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

London, 5 June 2003
EMEA/CPMP/2568/03/Rev 01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
20 – 22 MAY 2003 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 93rd plenary meeting from 20 – 22 May 2003.

The CPMP Chairman, Dr Daniel Brasseur, welcomed the participation of Dr. Milan Smid (Czech Republic) and Dr. Alar Irs (Estonia), who were attending the CPMP for the first time.

Product related issues

Centralised procedures

The CPMP adopted 3 opinions on an initial marketing authorisation application at this meeting:

- Positive opinions for **Humira** and **Trudexa** (adalimumab) from Abbott Laboratories, which are intended for the treatment of moderate to severe active rheumatoid arthritis. EMEA review began on 22 April 2002 and the opinion was adopted on 22 May 2003, with an active review time of 153 days.
- A positive opinion for **Ventavis** (iloprost) from Schering, which is intended for the treatment of primary pulmonary hypertension. EMEA review began on 28 January 2002 and the opinion was adopted on 22 May 2003, with an active review time of 205 days. Ventavis was designated an orphan medicinal product on 29 December 2000 and is the **eleventh orphan medicinal product** to receive a CPMP positive opinion.

Summaries of these opinions are available on the EMEA web site: http://www.emea.eu.int

The Committee also adopted 2 Lists of Questions (Part B).

The Committee gave positive opinions for a number of new indications for medicinal products that are already authorised in the EU:

- Extension of indication for **Actos** and **Glustin** (pioglitazone) from Takeda Europe to allow its use as a second-line monotherapy, particularly in overweight type 2 diabetes patients where other measures (such as diet and exercise) have failed and treatment with metformin is not suitable. Actos and Glustin were first authorised in the European Union in October 2000.
- Extension of indication for **Avandia**, **Nyracta** and **Venvia** (rosiglitazone) from GlaxoSmithKline to allow its use as a second-line monotherapy, particularly in overweight type 2 diabetes patients where other measures (such as diet and exercise) have failed and treatment with metformin is not suitable. Avandia, Nyracta and Venvia were first authorised in the European Union in July 2000.
- Extension of indication for **Aranesp** (darbepoetin alfa) from Amgen and **Nespo** (darbepoetin alfa) from Dompé Biotec to include the treatment of anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy. Aranesp and Nespo were first authorised in the European Union in June 2001.
- Extension of indication for **Cerezyme** (imiglucerase) from Genzyme to include type 3 Gaucher's disease. Cerezyme was first authorised in the European Union in November 1997.

Further information on these extensions will be included in the public assessment report (EPAR) once the European Commission has granted final approval.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 84 16
E-mail: mail@emea.eu.int http://www.emea.eu.int

An overview of centralised procedures since 1995 is given in **Annex 1.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 2**.

Referrals

The CPMP adopted a revised final opinion on a referral from Aventis Behring GmbH for **Beriate P** (human coagulation factor VIII) following the European Commission's request for clarification of the opinion adopted in February 2003. The CPMP revised final opinion removes the recommendation that the marketing authorisations may be revised in accordance with the Summary of Product Characteristics. In addition, the CPMP confirms its agreement with the decision taken in the mutual recognition procedure to refuse the variation application, which proposed to include the addition of HIV and HBV NAT testing in Section 4.4 (Special Warnings and Precautions) of the SPC. In consequence the Summary of Product Characteristics remains unchanged from the one finalised in the framework of the Mutual Recognition Procedure.

Non-product related issues

CPMP Working Parties, Ad Hoc Groups, Informal meetings

The CPMP was informed of the outcome of the discussions of the Scientific Advice Working Group (SAWG) meeting, which was held on 12 – 13 May 2003. For further details, please see **Annex 3**.

Documents prepared by the CPMP Working Parties and Ad Hoc Groups adopted during the May 2003 CPMP meeting are listed in **Annex 4**.

The Ad Hoc CPMP Vaccine Expert Group (VEG), chaired by Dr Dobbelaer, held its meeting on 20 – 21 March 2003 and the next meeting will be held on 18 – 20 June 2003

The Ad Hoc Expert Group on Gene Therapy (Chairperson Prof. Cichutek) will hold its next meeting on 26 – 27 June 2003.

The CPMP Paediatric Expert Group (Chairperson Dr Brasseur) will hold its next meeting on 23 May 2003.

