INFORMATION ON THE OUTCOME OF THE 49th MEETING OF THE PHARMACEUTICAL COMMITTEE

22-23 March 2000

The meeting was opened by Mr. Paul Weissenberg, the new Director of Directorate F of DG Enterprise. In an introductory statement, Mr. Weissenberg informed the Committee about the recent organisational changes within DG Enterprise (formerly DG III). He then started the meeting with a general exchange of views on three items of horizontal interest: the review of the pharmaceutical legislation (point 2.a of the agenda), ICH (point 7.a of the agenda) and information society in the pharmaceutical sector (point 6.1 of the agenda). The outcome of the discussion on these points is described under the respective points of the agenda.

AGENDA

The draft agenda of the 49th meeting (PHARM 285, version 14.3.2000) was adopted without amendment.

SUMMARY RECORD

The summary record of the 48th meeting on 27-28.9.1999 was adopted without amendment.

1. INTERPRETATION/IMPLEMENTATION OF LEGISLATION

a) Colourants

The Commission services representative informed the Committee on recent developments concerning the interpretation and application of Directive 78/25/EEC on colouring matters in medicinal products (PHARM 287). The Committee took note of the recent scientific opinions delivered by the Scientific Committee on Medicinal Products and Medical Devices (SCMPMD) on *E 123 Amaranth, E 127 Erythrosin, E 161g Canthaxatin, E 173 Aluminium*. (In these opinions the SCMPMD concluded that it would seem "*paradoxical to prohibit*", respectively "*reasonable to allow*" the use of these colourants in medicinal products.) The Commission representative suggested that - based on these scientific answers of the SCMPD - one might consider to interpret the references in Directive 78/25 in a way which would permit the use of these colourants in medicinal products. The Committee agreed with this suggestion but stressed that – in the interest of legal certainty – it seemed appropriate to amend Directive 78/25 accordingly and to replace the outdated references by clear new references. The Commission representative agreed with the need for legal certainty and announced that the Commission services would get into touch with the Commission Legal Service in order to examine practical solutions (e.g. the possibility to adopt an "adaptation to technical progress" of Directive 78/25 via Comitology) to answer this need.

b) Interpretation of Article 4(8)a ii of Directive 65/65

An updated draft of relevant parts of NTA – chapter 1 and letters from Member States on implications of Commission Directive 99/83 (on "well established use") and the role of "core SPCs" had been sent out before the meeting. Members of the Committee generally agreed that the text of the updated NTA had significantly improved and it was announced that the text would be further discussed – and hopefully finalised – at the next NTA meeting. Following specific questions raised by Members of the Committee, the Commission representative gave clarification on the following points:

- Interpretative Guidance on the application of Directive 99/83 (on "well established use") will be given both by the Commission (through the updated NTA) and the CPMP (through Guidance documents on the safety and efficacy of "old" substances)
- The so-called "core SPCs" (e.g. those elaborated by the Herbal Working Group of the EMEA) are legally not binding. The value of these "core SPCs" is based on their "persuasive power", underpinned by the fact that technical experts of all EU competent authorities have considered and agreed upon them.
- Bibliographic dossiers must always be "full dossiers". Whenever information on specific points is missing, justification must be given why demonstration of an acceptable level of safety and efficacy can be supported although some studies are lacking.
- "Well established use" always refers to the use of a specific substance for a specific theapeutic use. If well-known substances are used for entirely new therapeutic indications, it is not possible to refer to "well established use".

c) Interpretation of Article 4(8)a iii of Directive 65/65

An updated draft of relevant parts of NTA – chapter 1, a report from EMACOLEX discussion (PHARM 298) and comments from industry had been tabled for discussion. Members of the Committee generally agreed that the text of the updated NTA had significantly improved and it was announced that the text would be further discussed – and hopefully finalised – at the next NTA meeting. The Commission services representative stressed that the current draft was to a large extent based on the agreement achieved in the EMACOLEX group and that it was seeking ways of interpreting existing legislation in a way that would help to reinforce the balance of interests which Article 4.8 (a) (iii) of Directive 65/65/EEC has tried to establish. If this exercise would not prove successful (particularly with regard to the problem of withdrawals of originator products) changes to legislation would have to be considered within the review of the pharmaceutical legislation.

d) Plasma Master File (PMF)

The Commission services representative updated the Committee on recent developments and a CPMP response to the Commission proposal for the Plasma Master File (PHARM 306) was tabled for information. The Commission services representative highlighted that the BWP/CPMP endorsed most of the Commission proposal with the exception of Community assessment of the PMF, whereas the relationship of the PMF vis-à-vis the whole Marketing Authorization dossier remained to be clarified. He stated that it was envisaged to prepare a concrete legislative proposal during summer with a view on submitting and discussing it at the next meeting of the Pharmaceutical Committee in September.

