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

04 March 2004
EMEA/CPMP/537/04

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS FEBRUARY 2004 PLENARY MEETING MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 101st plenary meeting from 24-26 February 2004.

The CPMP Chairman, Dr Daniel Brasseur, on behalf of the Committee welcomed the new Danish CPMP member Prof. Gorm Jensen, who replaces Dr. Mark Ainsworth. The CPMP Chairman also extended a welcome to Prof. Michal Pirozynski, Poland and Pharm. Arthur Isseyegh, Cyprus who were attending the CPMP for the first time in their capacity of Accession Countries' Observers.

Product related issues

Centralised procedures

The Committee adopted three opinions on initial marketing authorisation applications at this meeting:

- A positive opinion on the marketing authorisation for **Abilify** (aripiprazole), from Otsuka Pharmaceuticals Europe Ltd, intended for the treatment of schizophrenia. EMEA review began on 24 December 2001 and the opinion was adopted on 26 February 2004, with an active review time of 206 days.
- A positive opinion on the marketing authorisation for **Levemir** (insulin detemir), from Novo Nordisk, intended for the treatment of diabetes mellitus. EMEA review began on 18 November 2002 and the opinion was adopted on 26 February 2004, with an active review time of 179 days.
- A positive opinion on the marketing authorisation for **TachoSil** (human fibrinogen and human thrombin), from Nycomed. TachoSil is a medicated sponge intended as supportive treatment in surgery for improvement of haemostasis where standard techniques are insufficient. Efficacy has only been demonstrated in liver surgery. EMEA review began on 22 July 2002 and the opinion was adopted on 26 February 2004, with an active review time of 225 days.

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

The Committee also gave a positive opinion on the extension of indication for **Enbrel** (etanercept), from Wyeth Europe Ltd, to include its use with methotrexate in adults with rheumatoid arthritis. Enbrel was first authorised in the European Union on 3 February 2000.

Further information on this extension will be included in the European 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

The Committee also adopted three Lists of Questions (Part B)

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**. No Commission Decision was granted since the CPMP meeting in January 2004.

Non-product related issues

CPMP Working Parties and Ad Hoc Groups

- The CPMP was informed of the outcome of the discussions of the Scientific Advice Working Group (SAWG) meeting, which was held on 10-11 February 2004. For further details, please see **Annex 3**.
- Documents prepared by the CPMP Working Parties and Ad Hoc Groups adopted during the February 2004 CPMP meeting are listed in **Annex 4**.

Organisational Matters

The 30th CPMP Organisational Matters (ORGAM) meeting took place on Monday 23 February 2004, chaired by Dr D. Brasseur. During the meeting the following principle topics were presented/discussed:

- Issues related to **CPMP Working Parties/Ad Hoc Working Groups** (Guidelines, Concept Papers, Points to Consider and Discussion Papers) (see **Annex 4**).
- **Achievements of ORGAM in 2003**

  An overview of the main ORGAM achievements in 2003 was presented. Areas of achievements related to:

  a) CPMP meeting Organisation [development of the scope of the ORGAM meetings, improvement of use of IT tools, preparation of CPMP and its Working Parties (WPs) for the EU Enlargement, CPMP organisational aspects],

  b) CPMP Centralised Review procedures [establishment of Therapeutic Advisory Groups (TAGs), CPMP audit plan, Requests for Scientific Advice on post authorisation issues, review of SPC Guideline, creation or update of templates for centralised procedures for assessors, organisation of training for CPMP assessors],

  c) Pharmacovigilance procedure (handling of safety concerns by the CPMP, EudraVigilance implementation),

  d) Transparency and Communication (CPMP /EMEA Working Group with Patients Associations, confidentiality issues),

  e) Issues related to CPMP Working Parties/Ad Hoc Working Groups Working Parties (discussions on Guidelines, Notes for Guidance, Position Papers etc) and

  f) Regulatory issues (implementation of the Commission Variation Regulation, definition of Similarity of Orphan Medicinal Products).

Upcoming meetings following the February 2004 CPMP plenary meeting:

- The next CPMP Gene Therapy Expert Group (Chairman K. Cichutek) will be held at the EMEA on 26-27 February 2004.
- The next Ad Hoc Working Group on (non)-clinical comparability of Biotechnology products (Chairman Dr P. Kurki) will be held at the EMEA on 18 March 2004.
- The 102nd plenary meeting of the CPMP will be held from 23-25 March 2004.
- The next CPMP Organisational Matters meeting will be held on Monday 22 March 2004.
- The next Invented Name Review Group meeting is scheduled to take place on Monday 22 March 2004.
- An Introductory session for new CPMP Members including CPMP Members from the new EU Members States (in view of the new mandate of the CPMP) will be held at the EMEA on 5 May 2004.
- An Extraordinary Organisational CPMP meeting will be held at the EMEA on 6 May 2004.

PROCEDURAL ANNOUNCEMENT

Announcement in relation to new and on-going post-authorisation procedures with all or part of CPMP Opinion Annexes affected.

