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

25 May, 1999
CPMP/1434/99

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 49th plenary meeting from 18 May to 20 May, 1999.

Centralised Procedures

The Committee adopted:

- Opinions[1] on initial centralised applications:

  - One positive opinion was adopted by majority vote relating to a medicinal product containing a new active substance (Part B), an antirheumatic agent indicated for the treatment of adult patients with active rheumatoid arthritis as a "disease modifying antirheumatic drug" (DMARD).
  - One positive opinion was adopted by majority vote relating to a medicinal product containing a new active substance (Part A), a monoclonal antibody indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children.
  - One positive opinion was adopted by consensus relating to a medicinal product containing a new active substance (Part A), a fast acting human insulin analogue indicated for treatment of patients with diabetes mellitus.
  - One positive opinion was adopted by consensus under exceptional circumstances relating to a medicinal product containing a new active substance (Part A), an immunomodulating agent indicated for treatment of severe, active Crohn's disease.

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

  - Two positive opinions were adopted by consensus relating to two applications for an additional strength concerning an already centrally authorised medicinal product containing a dopaminergic agent (Part B), indicated for symptomatic treatment of advanced idiopathic Parkinson's disease in combination with levodopa.
  - Three positive opinions were adopted by consensus relating to three applications for an additional strength, concerning an already centrally authorised medicinal product containing an angiotensin II antagonist (Part B), indicated for treatment of essential hypertension.

The CPMP agreed five lists of questions (two part A/three part B) (concerning four active substances) of which three products were considered to be approvable and two non approvable based on the information available to the CPMP at this time.

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

[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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Rapporteurs and Co-Rapporteurs were assigned for twelve applications forthcoming in the centralised procedure within the next four months (one Part A/eleven Part B), including five applications for the same active substance (Part B), and also including re-submission of an application previously withdrawn (Part B).

The CPMP adopted the GMP inspections requests for 12 medicinal products (2 for Part A/10 for Part B).

Since the CPMP meeting in April 1999, the Committee noted the withdrawal of one application (Part A) from the centralised procedure.

An overview of centralised applications is given in Annex I.

For marketing authorisations granted by the European Commission since the last CPMP in April 1999, see Annex II.

Pharmacovigilance

Following reports of serious, severe and unpredictable liver injuries associated with the antiinfective products Trovan/Trovan IV and Turvel/Turvel IV (containing trovafloxacin/alatrofloxacin) the CPMP finalised an urgent safety restriction to amend the SPC and patient information. Full information is available on the Internet in a special Public Statement addressing this issue (EMEA/15770/99).

Scientific Advice

The Committee:

- Adopted six scientific advice letters (four Part A/two Part B) on stability, preclinical and/or clinical development, concerning seven new medicinal products, intended for:

    - Needle free injection system for the treatment of anemia
    - Treatment of Crohn's disease
    - Prevention and clinical management of ischemic complications in patients with acute coronary syndromes
    - Treatment of chronic schizophrenia
    - Treatment of unstable angina or non-Q-wave myocardial infarction
    - Reduction in the duration of chemotherapy-induced neutropenia

Working Parties, Ad Hoc Expert Groups and Organisational Matters

EFFICACY WORKING PARTY

Two documents were adopted*:*

- Points to consider on clinical investigation of medicinal products in the chronic treatment of patients with chronic obstructive pulmonary disease (COPD) (CPMP/EWP/562/98)
- Note for guidance on clinical evaluation of new vaccines (CPMP/EWP/463/97)

Organisational Matters

The CPMP heard a presentation from EFPIA on *Regulation 2000,* followed by the third annual EMEA v. EFPIA football match (Annex IV).
The CPMP agreed that the August 1999 meeting will not take place and applications will be dealt with by written procedure. A revised calendar for the year 2000 has been adopted (Annex V).

Mutual Recognition

The CPMP noted the report from the mutual recognition facilitation group (MRFG) 17 May 1999, which is circulated together with this Press Release (Annex VI).

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The report from the meeting with interested parties of 21 April 1999 is circulated together with this Press Release (Annex III).

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

EMEA CENTRALISED PROCEDURES

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific advice	33	45	78	12	14	26	104
Follow-up to scientific advice	9	4	13	1	1	2	15

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	62	115	177	7	11	18	195
Withdrawals	11	19	30	1	3	4	34
Positive CPMP opinions	35	65	100	5	11	16	116[2]
Negative CPMP opinions[3]	1	2	3	0	0	0	3
Marketing authorisations granted by the Commission	28	60	88	9	7	16	104[4]

	1995-1998			1999			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	99	168	267	13	88	101	368
Positive opinions, variations type II	41	77	118	15	15	30	148
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	25	6	31	1	7	8	39

