EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Health systems, medical products and innovation
Medicines: policy, authorisation and monitoring

PHARM 714

PHARMACEUTICAL COMMITTEE
28 April 2016

76th meeting

SUMMARY RECORD

The Pharmaceutical Committee held its 76th meeting on 28 April 2016, in Brussels, chaired by Robert Vanhoorde, Head of Unit SANTE B5 – *Medicines: policy, authorisation and monitoring*.

Agenda

- **The draft agenda (PHARM 701) was adopted.**

1. INTERPRETATION OF PHARMACEUTICAL LEGISLATION

i. Update on Court cases

The Commission called the Pharmaceutical Committee's attention to some pending cases as well as recent rulings of the European Court of Justice, and the General Court, especially:

- Case C-82/15P, judgment of 3 December 2015 (PP Nature Balance v Commission)

- Case C-138/15P, judgment of 3 March 2016 (EMA v Teva)

Additionally, reference was made to the pending case C-276/15 – Hecht Pharma on the pharmacy exemptions in Article 3 of Directive 2001/83/EC and its link with the previous Abcur case law (C-544/13 and C-545/13).

ii. Legal and Regulatory news

The Committee was informed about new regulatory acts and Commission Guidelines that have been adopted since the last Pharmaceutical Committee held in October 2015.

iii. Update on the study of off-label use

The Commission informed the Committee that the study being carried out by the Netherlands Institute for Health Services Research (NIVEL), in cooperation with, the national Institute for public health and the Environment (RIVM) and the European Public Health Alliance (EPHA) was ongoing but was delayed. Consultation of the Member States on the draft final report would be through the next STAMP meeting planned for 28 June. The Heads of Medicines Agencies group, the European Medicines Agencies Co-operation on Legal and Legislative Issues (EMACOLEX), will be consulted by written procedure on the preliminary findings of the contractor regarding the collection of information related to Court cases relevant to off-label use of medicinal products at both national and EU level.

2. IMPLEMENTATION OF PHARMACEUTICAL LEGISLATION

i. GMP Guidelines specific to ATMPs

The Commission explained the activities that had taken place in connection with the development of the Good Manufacturing Practice (GMP) Guideline specific for Advance Therapy Medical Products (ATMPs) since the last Pharmaceutical Committee meeting. The Commission also explained the questionnaire submitted to the Member States in connection with this topic and stressed the importance that it attaches to the experiences of Member States in this field.

Several Member States questioned the development of a specific document (as opposed to developing a separate annex to the general GMP guidelines) and concerns were also raised regarding the timeline of the project. There was agreement that this project was relevant for the development of the field and the importance of relying on the expertise of the Committee for Advanced Therapies (CAT) and the Inspectors Working Group (IWG) to find the right balance between additional flexibility and safeguarding a high level of quality and safety was stressed. The Commission explained that the development of a specific Guideline is mandated by the ATMP Regulation and also noted that, from a practical standpoint, the annex approach would be unworkable (too many cross-references would be required and the document would be unreadable). As per the time-line, the Commission noted that the project started in January 2015 and that good progress had been done in the revision of the core sections of the Guideline. The Commission finally stressed the value of the input provided by the experts in CAT and IWG and invited all Member States to provide their views on the questionnaire submitted.

ii. Review of the regulatory framework on orphan medicinal products

The Commission presented the activities to streamline the regulatory framework for orphan medicinal products.

As far as the **notice** is concerned, the Commission asked the views of the group concerning the proposals for which diverging opinions had been expressed during the public consultation, in particular:

1. **Introducing the reassessment of the orphan criteria for a new subset of the condition when a sponsor extends the use of its product after marketing authorisation**: Commission explained the diverging views in relation to the proposal to reassess the criteria and the fear that this proposal would discourage development in the area of rare diseases. Many Member States were in favour of reassessing the orphan criteria for any change in therapeutic indication of the product. The orphan designation should systematically be given to the best product available for the disease;

2. **Simplifying the procedure for the reassessment of orphan criteria when two authorisation application procedures are pending in parallel for two orphan medicinal products**. Commission explained the proposal made by many respondents that a sponsor should not provide evidence of significant benefit over a medicine that has obtained a marketing authorisation after his marketing authorisation has been submitted/validated. The Member States supported to bring flexibility for the reassessment of the criteria when two products are running in parallel. Nevertheless, the proposal to stop the assessment at the time of the validation (more or less one year before the final Committee for Medicinal Products for Human Use (CHMP) opinion) is too long;

