The European Agency for the Evaluation of Medicinal products
Evaluation of Medicines for Human Use

24 January 2000
CPMP/122/00

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 56th plenary meeting from 18 January 2000 to 19 January 2000.

The CPMP welcomed six new members, who are Dr Mark Ainsworth from Denmark succeeding Dr Gorm Jensen, Prof. José Augusto Guimarães Morais from Portugal succeeding Prof. Rogerio Gaspar, as well as Dr Sigurdur Thorsteinsson and Dr Magnús J?hannsson from Iceland, and Dr Lars Gramstad and Dr Tove Karlsrud from Norway.

The CPMP noted the report from the Informal CPMP meetings held in Berlin and Helsinki, which is circulated together with this Press Release (Annex II).

Centralised Procedures[1]

The Committee adopted:

- Opinions on centralised marketing authorisation applications:

  - One positive opinion was adopted by consensus relating to a medicinal product containing a new active substance (Part B), a gonadotropine releasing hormone antagonist indicated for the prevention of premature luteinising hormone surges in women undergoing controlled ovarian hyperstimulation.

- Opinions on “line extension” applications (in accordance with Annex II of the Commission Regulation (EC) No 542/95 as amended):

  - One positive opinion was adopted by consensus relating to an application for a new route of administration concerning an already centrally authorised medicinal product containing an insulin (Part A), indicated for diabetes mellitus.

- Seven positive opinions by consensus for centralised type II variations.

- One positive opinion by consensus following the annual re-assessment of Betaferon (interferon beta 1-b) indicated for the treatment of multiple sclerosis. The CPMP recommended that the marketing authorisation for this product should remain “under exceptional circumstances”.

An urgent safety restriction concerning Ziagen (abacavir) to include further information regarding respiratory symptoms associated with hypersensitivity reactions which could be life threatening if treatment were continued or reintroduced, has been published and is available on the Internet: EMEA public statement (EMEA/1952/00).

The Committee considered the need for GMP inspections for six medicinal products (four Part A / two Part B) and requested five inspections for four of them (Part A).

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[1] Note for Editors:
Applicants may appeal any CPMP opinion, provided they notify the EMEA in writing of their intention to appeal within 15 days of receipt of the opinion.

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The Committee heard two oral presentations from applicants concerning ongoing procedures.

An overview of centralised applications is given in Annex I.

Scientific Advice

The Committee adopted the following scientific advice letters:

Part	Indication(s)	Topic
B	Hypercholesterolemia	Quality, pre-clinical and clinical development programme
B	Reduction of the frequency of relapse in patients with relapsing – remitting multiple sclerosis	Pre-clinical and clinical development programme
B	Alzheimer's disease	Clinical development programme
B	Chronic heart failure	Clinical development programme

The Committee accepted three new requests from companies for scientific advice. Co-ordinators were appointed.

Referrals

Referral under Article 7(5) of Commission Regulation (EC) No 541/95

Three positive opinions for arbitration for three variation type II procedures regarding the same medicinal product referred by Germany for safety concerns to the EMEA under the mutual recognition procedure were adopted by consensus and will be forwarded to the Commission.

Referral under Article 10 of Council Directive 75/319/EEC, as amended

A positive opinion for arbitration referred by Germany to the EMEA under the mutual recognition procedure because of lack of scientific justification of the dose recommendation was adopted by consensus and will be forwarded to the Commission.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

The CPMP heard reports from its Quality, Biotechnology, Safety, Efficacy and Pharmacovigilance Working Parties and from the Ad Hoc Working Group on Blood Products.

BIOTECHNOLOGY WORKING PARTY

The following document was released for 6 months' consultation:

- Note for guidance on the Production and quality control of animal immunoglobulins and immunosera for human use (CPMP/BWP/3354/99 Draft)

ICH

The CPMP in the presence of the European Commission has started a reflection on the ICH process and its future after ICH-5 in San Diego in November 2000.

The CPMP expressed its satisfaction in the achievements realised since ICH-1 (1991) for the harmonisation of requirements for the development of medicinal products in the three regions.

ICH-5, with the expected discussion of the Common Technical Document (CTD), will complete a cycle of the ICH process as planned 10 years ago.

