EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA
Head of Unit

PHARM 606

PHARMACEUTICAL COMMITTEE

28 March 2012

68th meeting

SUMMARY RECORD

The Pharmaceutical Committee held its 68th meeting on 28 March 2012, in Brussels, chaired by Patricia Brunko, Head of Unit SANCO D5 - *Medicinal products – authorisations, EMA*.

1. Agenda

- **The draft agenda (PHARM 599) was adopted, with additional items under A.O.B.**

2. Legislative issues

- **Hospital exemption for ATMPs (implementation of Art 28(2) of the ATMP regulation): update on feedback received by the Commission**

The Commission presented a first feedback received from some Member States on ATMP products and reminded its query to those Member States which have not responded yet.

- **Pharmacovigilance legislation: state of play of ongoing preparatory work**

The Commission provided an update on the state of play with respect to the draft implementing act on the performance of pharmacovigilance activities, transitional arrangements and the process of appointing members to the Pharmacovigilance Risk Assessment Committee. Additionally, Member States were invited to provide an update on their respective preparatory work. The new legislation will become applicable as from July 2012.

The Commission also explained the possibility for a Joint Action to facilitate collaboration among Member States for the effective operation of the pharmacovigilance system in the EU after the implementation of the 2010 Pharmacovigilance legislation. The objective of such Joint

Action would be to support Member States in the optimal organisation and operation of a pharmacovigilance system and the fulfilment of their pharmacovigilance tasks, by means of collaboration and knowledge sharing. Member States were asked to express their interest by 3 April 2012.

- **Directive on Falsified medicines: transposition and implementation, state of play**

The Commission representative stressed the particular importance for a correct transposition and implementation of the 'Falsified Medicines Directive' 2001/62/EU. An update of the Commission's implementation work was given:

Delegated act on the criteria to be considered and the verifications to be made when assessing the potential falsified character of medicinal products introduced in the union but not intended to be placed on the market (article 52b): The Commission is currently preparing a public consultation paper.

Implementing act on the design of a common logo identifying legally online pharmacies and the technical detail for the verification of the authenticity of this logo (article 85c): A public consultation is expected to be launched later in 2012. It was clarified that national rules on online sale of medicines will continue to apply until one year after the publication of the implementing act.

Delegated act on the detailed rules for a unique identifier for medicinal products for human use, and its verification: a public consultation has been launched and closes on 27 April 2012. The next meeting of the expert group on this topic is scheduled for autumn 2012. Adoption of the act is planned in 2014.

As regards the tasks of the Agency, the extension of the existing EudraGMP database and the developments of templates, work is on track.

Regarding the file 'importation of active substances', the Commission representative informed participants of its ongoing dialogues with various third countries to ensure smooth implementation of the new rules.

- **Paediatrics Regulation : lessons learnt after five years of application**

In view of the upcoming Commission report on experience acquired as a result of the application of the Paediatric Regulation, the Commission invited the Committee to share its experience with the Regulation so to take those reflections on board in the further preparation of the Commission report. Several Member States commented by referring to the achievements of the regulation, but also highlighting areas for improvement.

- **Recent judgments of the European Court of Justice**

The Commission called the Committee's attention to recent rulings and to the Court's conclusions concerning advertising provisions for medicinal products:

- Case T-52/09, judgment of 14 December 2011, "Nycomed"
- Case C-125/10, judgment of 8 December 2011

- **Interpretation of the legislation on biosimilars**

The Commission explained the current interpretation of the legislation for authorising biosimilars. The authorisation of generics is based on the comparison of a medicinal product with a reference product authorised in the EU as laid down in Directive 2001/83/EC. The forthcoming revision of the EMA guideline on similar biological products (CHMP/437/04) is currently subject to various expectations to promote a global biosimilar development which would avoid repeating clinical trials against reference biological product sourced from different territories.

The Commission sought the views of the Committee on the approach whereby, on a case by case basis, batches of a reference product from a non-EU country could be used to support the authorisation of a biosimilar product. In such case, an applicant would have to demonstrate by state-of-the-art analytical tests that the level of similarity of the two reference products is high enough to allow that one can be substituted by the other in the clinical trial. The Committee supported this proposal.

