INFORMATION ON THE OUTCOME OF THE 45th PHARMACEUTICAL COMMITTEE

16-17 March 1998

AGENDA
The draft agenda of the 45th meeting (PHARM 202, version 11.3.1998) was adopted.

SUMMARY RECORD
The summary record of the 44th meeting on 16-17 September 1997 (PHARM 203) was adopted, subject to the following modification:
- Under item 1b "Borderline between medical devices and medicinal products", the third sentence should be replaced by the following text: "*In this context attention should be paid to the fact that Article 33 of Directive 75/319 is applicable regarding revocations of marketing authorisations following the reclassification of products. Therefore any relevant decision should be notified to the CPMP and a compiled list should be circulated to all Member States and the Commission.*"

Joint meeting of the Pharmaceutical Committee and the Veterinary Pharmaceutical Committee:

1. INTERPRETATION/IMPLEMENTATION OF LEGISLATION
a) Commission Communication on the Community marketing authorisation procedures for medicinal products
The Commission representative informed the Committee on the likely timing for the adoption of this draft Communication: after an interservice consultation in April it would hopefully be possible to have the text adopted by the Commission in May. He stressed that – following suggestions made by the Legal Service of the Commission - it had been necessary to significantly redraft the text. The Commission representative asked for understanding that advance copies of the text could not be made available before the end of the interservice consultation. Following questions by Member States, the Commission clarified that the draft Communication could not directly answer all detailed and practical questions brought forward by Member States, applicants and the Mutual Recognition Facilitation Group. The purpose of the Communication was to lay down the basic principles, based on which practical and detailed questions could be answered.
b) Borderline between medical devices and medicinal products
The most recent draft Guidelines relating to the demarcation between Directives 90/385 and 93/42 on medical devices and Directive 65/65 relating to medicinal products (MEDDEV.2.1/3, Rev.5.1-March 1998) were tabled (PHARM 213) for information and the Commission representative expressed his hope that these Guidelines would be finalised shortly.
c) CFC's in medicinal products
Chapter 6 of the finalised draft Commission Communication regarding the phasing out of CFC´s was tabled for information (PHARM 212). After interservice consultation, the draft Communication will be adopted by the Commission (probably in May/June 1998).
d) Official Batch Release

The Commission representative stressed the validity of the final interpretation of the legislative framework concerning official batch releases provided for in Directives 89/342 and 89/381, distributed and discussed as "PHARM 192" at the occasion of the last Pharmaceutical Committee. The Commission alerted those Member States which were reluctant to accept this interpretation that they might receive "pre-169 letters" shortly.
The Commission also clarified some issues which had been raised at the EU OMCL network in Strasbourg and stressed that official batch release is a post-marketing activity whereas batch release by the manufacturer is a pre-marketing activity.

e) Third country imports

The Commission tabled a compilation of documents concerning the interpretation of Article 22 of Directive 75/319 and Article 30 of Directive 81/851 (PHARM 217). According to the interpretation given in these letters, "importing country" means the Member State in which the imported batch is controlled for the purpose of the release of that batch for marketing in the EU, and not necessarily the Member State through which the batch first physically enters the EU (the Member State in which customs controls have been carried out). Furthermore, importation from third countries includes the responsibility for storing the medicinal product prior to carrying out batch control for release onto the market in a Member State (i.e. onto the Community market), as well as the responsibility for batch control to release each batch of the medicinal product onto that market. Those responsible for these activities are required to have a manufacturing authorisation.

f) recent case law of the ECJ – interpretative issues

- The Commission representatives outlined the main findings of the Court of First Instance of the EC in its judgement in the "Pharos"-Case (Judgement of 17.2.1998, Case T-105/96, not yet published) and the conclusions which Advocate General Colomerin presented on 22.1.1998 in Case C-368/96 (The Queen vs MCA ex parte Generics).
- The Commission also alerted Member States to the fact that it had – in a recently opened infringement case - interpreted the term "*well established medicinal use*" in Article 4 paragraph 3 (8) lit a (ii) of Directive 65/65/EEC. According to this interpretation the factors which have to be considered in order to establish a "well established medicinal use" are: the time over which a substance has been used, quantitative aspects of the use of the substance, the degree of scientific interest in the use of the substance (reflected in the published scientific literature) and the coherence of scientific assessments (absence of significant disputes) regarding the safety and efficacy of a substance. These factors may lead to the result that different periods of time may be necessary for establishing "well established use" for different substances. However, considering that a "use" cannot be "well established" unless a certain minimum period of time had been elapsed, the Commission stressed that – as a general rule and for varioust reasons – this <u>minimum period of time</u> had to be at least one decade from the first systematic and documented use of that substance in the world.