3. **Reference to medicines prepared in a (hospital) pharmacy as a satisfactory method of treatment**: the Commission suggested to have a case by case assessment when considering hospital preparations. In certain cases, hospital preparations should be considered if the product can be prepared very easily in the pharmacy and if this is a general practice in the EU. Some Member States

supported a case by case assessment but suggested to have a prudent wording e.g. *'when used significantly amongst the Member States*". One Member State considered that we should encourage industrially produced products. It was also recognized that the market exclusivity is excessive for the hospital preparations that may subsequently be authorised with a well established use application. Nevertheless, it will not be possible for the Committee for Orphan Medicinal Products (COMP) to collect the information on the use of the hospital preparations in the EU and legal certainty is needed. Commission proposed to further discuss with the COMP if clear criteria could be established.

One Member State also asked to look broader than the current notice and to examine how the orphan Regulation functions, what works well and what does not work. There is room to review more regularly the orphan criteria and see how we can address the excessive profit made by certain companies.

As far as the **review of the Commission Regulation (EC) No 847/2000 is concerned**, the Commission explained the ongoing revision of the concept of similarity. The Commission explained that the European Medicine Agency (EMA) has kindly provided technical input developed by the CHMP and the CAT to update the definition of "similar products". The member States were invited to provide their views. It was proposed to launch the text in public consultation to collect the views of all stakeholders.

Member States were invited to provide further comments by 13 May.

iii. Implementation of the Clinical Trials Regulation

The EMA updated on the main developments in the preparation of the EU portal and database. In particular the Committee was informed that the EMA Management Board agreed during the December meeting on the timing of the process. It was stressed both by the EMA and by the Commission that the agreed timelines have to be seen as maximum timelines and every effort has to be made to advance them. Therefore a constructive collaboration by all interested parties is essential.

The Commission informed the group on the progress on the legal deliverables of Regulation (EU) No 536/2014 as well as on the ongoing work as regards the update of the whole Volume 10 of EudraLex. The Commission thanked Member States for their support in the revision of existing guideline documents and in the drafting of new ones. The Commission also stressed the importance of the constant involvement and timely contributions by all actors.

Finally an update on the discussions which took place during the last Commission expert group on clinical trials (the ad hoc group) was given. The Commission representative informed that the group discussed the rules for the transitional period foreseen by Regulation (EU) 536/2014. The Committee was informed as well that at the last meeting some Member States raised the issue of the rules for the access to specific clinical trials documents by non-concerned Member States. The Commission recalled that the Regulation clearly indicates who is an addressee of the various documents that will be stored in the EU clinical trials database. The system will facilitate the exchange of these documents between Member States, however it will depend on the applicable legal requirements of the Member State concerned by a specific trial whether and on which

conditions the documents stored in the EU database can be shared with non-concerned Member States. For example, if its national legislation allows so, a Member States may decide to give automatically full access to non-concerned Member States to all documents for which that specific Member State is a concerned Member State. The prerequisite for discussing technical IT solutions with EMA is that the Member States clarify what are their national applicable rules. The Commission thanked the Netherlands and Sweden for volunteering in the framework of the Heads of Medicines Agencies (HMA) Clinical Trial Facilitation Group (CTFG) group to collect such information and come up with a common proposal.

iv. Implementation of the Falsified Medicines Directive

o Notifications under Article 117a

The Commission started by reminding France and Luxembourg of their legal obligation to notify the Commission as soon as possible of the details of their respective national systems for the receipt and handling of notifications of suspected falsified medicinal products as well as of suspected quality defects of medicinal products, in accordance with Article 117a of Directive 2001/83/EC.

The Commission then presented the state of play of the implementation measures tasked to the Commission.

o Delegated act on the safety features

Concerning the safety features for the identification and authentication of medicinal products, it was mentioned that the delegated Regulation on the safety features was published in the official Journal and will apply as of 9 February 2019. Member States were informed that, in order to facilitate the implementation of the new rules, the Commission published a Q&A document on its Public Health website, while the EMA and the Co-ordination group for Mutual Recognition and Decentralised Procedures, human (CMDh) published on their websites the regulatory requirements for the implementation of the safety features for centrally- and nationally-authorised medicinal products, respectively.