Marketing Authorisation Holders are informed that as of now, the Annexes to centralised Marketing Authorisations will always be handled as one individual document per EU language throughout the life of the medicinal product.

Thus, all on-going and new post-authorisation procedures to start in February/March 2004, with affected Annexes to the Marketing Authorisations, will need to include the revised product information as a full set of Annexes (i.e. Annex I, II, IIIA & IIIB[1]) in one Word document per language, even when not all Annexes are affected.

Marketing Authorisation Holders are strongly advised to follow carefully the revised Post-Authorisation Guidance Document (http://www.emea.eu.int/htms/human/postguidance/list.htm) and the QRD templates which provide clear information regarding specific requirements for format and submission timelines for all 22 languages.

Regarding applications for post-authorisation procedures which are on-going or have already been submitted due to start in February 2004, Marketing Authorisation Holders are advised to liaise with the respective EMEA Product Team Leader.

[1] Annex I: SPC, Annex II: Conditions of the Marketing Authorisation, Annex IIIA/B: Labelling and Package leaflet

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on Monday 23 February 2004. For further details, please see **Annex 5.**

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 - 2003	2004	Overall Total
Scientific Advice	367	10	377
Follow-up to Scientific Advice	60	0	60
Protocol Assistance	30	5	35
Follow-up to Protocol Assistance	9	1	10

	1995-2003			2004			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	134	271	405	2	2	4	409
Consultation for Medical Device[2]	0	1	1	0	0	0	1
Withdrawals	22	55	77	0	0	0	77
Positive CPMP opinions[3]	99	172	271	2	3	5	276[4]
Negative CPMP opinions[5]	2	5	7	0	0	0	7[6]
Marketing authorisations granted by the Commission	91	164	255	0	0	0	255[7]

	1995-2003			2004			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	771	1505	2276	5	69	74	2350
Positive opinions, variations type II	583	697	1280	29	31	60	1340
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	49	56	105	0	1	1	106

[2] 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.
[3] 15 positive opinion corresponding to 15 Orphan Medicinal Products
[4] 276 positive opinions corresponding to 212substances
[5] In case of appeal, the opinion will not be counted twice
[6] 7 negative opinions corresponding to 6 substances (2 of these negative opinions correspond to 2 Orphan Medicinal Products)
[7] 255 marketing authorisations corresponding to 193 substances

ANNEX 2 to CPMP Monthly Report February 2004

OUTCOME OF THE FEBRUARY 2004 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
1 Extension of indication	1 Positive opinion
22 SPC changes	22 Positive opinions
11 Quality changes	11 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Benefix (nonacog alfa) Genetics Institute of Europe B.V	Positive opinion	Marketing Authorisation will remain under exceptional circumstances
Cancidas (caspofungin) Merck Sharp & Dohme	Positive opinion	Marketing Authorisation will remain under exceptional circumstances
Zavesca (miglustat) Actelion Ltd	Positive opinion	Marketing Authorisation will remain under exceptional circumstances
Ammonaps (phenylbutyrate) Orphan Europe SARL	Positive opinion	No remaining grounds to keep the Marketing Authorisation under exceptional circumstances

Opinion for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Beromun (tasonermin) Boehringer Ingelheim International GmbH	Positive opinion	---
Procomvax (haemophilus b conjugated and hepatitis B vaccine) Pasteur Merieux MSD	Positive opinion	---
Sustiva (efavirenz) Bristol Myers Squibb Pharma EEIG	Positive opinion	---
Stocrin (efavirenz) Merck Sharp & Dohme	Positive opinion	---

OUTCOME OF THE FEBRUARY 2004 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				
Chemical	Ulcerative colitis	X						X	
Chemical	Deep vein thrombosis	X						X	
Chemical	Chronic pain	X						X	
Biological	Cystic fibrosis		X			X	X	X	
Chemical	Cystic fibrosis		X			X	X	X	X
Chemical	Cystic fibrosis		X			X	X	X	X
Chemical	Low flow priapism		X				X		

SA: Scientific Advice

PA: Protocol Assistance

In February 2004, the above-mentioned 3 Scientific Advice letters and 4 Protocol Assistance letters were adopted.
The Committee accepted 4 Initial Scientific Advice new Requests and 2 Initial Protocol Assistance new Requests.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD HOC GROUPS ADOPTED DURING THE FEBRUARY 2004 CPMP MEETING

BIOTECHNOLOGY WORKING PARTY

Reference number	Document	Status
CPMP/BWP/3794/03	Guideline on the Scientific Data Requirements for a Plasma Master File (PMF)`	Adopted. Released on the EMEA website.
CPMP/BWP/4663/03	Guideline on Requirements for Plasma Master File (PMF) Certification	Adopted. Released on the EMEA website.
CPMP/BWP/4548/03	Vaccine Antigen Master File: Guideline on requirements for Vaccine Antigen Master File (VAMF) Certification	Adopted. Released on the EMEA website.
CPMP/BWP/3734/03	Guideline on the scientific data requirements for a Vaccine Antigen Master File (VAMF)	Adopted in December 2003. Released on the EMEA website.