- **Comparators in the context of marketing authorisation**

  France presented to the Committee its views on the use of comparators in the marketing authorisation procedure: a reflection on the subject of including a systematic assessment against a reference medicinal treatment, i.e. the introduction of a criterion of relative efficacy in the authorisation process.

  The Commission pointed out that the legal framework for the authorisation of medicines examines the molecule *per se* (quality, efficacy and safety) and provides flexibility for the design of clinical trials, as it takes into account the scenario where there is no similar product. It also indicated that a potential introduction of a criterion of relative efficacy in the marketing authorisation process would blur the limit with health technology assessment. The Commission underlined that such an approach could also endanger the authorisation of new molecules. Finally, the Commission stressed that this discussion has no connection with the Clinical Trials Directive, which only deals with the authorisation of clinical trials in view of the risk or the value for patients, whereas this discussion is related to data and criteria for the granting of a marketing authorisation.

  Several Member States took the floor and fully supported the Commission analysis.

  The Commission took note of the views expressed and explained that a reflection paper is currently under development at the EMA on the need for active control in therapeutic areas where use of placebo is deemed ethical and one or more established medicines are available . The Commission proposed to put on the agenda of the CHMP for information the status of this scientific reflection paper. This would provide an opportunity to present to the CHMP the issues raised by France and have a scientific discussion on that matter. The scientific views expressed in this document will be useful for this discussion.

- **Reform of ICH and international collaboration on generics**

  The Commission informed the Committee on the outcome of the meeting of the International Conference on Harmonisation of Technical Requirements for the Registration of Medicinal Products for Human Use ('ICH') held at Seville, Spain 6-10 September 2011. This meeting was marked by the proposal of the European Commission to reform ICH in order to address shortcomings related to governance, international outreach, consultation and transparency. It was announced that a dedicated discussion would take place at the next ICH meeting in Fukuoka in June 2012 on these topics.

  An initiative has also been launched with a view to improving international collaboration in the field of generics: e.g. harmonisation of authorisation criteria, exploring possible sharing of evaluation dossiers, mutual recognition of generics authorisations issued by third countries, harmonisation of legislation in the field of generics authorisation. However, creating a new structure for generics seems premature at this point. The Commission is therefore proposing to include generics in the framework of ICH discussions, which would avoid overlaps in terms of topics and resources.

- **AOB 1 - Project on possible unilateral recognition by Mexico of EU marketing authorisations**

  The Commission informed that a visit of Mexican representatives to the EMA is scheduled. The aim for Mexico is to assess how the EU authorisation system operates with a view to a possible unilateral recognition of the EU authorisations.

- **AOB 2 - Update on Commission proposal amending the Water Framework Directive**

  The Committee was informed of the adoption by the Commission of a proposal to amend the Water Framework Directive, which has now entered the ordinary legislative procedure ('co-decision'). The proposal identifies three substances used in medicinal products as 'priority substances'. This means that the presence of these substances would have to be monitored by Member States in surface waters and that control would have to be taken by Member States for progressive reduction of discharges, emissions and losses. (These substances are not proposed as "priority hazardous substances" for which the legislation requires a progressive phasing-out.) The three substances are two contraceptives (17alpha-ethinylestradiol and 17beta-estradiol) and one pain killer (Diclofenac).

  The proposal contains a footnote specifying that this measure is without prejudice to the legislation on authorisation of medicines.

- **AOB 3 - Study on the environmental risks of medicines: update on MS participation in an upcoming workshop**

  The Commission has contracted out this study which will take place in 2012. The two main objectives are to quantify the extent of the problem and to assess the operation of the EU legislation regarding environmental effects of medicines. A workshop in the framework of the study is currently scheduled for September 2012. One section of this workshop will be dedicated to an exchange of views on the application of pharmaceutical legislation in this respect. The Commission invited MS to express in writing, within a week after the meeting of the Pharmaceutical Committee, their possible interest for participating in this workshop. The Commission underlined that no commitment can be made as to the actual participants who are going to be invited at the workshop.

  Several MS expressed interest during the meeting.

