EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 701

PHARMACEUTICAL COMMITTEE
21 October 2015
75th meeting

SUMMARY RECORD

The Pharmaceutical Committee held its 75th meeting on 21 October 2015, in Brussels, chaired by Sabine Jülicher, Head of Unit SANTE D5 - *Medicinal products – authorisations, EMA*.

Agenda

- **The draft agenda (PHARM 688) was adopted without changes.**

1. **Interpretation of Pharmaceutical legislation**
    - **1a) Court cases**

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

- Case E-16/14, judgment of 9 April 2015 (Intervet)
- Case T-452/14, judgment of 11 June 2015 (CTRS v Commission)
- Case C-544 and 545/13, judgment of 16 July 2015 (Abcur)
- Case T-472/12, judgment of 15 September 2015 (Novartis v Commission)

Additionally, reference was made to one pending case (C-276/15 – Hecht Pharma).

- **1b) 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 March 2015.

- **1c) Variations and the use of the Article 57 database**

Together with the European Medicines Agency the Commission informed the Committee about the state of play of the project to use the Article 57 database to update information about the Qualified Person for Pharmacovigilance (QPPV) and the Pharmacovigilance System Master File (PSMF). This administrative simplification, which would replace some type IA variations, is foreseen in the Commission guidelines on details of categories of variations.

The programming and the upgrade of the Article 57 database has been recently completed. Subject to confirmation by the Management Board of EMA in December that the Art 57 database is functional for the notification of QPPV and PSMF details, this new service will go live in the coming months. National competent authorities, who are supportive of the project, will have direct access to the information and have been informed by the EMA regarding its progress and training opportunities also through different fora. The roll-out of this new feature will be complemented by direct information/training to stakeholders.

2. **Implementation of Pharmaceutical legislation**
    - **2a) Written procedure of Standing Committee – Scientific accelerated procedure**

The Commission (COM) services proposed at the Pharmaceutical Committee meeting in October 2014, that in cases when the Committee for Human Medicinal Products (CHMP) has performed its assessment under the accelerated procedure in accordance with Article 14.9 of

regulation 726/2004, this would be highlighted by COM services when launching the written comitology procedure. COM services would then have the possibility to proceed with the decision making process without having to wait until the deadline of the procedure. It was underlined that this modus operandi implies that members would have to provide their position and would not refer to the tacit agreement (absence of answer within the deadline). It will be then at the discretion of all Member States to proceed in a shorter time with the decision making process by reducing the comitology consultation period.

A state of play was done at the Pharmaceutical Committee meeting of March 2015, where two procedures have been launched following this principle. Only 2 Member States gave a favourable opinion on the decision before the deadline. Since then, three other procedures were launched. However, only 2 to 5 Member States gave a favourable opinion on the decision before the deadline.

In view of this and the objective to accelerate access to medicinal products which are of major interest from the public health point of view, COM services propose to reduce to 10 days the written comitology procedure in compliance with Article 10.3 of Regulation 726/2004 (instead of 22 days). This will only apply to accelerated scientific assessment and implies that the tacit agreement will be applicable. As the pharmaceutical committee members were favourable to such approach, COM services will write to the Permanent representations/members of the Standing Committee on Medicinal Products for Human Use in order that this approach is endorsed.

In parallel to this, COM services will consider if it would be possible to further reduce the time associated with the decision making process at the Commission in order to support timely access of medicinal products which are of major interest from the point of view of public health.

- **2b) Review of the 2003 Communication on orphan medicinal product**

The Commission presented the proposals for the review of the 2003 communication on orphan medicinal products in particular:

- Facilitating the entry into the European market of innovative products with a significant benefit over existing products;

- Encouraging the development of orphan medicinal products for communicable diseases (e.g. Ebola);

- Simplifying the procedure for the reassessment of orphan criteria when two authorisation application procedures are running in parallel for two orphan medicinal products;

- 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;

- Clarification of the process when transferring an orphan designation between sponsors.

One Member State welcomed the proposed changes and confirmed that the orphan Regulation is very important for the European market but further improvements could be put in place in particular:

- Better defining the criterion of significant benefit;

- Better harmonising the definition of 'significant benefit' in the context of orphans and 'unmet medical needs' in the context of the conditional marketing authorisation;

- Reassessing the criteria of orphan designation after marketing authorisation not only for the significant benefit but also if the product becomes profitable.