[2] 116 positive opinions corresponding to 90 substances
[3] In case of appeal the opinion will not be counted again.
[4] 104 marketing authorisations corresponding to 81 substances

Medicinal products granted a Community Marketing Authorisation under the Centralised Procedure since the April 1999 Press Release

Brand name	Procomvax
INN	*Haemophilus influenzae* type b capsular polysaccharide conjugated with the outer membrane protein of *Neisseria meningitidis* and recombinant hepatitis B surface antigen
Marketing Authorisation Holder	Pasteur Merieux MSD, FR
ATC code	J07CA
Indication	Indicated for vaccination against invasive disease caused by *Haemophilus influenzae* type b and against infection caused by all known subtypes of hepatitis B virus in infants of 6 weeks to 15 months of age.
Opinion receipt date	03.03.99
Date of Commission decision	07.05.99

Brand name	Rotashield
INN	One rhesus rotavirus serotype (serotype 3) and three reassortant rotavirus serotypes derived from rhesus and human strains (serotypes 1, 2 and 4)
Marketing Authorisation Holder	Wyeth-Lederle Vaccines S.A., BE
ATC code	JO7BH
Indication	Both indicated for active immunisation of infants aged 6 weeks to 30 weeks for prevention of severe clinical manifestations of gastro-enteritis caused by rotavirus serotypes 1, 2, 3, and 4 of group A.
Opinion receipt date	05.03.99
Date of Commission decision	07.05.99

Brand name	Rebetol Cotronak
INN	ribavirin
Marketing Authorisation Holder	Schering-Plough, USA
ATC code	J05AB040
Indication	both are indicated, in combination with interferon alfa-2b: - for the treatment of adult patients with chronic hepatitis C who have previously responded (with normalisation of ALT at the end of treatment) to interferon alpha therapy but who have subsequently relapsed. - for the treatment of adult patients with histologically proven chronic hepatitis C, not previously treated, without liver decompensation, with elevated ALT, who are positive for serum HCV-RNA and who have fibrosis or high inflammatory activity. Patients with only portal fibrosis (minimal fibrosis) should have a high inflammatory score.
Opinion receipt date	19.03.99
Date of Commission decision	07.05.99

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

ANNEX III to CPMP May 1999
Press Release

London, 25 May, 1999
EMEA/CPMP/1434/99

REPORT ON INTERESTED PARTY MEETING HELD ON 21 APRIL 1999

In continuation of the cycle of quarterly meetings with European Interested Parties, discussions were held on 21 April 1999 with representatives of European Federation of Pharmaceutical Industries Associations (EFPIA), Association Européenne des Spécialités Grand Public (AESGP), Groupement des Pharmaciens de l'Union Européenne (GPUE), Health Action International (HAI). European Generic medicines Association (EGA) and Bureau Européen des Unions de Consommateurs (BEUC) and Standing Committee of European Doctors (CP) were unable to attend the meeting.

The Chairman of the CPMP, Prof. Jean-Michel Alexandre presented the main results of the April CPMP meeting. Dr Mary Teeling, Vice Chairman of the CPMP, together with a number of CPMP members and experts also participated in the meeting. It was clarified that companies do have the opportunity to justify tradenames following receipt of objections from CPMP.

Dr Teeling reported from the April 1999 Scientific Advice (SA) Review Group meeting and informed the attendance of the increase in Scientific Advice requests (78 SA given from 1995 until 1998 and 30 SA currently ongoing). It was emphasised that the Scientific Advice letters are not legally binding for the CPMP, but have to be considered as an advice in line with the current scientific knowledge. In the event of a change of position it is to be anticipated that the CPMP would explain why new scientific knowledge would override positions taken earlier. In a similar way, companies are expected to present arguments in cases where they do not follow the advice given. The number of questions are increasing and broader (covering the overall pharmaceutical, preclinical and clinical drug development programmes). The group was informed that the SOP for Scientific Advice available on the Internet is being updated and that an interactive Scientific Advice Guidance is under preparation. They were also informed that opportunities to electronically submit Scientific Advice requests are under investigation.

The recent increase in pre-approval withdrawals from Marketing Authorisation applications triggered an extensive discussion of underlying causes. Prof. Bass presented the preliminary report on "withdrawn centralised applications" and announced that the final report will shortly be made available on the EMEA website. Promotion of Scientific Advice and of pre-submission meetings could reduce withdrawals from the current rate of approximately 25%.

The next meeting will be held on Wednesday, 20 October 1999. In preparation for this meeting, participants agreed to discuss how to update the structural and scientific content of the EPAR and ways and means towards more user-friendly patient leaflets should be put on the agenda.