The 1st CPMP/EMEA Working Group with Patients' Associations meeting, Co-chaired by Dr. Frits Lekkerkerker (CPMP member) and Mr Noël Wathion was held on the 8 May 2003. A Press Release and the attachments concerning this meeting are available on the EMEA website http://www.emea.eu.int/pdfs/human/patientgroup/1253603en.pdf.

The Informal CPMP meeting under the Greek presidency was held on 5-6 May 2003 in Athens, Greece. The Committee discussed internal organisational matters, management of European Risk programmes, SPC guideline issues (content of sections 4.1 and 5.1 of the SPC) and the scope and aim of the EMEA/CPMP Working Group with Patients Associations.

Interested Parties meetings:

A EMEA/DIA//EFPIA Pharmacogenetics Conference will be held on 29 and 30 October 2003. The CPMP appointed Dr. E. Abadie as chairperson of the plenary sessions.

Organisational Matters

The 23rd CPMP Organisational Matters meeting took place on Monday 19 May 2003, chaired by Dr D. Brasseur. During the meeting the following principle topics were presented/discussed:

- CPMP internal organisational matters (improvement of IT tools, optimum link between Organisational Matters meetings and CPMP plenary meetings)
- SPC Expert Group proposals
- CPMP Type II Assessment Report (AR) and Response AR templates were released for an internal 2 month consultation by the CPMP members

The next CPMP Organisational Matters meeting is scheduled to take place on Monday 23 June 2003.

PROCEDURAL ANNOUNCEMENT

Applicants are reminded that it is expected that the revised Annex I to Directive 2001/83/EC, which will include the CTD in its Part I, will enter into force in July 2003. The EMEA will therefore accept submissions in the 'old' NTA format only **until Monday 30 June 2003**. Any application received as of 1 July 2003 should be presented in accordance with the 'new' NTA format.

For further information on the CTD and the 'new' NTA format, please refer to the WebSite of the European Commission:
http://pharmacos.eudra.org/F2/eudralex/vol-2/B/ctdmay02.pdf

For further information on the handling/format of variations, reformatting of dossiers etc.. please refer to the Question & Answer section on the WebSite of the European Commission:
http://pharmacos.eudra.org/F2/eudralex/vol-2/B/ctdqa_032003.pdf

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 19 May 2003. For further details, please see **Annex 5.**

The 94th plenary meeting of the CPMP will be held from 24 – 26 June 2003.

Noël Wathion
Head of Unit
Post-Authorisation Evaluation of Medicines for Human Use, Tel. (+44-20) 74 18 85 92
This CPMP Monthly Report and other documents are available on the Internet at the following address:
http://www.emea.eu.int

EMEA CENTRALISED PROCEDURES

	1995 - 2000	2003	Overall Total
Scientific Advice	302	27	329
Follow-up to Scientific Advice	50	5	55
Protocol Assistance	13	4	17
Follow-up to Protocol Assistance	4	1	5

	1995-2002			2003			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	127	239	366	3	13	16	382
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	20	53	73	1	2	3	76
Positive CPMP opinions[2]	92	155	247	3	3	6	253[3]
Negative CPMP opinions[4]	1	4	5	1	0	1	6[5]
Marketing authorisations granted by the Commission	88	146	234	0	9	9	243[6]

	1995-2002			2003			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	585	1132	1717	72	159	231	1948
Positive opinions, variations type II	405	511	916	69	73	142	1058
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	44	44	88	1	0	1	89

[1] Consultation in accordance with Council Directive 93/42/EEC concerning medical devices as amended by Directive 2000/70/EC as regards medical devices incorporating stable derivatives of human blood or plasma and Directive 2001/104/EC.
[2] 2 positive opinion corresponding to 2 Orphan Medicinal Product
[3] 253 positive opinions corresponding to 190 substances
[4] In case of appeal, the opinion will not be counted twice
[5] 6 negative opinions corresponding to 5 substances
[6] 243 marketing authorisations corresponding to 182 substances

OUTCOME OF THE MAY 2003 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
8 Extension of indication	8 Positive opinion by consensus
9 SPC changes	9 Positive opinions by consensus
10 Quality changes	10 Positive opinions by consensus

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	N/A	N/A

Opinions for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Novonorm (repaglinide), Novo Nordisk	Positive opinion by consensus	---
Prandin (repaglinide), Novo Nordisk	Positive opinion by consensus	---
Optruma (raloxifene), Eli Lilly Nederland B.V	Positive opinion by consensus	---
Evista (raloxifene), Eli Lilly Nederland B.V.	Positive opinion by consensus	---