➢ 2c) Specific GMP guidelines for Advanced Therapy Medicinal Products (ATMPs)

The Commission presented the initiative to develop the GMP guidelines specific to ATMPs as provided for under Article 5 of the ATMP Regulation. The Commission services evoked the specific characteristics of ATMP that warrant adaption of the general GMP requirements, as well as the need to reduce burdens, streamline and clarify requirements considering the fact that most developers are not traditional pharma companies and they are therefore not familiar with the GMP system.

The Commission services stressed, however, that the main guiding principle of the specific Guidelines for ATMPs should continue to be the protection of public health. A Member State questioned the need for this project and asked whether this was the only initiative that the Commission was going to take in connection with ATMPs. The need to ensure public health protection and cooperation with the inspectors was also highlighted. Another Member State expressed support for the initiative considering that it is important to introduce the risk-based approach, while - at the same time - assuring that sufficient details would be given to ensure proper enforcement by inspectors. The Commission services reassured the members of the Commission's commitment to protect public health and stressed the importance of putting together all expertise available in the MS both from the advanced therapy field and the inspector's side to finalise the guideline. Other initiatives to improve the regulatory environment for ATMPs were also explained.

➢ 2d) Feedback from the 2nd meeting of the Commission Expert Group on "Safe and Timely Access to Medicines for Patients" (STAMP)

The Commission services gave an update of the second and third meeting of the STAMP Expert Group which took place on 6 May and 20 October 2015. The STAMP discussed the conditional marketing authorisation and accelerated assessment procedure and possible ways to optimise their use. EMA gave an update on its pilot project on Adaptive Pathways.

EMA's new scheme to facilitate patient access to innovative medicines, called Priority Medicines (PRIME) was also discussed. The related reflection paper is under public consultation until 23 December 2015. More information can be found on EMA website.

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.

➢ 2e) Clinical Trials Regulation: update on the implementation

The Commission services gave an update on the ongoing activities related to the implementation of the Clinical Trials Regulation (CTR). The Committee was informed that the ad hoc group on clinical trials held two meetings - in April and in September - during which EMA gave an update on the progress of the development of the EU Portal and database – mainly regarding specifications concerning transparency. Work in this area was done in two steps. As a first step, EMA in collaboration with the Commission and the Member States (MS), prepared a document outlining the technical features of the Clinical Trial (CT) EU portal and database in relation to the publication of information, as a revision of section 6 of the functional specifications. EMA informed the ad hoc group in April that this document was endorsed by the EMA Management Board during the March meeting and was published on the EMA website.

During the meeting in September EMA gave an update on the second step, regarding the preparation of an addendum to the "Functional specifications for the EU portal and database to be audited", outlining the practical implementation of the transparency rules – that is, the rules and criteria of what documents and data would be published and at what time. The Commission services explained to the Committee that these rules, which were also prepared by EMA in collaboration with the Commission and the MS, will ensure access to the public of the content of the EU database but at the same time give the possibility for the sponsor to request a delayed publication of documents containing commercial confidential information (specific conditions and maximum time limits have been put in place for the various types of documents and types of trial).

The Committee was informed that the content of this addendum was subject to a large public consultation exercise. EMA also held meetings with different stakeholder groups (industry, patients, consumers groups, civil society representatives) during the various phases of development. The addendum was endorsed by the EMA Management Board during the October meeting and published on 6 October 2015.

Additionally, during the September ad hoc group meeting EMA gave an outline of the plan with timelines for the various milestones of the EU portal and database project. The Commission services explained that the plan of EMA is to have the system available for an independent audit by the end of the third quarter of 2016. If the portal and database get a green light from the audit, the Regulation will come into application by the end of 2017. These timelines are currently being discussed with MS.

The Commission services provided an update to the Committee on other topics discussed during the ad hoc group meeting, which were in relation to the procedures and the rules for the implementation of the Regulation. During both meetings the Commission services gave presentations to the group with the aim of clarifying and discussing with delegates certain outstanding issues that have arisen during discussions held with different groups. These included clarification of the possibility of a negative opinion by an Ethics Committee (art 8.4) and the extension of timelines, such as in the case of Advanced Therapy Medicinal Products (ATMPs).

Moreover the Commission services sought to understand during the ad hoc group meeting what MS consider to be "conditions", referred to in the CTR when a decision is issued stating that a Clinical Trial (CT) is "acceptable subject to compliance with specific conditions". Preliminary discussions were held on what MS consider to be tasks and responsibilities of a legal representative of a non-European Economic Area (EEA) sponsor.