On this point, Slovenia informed the audience on the progresses of national stakeholders in setting up the Slovenian repository and the intention of Slovenia to issue national legislation to guide implementation (penalties, categories of people exempted from the decommissioning obligations, etc.).

o Active substances

Concerning the importation of active substances (APIs), the Commission informed that (1) the assessments of New Zealand and South Korea are still ongoing and that the on-site audit of Korea is planned for December 2016; (2) Poland communicated to the Commission its intention to use the waiver referred to in Article 46b(5) of Directive 2001/83/EC.

The Commission requested the Member States feedback on a proposed addition (Q&A n°35) to the Q&A document on API importation. The new Q&A aims at clarifying the

requirements in case of importation of active substances with an expired written confirmation but released for sale before the expiration date of the written confirmation. Member States comments were requested by 20 May 2016.

Concerning the new Q&A n°35, Portugal asked the Commission whether a specific type of documentation was requested in order to prove release for sale before the expiry date of the written confirmation. The Commission clarified that the choice of the type of documentation to provide was left to the company but it had adequately prove to the competent authority that the active substance has been released for sale during the period of validity of the written confirmation.

- **Common logo**

The Commission stressed that the provisions on the common logo for the retail at a distance of medicinal products are applicable since July 2015. In this context the Commission thanked Greece who recently contacted the Commission in order to arrange for the signature of the licence agreement on the use of the common logo. The Commission also urged Romania to proceed with the same procedure. The Commission recalled the request to be kept informed on national information campaign on the common logo and the dangers of purchasing medicines on the internet. Finally, the Commission invited the Member States to fill in the questionnaire submitted to the committee members on the national implementation of the Article 85c.

v. Feedback from Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP)

The Commission reminded the Committee of the work of the STAMP Expert Group during 2015 and gave an update of the meeting of the 4th meeting of the STAMP Expert Group on 10 March 2016. During the meeting on 10 March there was discussion on the following new topics: repurposing of established medicines; real world evidence; compassionate use; and, personalised medicine. In addition, the STAMP had been updated on: the Commission activities in the area of health technology assessment and pricing and reimbursement; the EMA activities on the PRIME (PRIority Medicines) scheme which had been launched on 7 March and the adaptive pathways pilot; and, the Netherland Presidency's meeting on 1-2 March 2016 concerning adaptive pathways, incentives and market access.

All related documents and presentations can be found to the webpage of the STAMP Expert Group:
http://ec.europa.eu/health/documents/pharmaceutical-committee/stamp/index_en.htm.

3. PHARMACOVIGILANCE

i. Update on pharmacovigilance related reports

The Commission updated the Committee on the reporting obligations in the area of pharmacovigilance. With regard to the report on the performance of pharmacovigilance tasks by the Member States, the Committee had been consulted on the draft report and

the accompanying document covering the activities of both the Member States and the EMA. The process for the adoption of the report was ongoing.

Regarding the Reports of Member States pharmacovigilance audits, 26 Member States and 1 EEA country had submitted their report and it was planned to prepare an overview document.

4. LEGISLATIVE ISSUES

i. Update on the preparation of the Commission report on the Paediatric Regulation

The Commission provided an update regarding the progress made for preparing the 2nd report to the European Parliament and the Council on the Paediatric Regulation, which is due in 2017. The 2017 report is supposed to cover an analysis of the public health and the economic impact of the Regulation. As far as the economic side of things is concerned, the Committee was informed that the Commission commissioned a study, the results of which are expected in the second half of 2016. The study will assess the rewards and incentives provided by the Regulation, but will also reflect on other indicators that are economically quantifiable.

For judging the public health impact, the Commission will rely on information to be collected by the EMA together with its Paediatric Committee and with support of national authorities. Moreover, a public consultation is planned in the second half of 2016 as well as a bilateral meeting between the US Food and Drug Administration (FDA) and EU to exchange views on the paediatric regulatory framework and future developments.