2. LEGISLATIVE ISSUES

a) Starting materials

Following comments received by interested parties (a compilation of the comments received was tabled as PHARM 209 and 209a), the Commission Services had redrafted the amendment to Directives 75/319/EEC and 81/851. The Commission representative described the essential elements of the adapted draft (PHARM 215) and the modifications which had been inserted. It was announced that the draft would be further discussed at a technical level in the Inspectors Working Group and that a final Commission proposal could be adopted before the end of this year. In general, Member States welcomed the new proposal. As in previous discussions, several Member States

expressed, however, their concern with regard to the proposed system of Community inspection. Some Member States also criticised that the draft text was delegating too many issues to future Guidelines. In this context the Commission representative stressed that some of the guidelines to which the text referred already existed. Other Guidelines were currently being drafted in parallel, like for instance the Guidelines on GMP for starting materials (PHARM 210). This Guideline, which will be drafted within the framework of ICH, should be at an advanced stage by the end of this year

b) Transmissible Spongiform Encephalitis (TSE)

The Commission representative updated the Committee on recent developments, informed the Committee about the content of the new draft horizontal SRM-Decision (elaborated by DG VI and presented by the Commission on 25.2.1998) and outlined several possible scenarios for the pharmaceutical sector – whilst stressing the uncertainties of any prediction.

- Member States might agree on the new draft horizontal SRM Decision. In this case the new SRM Decision would formally enter into force on 1.4.1998. The first substantive effects of the new decision would enter into effect on 1 July. Therefore, under this scenario, the Commission would have three additional months (April-June) to prepare and adopt specific sectoral legislation (amendments to the annex of Directive 75/318 and 81/851) in the pharmaceutical field.
- Member States might not agree on the new draft horizontal SRM Decision. In this case the "old" SRM Decision of July 1997 (Decision 97/534) could formally enter into force on 1.4.1998. This scenario could legitimately be called "catastrophic scenario", because the text of the July 1997 Decision does not allow for specific derogations in the pharmaceutical field. Full implementation of the July 1997 Decision by Member States at 1 April would therefore lead to shortage of supply of medicines in the marketplace. (see "Statement" of the 44th Pharmaceutical Committee of 16.9.1997 on this issue)
- Member States might not agree on the new draft SRM Decision and the Commission could propose (and Member States could accept) a further postponement or revocation of Decision 97/534. In this case it could be necessary to await further political and scientific developments and to propose and adopt specific sectoral legislation (amendments to the annex of Directive 75/318 and 81/851) in the pharmaceutical field afterwards.

The Commission representative regretted that no further clarification or decision was possible at this point in time and stressed that the Commission Services envisaged to draft and propose adapted amendments to the annex of Directive 75/318 and 81/851 as soon as the situation regarding the horizontal SRM-Legislation was sufficiently stabilised.

c) Fees payable to the EMEA

The Commission tabled its proposal of 21.1.1998 (COM(1998) 21 final = PHARM 204) concerning an amendment of Council Regulation 297/95 on fees payable to the EMEA and shortly highlighted the main points of the proposal. The proposal is currently discussed in Council and could be adopted before summer.

d) Variations Regulations 541/95 and 542/95

The Commission informed the Committee on the successful outcome of a Standing Committee of 6.3.1998 on which amendments to the Variations Regulations 541/95 and 542/95 (PHARM 216) were discussed and accepted by Member States. The eleven linguistic versions of the text were distributed and the Commission asked Member States to check the translations and to send their comments back to the Commission Services in order to prevent linguistic inconsistencies. Greece, Finland and Italy asked for a complete retranslation of the texts. Following a comparison of the French and the English version it was also clarified that under point 18 of the amendment to Directive 541/95, the third

sentence in the second paragraph should read: "…. Proteinaceous component obtained through **a** biotechnology process …."

e) Codification

The Committee was informed that draft codified texts would be finalised in April and that they would be submitted to Council and European Parliament under the simplified procedure foreseen for codification before summer.