e) Information on new Case law

The Judgement of the ECJ of 16.12.1999 in case C-94/98 on parallel imports (Rhone-Poulenc) (PHARM 289) was tabled for information. Following a specific request from a member of the Committee, the Commission services representative stressed that the findings of the ECJ must be read within the context of parallel imports and that it was not possible to directly apply all the principles elaborated in this parallel import case to the interpretation of Article 4(8)a iii of Directive 65/65 (the "generic provision").

f) Borderline medicinal products/biocides

The document PHARM 304 was presented for discussion and members of the Committee were asked to send their comments on the options proposed in this paper in writing to the Commission services by 2 May 2000.

g) Combination packs
A letter from the Swedish authorities and a Commission note to the MRFG concerning the possibility to authorise combination packs was presented to the Committee and the Commission services representative reaffirmed the position expressed in the note to the MRFG that – under the current legal framework and contrary to fixed-combination products – "combi-packs" or "convenience packs" cannot be the subject of ONE marketing authorisation. The Committee took note of this position.

2. LEGISLATIVE ISSUES
a) Review 2000 - Audit of the new marketing authorisation procedures
The Commission services representative highlighted that the Commission was obliged under Article 71 of Regulation 2309/93 to publish a general report on the experience acquired with the new marketing authorisation procedures (central procedure and mutual recognition procedure) by 1.1.2001. Based on this report, the Commission might take the decision to propose legislative changes. He reported that the Commission services had commissioned an independent audit to be carried out over the year 2000. This audit should provide a sound basis for the elaboration of the report to be drafted. He also stressed – following specific remarks by members of the Committee - that
- all Member States (in particular those which will keep the presidency in the upcoming period) would be closely involved in the exercise from the very beginning
- a special Pharmaceutical Committee to discuss the "review 2001" would be convened in November 2000
- care should be taken to avoid overlaps between the activities (meetings, workshops etc) dedicated to the review 2001
- everybody was invited to contribute to the audit and to make his view known
- the "questionnaires" which have been recently circulated by the contractor should help to focus contributions on some key points but that there were, however, no limits whatsoever on the scope of comments which may be made.

b) Transmissible Spongiform Encephalopathy (TSE)
Letters of November 1999 from the European Commission and letters from NL and Fin (PHARM 290 and 290a) on the practical application of Directive 99/82/EC on medicinal products and TSE were presented for discussion. After an intensive debate which helped to clarify certain misunderstandings, the Commission services reiterated the position already taken in November 1999 that for marketing authorisations not falling under the scope of the two Variations Regulations (=purely national authorisations), Member States were free to follow appropriate national procedures, ensuring that demonstration of compliance with the TSE-Directive takes place in an appropriate form. The Commission representative stressed that requiring the marketing authorisation holder to produce a certificate of suitability of its product with the newly created Pharmacopoeia monographs on TSE has significant merits and that the use of this model in the national context should be encouraged. The Dutch representative proposed to prepare within the NTA-Group specific templates to be used by competent Member States authorities.

c) Working Group on "Traditional medicinal products"
The Commission services representative reported that – after receipt of nominations for membership – a first meeting of this newly established brainstorming group was convened for 5 April 2000.

d) Draft proposal for changing chapter Va of Directive 75/319 (pharmacovigilance)
The updated proposal for a Commission Directive amending chapter Va of Directive 75/319/EEC and explanatory remarks (PHARM 299) were presented to the

Pharmaceutical Committee and were subject of a general discussion and exchange of views, particularly with regard to the explanatory notes and legal basis for adopting this Directive. The Commission was asked to confirm the legal basis. Subsequently the draft was the subject of a special Standing Committee, starting on 23.3.2000 at 10.30, which delivered a positive opinion on the draft (see separate minutes of this meeting).

e) 'Orphan medicinal products'
The text of the recently adopted EP and Council Regulation 141/2000 (PHARM 291) was tabled for information and the Commission services representative presented the draft of an implementing Commission Regulation (PHARM 305) to the Committee. This draft was the subject of a general discussion and exchange of views, particularly with regard to the possibility of improving the definitions contained therein. Subsequently the draft was the subject of a special Standing Committee, starting on 23.3.2000 at 10.30, which delivered a positive opinion on the draft (see separate minutes of this meeting).

f) 'Good Clinical Practice in the conduct of clinical trials'
The Commission services representative informed the Committee that the Portuguese Presidency was trying hard to arrive at a common position before the end of June. A lot of progress had been made under the Portuguese Presidency, but due to a multitude of - mainly technical - requests and reservations from Member States it was difficult to foresee whether this aim could be achieved.

