EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

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PHARM 561

PHARMACEUTICAL COMMITTEE - HUMAN
SUMMARY RECORD
63rd meeting, 10th December 2007
Conference Centre Albert Borschette, Brussels

OPENING

Irene Sacristán Sánchez opened the meeting on behalf of Mr Martin Terberger, Head of the Pharmaceuticals Unit of DG Enterprise and Industry, who chaired the meeting.

AGENDA

The draft agenda of the 63rd meeting (PHARM 556) was adopted.

1. LEGISLATIVE ISSUES

a) State of play and discussion on the revision of the EU system of pharmacovigilance

The Commission representative presented the draft pharmacovigilance legislative proposal, which was under public consultation until 1 February 2008. The legislative proposal was strongly welcomed overall and Committee members particularly welcomed proposals to rationalise reporting procedures, clarify medication error reporting and strengthen public health protection through more proactive pharmacovigilance. Members of the Committee made various comments and suggestions regarding the best possible EMEA committee structure, the best way to improve product information, and the way the public might perceive intensively monitored products. The proposal for patient reporting of adverse reactions was welcomed, however, some Committee members questioned the marketing authorisation holder being the direct recipient of such reports. Additional comments were made regarding the critical role of the Member States in pharmacovigilance particularly given their closeness to stakeholders for the receipt of data and dissemination of information on the safety of medicines. The Commission services strongly supported the critical role of the Member States as regards pharmacovigilance.

b) State of play and discussion on Communication on the future of the single market in pharmaceuticals for human use

The Commission representative updated the Committee on the planned Communication, which is scheduled for adoption by the Commission by October 2008 as a part of a "Pharmaceutical package" together with proposals on "Information to patients" and "Strengthening of EU Pharmacovigilance".

It will provide an opportunity to outline the challenges ahead of the European single market in pharmaceuticals and set out a vision for the future of the sector by proposing concrete deliverables for the Commission and Member States over the next few years. It will focus on the three pillars of the sector: enhancing public health, stimulating innovation, and strengthening the competitiveness of our pharmaceutical industry. The Committee was informed that public consultation summary was available at the website of DG Enterprise and Industry.

c) State of play of a possible legal proposal for a Commission Directive on excipients

The Commission representative presented an impact assessment study on the preparation of a Commission Directive on GMP for certain excipients used in the manufacture of medicinal products for human use as currently foreseen in Article 46 (f) of Directive 2001/83/EC, as amended. The study suggested that the least costly option based on the application of principles of risk assessment and management should be preferred to select excipients to be subject to GMP requirements. The Committee was informed that a decision would be taken upon finalisation of the impact assessment study. A number of Member States intervened to support a rational and sensible approach to address the problem.

2. INTERPRETATION/IMPLEMENTATION OF PHARMACEUTICAL LEGISLATION

a) Transposition of Community Legislation by the Member States

The Commission representative provided an update on the transposition of Directives 2004/24/EC, 2004/27/EC and 2005/28/EC as well as reminded the Committee of the duty of Member States to fully transpose these pieces of legislation and notify the transposition measures to the Commission. While there has been a progress in transposition of these Directives on the one hand, several infringement cases have been referred to the European Court of Justice due to the lack of transposition measures on the other hand. A number of these cases are now withdrawn from the court, as the Member States concerned have communicated national transposition measures. In all cases decided upon by the Court, the Court has ruled that the Member States concerned had failed to fulfil their obligations to communicate national transposition measures. The Commission representative stressed that these countries will immediately have to communicate their measure to avoid launching of infringement procedures in accordance with Article 228 of the EC-Treaty.

b) Implementation of Regulation (EC) No 1901/2006 on medicinal products for paediatric use

The Commission and EMEA representatives updated the Committee on the progress of implementation of the paediatric regulation. The Paediatric Committee (PDCO) had met for the first time in July 2007 in line with the legal provisions (6 month deadline) and has rapidly become fully operational. Appointment of the Commission nominees to represent healthcare professionals and patients was ongoing and due to the need to consult the European Parliament is not anticipated before 2008.

The guideline on the format and content of applications for agreement or modification of a paediatric investigation plan and requests for waivers or deferrals and concerning the operation of the compliance check and on criteria for assessing significant studies was being finalised taking into

accounts comments from the last Pharmaceutical Committee meeting and comments from the public consultation. Commission adoption in 2008 is anticipated.

Member State representatives were reminded of their reporting obligations stemming from Articles 39 (to inform Commission on national provisions for penalties by 26 October 2007) and 49 (to inform on measures to support research and development of medicines for children) of the Regulation. The Commission will publish an inventory of incentives for stakeholders based on the responses received under Article 49.

The Committee was informed that a recommendations document on ethical considerations for clinical trials in children was being finalised by the "Ad hoc group" on clinical trials. It was anticipated that this would be made public in the New Year.