3. MARKETING AUTHORISATION PROCEDURES

a) Mutual recognition

1. Status Report (UK) – The UK representative made available a written Status Report of the MRFG.
2. Ad hoc Working Group on Herbal Medicinal Products – A copy of the final report to the EMEA and the Commission (PHARM 206) was tabled for information. The Commission representative clarified that this report was a not a "final", but just a "final 1997" Report. He reported that the mandate for the Group had been extended for one year. In this context he also informed the Committee that the Commission had finally awarded a contract concerning a study on herbal medicinal products to a contractor (AESGP) which would carry out the study and present results before the end of 1998.

b) Centralised procedure

EMEA representatives presented new 1998 forecasts for the centralised procedure: According to these forecasts, around 63 new applications concerning 48 new substances were expected to be dealt with by the CPMP in 1998.

c) Notice to Applicants

The Committee discussed the inclusion of a new paragraph in chapter I.4.2, concerning the role of scientific monographs (PHARM 207). Several Member States expressed the view that the inclusion of such paragraph would be premature and/or that the wording should at least be more neutral. The Commission representative stressed that the proposed text would just suggest to make systematic use of these monographs and that it would not confer any legal or other obligation on authorities. It was agreed that the NTA-Group could follow up and reconsider the issue.

4. INTERNATIONAL RELATIONS

a) ICH

Not covered at the meeting.

b) Relations with 3rd countries

The Commission representative presented a progress report on negotiations with USA, Canada, Switzerland, Australia, New Zealand, Japan (PHARM 214).
The entering into force of the agreements with USA, Australia and New Zealand is expected – under a best case scenario - for this summer. The entering into force of the agreements with Switzerland and Canada are blocked (the reasons for the blocking are not directly linked to the pharmaceutical sector) and the agreement with Japan is still under negotiation.

c) Enlargement

The Commission representative stressed that the first phase of accession negotiations with the accession candidates would start shortly. As in precious enlargement exercises,

the first main activity would be to define and to explain the existing "acquis communautaire" to the accession candidates. It was stressed that the "pharmaceutical acquis" did not only cover those Regulations and Directives which were listed in the "Directory of Community Legislation", but also the Decisions which had been and will have been adopted on the basis of these legal instruments (particularly the Community marketing authorisations). Other activities would involve an Institution Building Program (through an exchange of experts) and Member States were asked to actively support these projects.

Electronic communication of information in the pharmaceutical sector:
The Commission representative explained the function and content of EUDRALEX, EUDRAWATCH, EUDRAMAT, EUDRANET and EUDRATRACK. He announced that the EUDRA-website, which was currently only open for competent authorities only, would be opened to the public as of the end of March 1998 under the following address: http://DG3.EUDRA.ORG.

At this point of the agenda, the joint meeting of the Pharmaceutical Committee and the Veterinary Pharmaceutical Committee ended.

The Pharmaceutical Committee continued and addressed the following items:

6. LEGISLATIVE ISSUES (continued)
a) 'Good Clinical Practice in the conduct of clinical trials'
The Commission representative informed the Committee that this point was currently actively discussed in Council.
b) 'Orphan medicinal products'
A revised draft proposal for a European Parliament and Council regulation on orphan medicinal products (PHARM 219) was tabled for information. The Commission representative informed the Committee that this draft had already gone into a new round of interservice consultation and that it was hoped that a final Commission proposal could be adopted before summer.

7. RATIONAL USE OF MEDICINAL PRODUCTS
The Commission Report of 14.11.1997 on the Application of Directive 92/26 concerning legal status (COM(97)581 final = PHARM 205) was tabled for information.
In this context and following a question from a Member State, the Commission representative stressed that an updated version of the "Switching-Guideline" would be presented to the Pharmaceutical Committee in September 1998.

8. GOOD MANUFACTURING PRACTICE AND INSPECTION
A revision of Annex 14 to the EU Guide to Good Manufacturing Practice (PHARM 208) was tabled for information.

9. A.O.B..
a) Internet selling of medicinal products – A resolution of 23.1.1998 of the Executive Board of the WHO on cross-border advertising, promotion and sale of medical products through the Internet (PHARM 211) was tabled for information.
b) The next meeting will take place on **23.-24. September 1998**, subject to further confirmation.