some specific needs. First, the European Parliament and the Council needed deeper studies into paediatric drugs. Then, from a commercial point of view, there was the need to remove obstacles to the free circulation of such drugs. The need to provide a free consulting service to encourage sponsors was particularly felt, as well as the need to label paediatric drugs with a clear logo. The regulation also has the task to maximise the access of Union people to paediatric drugs. Finally, there was the need to optimise both availability of information about paediatric drugs and the number of studies.

INTRODUCTION AND DEFINITIONS

The Regulation is intended to rule the development of human drugs for children, without submitting them unnecessarily to clinical trials. Patients under 18 are meant as paediatric patients.

A paediatric committee is to be appointed within EMEA (European Medicines Agency), and it is meant to be coordinated by the executive director of EMEA.

The committee members change every three years. A unanimous consent should be reached inside the committee. In case it is not possible, decisions are taken by a majority of votes.



The tasks of the paediatric committee are the evaluation of any paediatric investigation plan (PIP) for any drug under trial, the evaluation of derogations and delays and the preparation of an opinion; the evaluation of data from trials according to the paediatric investigation plan; the release of opinions.

PROVISIONS RELATED TO THE AUTHORISATION

An application for the authorisation of any drug should enclose, if appropriate, the results of any study according to the approved paediatric investigation plan, a decision of EMEA allowing a derogation for a specific product, a decision of EMEA allowing a derogation for a class, a decision of EMEA allowing a delay.

In case results of studies are enclosed, the approved paediatric investigation plan should be annexed to the application. In case of drugs covered by a patent or a supplementary protection certificate (SPC), the above is applied to any application for registration of new drugs or of new administration routes.

Derogation about the provision of information can be allowed if there is the likelihood that the drug is not suitable for children, if the disease is not likely in paediatric people or if the drug gives no benefit to children. As previously seen, the derogation should be decided by the committee, which keeps a list of allowed derogations. A revision of derogations is possible.

The paediatric investigation plan is the core of this provision. It is to be submitted to EMEA for approval before applying for the authorisation of any drug. The deadline to submit the plan is by the end of trials for adults. A delay in starting of one or more provisions of the plan, which could be particularly useful to carry out studies on adults first, can be requested when filing the plan. Thus, requirements for studies on children should not delay the authorisation of medicines for adults.

The paediatric investigation plan can be modified by filing an application if it cannot be carried out as such or if it is no longer suitable. The application should be evaluated by the Committee within sixty days. The compliance to the plan is checked by



EMA. The lack of compliance results in the exclusion from possible incentives. An opinion about the compliance can be requested to the Committee and a revision of the same can be requested by the Applicant. EMA should decide within ten days after the opinion.

The Applicant can request the advice of EMA during the preparation of the paediatric investigation plan.

The authorisation procedure is under EU regulation 726/2004 and directive 2001/83/EC.

The explanatory sheet enclosed to the drug should bear the results of trials.

The request of an authorisation for paediatric use does not prevent the request of authorisation for other purposes. An application should be connected with information and documents to assess quality, safety and efficaciousness for paediatric patients and the approval of the paediatric investigation plan by EMA. Reference could be made to the authorisation of a EU country.

Setting up a system of risk management can be required for a paediatric drug to be authorised.

AUTHORISED PAEDIATRIC DRUGS

A symbol (paediatric label) will be chosen, in order to show that a drug is authorised in the paediatric field.

If an authorisation for paediatric use upon implementation of a paediatric investigation plan is granted for a drug already authorised for other purposes, the owner of the authorisation puts the drug on the market within two years from the grant.

PATENTS AND SUPPLEMENTARY PROTECTION CERTIFICATES

Patents and supplementary protection certificates are referred to in three articles (8-10).



If the application for the authorisation includes results got according to the approved paediatric investigation plan, the owner of the patent or of the SPC enjoys a six-month extension of the protection. This provision applies even if no paediatric labelling is granted and applies to all of the authorised indications for the product including the non-paediatric indication. If a paediatric indication is granted it must be authorised in all the member states. This constitutes a clear incentive for the use of the centralised procedure, where a single approval is automatically valid in the whole EEA. The application to the national patent offices for the SPC extension must be lodged no later than six months before the expiry of the SPC. However, after a five-year period from the entry into force of the paediatric regulation, such an application should be lodged no later than two years before the SPC expiry. This does not apply to drugs called “orphan” according to the regulation EC 141/2000. Such drugs are drugs for very rare diseases, often not patent protected, but already enjoying EU incentives since their production is not profitable otherwise. In case of orphan drugs, if the application includes results according to the approved paediatric investigation plan and gets a declaration in this sense by EMEA, the ten-year term for exclusive authorisation is extended to 12 years, even in case of non authorisation. During this period, no other subject can get an authorisation for the same drug.

PRODUCTS NOT COVERED BY INTELLECTUAL PROPERTY RIGHTS

For products not covered by intellectual property rights Article 38 provides for a new type of marketing authorisation, Paediatric Use Marketing Authorisation (PUMA) allowing 10 years of data exclusivity.

Regulation 1901/2006 relates to any product authorised for the first time in the EU after 26th July 2008 even when it does not take advantage of an SPC. Further, it relates to any product already authorised in the EU when a new authorisation is applied after 26th January 2009 for a new indication, a new pharmaceutical form or a new route of administration provided that it benefits from an SPC or from a patent which qualifies for the granting of the SPC. In the latter case the company will have to provide paediatric studies relating to both the existing and the new indications, pharmaceutical forms and routes of administration.



The six -months extension will only be granted on condition that significant studies contained in agreed Paediatric Investigation Plan are completed after the entry into force of the regulation. Paediatric studies already submitted in e.g. USA will therefore not qualify for the EU paediatric incentive.

MISCELLANEOUS

There is a trial data base wherein data can be inserted according to directive 2001/20/EC. Data refer to trials which have been performed in foreign Countries.

Member States collect data available about all uses of drugs existing in paediatric people and communicate them to EMEA by 26 January 2009.

EMEA should implement a network of researchers and centres with special skill in performing studies on paediatric people.

The evaluation and approval of a paediatric investigation plan is cost-free.

Fines for infringement of the present Regulation are set by the member States.