The CPMP considered that an evaluation of the impact of the ICH process at Regulatory and Industry level should be performed. The CPMP has reinforced the importance of a continued revision of adopted guidelines according to the scientific State of the Art, of international co-operation and of globalisation activities. Nevertheless, objectives and priorities for new or challenging scientific areas for pharmaceutical products have to be agreed, as well as possible new mechanisms for their completion. The CPMP has agreed to continue its reflection in the coming months, for the preparation of the Brussels meeting in July 2000.

Organisational Matters

The CPMP adopted a template for the list of questions which is sent to the applicant by the CPMP at day 120 of the Scientific Evaluation of a new application for marketing authorisation. The document will be made available on the Internet (CPMP/1775/99).

Mutual Recognition

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) dated 17 January 2000, which is circulated together with this Press Release (Annex III).

Prof. Rolf Bass
Head of Unit
Evaluation of Medicines for Human Use

This Press Release and other documents are available on the Internet at the following address: http://www.eudra.org/emea.html

EMEA CENTRALISED PROCEDURES

	1995-1999			2000			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	61	77	138	0	4	4	142
Follow-up to scientific advice	11	6	17	0	0	0	17

	1995-1999			2000			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	80	144	224	5	16	21	245
Withdrawals	12	26	38	0	0	0	38
Positive CPMP opinions	44	82	126	0	1	1	127[1]
Negative CPMP opinions[2]	1	6	7	0	0	0	7[3]
Marketing authorisations granted by the Commission	40	78	118	0	0	0	118[4]

	1995-1999			2000			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	159	346	505	1	26	27	532
Positive opinions, variations type II	89	131	220	2	5	7	227
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	32	15	47	1	0	1	48

[1] 127 positive opinions corresponding to 99 substances
[2] In case of appeal the opinion will not be counted again
[3] 7 negative opinions corresponding to 4 substances
[4] 118 Marketing Authorisations corresponding to 94 substances

OUTCOME OF INFORMAL CPMP MEETINGS HELD IN BERLIN AND HELSINKI

The CPMP, during its informal meetings held in Berlin on 7 and 8 June 1999 and in Helsinki on 30 September and 1 October 1999, addressed a number of organisational issues which were further discussed during its December 1999 and January 2000 plenary meetings.

The main results of such discussions can be summarised as follows:

Organisation of the CPMP week

As of February 2000, discussions on Scientific Advice requests will continue to be held on Mondays of the CPMP week, but continue, when necessary on Tuesday mornings. CPMP plenary meetings will necessitate 3 full meeting days, starting on Tuesday mornings and finishing on Thursday afternoons.

The CPMP will continuously review this situation in order to accommodate the increasing involvement of the CPMP in various public health matters.

Processing of Centralised applications

- Pre-authorisation phase

- As of the September meeting, the adoption of the CPMP List of Questions at day 120 will coincide with a CPMP meeting. This will necessitate changes in the dates for submission of applications for marketing authorisation.

- As of January, the EMEA Secretariat will send the Rapporteur / Co-Rapporteur Assessment Reports to applicants / Marketing Authorisation Holders (both in the Centralised Procedure and in the Referral / Arbitration Procedure) prior to discussion at CPMP level. It should be noted that such Assessment Reports are sent for information only; they set out only the preliminary conclusions of Rapporteur and Co-Rapporteur and in no way bind the CPMP.

- Timing of oral explanations will be carefully monitored and discussions should be limited to key outstanding issues, resulting, where possible, in 1-hour oral explanations (30 minutes for the presentation of such key issues and 30 minutes for subsequent discussion).

- In order to allow a better finalisation of the product information (Summary of Product Characteristics, Package Leaflet and Labelling) and the CPMP Assessment Report, adoption of CPMP Opinions will, in the future, take place during the month following the oral explanation, whilst the legal timeframe for the review will continue to be adhered to. Such timeframe could also be used for finalisation of product information translations.

- Post-authorisation phase

- In the future, Co-Rapporteurs will become systematically involved in post-authorisation activities. The CPMP will have to further define the exact role of Rapporteurs and Co-Rapporteurs in the post-authorisation phase.

