



EUROPEAN COMMISSION  
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

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

PHARM 742

**PHARMACEUTICAL COMMITTEE**  
**27 October 2017**

**79<sup>th</sup> meeting**

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SUMMARY RECORD

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The Pharmaceutical Committee held its 79<sup>th</sup> meeting on 27 October 2017, in Brussels, chaired by Olga Solomon, Head of Unit SANTE B5 – *Medicines: policy, authorisation and monitoring*.

**Agenda**

- **The draft agenda (PHARM 733) was adopted.**

## **i. INTERPRETATION OF PHARMACEUTICAL LEGISLATION**

### **i. Update on Court cases**

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

- Joined Cases C-629/15P and C-630/15P, judgments of 28 June 2017 (global marketing authorisation concept)
- Case C-621/15, judgment of 21 June 2017 (liability for medicinal products)
- Additionally, reference was made to some pending cases, including case T-191/17 (therapeutic indication of a centrally authorised product).

### **ii. Legal and Regulatory news**

The Committee was informed about new regulatory acts and Commission reports that have been adopted since the last Pharmaceutical Committee held in March 2017.

## **2. IMPLEMENTATION OF PHARMACEUTICAL LEGISLATION**

### **i. Falsified Medicines Directive – Update on the implementation of the safety features (medicine traceability)**

The Commission shared with the Committee the state of play of the implementation of the safety features and the new medicine verification system which will become applicable as of February 2019. In particular, the Commission informed Member States of delays in the setting up of the repositories system, in particular the creation of national medicines verification organisations and the signature of the IT contracts for the infrastructures; good progress in the discussion between the European Medicines Verification Organisation (EMVO) and the Member States concerning the national competent authorities' access to the repositories system; and difficulties with regard the preparedness of hospitals (lack of budget plans for the required equipment/resources) and the regulatory implementation of the safety features by marketing authorisation holders.

In the discussion which followed, one Member State asked about a possible postponement of the application of the new rules, which the Commission confirmed was legally not possible. Another Member State pointed out that the future system is not a medicine traceability system and should not be referred to as such, whilst another Member State stressed that the slow set up of National Medicines Verification Organisation is also due to the flat fee model chosen by the EMVO: it is too penalising for smaller players, which are therefore reluctant to join. The Member State further asked whether vaccination centres needed to decommission the safety features, which the Commission tentatively confirmed but advised Member State to send the question in writing with more details on the Member State's supply for a more informed reply.

## **ii. Draft Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products**

The Commission addressed the comments received during the consultation period. One Member State maintained objections to the document, in particular regarding the risk of double standards and the style of the document (lack of sufficient precision), the provisions on out of specification products, manufacturing at the operation theatre, and the quality of air requirements for first-in-man trials.

In connection with the risk of double standards, the Commission explained that ATMP manufacturers will not be confronted to different standards because the guidelines constitute a comprehensive framework for Advanced Therapy Medicinal Products (ATMPs). It was recalled that during the drafting process there has been a detailed analysis of the general Good Manufacturing Practice (GMP) Guidelines and that adaptations have been made as necessary. Comments on style were also addressed and specifically it was shown that the language of the text does not differ from the language used in the general GMP guidelines. On the legal concerns raised regarding out of specification products and manufacturing in the operation theatre the Commission explained that the text of the guidelines is consistent with current legal framework. Finally, regarding quality of air requirements, the Commission stressed that the conditions foreseen permit Member States to disagree if they consider that trials should not be conducted with products manufactured in A/C. In connection with the concern that this approach will lead to dis-harmonisation, the Commission explained that first-in-man trials are typically limited to one Member State. Moreover, in case a Member State disagrees, the clinical trial would not be conducted in its territory but would be no effect on free-movement of ATMPs. It was also recalled that several consultations had been made to the committee regarding this question and that the proposal had been accepted by 27 Member States.

Another Member State considered that it is important that the Guidelines can be updated within appropriate timelines. The Commission agreed on the need to keep the field under monitoring so as to ensure that document can be updated to take into account technological changes or new knowledge on risks.

Having regard to the outcome of the consultation process and the discussion at the Committee, the Commission announced that the Guidelines will be adopted and published in Eudralex.

It was agreed to allow for a maximum period of 6 months before the application of the document in the understanding that Member States that are ready should be able to apply it earlier.

## **iii. Feedback from 7<sup>th</sup> meeting of the Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP)**

The Commission presented an update on the 7th meeting of the STAMP which had taken place on 27 June 2017. The meeting included continuation of the discussion on the compassionate use of medicinal product as well as the repurposing of established medicines/active substances, for which it was agreed that there should be an examination of case studies to identify best practices. There were presentations and updates on the United States 21st Century Cures Act; the first years' experience of the PRIME (PRiority

Medicines) scheme; and the ad hoc Synergy Group of health technology assessment and regulatory bodies.