Additionally discussions were held with the ad hoc group on a number of priority Questions and Answers (Q&As), the outcome of which would have an impact on the structure of the EU portal and database. This included discussions on:

- the processes that can occur after the end of a trial: e.g. the possibility of a MS taking a corrective measure;
- the timing of the submission of interim and sub-study results; and
- which scientific reasons would allow the extension of the time for publication of the summary of results.

The Committee was informed that as part of the ongoing update of the Q&A document, the Commission asked for volunteers from the ad hoc group to form task groups to provide their expertise to review and update certain sections. The aim is to start work in Q1 2016. Some MS have already indicated their interest. The Commission services would greatly appreciate the support of other MS.

As a further update on the ad hoc group, the Committee was informed that a presentation, which was prepared by the Clinical Trials Facilitation Group (CTFG), was given in April regarding the criteria for the selection of the Reporting Member State (RMS) during validation period. Additionally in the September meeting presentations on Good Laboratory Practice (GLP) principles, also related to ATMPs, were given by colleagues from DG GROW (D2) and DG SANTE (D5). The current statement on GLP available on Heads of Agencies (HMA) websites will be updated, taking into consideration the particular case of ATMPs and will also be included in the Q&A.

Additionally, during the ad hoc meeting in September an update was given by three lead Member States (DE, NL, UK) on the progress of the ongoing work on the update of two existing guidelines and on the preparation of two new ones, which fall under the responsibility of the ad hoc group.

The Committee was informed that the Commission services still continue to closely follow the work of other bodies and groups involved in the preparation of the implementation of the new Regulation, such as:

- the various EMA working groups (Good Clinical Practice Inspectors Working Group (GCP IWG), Good Manufacturing and Distribution Practice (GMDP) IWG, Committee for Advanced Therapy Medicinal Products (CAT) etc.),
- the Clinical trials Facilitation Group (CTFG), and
- the EU Clinical Trials Regulation Coordination Group.

The Commission services are also steering the process for the update of the related guidelines (e.g. those in Eudralex) as well as for the preparation of new guidelines.

The Commission services reminded those Member States who did not yet inform the Commission of the national contact point for the facilitation of the functioning of the procedures related to the CTR (Art 83 of the Regulation), to send this information to the Commission as soon as possible. As mentioned previously, the contact point will also be the member of the Clinical Trials Advisory Group (CTAG) (art 85 of the Regulation).

A Member State asked the Commission services to confirm that the finalisation of the EU Portal and database is set for December 2017, as this is relevant for the application of the legislation nationally. Commission services stated that EMA will launch the independent audit by the end of the third quarter of 2016, which will take around 4 months. Once the EMA Management board verifies that full functionality of the EU portal and database has been achieved, it will inform the Commission who will publish a notice in the Official Journal once the latter is satisfied that the conditions have been fulfilled. The Regulation would come into application 6 months later. Considering the time required for these requirements it is envisaged that this will happen at the end of 2017. The Commission services stated that they have no indication from EMA that this will be further delayed. EMA has set contingency plans within their timelines. They will carry out user acceptance testing to ensure the needs of the Member States are taken into account. Additionally a workshop for IT Directors of MS was held on the 21 October in order to start preparations for setting up the IT system in MS.

- **2f) Falsified Medicines Directive: update on the implementation**

The Commission started by reminding Bulgaria, France, Greece, Luxembourg and Slovenia of their legal obligation to notify the Commission 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.

Concerning the safety features for the identification and authentication of medicinal products, it was mentioned that the delegated Regulation on the safety features was adopted – together with the relative impact assessment – on 2 October 2015 and is currently undergoing scrutiny by the European Parliament and the Council. If no objections are raised, publication is expected by mid-February 2016.

A Member State asked whether the Commission is planning to facilitate the exchange of information and best practices among Member States on the implementation of the new rules on the safety features. The Commission confirmed that such exchanges could take place within the framework of the expert group on the safety features, and that meetings of the expert group will be organised throughout the implementation phase of the new rules.

Concerning the importation of active substances (APIs), the Commission communicated that:

(1) in July 2015, Brazil and Israel were added to the list of countries having a legislative/regulatory framework for APIs equivalent to that of the EU;

(2) the assessment of New Zealand and South Korea are still ongoing;

(3) Finland 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 the proposed changes to the Question n°3 of the Q&A document on API importation. The change aims at clarifying the requirements in case of importation of active substances to be used in the manufacture of authorised medicinal products intended for research and development trials. Comments are requested by 15 November 2015.

