PHARMACEUTICAL COMMITTEE
SUMMARY RECORD OF THE 54th MEETING
13th November 2002

OPENING

Mr Paul Weissenberg, Director of Directorate F of DG Enterprise, opened the meeting and chaired the discussions on points 2, 3.1, 3.2 and 6.

AGENDA

The draft agenda of the 54th meeting (PHARM 418) was adopted.

SUMMARY RECORD

The summary record of the 53rd meeting on 14th May 2002 (PHARM 419) was adopted without amendment.

1. INTERPRETATION/IMPLEMENTATION OF LEGISLATION

1.1 Information on recent case law and pending cases

The Committee was informed about the judgement of 3 July 2002 in Case T-179/00 "Menarini" by the Court of First Instance. The Court held that the local representative's logo may be included in the so-called blue box. In addition, the Court clarified the limits of judicial review of decisions in the pharmaceutical sector and the role of the Pharmaceutical Committee. The Commission will not appeal against the judgement as similar provisions are foreseen in the Review.

1.2 Implementation of TSE requirements (ex-Directive 1999/82)

In introducing the subject, the Commission representative stressed the urgency to ensure that all provisions protecting against TSE are fully complied with. The EMEA as well as some Member States are still waiting for some EDQM certificates. The EDQM representative confirmed that all pending dossiers should be finalised by the end of the year, apart from some recently approved products. In some cases though the producers did not submit the information requested by the EDQM so that no certificate could be granted. In such case, the marketing authorisation holder has to find another producer who has obtained the necessary certificate; otherwise the marketing authorisation has to be withdrawn.

1.3 Implementation of Title VIII of Directive 2001/83/EC

The Commission representative informed the Committee that there had been some uncertainty on the part of Member States about their responsibility to enforce the Community legislation on information/advertising in case of centrally approved medicines. Interpretative guidelines could help to clarify that Member States are responsible for such enforcement. The contents of such guidelines would need to take account of whether or not the Commission's proposal for a test case on information to

patients, which is part of the Review, will find support. The outcome of the Review should therefore be awaited.

1.4 Provisions on data protection

The subject was introduced by the Commission representative. He clarified that a generic application that is submitted when the reference product is still under data production must not be validated or processed before the data protection has expired.

2. LEGISLATIVE ISSUES

2.1 Review 2001

The Commission representative informed the Committee on the ongoing preparation of the Commission's modified proposals on the regulation and the two directives, following the European Parliament's vote in the first reading in October 2002. Taking into account the priorities of the Danish Presidency, the modified proposal for the regulation would be adopted and released first. The modified proposals for the two directives would follow as fast as possible.

The Danish representative clarified that as a consequence of the late vote in the Parliament and the late availability of the Commission's modified proposal for the regulation, it would not be possible to achieve political agreement on this text during the Health Council of 2 – 3 December 2002. The Review would remain on the Health Council's agenda, but only as a point for information.

The EMEA representative reminded the Committee that the day-to-day work in the EMEA and its scientific committees would become very difficult if the Review were not adopted before the accession of ten new Member States in May 2004.

2.2 Annex I to Directive 2001/83/EC

After a brief introduction of the topic by the Commission representatives, a detailed discussion was held on the draft proposal sent in advance of the meeting. Overall, the Member States acknowledged the work by the Commission services and the progress made as compared to earlier drafts. Nonetheless, Member States expressed concern on some aspects of the draft and declared that they would send further comments in written or raise issues in the Standing Committee. The Commission's idea to set out specific provisions on advanced therapy medicinal products, as contained in Part IV of the draft, was supported by various Member States, while others were more hesitant or even opposed to it. Further comments related to various terminological aspects, e.g. on similar biological and herbal medicinal products, as well as to the Plasma Master File.

