EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems and products
Medicinal products – authorisations, EMA

PHARM 687

PHARMACEUTICAL COMMITTEE
17 March 2015
74th meeting

SUMMARY RECORD

The Pharmaceutical Committee held its 74th meeting on 17 March 2015, in Brussels, chaired by Sabine Jülicher, Head of Unit SANTE D5 - *Medicinal products – authorisations, EMA*.

Agenda

- **The draft agenda (PHARM 677) was adopted, after accepting the request to table an additional point under AOB (see request AOB 5c).**

1. Interpretation of Pharmaceutical legislation

➢ 1a) Update on the study of off-label use

The Commission services informed that on 16 December 2014, the request for Specific Services № CHAFEA/2014/Health/27 for the implementation of Framework Contract № EAHC/2013/Health/01 - lot 1 Health reports - for the provision of a study on off-label use of medicinal products in the European Union has been sent by the Consumers, Health and Food Executive Agency (CHAFEA) to the service providers of the framework contract. The Commission services have selected one offer. The study should commence in April 2015, for a maximum duration of 14 months. Although the way the work will be performed should be finalised with the contractor, it was mentioned that it is requested to involve stakeholders such as patients, healthcare professionals, Member States (responsible for marketing authorisation and for prices and reimbursements) and the pharmaceutical industry.

The first part of the study will consist in collecting information, which will then be confronted (brainstorming method). The study will also include a legal analysis.

Members of the committee were asked to support the contractor in collecting information and identifying relevant contacts at national level. Lastly it was explained that the consultant will not provide recommendations, but a state of play, for further discussion with Member States.

Post meeting note: The study will be 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), a platform of non-governmental organisations working in the area of public health in Europe.

➢ 1b) On-going cases

The Commission services called the 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-104/13, judgment of 23 October 2014 (Olainfarm).

➢ 1c) Legal and Regulatory News (new pieces of legislation, COM guidelines)

The Committee was informed about new regulatory acts and Commission Guidelines that have been adopted since the last Pharmaceutical Committee held in October 2014.

➢ 1d) The use of registries in the context of marketing authorisations: experiences and legal framework

The Commission services addressed the legal status of registries that are imposed as post-marketing obligations. It was noted that the definitions of low intervention clinical trial and non-interventional study under the Clinical Trials Regulation (EU) No 536/2014 of the European Parliament and of the Council provide for some margin of interpretation. In this scenario, it becomes very important to look at the consequences of regulating such registries under the clinical trials regulation (risk of contradictory decisions, excessive burden for the

Marketing Authorisation Holder (MAH), different reporting channels, etc.). The Commission services called for a common approach by all Member States on this issue.

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 when the Committee for Human Medicinal Products (CHMP) has performed its assessment under the accelerated procedure, this would be highlighted by COM services when launching the comitology phase. 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. Since then, two procedures have been launched following this principle. Only 2 Member States have given a favourable opinion on the decision before the deadline.

Commission services called the attention of Member States on this matter and proposed to debrief at the next Pharmaceutical Committee and on this basis discuss the way forward.

➢ 2b) Feedback from the 1st meeting of the Commission Expert Group on "Safe and Timely Access to Medicines for Patients"

A summary of the topics discussed in the first meeting of the Commission expert group on Safe and Timely Access to Medicines for Patients (STAMP) was presented to the Pharmaceutical Committee. The first meeting of the STAMP took place on 27 January 2015 with the participation of experts from 23 Member States and from the European Medicines Agency (EMA).

The mandate of the expert group was presented in detail. The STAMP will discuss experience acquired so far with the implementation of the EU legislation and national initiatives with the aim to identify ways to optimise the use of existing regulatory tools. This is expected to further improve timely and safe access and availability of medicines for patients. The pilot project on adaptive pathways carried out by the EMA will be part of this discussion. Since the issue of timely access to innovative medicines is strongly linked to pricing and reimbursement decisions, it was agreed that synergies should be created with other fora dealing with these issues, such as the Health Technology Assessment (HTA) network and the Network of Competent Authorities on Pricing and Reimbursement (CAPR).