Concerning the delegated Regulation on GMP for APIs, the Commission informed that the Polish, French and German corrigenda were published in the Official Journal.

Concerning the logo for online pharmacies, the Commission reminded that Article 85c of Directive 2001/83/EC of the European Parliament and of the Council is fully applicable in all Member States as from 1 July 2015. As a consequence, each legally operating on-line retailer of the medicinal products should display on every page of his/her website the common logo established by the Commission Implementing Regulation (EU) No 699/2014 on the design of the common logo to identify persons offering medicinal products for sale at a distance to the public and the technical, electronic and cryptographic requirements for verification of its authenticity.

The Commission informed that almost all Member States have signed the licence agreement for the use of logo. The Commission recalled that the signature of the licence agreement is a prerequisite for the correct implementation of the provisions on the common logo since the common logo is a registered trademark on behalf of the European Commission. The Commission urged two outstanding countries, namely Romania and Greece, to proceed in order to arrange for the signature.

The Commission stressed as well that in order to fully comply with the requirements established in the legislation, the Member States should ensure that the hyperlinks between the online logo and the national list of the persons offering the medicinal products for sale at a distance to the public by means of information society services are permanent and secured. Furthermore the websites hosting those national lists have to be secured and hosted on trusted domains.

The European Commission invited the Member States to inform about the national information campaigns, mentioned in Article 85d of Directive 2001/83/EC, they are conducting or they plan to conduct.

Finally, EMA provided an update to the Pharmaceutical Committee on the EMA deliverables completed since the last Pharmaceutical Committee.

In accordance with Article 85c(5) of Directive 2001/83/EC, the Agency website was amended to add a dedicated webpage on falsified medicinal products. This new page was launched on 1 July 2015. It provides information on the EU common logo to be displayed on the websites of

authorised on-line medicines retailers and provide a list with the links to the Member States' dedicated websites.

In line with Articles 111(6) and (7), 524(7), 77(4), 40(4), 111a of Directive 2001/83/EC, EudraGMDP database was extended since April 2013 to accommodate new information required by the falsified medicines Directive (i.e. Good Distribution Practices (GDP) certificates, wholesale authorisations and active substance manufacturers, importers and distributor registration). To date, Member States have populated the new EudraGMDP modules with:

- Over 6600 wholesale distribution authorisations

- Over 4000 GDP certificates

- Over 1000 active substances manufacturer registrations.

Post-meeting note: Poland communicated to the Commission its intention to use the waiver referred to in Article 46(b)(4) of Directive 2001/83/EC.

3. Pharmacovigilance

➢ 3a) Report on the performance of pharmacovigilance tasks by the Member States

The Commission thanked the Member States for the information they had provided for the preparation of the report on the performance of pharmacovigilance tasks by the Member States and the European Medicines Agency. The publication is expected to be early in 2016.

➢ 3b) Reports of Member States pharmacovigilance audits

The Commission presented an overview of Member States biennial reports on audits of their pharmacovigilance systems for the 2013 reporting year (Pharma 693). The Commission thanked the Member States for the prompt submission of the 2015 reports and would report on these in a future meeting.

4. Legislative Issues

➢ Paediatrics

The Commission reported on its planning for the 2nd report to the European Parliament and the Council on the Paediatric Regulation, which is due in 2017. Since the last report in 2013, further promising signs have been noted regarding the impact the Regulation had on better medicines for children. For example, the number of completed paediatric investigation plans has increased in 2014 to over 30 per year.

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 2016 as well as a workshop between the US Food and Drug Administration (FDA) and EU to exchange views on the paediatric regulatory framework and the experience with paediatric legislation.

The Pharmaceutical Committee itself will be again updated on the progress of the preparatory work at the next meeting in 2016.

5. International Developments

- **5a) Update on multilateral collaborations:**

The reform of the International Conference for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH)

The Commission informed the Committee that the reform of ICH that was launched four years ago was about to be completed. Considering the importance of ICH for international harmonisation of guidelines for the authorisation of medicinal products, this is a major development in the field of international collaboration on medicinal products. Detailed information on the different aspects of the reform which results in improved governance and increased involvement of key regulatory authorities and concerned pharmaceutical industry organisations was provided.

The establishment of ICH as a legal entity (non-profit Association under Swiss law) was due to take place on 23 October 2015. The first face-to-face meeting of the new Association will take place on 5-10 December 2015 in Jacksonville, USA. The Commission, as a founding member of ICH, will continue, with the support of the European Medicines Agency (EMA), to play a leading role in the further development of ICH activities.