Member States requested more time for detailed analysis and discussion of the proposal. The Commission representative explained that due to international obligations Parts I to III of the Annex I need to be in place by 1 July 2003. Part I implements the "Common Technical Document", agreed within the framework of ICH. Parts II and III are intrinsically linked with Part I, as the CTD applies to all kind of applications and hence also to those for which Parts II and III contain specific rules on the application dossier. For the advanced therapy medicinal products as referred to in Part IV, full coherence with other ongoing legislative initiatives would be ensured. The proposal for a new directive

on tissue engineering as prepared by Directorate-General Health and Consumer Protection would cover the tissues until they are stored in a tissue bank. Once the tissue leaves the bank to be processed to a medicinal product, the pharmaceutical legislation would apply. The Commission representative explained that the revised Annex I is needed to set out rules on the contents of an application dossier for different categories of medicinal products. Once these rules are in place, interpretative guidance might have to be adopted by the CPMP.

The Commission representative concluded that the text would be further improved once all comments have been received from the Member States. It would then be important to move on with the consultation of the Standing Committee as swiftly as possible to meet the strict deadlines.

2.3 Paediatric medicines

The Commission representative introduced the current reflections on paediatric medicinal products, as set out in the reflection paper circulated in advance of the meeting.

The Member States representatives expressed clear support for the initiative, while stressing that a number of aspects require further discussion. Several Member States highlighted that it would be crucial to achieve a sound balance between establishing the necessary incentives for research and development in paediatric medicines on one side and ensuring appropriate price levels by maintaining sufficient competition on the other. Further comments related to the equal level of incentive, irrespective of the positive or negative outcome of the research, to the ready accessibility of scientific advice and to the coherence between paediatric and orphan legislation in terms of fee reductions and market exclusivity.

Several Member States indicated that detailed comments would be sent in written, but that more time would be needed for reflection. The Commission representative explained that a tentative draft should be presented in the beginning of 2003, taking into account the Member States' comments. A detailed discussion would be held during the next meeting of the Committee.

2.4 Traditional herbal medicinal products

The Commission representative informed the Committee about the vote of the European Parliament's Committee on Environment, Public Health and Consumer Policy of 5 November 2002. In this vote, the Parliament Committee supports the gist of the Commission's proposal, while asking for a number of amendments. The changes relate to extending the scope of the new simplified procedure to combination products, to lowering the minimum time of use in the Community to 10 years and to fully replacing the CPMP by the new Committee on Herbal Medicinal Products for all herbal medicines. The European Parliament's vote in plenary session is scheduled for 20 November 2003. The Commission will then prepare it's modified proposal to be presented beginning of 2003.

2.5 Variations regulations

The Commission representative updated the Committee on the ongoing work to review the two regulations on variations to marketing authorisations. There has been broad

consultation of scientific committees and working groups as well as of external stakeholders. The numerous comments have been analysed and discussed in detail within the "Notice to Applicants" Working Group. At present, a number of issues still need to be solved such as certain terminological questions and the optimal approach for variations concerning medicinal products containing biological active substances. The two regulations will replace the existing Regulations 541/95 and 542/95. It is expected that they could be adopted during the first half of 2003.

3. MARKETING AUTHORISATION PROCEDURES

3.1 Mutual recognition procedure

The Danish Chairperson of the MRFG gave an update on important activities of the group. The preparatory discussion on SmPC harmonisation within the Joint CPMP/MRFG Working Group and with the concerned industry has progressed. The first referral procedure has been initiated by the Commission on 8 November 2002. The Member States expressed different views on the relevance of aspects of intellectual property rights and in particular of usage patents for the future success of SmPC harmonisation. It was proposed to refer this question to the EMACOLEX group for analysis.

The Danish representative explained that further priorities of the MRFG have been to discuss the Review 2001 and its implications for the mutual recognition procedure. To prepare an effective functioning, it was agreed that the rules of procedure of the future Co-ordination Group should already be prepared, even if the Review has not yet formally been adopted.