Moreover, three Member States (BE, FR, ES) have presented to STAMP their national routes for making medicines available before authorisation. The STAMP also discussed the developments as regards EMA's pilot project on adaptive pathways and the experience with conditional marketing authorisation and accelerated assessment. Finally, it identified several

points to be discussed and addressed in the future with the aim to optimise the use of these regulatory tools.

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

The Commission services gave an update on the progress of the work with respect to the implementation of the Clinical Trials Regulation. It was stated that two working documents have been drafted:

- detailed arrangements for inspection procedures including qualification and training requirements of inspector, in preparation for an Implementing Regulation by the Commission and

- Good Manufacturing Practices for Investigational Medicinal Products, in preparation for a Delegated Regulation by the Commission.

Both working documents have been updated following comments received from the ad hoc group for Clinical Trials. In addition the Good Clinical Practice Inspectors Working Group (GCP IWG) and Good Manufacturing Practice/Good Distribution Practice Inspectors Working Group (GMP/GDP IWG) of EMA are currently being consulted on both working documents.

The committee was also informed about the ongoing work with the ad hoc group, such as clarifications on certain issues regarding procedures and rules related to the implementation of the Regulation. In addition it was explained that new guidelines are being prepared and existing guidelines are being updated. In this respect Member States were asked to contribute to the update of the Q&A document.

Member States (MS) were reminded to inform the Commission as soon as possible of the contact point for the facilitation of the functioning of the procedures related to the Clinical Trials Regulation (Art 83), who will also be the member on the Clinical Trials Advisory Group (CTAG) (Art 85 of the Regulation).

Member States should also be prepared for the implementation of the Regulation at national level with respect to the legal environment, preparation of IT requirements, including the interface with the EU Portal as well as the internal organisation and liaison with ethics committees.

A Member State asked about access to documents within the EU Clinical Ttrial (CT) Portal and database. The Commission explained that MS who are not concerned with a particular CT cannot receive nor have access to documentation related to it. MS will be able to search for certain information on a Clinical Trial in the database, which will also be made public. However, sharing of documents is possible only outside the database. In this respect, MS can continue to follow their current procedures on the management of documents they have access to. Member States remain responsible for any exchange of documents between themselves.

Another Member State asked about the legal status of the Commission Directive 2003/94/EC on GMP once the Delegated Act on GMP for Investigational Medicinal Products (IMP) is applicable and of Annex 13 of the GMP guidelines. The Commission explained that Directive 2003/94/EC will be repealed and replaced with a new implementing directive covering only GMP for finished products. Annex 13 will be replaced with a new guideline on GMP for IMPs that will be adopted and published by the Commission.

Member State representatives asked for the expected date of completion of the EU Clinical Trial Portal and consequently of the applicability date of the Regulation. The Commission representative explained that EMA is currently preparing the business requirements for the development of the EU Portal and database. In order to determine the underlying principles concerning the transparency of the EU database, EMA had published for consultation a document where different possible scenarios were presented. EMA is currently reviewing the received feedback to proceed to set out the rules and criteria in collaboration with COM and MS, in order to be able to start the IT development of the portal and database. The Commission added that EMA tentatively indicated the applicability date to be beginning of 2017.

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

The Commission informed the Member States representatives of the closure of all infringement procedures for non-transposition of the Directive 2011/62/EU of the European Parliament and of the Council with the exception of one, for which a decision will be taken shortly.

The Commission also requested the 10 Member States who still have not notified the Commission of their national systems for the receipt and handling of notifications of suspected falsified medicinal products and quality defects, in accordance with Article 117a of Directive 2001/83/EC of the European Parliament and of the Council, to do so as soon as possible – the notifications being overdue by almost 2 years.

The Commission presented an overview of work on the different implementation measures of the Falsified Medicines Directive under its responsibility. The adoption of the delegated act on the detailed rules for the safety features of medicinal products for human use is planned by July 2015, and its publication in the Official Journal by the fourth quarter of 2015.