Related documents and presentations can be found on the webpage of the STAMP Expert Group:

[http://ec.europa.eu/health/documents/pharmaceutical-committee/stamp/index\\_en.htm](http://ec.europa.eu/health/documents/pharmaceutical-committee/stamp/index_en.htm).

**iv. Report on use of additional monitoring list – experience of Member States**

Following the discussion in the 27 March 2017 meeting it had been agreed that the European Medicines Agency (EMA) and the Member States would provide a joint submission to the Commission on their experience of the use of the additional monitoring list. The EMA presented the activities which had been initiated to collect relevant information. The Committee was consulted on the process for the finalisation and endorsement of the joint EMA/Member States submission. It was agreed that it should be a joint EMA/Heads of Medicines Agency submission.

**v. Members States' reports on the audits of their pharmacovigilance systems**

The majority of Member States had submitted a report on the audit activities of their pharmaceutical systems covering the 2015 – 2017 reporting period. The Commission thanked the Member States for the prompt submission of the reports and asked that the Member States who had not already done so to send their reports as soon as possible.

### 3. LEGISLATIVE ISSUES

#### i. Update on the Paediatric Report

The Commission highlighted some of the key results and conclusions of the recently published Commission Report on the Paediatric Regulation. This included the increase in authorised medicines and paediatric research, but also secondary effects such as increased involvement of patients in discussions about medicine development. At the same time, some of the weaknesses and the results of the economic impact study were highlighted too.

The Commission also explained the relation between the economic study on the impact of the pharmaceutical incentives (currently being carried out by DG SANTE and DG GROW), the 2017 Paediatric Report and a complementary study focused on orphans which will be conducted in 2018. On the basis of the results of these three studies, the Commission will evaluate the Orphan and Paediatrics Regulations.

The Evaluation Roadmap will be published before the end 2017 for a 4-week public consultation. As part of this evaluation process various stakeholders will also be consulted further in 2018.

#### ii. Commission's Report on Product Information Leaflets and related activities

The Commission provided a follow up activities on the Commission assessment report that was adopted on 22 March 2017<sup>1</sup> on current shortcomings in the summary of product characteristics (SmPC) and the package leaflet (PL). The report identified a number of recommendations on how to improve them in order to better meet the need of patients and healthcare professionals.

The EMA representative presented the EMA Action Plan<sup>2</sup> that was prepared on the basis of the Commission report for the implementation of the recommendations of the report with outlined priorities and indicative timelines. The highest priority is given to the activity on electronic PL formats, which will start in 2017<sup>3</sup>. Other actions will be initiated based on available resources in EMA. The overall implementation will be in close collaboration with National Competent Authorities and relevant stakeholders.

#### iii. Planned study on centralised and decentralised marketing authorisation procedures

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<sup>1</sup> Commission report on product information leaflets

[https://ec.europa.eu/health/sites/health/files/files/documents/2017\\_03\\_report\\_smpc-pl\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/documents/2017_03_report_smpc-pl_en.pdf)

<sup>2</sup> EMA Action Plan in relations to the Commission report on product information leaflets

[https://ec.europa.eu/health/sites/health/files/files/committee/pharm740\\_3ii\\_report-on-pil-and-ema-action-plan\\_0.pdf](https://ec.europa.eu/health/sites/health/files/files/committee/pharm740_3ii_report-on-pil-and-ema-action-plan_0.pdf)

<sup>3</sup> *Post-meeting note: EMA has initiated a survey* on the initiatives on electronic/digital formats for the product information leaflets by the end of February 2018

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2017/11/news\\_detail\\_002853.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/11/news_detail_002853.jsp)

The Commission presented the purpose and indicative timelines for the planned study on centralised and decentralised marketing authorisation procedures. The external study should be conducted in 2018. Once completed, results of this external study will provide evidence for the Commission Report to the European Parliament and the Council on the experience acquired with the operation of the centralised and decentralised marketing authorisation procedures. The report should be adopted before the end of 2019.

#### **iv. Adoption of GMP package**

The Commission Delegated Regulation (EU) 2017/1569 of 23 May 2017 supplementing Regulation (EU) No 536/2014 of the European Parliament and of the Council by specifying principles of and guidelines for GMP for Investigational Medicinal Products (IMP) for human use and arrangements for inspections was adopted on 23 May 2017 and published on 16 September 2017.

The Delegated Regulation was published as a package with Commission Directive (EU) 2017/1572 of 15 September 2017 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of GMP for medicinal products for human use.

The entry into application will be the date of entry into application of the Clinical Trials (CT) Regulation. This application depends on the setting-up of the clinical trial portal by EMA.