International Pharmaceutical Regulators Forum (IPRF)

The objectives of IPRF are to provide an environment for exchange of information amongst pharmaceutical regulators, for regulatory cooperation as well as to ensure pragmatic coordination of existing initiatives (avoid overlaps).

The IPRF has currently established working groups on the following specific topics: Gene Therapy, Cell Therapy Biosimilars, Nanomedicines.

The developments of the organisation, notably regarding how IPRF members could contribute to secretariat activities as well as the links between IPRF and IGDRP (International Drug Regulatory Program) and ICMRA (International Coalition of Medicine Regulatory Authorities), will be discussed at the next IPRF meeting that will take place on 7-8 December 2015 in Jacksonville, USA.

- **5b) Update on bilateral negotiations**

The Commission provided a state-of-play of the Transatlantic Trade and Investment Partnership (TTIP) negotiations on the pharmaceutical sector after the 11th round that took place during the weeks of 12 and 19 October 2015. The presentation focused on recent developments with respect to the objective of establishing mutual recognition of Good Manufacturing Practice (GMP) inspections and the preparation of an EU submission on collaboration on generics.

The FDA and EU are making good progress on collecting information on respective GMP inspection systems. This is mainly achieved through the attendance of FDA as observer to the audits of Member State inspectorates that are organised in the framework of the Joint Audit Program (JAP). Similarly, an EU team carried out an audit of FDA in September 2015. Equivalence of conflicts of interest rules and the possibility to exchange inspection reports that include confidential information and trade secrets are two important elements to enable this collaboration.

The Commission introduced a draft EU submission (under the format of a technical paper) identifying opportunities for further EU-US collaboration and regulatory convergence with respect to generics. The overall objective of the technical paper is to create conditions that facilitate timely access to generic medicines and avoid unnecessary duplication of clinical trials and the associated exposure of human subjects. The draft technical paper identifies more specifically three types of opportunities:

- development of further collaboration in the context of the International Drug Regulatory Program (IGDRP),
- harmonisation of BCS (Biopharmaceutics Classification System)-based biowaivers, and
- harmonisation of clinical data requirements for products subject to hybrid applications**.**

The Pharmaceutical Committee was informed that Member States will be formally consulted on this technical paper in view of a submission in the framework of TTIP prior to the next round of negotiations.

The Pharmaceutical Committee welcomed the regular updates provided by the Commission on the TTIP negotiations for pharmaceutical sector. The Committee also indicated its interest to receive during one of its next meetings broader information on these negotiations and in particular on non-sectorial aspects, such as health services and regulatory cooperation that are of relevance for pharmaceuticals.

The Commission provided also an update on the ongoing negotiations with Free Trade Agreement negotiations with Japan as well as on the contacts with Canada related to the inclusion of the existing Mutual Recognition Agreement (MRA) in the Comprehensive Economic and Trade Agreement (CETA).

The Pharmaceutical Committee was informed that the Commission and EMA have concluded during summer 2015 confidentiality arrangements with Swissmedic and with the World Health Organisation (WHO). These two Confidentiality Arrangements will enable the sharing

of confidential information on the quality, safety and efficacy of medicines for human and animal use, further enhancing the relationship with these Parties in the interest of public health. The Arrangements foresee that information received from Swissmedic/WHO may be shared with Member States.

6. AOB

- **6a) Summary of comments to the study reports on the Patient Information Leaflet (PIL) and the Summary of Product Characteristics (SmPC)**

The Commission services presented the summary of comments of the Pharmaceutical Committee to the external study reports on the Patient Information Leaflet and the Summary of product characteristics, informing that some Member States have expressed willingness to contribute to further improvement of product information. The Committee members were reminded that the external study reports, the individual comments and the summary of comments will be published on the web page of the Committee.

- **6b) Biosimilars: World Health Organisation (WHO) Biological Qualifier**

A brief update was given on the developments of the WHO Biological Qualifier since October 2014, focusing on the revised proposal for the Biological Qualifier published in June 2015. The Pharmaceutical Committee was informed that at the previous week's meeting of the WHO INN Expert Group, the proposal for the Biological Qualifier was finalised and recommended to the WHO to consider its implementation. However, there was no indication of timing of next stages regarding future implementation of the Biological Qualifier.

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The next meeting of the Pharmaceutical Committee (human) is **tentatively** planned for **28 April 2016. No travel arrangements should be made until the final date is confirmed by the Commission in March 2016.**