EFFICACY WORKING PARTY

Reference number	**Document**	**Status**
CPMP/EWP/6235/04	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products for the prophylaxis of venous thromboembolism in non-surgical patients	Adopted
CPMP/EWP/6172/03	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products for the treatment of chronic hepatitis B	Adopted
CPMP/EWP/438/04	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products for the treatment of psoriatic arthropathy	Adopted
CPMP/EWP/422/04	Concept paper on the development of a CPMP points to consider on clinical investigation of medicinal products for the treatment of juvenile idiopathic arthritis (JIA)	Adopted
CPMP/EWP/2339/02	Draft Note for guidance on the evaluation of the pharmacokinetics of medicinal products in patients with impaired hepatic function	Released for 6 months consultation

CPMP/EWP/2158/99	Draft CPMP points to consider on the choice of non-inferiority margin	Released for 3 months consultation
CPMP/EWP/252/03	Draft CPMP points to consider on clinical investigation of medicinal products for the treatment of neuropathic pain	Released for 3 months consultation
CPMP/EWP/2459/02	Concept paper on the development of a CPMP points to consider on data monitoring committees	Adopted

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/4359/03	Joint CPMP/CVMP Guideline on Plastic Primary Packing Materials (Revision of 3AQ10a)	Adopted. Released for 6 months consultation.
CPMP/QWP/6142/03	CPMP Guideline on Stability testing for Active Substances and Medicinal Products Manufactured in Climatic Zones III and IV and to be marketed in the EU	Adopted. Released for 6 months consultation.
CPMP/QWP/6239/03	Joint CPMP/CVMP concept paper on the need for updating the quality part of the dossier for existing marketing authorizations	Adopted. To be forwarded to CVMP for adoption prior to release for 2-months consultation.

PAEDIATRIC EXPERT GROUP

Reference number	Document	Status
CPMP/PEG/35132/03	Discussion paper on the impact of renal immaturity when investigating medicinal products intended for paediatric use.	Adopted. Released for 3 months consultation

Report from the meeting held on 23 February 2004

General Issues

Update of the document: Notification to the EMEA/CPMP in the MRFG
An updated version of the document, in line with the new version of chapter 5 of the Notice to Applicants, has been published on the website.

Document: Recommendation for Mutual Recognition Procedure after finalization of an arbitration procedure with a positive opinion by the CPMP and a positive decision by the EU-Commission
An updated version of the document has been adopted by the group and will be published on the website.

Questions and answers on MRP and enlargement

A questions and answers document on enlargement related issues in the framework of MRP has been agreed by the group and will be added to the Frequently Asked Questions section of the MRFG website.

MRFG expert group on the core SPC for HRT
The expert group met on 23 February 2004. A timetable for the next steps in the variation procedure was agreed by MRFG.

Meeting schedule
The next MRFG meeting will be held on 22 March 2004.

Mutual Recognition Monitoring

The MRFG noted that **30** new mutual recognition procedures were finalised during the month of January 2004, as well as **19** type I variations, **208** type IA variations, **142** type IB variations and **52** type II variations.

The status as of 31st January 2004 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 IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CPMP
2004	30	145	19	208	142	52	--

48 new procedures (regarding **11** products) started in January 2004. The categories of these procedures are as follows:

3 new active substance (first authorisation in the European Community after RMS approval) classified as repeat use.

15 known active substances (already authorised in at least one member state), of which **5** are classified as multiple applications and **1** is a repeat use.

30 abridged applications; including **14** multiple applications and **1** is a repeat use.

The new procedures started related to **16** full dossiers, **18** generics, **2** bibliographic applications and **12** for different use, route or dose.

The procedures consisted of **46** chemical substances, **1** biological-blood product and **1** biological-other[1].

47 of these procedures were prescription-only medicinal products in the reference Member State and 1 procedure was classified as a Non-prescription (including OTC) medicinal product[2].

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 January 2004

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (1)	4
DE (1)	13
DE (1)	13
DE (5)	2
DE (5)	2
DE (5)	2
DE (5)	2
DE (4)	2
DE (1)	10
DK (2)	6
ES (2)	4
ES (1)	2
FI (3)	1
FI (3)	11
FI (3)	12
FI (3)	1
FI (3)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
FI (3)	7
FI (2)	1
FI (2)	1
FI (2)	1
FI (2)	8
FI (2)	1
FI (1)	1
FI (1)	1
FI (1)	1
FI (2)	3
FI (2)	2
FI (2)	1
FI(2)	1
FI (2)	2
FR (1)	8
IE (5)	3
NL (1)	4
NL (2)	1
NL (2)	1
PT (1)	1
SE (4)	2
SE (4)	2
SE (1)	1
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	1
UK (1)	2
UK (3)	3
UK (3)	1

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

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

*Dr. Caitríona **FISHER***
Irish Medicines Board
The Earlsfort Centre
Earlsfort Terrace
Dublin 2 - IRELAND

Phone: + 353 1 676 4971
Fax: + 353 1 676 8490
e-mail: caitriona.fisher@imb.ie

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