The Committee was informed about recent developments in the mutual recognition procedure: From 1 January to 31 October 2002, 360 new applications regarding medicinal products for human have been submitted (as compared to 394 in 2001). There is still a trend to involve just one concerned Member State (115 procedures – as compared to 136 in 2001) or two to five (121 procedures – as compared to 115 in 2001).

3.2 Centralised procedure

The EMEA representative gave an update on the centralised procedure. He highlighted that in 2002 the number of applications for a Community marketing authorisation has dropped significantly. So far, there had been only 21 new applications in 2002, as compared to 48 applications in the same period in 2001. This means a slide by more than 50%. The forecast for 2003 and 2004 is similarly negative and an increase of the figures cannot be expected before 2005, if at all. While the reasons for this development are still to be analysed, it has important financial implications for the EMEA. As urgent measure, additional subvention by the Community would be necessary for 2002. On the long run, the structure of the EMEA funding including the fees might have to be reconsidered.

The EMEA informed the Committee that on various occasions the scientific evaluation of recent applications demonstrated that improved risk management procedures are necessary. It was discussed that the current legislation already provides for a legal basis,

but that the Review 2001 could introduce specific provisions on such risk management in order to enhance legal certainty.

In the same context, the Commission representative highlighted the need that all Member States fully and correctly implement binding Commission decisions containing a Community marketing authorisation.

Finally, the Committee was informed about a recent case of illegal re-importation into the EU of centrally approved medicines. The Commission representative stressed that the existing law allows stopping such re-importation on three grounds. First, the importer needs a manufacturing authorisation according to Article 40(3) of Directive 2001/83. The importer has to indicate in his application which products he intends to import. As he will not declare his intention to illegally import a product, he will not possess the necessary authorisation. Second, Article 51(1)(b) of Directive 2001/83 requires for products coming from non-EU countries that each production batch is reanalysed; in case of illegal re-importation, the importer will not submit the products for such reanalysis. Third, the importer will not be able to prove that the requirements of Good Distribution Practice are complied with from the moment of production until the time of importation.

In addition, the Committee was informed about a proposal for a regulation to avoid trade diversion into the European Union of certain key medicines. This regulation provides for a preferential price of medicinal products for certain diseases in the world's poorest countries. The regulation could be adopted in the near future.

4. TELEMATICS

4.1 EudraTrack

The Danish representative updated the Committee that the German Federal Institute for Drugs and Medical Devices (BfArM) is willing to take over the management of EudraTrack. The Commission, the Joint Research Centre and the BfArM are currently preparing a contract to ensure a smooth hand-over as well as the necessary support. Final agreement could be achieved before the end of the year. The German representative explained that certain financial questions still need to be solved.

4.2 EudraVigilance

The EMEA representative explained that so far just two Member States and one company are regularly reporting electronically in compliance with the new provisions on pharmacovigilance. Seven further Member States and 19 other companies are testing the electronic reporting. The electronic reporting of pharmacovigilance information is a high priority for the EMEA, but its success depends on the co-operation by all national agencies and by the marketing authorisation holders. A number of issues are still under discussion, e.g. the role of Member States in communicating information on EudraVigilance, the use of a drug dictionary, support for SMEs as well as training programmes for all companies.

In this context, the EMEA representative updated the Committee on the preparation of Interchange Agreements on the transmission of pharmacovigilance data. The current draft Agreement has two parts, one legal part covering issues like confidentiality and one technical part. Some discussion was held on the question whether it would be preferable

to have two separate agreements, one to be concluded between the EMEA and the competent authority and the other between the competent authority and the marketing authorisation holder.

It was agreed that written comments on this issues should be sent to the EMEA within one week so that the preparation of the Interchange Agreements could be finalised before the end of the year.

5. INTERNATIONAL ASPECTS AND ENLARGEMENT

5.1 ICH

The Commission representative updated the Committee on recent developments within ICH. A working group on gene therapy shall be established soon. The preparations for "ICH 6" are under way.

5.2 MRA

The Commission representative explained that several Commission services are currently analysing the legal situation of the MRAs for the acceding Member States and what practical steps need to be taken. No final solution has yet been determined.