The Guidelines on "principles of good distribution practices for active substances" and on "the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients" are to be adopted and published by the end of March 2015 (post-meeting note: they were published in the Official Journal of the European Union on 21 March 2015[1]).

With regard to active substances, the Commission also informed on the progress of the equivalence assessments of Brazil, Israel, New Zealand and South Korea.

EMA informed on implementation measures under its responsibility, namely:

[1] C 95, 21 March 2015, p.1, p.10, http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:C:2015:095:TOC

- the extension of the Community database on manufacturing, import and wholesale-distribution authorisations, and good manufacturing-practice and good-distribution-practice (EudraGMDP) to accommodate the submission by Member States of the additional information required by the Falsified Medicines Directive,

- the sharing of information on GDP inspection and planned GMP inspections, and

- the coordination of inspections in third countries.

Finland informed the Commission that they will send in their Article 117a notification shortly.

➢ 2e) Falsified Medicines Directive: update on the common logo for online pharmacies

The Commission representatives clarified that the common logo will have to be used by any natural or legal person offering medicinal products for sale at a distance to the public by means of information society services, in accordance with national legislation, not only by online pharmacies.

It was reminded that Article 85c of Directive 2001/83/EC of the European Parliament and of the Council will become fully applicable in all Member States as from 1 July 2015.

In addition, the online logo, established with the Commission Implementing Regulation (EU) No 699/2014, has been protected by copyright by the Commission. The Member States that have not yet signed or initiated the procedure to sign the license agreement for the use of the logo were invited to proceed as soon as possible. The trademark protection will allow Member States to use also the trademark law and not only the pharmaceutical legislation to enforce unauthorised use of the logo.

Some Member States informed the Commission that they are consulting their legal departments on the text of the license agreement; others indicated that they are verifying internally who should sign it.

One Member State representative requested feedback from other Member States on how health inspectorates plan to enforce trademark law. The Commission reminded that the enforcement of trademark law may well be carried out by bodies other than health inspectorates.

One Member State requested details on which medicinal products can be sold to a patient in one Member State from an online retailer of medicinal products situated in another Member State. The Commission representative explained that this is covered by Article 85c (1) (c) of Directive 2001/83/EC. To ensure a coherent application of such provision in all Member States, an exchange of views is ongoing in the framework of the Heads of Medicines Agencies (HMA) taskforce on the implementation of the Falsified Medicines Directive and of the HMA Working Group of Enforcement Officers (WGEO).

➢ 2f) Forthcoming activities on orphan medicinal products

The Commission presented the forthcoming activities on the orphan legislation. As far as the revision of the Commission Communication is concerned, the Member States are invited to provide suggestions for the review by mid-April. As far as the updated version of the inventory of incentives is concerned, the Commission will send a letter in the coming weeks to collect information on the incentives available in the Member States.

➢ 2g) Update on activities regarding Advanced Therapy Medicinal Products (ATPMs)

The latest developments on ATMPs were presented both at European Union (EU) and international level. At the level of the EU, no decision has been taken on a possible review of the ATMP Regulation but work is ongoing to further exploit the flexibilities that exist under the current legal framework.

At international level, reference was made to:

- the Council of Europe draft Guide to the Quality and Safety of Tissues and Cells for Human Application (second edition)
- the WHO projects on International Nonproprietary Names (INNs) or ATMPs, on the regulation of ATMPs (16th International Conference of Drug Regulatory Authorities (ICDRA) recommendations), and
- a draft Decision on Medicinal Products of Human Origin.

Member States were encouraged to follow these developments. Finally, Member States were also encouraged to follow the Council discussions on the scope of the new rules on medical devices, having particular regard to the impact on the application of the authorisation system for combination ATMPs foreseen under the ATMP Regulation.

3. Pharmacovigilance

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

The Commission updated the Committee on the data collection for the report on the performance of pharmacovigilance tasks by the Member States and the European Medicines Agency. In the first instance information would be collated through existing sources such as the European Medicines Agency and the Strengthening Collaboration for Operating Pharmacovigilance in Europe Joint Action. Member States would be contacted for additional information if necessary.