The Commission representative updated the Committee on the symbol for medicines approved for their use in children and it was noted that a recommendation on this from the PDCO was anticipated for December 2007.

It was noted that the EMEA had done excellent work on the implementation of the paediatric regulation and that the first EMEA Decisions relating to the regulation had been issued.

3. INTERNATIONAL ASPECTS

a) EU-US Workshop on administrative simplification

The Committee was informed about the Transatlantic Administrative Simplification Workshop, which was co-chaired by the Commission and the United States Food and Drug Administration and organised in collaboration with the EMEA and the Heads of the EU National Medicines Agencies. The key objective was to identify opportunities for administrative simplification through transatlantic cooperation at the level of administrative practices and guidelines, which should not necessitate changes to legislation.

During the workshop industry presented a diverse range of proposals for administrative simplification through transatlantic and international collaboration and harmonisation. The proposals were presented in four thematic panels (on 1. quality and inspections, 2. pharmacovigilance, 3. scientific collaboration, 4. guidelines, format harmonisation and electronic submission) and the subsequent discussion offered a unique opportunity to build a mutual understanding between senior regulators and senior pharmaceutical industry executives from both sides of the Atlantic.

The next steps in the process would be careful consideration of the proposals by the EU and U.S. regulators with a view to making public, in the context of the bilateral collaboration, joint prioritised roadmaps for administrative simplification by June 2008.

b) ICH: Update on activities: ICH and international standard setting with CEN/ISO

The Committee was reminded of the important move to work towards elevating certain ICH guidelines to CEN/ISO standards, and was encouraged to follow the development of these standards carefully. It was noted that both CEN and the EMEA were working to coordinate European input to the standards and Member States were encouraged to make contact with their national standardisation bodies to ensure that the voice of the medicines regulator was heard.

Detailed feedback from the ICH meeting in Yokohama Japan was provided including feedback on the progress of the technical working groups

It was noted that the ICH Steering Committee has agreed to open up the Global Cooperation Group to certain individual drug regulatory authorities which should facilitate the use of ICH guidelines in countries such as China, India and Russia, which are of public health importance for the EU given their role in the manufacture of active ingredients and medicinal products and for clinical trials. It was also noted that starting at the next ICH meeting these additional drug regulatory authorities would be invited to a 'Regulators Forum' which will focus on the practical implementation of ICH guidelines.

The Committee noted that there were ongoing reflections at ICH on whether there is a need for a major revision of electronic Common Technical Document (e-CTD).

c) WHO International Medical Products Anti Counterfeiting Task Force (IMPACT)

The Committee was informed that "Principles and Elements for National Legislation against Counterfeit Medical Products" developed the IMPACT working group on legislation would be finalised and agreed by the IMPACT General meeting, taking place on 10-13 December 2007 in Lisbon, and subsequently published on the WHO/ IMPACT website. The European Commission had supported and closely monitored this specific project.

There is a continuous support for IMPACT amongst Member States and several of them had been actively participating in task force activities. The European Commission expressed its high interest for IMPACT to be continued as a high priority project after the planned reorganisation of WHO. Member States as WHO members could influence future priorities in this respect. The representative of the Portuguese presidency expressed his pleasure to host the 2007 IMPACT meeting as his country had highly supported the process.

d) International MRA EC-Australia

The Committee was informed that after long negotiations between the European Commission/ EMEA and Australia, an agreement had been reached for use of Canadian assessment reports as a primary means of assessment. This way forward was possible as "Health Canada" had agreed that the EU shares their assessment reports with Australia, if the Member States concerned have agreed to this on a case-by-case basis.

During the negotiations, Australia had requested an amendment of the MRA GMP Annex to allow additional information exchange. It was finally approved that such information exchanges would be limited to specific cases. The amendment would need to be agreed in the Council.

4. A.O.B.

The following items were discussed under A.O.B.

a) Radiopharmaceuticals

The Commission informed the Committee in its note of 13 November 2007 about concerns expressed by some stakeholders with regard to the legal status of radiopharmaceuticals in the Member States. Member States were invited to report on this situation.

b) Clinical Trials

The Commission representative provided a progress report on the preparation of "Draft Guideline on the data fields contained in the clinical trials database provided for in Article 11 of Directive 2001/20/EC to be included in the database on medicinal products provided for in Article 57 of Regulation (EC) No. 726/2004".

c) Active Substances

The Committee was informed that, as a response to the EP Resolution on Pharmaceutical Active Substances, the EMEA had undertaken a survey of a current self-control system relying the on self-declaration by manufacturers. Results of the Member States survey pointed out some concerns on quality of API manufacturers' internal audits. Member States were invited to reflect experience on their national inspections, which would be helpful for decisions on next steps to be taken.

d) Organisational matters

The Commission representative informed the Committee of the need to update the Committee's mailing list. In this context use of functional EUDRA mailbox by Member States was also encouraged. In addition implementation of CIRCA system for document management will be considered during 2008.

e) Enlargement of the mandatory scope of the centralised procedure

The EMEA representative updated Member States on the state of play of the document "Enlargement of the mandatory scope of the centralised procedure in 2008: Scientific aspects and working definitions for the mandatory scope of the centralised procedure". Following discussion in the previous meeting several changes had been implemented, in particular reducing the scope of autoimmune diseases. As no further substantial comments were received during public consultation, the guideline should be adopted by the CHMP in December 2007 and applied since January 2008.