g) Codification of Pharmaceutical Legislation
The Commission services representative informed the Committee that Council and EP were currently examining the codified text and that it was expected to have it adopted before the end of 2000. Due to a multitude of - mainly technical - request and reservations from Member States it was, however, difficult to foresee whether this aim could be indeed achieved.

h) Variations Regulations
The Commission services representative informed the Committee of the intention to carry out a revision of Regulations 95/541 and 95/542 on variations to the terms of a Marketing Authorization, taking into account the practical experience accumulated so far. For the purpose of this exercise, contributions from Member States were requested and it was announced that a special meeting on this issue would probably be convened in October 2000.

3.MARKETING AUTHORISATION PROCEDURES
a) Mutual recognition
The Portuguese Presidency tabled a written Report from the MRFG.

b) Centralised procedure
1. Status Report
The EMEA representative updated the Committee on the functioning of the centralised procedure and referred to the fact that detailed information was also available at the EMEA-website (http://www.eudra.org)
2. Labelling, indication of the logo of the local representative
The Commission services representative conveyed a request submitted by an interested party to allow the mentioning of the logo of the local representative in the labelling (in the blue box) of centrally authorised medicinal products.
Whilst representatives of some Member States expressed sympathy with the proposal, a large majority of representatives of Member States declared that they would consider the

inclusion of the logo of the "local representative" at the packaging of centrally authorised products as not acceptable. The main reason for this position was the argument that the indication of the name and address of a "local representative" has to serve as a national contact point for patients and that it was not necessary for *health* purposes to add a company logo to this information. Moreover certain delegations raised the point that such an inclusion would induce a confusion for the patient between the marketing authorisation holder (who bears all the responsibilities for the product) and the local representative who – by definition – has none.
Taking into account the fact that any modification of the "blue box" Guideline would need the support of the Pharmaceutical Committee, the Commission services representative noted that a positive response to the request for a change of the Guideline was not possible

c) Notice to Applicants
The Commission services representative informed the Committee that the guideline on renewal and chapter 7 would be finalised by written procedure. The main topics of the next NTA meeting (3-4 May 2000) would be chapters 1 and 3, the template in part IA and the Guideline on classification "new applications vs variations". Comments received by interested parties for chapter 2 would also be examined.

4. RATIONAL USE
a) Working group on information/advertising and working group on electronic commerce
The Commission services representative informed the Committee that a first joint brainstorming meeting of both groups had taken place on 21 March in Brussels. At the occasion of this meeting it was agreed that the Commission services would send out – as a next step - a questionnaire, asking concrete questions and proposing concrete options on possible ways forward. Based on the answers to this questionnaire, the future work of the group would be determined. Following requests from members of the Committee it was agreed to copy this questionnaire also to all members of the Pharmaceutical Committee.

b) Indication of additional items at the packaging of medicinal products
The Commission services representative presented proposals submitted by interested parties concerning the mentioning of additional items at the packaging of medicinal products:
With document PHARM 293 the indication of "accreditation logos", like the "Kosher" and "Halal" or the "organic farming" logo was proposed. 14 out of 15 Member States representatives rejected this proposal (one Member State abstained from expressing its view). The main reasons given for the rejection of the proposal were that these logos could not be considered as "health-information" and that the risk of an inflation of additional items on the packaging required a restrictive interpretation of Directive 92/27. Moreover some representatives of Member States expressed concern that the indication of such items might negatively influence the compliance of some patients.
With document PHARM 293a the indication of the manufacturers name and of pictograms or symbols showing the therapeutic indication and/or the pharmaceutical form and/or method/route of administration was proposed. A large majority of members of the Committee rejected the possibility of mentioning the manufacturers name. With respect to the mentioning of pictograms or symbols showing the therapeutic indication and/or the pharmaceutical form and/or method/route of administration, the Committee considered that it was not possible to give a general answer to this question. It was agreed that it was

necessary to look into the details and that an answer could only be given with respect to concrete examples/scenarios on a case by case basis.

c) Doping/sport
The Commission services representative presented a questionnaire (PHARM 300) on the information on the labelling of medicinal products concerning doping. Member States were asked to return the completed questionnaire to the Commission services by 2 May 2000.

5. GOOD MANUFACTURING PRACTICE
The Commission services representative reported on activities within the Inspectors Group presented the papers PHARM 294 (Revision of Annex 14 to the EU Guide to Good Manufacturing Practice) and PHARM 294a (Revision of Annex 6 to the EU Guide to Good Manufacturing Practice) to the Committee. The Committee took note of these papers. PHARM 294 was adopted and PHARM 294a released for consultation. The Commission representative informed the group that a new annex on parametric release and a revised procedure for rapid alerts would be circulated by mail for information to the Pharmaceutical Committee in the near future.