OUTCOME OF THE May 2003 CPMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Influenza virus vaccine	X				X	X	X	
Chemical	Type 2 diabetes	X						X	
Chemical	Parkinson's disease	X						X	
Chemical	Renal Cell carcinoma	X						X	
Chemical	HIV-1 infection	X					X	X	
Chemical	Chronic Obstructive pulmonary disease (COPD)	X					X	X	
Chemical	Asthma	X					X	X	
Chemical	Non-small cell lung cancer			X				X	

SA: Scientific Advice

PA: Protocol Assistance

In May 2003, the above-mentioned 7 Scientific Advice letters and 1 Follow-up Scientific Advice letters were adopted. The Committee accepted 8 Scientific Advice New Requests and 3 Protocol Assistance New Requests.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE MAY 2003 CPMP MEETING

BIOTECH WORKING PARTY

Reference number	Document	Status
CPMP/BWP/2583/03 rev. 1	Theratope vaccines: BPW recommendation to CPMP	**Adopted**

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/558/95 rev.1	Note for Guidance on evaluation of medicinal products indicated for treatment of bacterial infections	**Released for 6 months consultation**
CPMP/EWP/2863/99	Revised Points to consider on adjustment for baseline covariates	**Adopted**
CPMP/EWP/1343/01	Points to consider on the clinical evaluation of new agents for invasive fungal infections	**Adopted**

Report from the meeting held on 19 May 2003

General issues:

EU Enlargement
Following the decision of the European Commission and the HoA, the MRFG has invited the Candidate Countries to nominate representatives to attend their monthly meetings as observers. The nominated representatives of four CEEC countries, which were present at the meeting were welcomed by the Chair. It is expected that all Candidate Countries would be represented in future meetings.

Annex 1

Joint CPMP/ MRFG Working Group on Harmonisation of SPCs:
The progress report of the working group, outlining the current situation and the perspectives of the SPC harmonisation exercise will be presented to the HoA at their meeting on the 28 May 2003 in Athens.

Meeting schedule
The next MRFG meeting will be held on Monday 23 June 2003.

Mutual Recognition Monitoring

The MRFG noted that 31 new mutual recognition procedures were finalised during the month of April 2003, as well as 228 type I and 41 type II variations.

The status as of 30th April 2003 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
2003	135	100	773	292	150	338	1 N.A.

42 new procedures (regarding 90 products) started in April 2003. The categories of these procedures are as follows:

2 new active substances, including 1 repeat use.

12 known active substances (already authorised in at least one member state), including 2 repeat use.

27 abridged applications including 11 multiple applications and 2 repeat use.

1 Line extension applications, classified as repeat use.

The new procedures started related to 7 full dossiers, 27 generics, 2 bibliographic applications and 1 for different use, route or dose.

The procedures consisted of 39 chemical substances, 2 biological- blood product and 1 biological-other1.

36 of these procedures were prescription-only medicinal products in the reference Member State and 6 were Non-prescription (including OTC) medicinal products2.

1. As considered by RMS.
2. In this category products are classified as prescription-only or Non-prescription (OTC) products when the RMS has approved them accordingly, although the legal status is not part of the Mutual Recognition Procedure.

Number of countries involved in the new applications procedures started in April 2003

Reference Member State (number of products involved in the procedure) Number of CMSs involved in the procedure

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (3)	2
AT (1)	1
DE (1)	5
DE (1)	2
DE (1)	10
DE (3)	1
DK (4)	2
DK (3)	1
DK (3)	1
DK (3)	1
DK (3)	1
DK (3)	1
FI (2)	3
FI (2)	1
FI (2)	7
FI (4)	3
FI (1)	1
FI (1)	1
FI (1)	1
FR (3)	11
FR (1)	8
FR (1)	9
FR (1)	6
IT (1)	16
NL (1)	16
NL (1)	1
NL (1)	14
NL (3)	1
NL (3)	1
NL (3)	1
NL (3)	2
NO (3)	2
SE (5)	7
SE (5)	1
UK (3)	2
UK (2)	6
UK (2)	6
UK (1)	12
UK (2)	5
UK (1)	4
UK (1)	10
UK (1)	7

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:

*Pharm. Julia **YOTAKI***
National Organization for Medicines (EOF)
284, Messogeion Avenue
GR 155 62 Holargos
GREECE

Phone: + 30 210 650 7209
Fax: + 30 210 6547 202
e-mail: yotakij@eof.gr

*Or you could visit the **MRFG web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*
http://heads.medagencies.org/