Finally, the Commission intends to organise an extraordinary meeting of the Pharmaceutical Committee dedicated to paediatrics, which is tentatively scheduled for the 19 September 2016. The purpose of the meeting is to debrief the Committee on the results of the economic study and the EMA data and to prepare the launch of the public consultation. The date of this meeting will be confirmed sufficiently in advance.

5. INTERNATIONAL DEVELOPMENTS

a) Update on multilateral collaborations:

i. The reform of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

The Commission updated the Committee on this harmonisation venue involving at present the Regulators and research-based Industries of US, EU and Japan as well as Health Canada and Swissmedic as members with World Health Organisation (WHO), International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) as

standing observers. The goals of the ICH reform and the new ICH structure and governance were explained to the MS.

ii. International Pharmaceutical Regulators Forum (IPRF)

The Commission provided a feedback on the last IPRF meeting that took place on 7-8 December 2015. IPRF allows to exchange information amongst regulators on recent regulatory development and to launch activities towards increased regulatory convergence/harmonisation and increased regulatory cooperation in identified areas. There are four Working Groups (WG) dedicated to these priority areas that are currently in place.

The Biosimilar WG is developing a standardized template that would allow for all authorities to communicate on their summaries of evaluation of biosimilars and a reflection paper on extrapolation of indication for biosimilars. The outcome of this work is intended to be published on the IPRF website in the second quarter of 2016.

There are the other WGs established working on gene-therapy, cell therapy and nanotechnology. As these areas are rapidly evolving, the main objectives of these WGs are similar and focusing in all MSs on the exchange of information, new development regarding regulatory requirements in order to gain a common understanding on these developments and opportunities for convergences.

In the last meeting it was proposed to establish a new group on Identification of Medicinal Products (IDMP) standards. This proposal will be further considered during the next meeting in Lisbon in June 2016.

b) Update on bilateral negotiations

i. Regulatory cooperation: China and India

The Commission informed the Committee on the outcome of the EU-China Working group on pharmaceuticals that took place in Beijing on 9 and 10 March 2016.

In addition, the Committee was informed about the next meeting of the EU-India Joint Working Group on pharmaceuticals, biotechnology and medical devices that will take place in Brussels on 5 and 6 July.

ii. Agreements on Conformity Assessment and Acceptance of industrial products (ACAA) / Mutual Recognition Agreements: recent developments with Swiss, Japan, Australia and Israel

The Commission updated the Committee on the recent developments with regard to the Mutual Recognition Agreements with Switzerland, Australia and Japan and to the Agreement on Conformity Assessment and Acceptance of industrial products (ACAA) with Israel. The Commission will reply in writing to a question concerning a revision clause in the ACAA.

Post meeting note in reply to the question concerning a revision clause in the ACAA:

Article 7 of the Protocol to the Euro-Mediterranean Agreement establishing an association between the European Communities and their Member States, of the one part, and the State of Israel, of the other part, on Conformity Assessment and Acceptance of Industrial Products (ACAA) states that the parties may discuss the amendments of the Annexes to this Protocol or conclusion of new ones if Israel aligns further its law with the EU law. This provision is not a revision clause but rather stipulates the conditions for the future expansion of the ACAA and the applicable procedure. Independently of Article 7, Section 2 of the Good Manufacturing Practice Annex of the ACAA stipulates that two years after the entry into force of the ACAA, the Parties should discuss the possibility of extension of the scope of that Annex to human blood and plasma derived products, investigational medicinal products and veterinary immunologicals.

iii. Transatlantic Trade and Investment Partnership

The Commission informed the Pharmaceutical Committee of the recent developments of Transatlantic Trade and Investment Partnership (TTIP) negotiations for the sector of medicinal products. A first exchange took place on the respective proposals of the EU and the US for legal text dedicated to the sector of medicinal products. Progress towards the development of a framework for mutual recognition of GMP inspections was also reported. The report of the round as well as the EU proposal for a legal text is made publicly available on the webpage of DG TRADE dedicated to the TTIP. The next round of negotiations is scheduled in July 2016.

6. AOB

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The next meeting of the Pharmaceutical Committee (human) is **tentatively** planned for **18 October 2016. No travel arrangements** should be made **until the final date is confirmed** by the Commission in September 2016**.**