6. INFORMATION SOCIETY IN THE PHARMACEUTICAL SECTOR:
1. New administrative structure concerning the management of Telematic projects in the pharmaceutical sector
In a lively exchange of views on the management of IT projects in the pharmaceutical sector, Member States expressed concern that there was an urgent need to streamline and co-ordinate initiatives better, to take operative decisions quickly and in full transparency and to get certainty about financial implications.
The Commission services representative took note of the concern expressed by Member States and stressed that a quick phasing-in of the agreed new management structures was a priority. He invited Member States to help creating a coherent and efficient frame in the coming weeks and he announced that
- a meeting of the Telematic Steering Committee would be convened on 12 June in Lisbon,
- a meeting of the Telematic Management Board would be convened on 17 May in Brussels, and
- that all pertinent information (Summary Record of the December 1999 Telematic Steering Committee and Commission services document of 22.12.99 on Pharmaceutical IT systems) would also be circulated to the members of the Pharmaceutical Committee.
2. MedDRA (Medical Dictionary for Drug Regulatory Activities)
A report and a draft paper on the implementation of MedDRA in the EU (PHARM 295) was distributed and discussed. Whilst everybody agreed on the merits of a – possibly mandatory - harmonised medical terminology, concern was raised on the financing of this project. It was agreed that Member States/regulators should have free access to all MedDRA data and that training on the use of these data needed to be mad available at a reasonable price.
The Commission services representative invited written comments on the proposal to make MedDRA mandatory and on the paper on LLT versus PTs by 7 April 2000.

7. INTERNATIONAL RELATIONS
a) ICH
The future of ICH was the subject of an intensive general debate of the Pharmaceutical Committee. The outcome of this debate can be summed up as follows:

1. It was agreed that ICH has done a good job in the past and that the development so far could be legitimately called a "success-story"
2. The future activities of ICH must be carefully considered taking into account resource considerations and the pros and cons of the exercise.
3. The exercise should continue for political and scientific reasons provided activities can be streamlined or downsized and priorities identified.
4. The need for the current administrative structure was questioned.

During the special session on the future of ICH with Members of the Pharmaceutical Committee and invited experts involved in ICH which subsequently took place on 23 March, the need to focus on activities where there is a high value added and to look carefully at the possibility of a lighter structure, involving videoconferencing if necessary, were stressed. It was agreed that the Commission services would develop a paper in association with the CPMP and EMEA by the end of May.

b) (Mutual) Recognition Agreement

1. Progress report on implementation of mutual recognition agreements:

The Commission services representative reported that the mutual evaluation of the EU and *Canada* was progressing well. Problems encountered in the evaluation of some EU Member States seemed to be based on misunderstanding and would hopefully be sorted out shortly. With regard to a possible future MRA with *Japan*, there had been no activity and no progress could be reported.

2. Implementation of chapter 15 of the MRA with Switzerland;

The final explanatory notes on the interpretation of chapter 15 of the MRA with Switzerland (PHARM 296) were tabled for information.

c) Enlargement - PERF

1. Report on the activities of the Pan European Regulatory Forum (PERF)

The Slovak CADREAC Member informed the Committee on the outcome of the Pan European Regulatory Forum (PERF) and a General Report of PERF was tabled as document PHARM 297. The Commission services representative highlighted its satisfaction with the PERF-exercise and announced that the financing of a possible future "PERF II" was the subject of ongoing discussions within the Commission services. A decision could be expected by May/June 2000. PERF II would focus on the following three key issues: Implementation of the acquis; GMP and Pharmacovigilance. The need for specific practical training was also stressed.

2. PECAs with Hungary and the Czech Republic

The Committee was informed about the draft Protocols to the Europe Agreements on Conformity Assessment and Acceptance of industrial products between the EC and Hungary and the Czech Republic ("PECA"), which are currently at the initialling stage (PHARM 301). The Commission services representative highlighted that Section 2.10 of the agreement with the Czech Republic and section 2.8 of the agreement with Hungary were dealing with GMP for medicinal products and clarified that the future application of these agreements was clearly limited to the pre-accession period of Hungary and the Czech Republic.

8. A.O.B.

- Food supplements: A Commission services representative informed the Committee on the content of a draft Directive on food supplements. It was envisaged that the text of this

draft Directive would be circulated to Members of the Pharmaceutical Committee in writing for comments within the weeks following the meeting.
- The next meeting of the Pharmaceutical Committee will take place on 21 and 22 September 2000.