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ANNEX IV to CPMP May 1999
Press Release

Third annual EMEA v. EFPIA football match
London, 19 May 1999

EMEA 3 – EFPIA 0

The third annual EMEA v. EFPIA football match was played on 19 May 1999. As part of the pre-match warm-up routine, a delegation from EFPIA took the opportunity to present the *Regulation 2000* concept paper to the CPMP in the afternoon of 19 May. The concept paper, adopted by the EFPIA Board on 30 April, sets out the innovative pharmaceutical industry's view on how it would like to see the European regulatory system for medicinal products evolve.

The game kicked off at 8.30 pm and was an anxious moment for the EMEA who had never beaten EFPIA. The final score of EMEA 3 – EFPIA 0 put all memories of the 5-1 defeat in 1997 and the 3-3 draw in 1998 firmly into the past.

The EFPIA team, once again captained by Richard Horne, put a lot of pressure on the EMEA team from the start. Resplendent in their new strip, the EMEA team, captained by David Drakeford, was initially nervous but took full opportunity of all their chances eventually leading 2-0 by half time.

Despite EFPIA winning much of the play in mid-field, the EMEA defence was very strong. EFPIA showed a lot of individual skill and ability throughout the match, but lacked teamwork, many passes – when they occurred – going astray. On the other hand, the EMEA played well as a team (both CPMP members and EMEA staff), both on the pitch and during the celebrations after the match.

Overall, it was a good result for the EMEA team after 3 years of working together. A metaphor perhaps for the progress the regulators are making with industry?

EMEA/CPMP team

Eric Abadie
Laurent Brassart
Paul Brown
Ruggero De Cristofano
Javier De Esteban
David Drakeford (*Captain*)
David Jefferys
Markey Kieron
Sergio Lucarelli
Jos Olaerts
Brian Ollivierre
Pasqualino Rossi
Per Sjöberg
Jan Stevens
Florence Villenave
Achilleas Voutsas

EFPIA team

Anthony Faupel, Glaxo Wellcome, London
Richard Horne, EFPIA, Brussels (*Captain*)
Anthony Pac-Soo, Fujisawa, Munich
Mike Page, Pfizer, Kent
Stratos Pegidis, EFPIA, Brussels
Piero Rijli, Menarini, Florence
Edwin Ruighaver, Eli Lilly, Surrey
Stefan Schwoch, Eli Lilly, Surrey
Fraser Stodart, Pfizer, Kent
Ivan Tommasini, Pfizer, Kent
Craig Whitehead, Smithkline-Beecham, London

Referee: Colin Walton, London Underground

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ANNEX V to CPMP May 1999
Press Release

London, 25 May, 1999
Doc. Ref: EMEA/CPMP/1434/99

Calendar for CPMP meetings in 2000

Month	Day
January	18, 19, 20
February	15, 16, 17
March	14, 15, 16
April	11, 12, 13
May	23, 24, 25
June	27, 28, 29
July	25, 26, 27
August	22, 23, 24
September	19, 20, 21
October	17, 18, 19
November	14, 15, 16
December	12, 13, 14

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MRFG
Mutual Recognition Facilitation Group

Report from the meeting held on 17 May 1999

The MRFG noted that 4 new mutual recognition procedures were finalised during the month of April 1999, as well as 55 type I and 23 type II variations.

The status as of 30 April 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	30	51	236	104	95	124	1 var.

28 new procedures (regarding 41 products) started in April 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]
4	3	2	15	0	1	0	2	1

1. When in one of the involved Member States it concerns a new active substance according to the definition in the Notice to Applicants Part IIA;
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 April 1999:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (3)	13
DE (1)	4
DE (1)	2
DE (1)	5
DE (1)	2
DE (1)	4
DE (2)	8
FR (1)	9
FR (1)	8
IR (2)	6

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
IR (2)	2
NL (1)	11
NL (1)	7
NL (1)	5
NL (1)	1
NL (1)	4
NL (1)	7
SE (1)	13
SE (1)	6
UK (1)	3
UK (1)	14
UK (1)	7
UK (1)	14
UK (1)	13
UK (3)	9
UK (3)	9
UK (3)	13
UK (3)	7

General issues

- The "recommendation on informed consent applications in mutual recognition procedures"* and the "position paper on repeat use ("second wave") of mutual recognition procedure" have been adopted and will be published on the Heads of Agencies Website as indicated below.
- The "recommendation on line extensions" will be adopted in June.
- The "recommendation on duplicate applications" will now read "recommendation on multiple applications".*
- The dates of MRFG meetings in the year 2000 will be published on the Heads of Agencies Website as indicated below.
- Comments concerning specific products in the MRP index should be addressed to the reference member state directly.
- The MRFG plenary meeting was followed by a meeting with representatives of EFPIA concerning Regulation 2000.
- No MRFG meeting will be held in August (initially proposed for 23 August 1999) – Break out sessions if necessary will be organised by the RMS.

*Recommendations released by MRFG reflect the current view of the group and are intended to facilitate and harmonise mutual recognition procedures

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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