- **AOB 4 - Update on the amended proposals on pharmacovigilance and information to patients on prescription-only medicines**

  The Commission gave a short presentation on the state of play of the proposals on "Pharmacovigilance" and "Information to patients" after the split of the proposals into the two respective parts on 10 February 2012.

  With regard to the proposals on Pharmacovigilance, progress in the Council is on-going and both the Council and European Parliament are interested in an agreement at first reading in order to close quickly the gaps identified in the legislation through the Mediator 'stress test'. Regarding information to patients, Member States at the Council Working group have expressed concerns about the proposals but, at the date of the meeting of the Pharmaceutical Committee, there had been no detailed discussion or a formal position of the Council on these proposals.

- **AOB 5 - Update from Belgium and Ireland on a review of marketing authorisations of cough syrups**

  Belgium announced that, for reasons of better and safer use of medicines, it had carried out a review of all the active substances used in cough medicines, especially when used in children. The conclusion was that most of these cough medicines should be contraindicated for children under 6 years, as there is no convincing evidence of their efficacy in this

population. Moreover, all cough medicines containing codeine have been put on prescription. Furthermore, all liquid forms will have a child-safe closure.

Ireland informed that it had conducted a similar exercise in 2011 for the same reasons. Manufacturers have been requested to modify labelling, so there are virtually no longer such products in use for children under 6. As regards codeine-containing products, strong restrictions apply: they can only be supplied in a pharmacy and by a pharmacist, with a restriction on a short-term use and only for adult users.

The Commission noted that this issue has been discussed in the framework of the Pharmacovigilance Working party.

- **AOB 6 - Non-compliance certificates issued by EDQM**

A discussion took place on the modalities to respond to GMP (Good Manufacturing Practices) non-compliance certificates issued by EDQM (European Directorate for the Quality of Medicines, Council of Europe). Ireland and Italy confirmed that measures are taken when such certificates are issued. The Netherlands pointed out that the availability of products may be a matter of concern if actions are taken.

- **AOB 7 - Update on a WHO informal consultation on vaccines in preparation for a UNEP-convened Intergovernmental Negotiating Committee Meeting on a global legally-binding Treaty on mercury**

The Commission informed the MS that in the framework of the on-going negotiations on the Treaty on mercury, a list of vaccines (some of which are for human use) has been prepared in collaboration with the EMA. For these vaccines it is considered that mercury is still necessary. This list has been provided to the negotiators.

A number of intergovernmental meetings (Intergovernmental Negotiating Committee Meeting) are scheduled before the signature of this Treaty and the fourth meeting will be held from 27 June to 2 July 2012. In preparation of this, WHO is organising the above-mentioned informal consultation on vaccines on 3 and 4 April. The COM invited MS to channel any message for this informal consultation through their MS representatives.

- **AOB 8 - Update from the Commission on a new alert on Sorbitol labelled products**

On 25 March 2012 Italy notified to the Commission and the Member States, through the Rapid Alert System for Food and Feed, of one death case and two hospitalisations with a serious condition, after ingestion of a product being labelled as Sorbitol, in the setting of a private medical practice, during a food intolerance test. Sorbitol is a food additive and the product thus ingested was labelled as Sorbitol but was in fact another substance.

The Commission informed the Pharmaceutical Committee of this food issue because some confusion was created by the initial information that this was a pharmaceutical used in an allergy test. The Commission also informed that the tracing of the problem was on-going and that it was probably an error in labelling and that several MS had been possibly affected, through imports or Internet purchases.

- **AOB 9 - Request from the Republic of Guinea to the EDQM to be granted a status of observer at the European Pharmacopoeia**

EDQM has received a request from the Republic of Guinea to be granted a status of observer at the European Pharmacopoeia Commission. For non-technical matters, the EU can vote on behalf of its members. The European Commission has sent letters to both Human and Veterinary Pharmaceutical Committees seeking their opinion on the subject, with a deadline for reply 28 March 2012. All replies received are in favour of that request. With this, the Commission will proceed and give a positive opinion to the European Pharmacopoeia Commission.

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Next meeting of the Pharmaceutical Committee (human) is **tentatively** planned for **11 October 2012 (final date to be confirmed by the Commission in early September 2012).**