5.3 Enlargement

The Committee was updated on the outcome of the special meeting of the Pharmaceutical Committee on 2 October 2002. The subject of this meeting, which was held on request of the Council, was the transitional clause on parallel imports of medicinal products. This clause will be part of the Accession Treaty for most of the acceding countries.

The Commission representative updated the Committee on the current planning for the third and last phase of the Pan-European Regulatory Forum (PERF). This phase shall last until end 2003 and shall cover similar priority areas as PERF II. To further improve interaction with stakeholders, it is envisaged to hold three conferences on specific topics during PERF III instead of one broad conference as during PERF I and II.

6. TRANSPARENCY COMMITTEE

The Commission representative informed the Committee on ongoing reflections to establish a Preventive Dialogue. The Preventive Dialogue is meant as an informal dialogue which could provide an alternative to formal infringement procedures to tackle more effectively problems of implementing the *acquis communautaire* in particular with regard to the forthcoming enlargement. It could deal, amongst others, with problems of correct implementation of Directive 89/105. The Member States supported this idea in principle, but asked to collect first of all correct and reliable data on national decisions on price/reimbursement of medicinal products. The Commission was asked to facilitate the collection of such standardised data. The Member States were reminded to communicate to the Commission data that is already existing, even if it is not yet standardised.

The Committee was updated on the discussion in the Transparency Committee on relative effectiveness. The Member States supported the idea that the Transparency

Committee should look into this issue. Several Member States (Denmark, Germany, Portugal and the United Kingdom) indicated their willingness to participate in a Task Force to prepare the discussion. At the same time, Member States stressed that the actual evaluation of relative effectiveness must remain a national competence.

7. WORKING GROUP ON INFORMATION TO PATIENTS

The Commission representative informed the Committee about the 1st meeting of the Working Group on Information to Patients that was held on 18 July 2002 as well as about a workshop with stakeholders that was organised on the same subject on 24 September 2002. The Working Group's next meeting is scheduled for January 2003. To prepare this meeting, Member States were invited to inform the Commission services by end of November 2002 about their national legislation on advertising for medicines available without prescription. In addition, Member States should communicate to the Commission any information and experiences they have on co-operation of public and private sector ("public-private partnerships") on information to patients.

8. GOOD MANUFACTURING PRACTICE

The Committee was informed about the ongoing revision of Annex I of the EU GMP Guide. The main objective of the proposed amendments is to harmonise the environmental standards for clean rooms with the international standards. Stakeholders will have the possibility to comment on the draft within three months. The Committee did not raise any objections against the draft proposal.

9. A.O.B.

9.1 Contamination of the feed and food chain with pharmaceutical waste containing Medroxyprogesterone

The Commission representative introduced the subject, describing the problem, the source of contamination, the distribution of contaminated products as well as measures taken and an estimation of the overall costs. She explained that studies on the ecological effects of Medroxyprogesterone Acetate are still ongoing.

The Committee felt it necessary to collect further information on the issue. It was agreed that all Member States should inform the Commission swiftly whether medicinal products containing Medroxyprogesterone Acetate are authorities in their respective countries. In addition, the Commission services will contact the holder of the marketing authorisation of those products, which have been determined as source of the contamination. Once all information is available, it has to be decided whether further action is necessary.

9.2 Translation of documents

The topic was postponed to the next meeting.

9.3 Distribution of medicinal gases

The topic was postponed to the next meeting.

9.4 Proposal for a regulation on sales promotion

The topic was postponed to the next meeting.

9.5 EU Action Plan on Drugs 2000 – 2004

The Commission representative summarised the responses received so far on the questionnaire circulated in advance of the meeting. The Member States that had answered (Greece, Belgium, United Kingdom and Greece) took different positions as to whether or not additional measures are necessary to control the diversion of Ketamine. The other Member States were invited to send their answers by the end of the year.