- The increasing difficulties encountered by the CPMP in relation to the fulfilment by Marketing Authorisation Holders of post-authorisation commitments (i.e. specific obligations and follow-up measures) will lead to a more careful review by the CPMP of timelines for such post-authorisation commitments proposed by the applicants at the time of the adoption of the CPMP Opinions. In addition, during such adoption, clear statements will be made in the SPC (e.g. Section 5.1) on the non-availability of certain data / studies.

Difficulties encountered with marketing authorisation applications in some therapeutic fields

The CPMP, having reviewed its approach towards applications in the different therapeutic fields, is of the opinion that its evidence-based medicine is a robust approach. There is, however, room for further improvement, especially in the anti-cancer field, and the CPMP agreed on the following action plan:

- A brainstorming session will be held with all stakeholders in the anti-cancer field in order to overcome the differences between the CPMP and such stakeholders.

- Contacts with industry will be maintained by establishing an anti-cancer Working Group in order to streamline views on anti-cancer medicines.

- Stronger scientific input will be ensured by relying on input from academia.

- The access of patients to promising anti-cancer medicines will be improved by accepting, on a case-by-case basis, phase II trials.

- Better interaction with interested parties will be allowed by further improving communication with such interested parties.

Report from the meeting held on 17 January 2000

The MRFG noted that 21 new mutual recognition procedures were finalised during the month of December 1999, as well as 46 type I, and 11 type II variations.

The status as of 31 December and for the whole year 1999 of procedures under mutual recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures from Type I variations finalised	Procedures from Type I variations pending	Procedures from Type II variations finalised	Procedures from Type II variations pending	Arbitrations referred to CPMP
1999	228	43	671	50	301	124	2 N.A. 2 var.

The status of the 5 years since the Mutual Recognition Procedure started is as follows (further detailed statistics can be found at the MRFG Website):

Years	Procedures from New applications finalised	Procedures from Type I variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CPMP
1995-1999	650	1176	776	6 New Applications + 8 Variations

In 1999 the categories of the finalised procedures are as follows:

New active substance[1]	Line extensions[2]	Fixed comb.	Generics	Herbal products[3]	OTC[4]	Blood products	Immuno-logicals	Others[5]
35	24	13	91	0	2	1	5	57

32 new procedures (regarding 47 products) started in December 1999. The categories of these procedures are as follows:

New active substance[1]	Line extensions[2]	Fixed comb.	Generics	Herbal products[3]	OTC[4]	Blood products	Immuno-logicals	Others[5]
10	4	4	8	0	1	0	0	5

1. When in one of the involved Member States it concerns a new active substance according to the definition in the Notice to Applicants Volume IIA; the number given includes multiple applications and repeat use

procedures.

2. Line extensions are those applications which extend a range of products, e.g. an additional strength, or a new pharmaceutical form from the same Marketing Authorisation Holder;
3. In this category products are classified as herbals when the RMS has considered them as herbal product;
4. In this category products are classified as OTC products when the RMS has approved it for OTC use, although the legal status is not part of the Mutual Recognition Procedure;
5. When the product is not classified in the other eight categories.

Each application can be classified in only one category.

Number of countries involved in the new applications procedures started in December 1999:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (1)	14
DE (1)	12
DE (1)	3
DK (4)	10
FI (1)	7
FR (1)	11
FR (1)	9
FR (1)	11
FR (1)	11
IT (1)	12
NL (2)	8
NL (2)	14
PT (1)	1
SE (1)	12
SE (1)	6
SE (2)	14
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	14
SE (2)	14
SE (2)	1
SE (2)	1
UK (1)	12
UK (1)	1
UK (1)	1
UK (1)	2
UK (3)	3
UK (1)	14
UK (1)	1
UK (1)	1

General issues

- The first MRFG meeting in 2000 took place under Portuguese chairmanship with an observer from the Cadreac countries and representatives from Norway and Iceland who have officially joined the Mutual Recognition procedure as of 1 January 2000.
- A proposal to amend the Core-SPC for flu vaccines regarding Guillan Barré syndrome is under discussion.

All documents mentioned in this press release can be found at the MRFG website at the European Medicines Authorities Windows under the heading SOP.

Information on the above mentioned issues can be obtained by the presiding chair of the MRFG:

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*Alternatively, you could visit the **MRFG web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*

http://heads.medagencies.org/