The Commission also reported the challenges faced by Member States in their preparation for implementation of the CT Regulation. There are some critical ones such as regarding resources and cooperation on safety assessment.

The Commission emphasised the importance of having adequate resources in order to ensure all arrangements are in place for the implementation of the CT Regulation.

#### **v. Shortages of medicines**

The Commission referred to the call of the Slovakian Presidency and the European Parliament report to find solutions to the problem of shortages of medicines. The Commission presented a questionnaire aiming at collecting information on national provisions related to the obligation for marketing authorisation holders and distributors to ensure continuous supply.

Member States expressed broad support to examine the legal obligation of continuous supply and stressed the seriousness of the situation. The Commission also explained that the feedback of the Member States will be examined in close cooperation with the HMA/EMA task force on availability. Member States are invited to reply to the questionnaire by 5 December 2017.

**vi. Questionnaire on the national law implementing Article 85c of Directive 2001/83/EC**

The Commission explained that the risk of fake medicines by internet is very serious despite the introduction of the EU logo on legal online pharmacies. The Commission has received 400 alerts of fake products during the last 3 years. Member States are encouraged to launch information campaigns to increase awareness on the risk of buying fake medicines online. To this end, the Committee members were reminded that the Commission has a communication kit available in all languages. Member States can contact the Commission to have the poster and the material in their national language.

**4. INTERNATIONAL DEVELOPMENTS**

**i. ICH Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management: Draft ICH Guideline**

The Commission informed the Committee that following its legal review of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Q12 (draft technical document), the Commission has put forward certain amendments to allow for regional flexibility for the implementation of certain parts of Q12 as the current text is not fully compatible with the EU legislative framework on variations. The proposed revision of the Q12 will be discussed at the ICH meeting in Geneva (11-16 November 2017) with the aim to reach an agreement that would allow for the adoption of Q12 as a draft guideline (under Step 2b) to be followed by the public consultation in the ICH regions.

**ii. Confidentiality Arrangement (Super-CC) between SANTE/EMA and US FDA**

The Commission explained that it has together with the EMA recently concluded a Confidentiality Commitment on medicinal products that covers trade secrets (referred to as 'Super-CC') with the US Food and Drug Administration (FDA). The Commission encouraged all the National Competent Authorities (human and veterinary) (NCA) to conclude similar bilateral arrangements with the US FDA as soon as possible e.g. as this will allow the NCAs to receive unredacted inspection reports from the FDA.

**iii. Consolidation of IPRF and IGDRP Initiatives**

The Commission provided an update on the consolidation of the International Pharmaceutical Regulators Forum (IPRF) with the International Generic Drug Regulators Programme (IGDRP) as agreed by the governance bodies of the two regulatory collaborative initiatives in June 2017. This consolidation is expected to realise several opportunities including, for example: enabling a shared vision for information exchange and regulatory cooperation; maximising synergies and avoiding duplication of efforts; creating the regulatory hub for pharmaceuticals that covers all medicinal products; simplifying the numerous forms of international collaboration; improving governance. The chairs of the IPRF and IGDRP are leading a joint Implementation Task Group which is

developing an implementation plan that will be submitted for adoption by each organisation at their respective next meetings in November 2017. The new joint initiative will be launched in January 2018 (with a new name to be decided) with the aim of a first face-to-face management committee meeting in June 2018 in conjunction with the ICH meeting in Japan. The initiative will remain informal and shall allow for opt-in or opt-out of regulators in different projects.

## **6. AOB**

### **i. The European Society of Oncology Pharmacy (ESOP) initiative on "Yellow Hand" symbol**

The Committee members were informed about the request from the European Society of Oncology Pharmacy (ESOP) for a "Yellow Hand" symbol to be added on the packaging of pharmaceuticals for human use to raise awareness about the issues of handling of cytotoxic/hazardous pharmaceuticals by healthcare professionals at their working place (e.g. pharmacies and hospitals).

The Commission explained that the EU pharmaceutical legislation regulates the particulars that appear on the outer and/or immediate packaging (labelling) and on the leaflet of the medicinal products. According to the current legislation the packaging and labelling may include symbols or pictograms designed to clarify certain information which is useful to the patients and where requested by the marketing authorisation holder. The so called "blue box" on the outer packaging of medicinal product may include some additional pictograms and information whether is required by Members States national legislation.

In regard to safety of employees at their work place, there are specific EU laws for occupational health that put an obligation on the employers (e.g. hospitals and pharmacies) to determine and assess the risks posed by the chemical and biological compounds and to take appropriate preventive and proactive measures.

The Commission will send a questionnaire to the National Competent Authorities of the Member States in order to gather information on national measures for handling such substances.

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