- **3b) Reports of Member States pharmacovigilance audits**

The Commission informed the Committee that a draft document giving an overview of the 2013 reports of the Member States' audit of their pharmacovigilance systems had been circulated to the relevant contact persons in the Member States. The comments received would be taken into consideration during the finalisation of the report.

4. International Developments

- **4a) International Conference for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH)**

The Commission gave a presentation about the state of play regarding the ongoing reform of ICH. The ICH meeting in Lisbon (8-13 November 2014) allowed reaching agreement on the future organisation of ICH. The Assembly will be the overarching body of the Association taking important decisions such as amendments to the Statutes as well as decisions to adopt ICH guidelines. A Management Committee will oversee operational aspects on behalf of all members of the Association and be primarily responsible for administrative and financial matters. Eligibility criteria as well as rights and obligations associated with the different types of membership and observership have been defined. A new ICH legal entity of which the Commission is due to be a founding member will be established. The ICH reform is expected to be fully completed by January 2016.

- **4b) Update on the Transatlantic Trade and Investment Partnership (TTIP)**

The Committee was informed of the main developments of the ongoing negotiations with the United States in the framework of the Transatlantic Trade and Investment Partnership (TTIP) for the sector of medicinal products. The objective of Mutual Recognition of GMP inspections has the highest priority. The organisation of the ongoing work on this matter and the relation between the TTIP and the Mutual Reliance Initiative allowing intensive technical exchanges amongst competent authorities was presented. A short term objective is to facilitate the exchange of GMP inspection reports containing confidential information.

The Committee was also informed on recent developments regarding Biosimilars as well as on the other regulatory topics that are currently under consideration in the TTIP.

5. AOB

- **5a) Presentation on the joint procurement agreement for medical counter-measures**

The joint procurement mechanism put in place according to Article 5 of European Parliament and Council Decision 1082/2013/EU on serious cross-border threats to health was presented. The state of play was described in the supporting document number 685.

With regard to a question on the pandemic vaccine joint procurement, it was explained that it is only possible, at this stage of Member States approval/ratification process, for those 18

Member States having fully approved/ratified the Joint Procurement Agreement to fully participate to a procurement procedure organised under the Joint Procurement. In general, 24 Member States confirmed interest in participating to the pandemic vaccine joint procurement.

It was also clarified that the Joint Procurement Agreement is only applicable within the remit of Decision 1082/2013/EU, which does not include veterinary medicines.

- **5b) 50 years of pharmaceutical legislation: communication activities and events**

The Committee members were informed that the European Commission is organising a conference to celebrate the 50th anniversary of the adoption of the first legislation on EU pharmaceutical legislation (Council Directive 65/65/EEC) in 1965. The conference will take place in Brussels on 28 September. It will provide an opportunity to highlight the achievements of the past 50 years while looking at the present and future role of EU pharmaceutical legislation in protecting the health of citizens in the EU and in the world and in promoting advance in science, innovation and public health.

- **5c) Request by one Member State regarding the applicability of Article 10.2 of Regulation 726/2004 in case of variations**

The Commission services explained that in application of Article 16(4) of Regulation (EC) No 726/2004 of the European Parliament and of the Council, the Commission Regulation (EC) 1234/2008 was adopted on 24 November 2008 concerning the examination of variations to the terms of marketing authorisation for medicinal products. This regulation (as its predecessor Commission Regulation (EC) No 1085/2003 and contrary to the initial Commission Regulation (EC) 542/1995) does not refer to the comitology procedure in case of variation. This explains why the Commission services do not launch a comitology procedure when varying marketing authorisations for centrally authorised medicinal products. This situation is described in Chapter 6 of the Notice to Applicants.

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The next meeting of the Pharmaceutical Committee (human) is **tentatively** planned for 21 October **2015. No travel arrangements should be made until the final date is confirmed by the Commission in September 2015.**