PHARMACEUTICAL COMMITTEE

JOINT MEETING WITH VETERINARY PHARMACEUTICAL COMMIITTEE

SUMMARY RECORD

10th December 2007

The joint meeting of the Pharmaceutical Committee (Human) and the Veterinary Pharmaceutical Committee dealing specifically with revision of the Variations Regulations was held during the afternoon session and chaired by Mr Martin Terberger, Head of the Pharmaceuticals Unit of DG Enterprise and Industry.

1. LEGISLATIVE ISSUES

a) Proposal for a Directive of the European Parliament and of the Council amending Directive 2001/82/EC and Directive 2001/83/EC as regards amendments to the terms of marketing authorisations for medicinal products Public consultation

The Commission representative updated the Committee on the progress of this legislative initiative aiming to harmonise variations procedures for all medicinal products independently on the kind of their marketing authorisation (centralised, decentralised/mutual recognition, purely national). Outcome of the public consultation had been published at the Commission website.

b) Update on the process of the revision of Commission Regulations (EC) No 1084/2003 and 1085/2003

The Commission representative presented the draft legal proposal on the comitology part of the revision of the Variations Regulations, which was a subject to public consultation until 4 January 2008. The draft single text was covering changes to all marketing authorisations (centralised, decentralised/mutual recognition, purely national). Major issues for discussion were:

"Do and Tell" procedure

No specific comments received on the "Do and Tell" procedure for type IA variations.

Grouping

The draft proposal outlines a series of cases where grouping of variations could be allowed. Those 'grouped variations' would be evaluated in accordance with the procedure of the 'highest-risk' variation included in the group and are also eligible to the 'worksharing' procedure.

These concepts have been in principle endorsed by Member States. Although an annual report grouped per marketing authorisation was fully supported, a number of MSs expressed their concerns about grouping per MAH due to foreseen consequences for their handling via e-CTD and workload of national agencies, particularly at the end of the calendar year. Some MSs supported a package of identical variations submitted for more marketing authorisations, what is already possible in some Member States. There were some comments that the fee structure would have to be adapted at national level. A need for further reflexion on grouping was expressed by certain Committee members.

Worksharing

The draft proposes to introduce a 'worksharing' procedure in the following two cases:

(a) where the change concerns one given medicinal product that is authorised at purely national level in several Member States;

(b) where the change is common to several, distinct medicinal products.

The procedure would be optional and would be applicable to variations of Type IB, Type II, line extensions and grouped variations.

While the principle of 'worksharing' was supported, some MSs did not agree with a principle of "downgrading" as an outcome of the worksharing procedure, particularly for line extensions. There were concerns about benefits of worksharing if not taken on board by all MSs. The role of the CMD and need of a strong ground for refusal were emphasised. Application of a voluntary worksharing within HMA (as for PSUR's or Paediatrics) was proposed by some Committee members.

Some concerns about resource availability in individual MSs were expressed and reimbursement proposed. Other comments related to the possibility for Member States to retain their power to check a dossier at a national level and possibly reject a variation. Marketing authorisation holders should be also encouraged to workshare.

Type IB by default

It is proposed that variations which are not explicitly recognised as Type IA, II or line extensions are handled, by default, as Type IB variations (and no longer as Type II).

The proposal was in general supported. Some concerns were expressed with regard to a shorter deadline (30 days). In the case of biological medicines even small variations could have great impact and therefore it was proposed by some Member States to leave type II as a default for them (with a possibility of downgrading to IB).

The proposal to have the list of variations in a guidelines rather than in a regulation's annex was welcomed, provided MSs are properly involved in guideline discussions.

ICH

The approach suggested by the Commission was broadly supported with regard to:

Design Space (DS)

Regulatory flexibility

Regulatory agreement

Other aspects discussed

Grouping of variations (Art. 7 and Annex II)

Deadlines for implementation of changes (Art. 21 and 22)

Notion of guidelines for classification of variations (Art. 3 to 6)

Downgrading of variations classification in relation to worksharing (Art. 24)

EMEA recommendation on classification of variations (Art. 5(1))

Multistrain approach for veterinary vaccines (Annex I and draft guideline on classification of variations)

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