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

29 January 2004
EMEA/CPMP/269/04

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
20-21 JANUARY 2004 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 100th plenary meeting from 20-21 January 2004.

The election of a new CPMP Chairperson and Vice-Chairperson took place on 20 January 2004. The Committee re-elected Dr Daniel Brasseur as its Chairman and Dr Eric Abadie as its Vice-Chairman (for further details please see separate EMEA press release published on 20 January 2004:http://www.emea.eu.int/htms/hotpress/d147604.htm).
The Committee agreed that the Chairpersons of the CPMP Working Parties, the CPMP Ad-Hoc Working Groups and the CPMP ICH representative for the ICH Steering Committee will remain as currently appointed.

The Committee welcomed Dr George Aislaitner as a new Greek CPMP Member replacing Prof. Nikolaos Drakoulis. The Committee noted the resignation of the Danish CPMP Member Dr Mark Ainsworth who will be replaced by Prof. Gorm Boje Jensen as of the February 2004 CPMP meeting.

Product related issues

Centralised procedures

The CPMP adopted two opinions on initial marketing authorisation applications at this meeting:

- A positive opinion on the marketing authorisation for **Lysodren** (mitotane), from Laboratoire HRA Pharma, intended for the symptomatic treatment of advanced adrenal cortical carcinoma. EMEA review began on 18 November 2002 and the opinion was adopted on 21 January 2004, with an active review time of 182 days. Lysodren was designated an orphan medicinal product on 12 June 2002 and is the **sixteenth orphan medicinal product** to receive a positive CPMP opinion.
- A positive opinion on the marketing authorisation for **Velcade** (bortezomib), from Millenium Pharmaceuticals Ltd, intended for the treatment of relapsed and refractory multiple myeloma. EMEA review began on 24 February 2003 and the opinion was adopted on 21 January 2004, with an active review time of 173 days.

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

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 gave positive opinions on the extension of indication for two medicinal products that are already authorised in the EU:

- **Ambirix** (inactivated hepatitis A virus and hepatitis B surface antigen, rDNA), from GlaxoSmithKline Biologicals, to extend its use to children aged 1 to 5 years. Ambirix was first authorised in the European Union on 30 August 2002.
- **Paxene** (paclitaxel), from Norton HealthCare Ltd, to extend its use to include treatment of metastatic breast cancer and metastatic cancer of ovary. Paxene was first authorised in the European Union on 19 July 1999.

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

The Committee also adopted one opinion (Part B) for a "line extension" application (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003).

An overview of centralised procedures since 1995 is given in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CPMP plenary meeting in December 2003 is provided in **Annex 2.** No Commission Decision was granted since the CPMP plenary meeting in December 2003.

Referrals

The Committee finalised two EU-wide reviews for:

- Four generic products containing **amlodipine maleate** for which marketing authorisation applications have been made in the mutual recognition procedure. The arbitration referral was initiated by Germany in September 2003 under Article 29 of the Community Code on human medicines and related to potential differences in the quality profile between the generic products and the innovator product. The Committee concluded that the quality differences in the generic products did not present a risk to public health. The objections raised in the arbitration should not therefore prevent the granting of marketing authorisations in the mutual recognition procedure.

- **Zocord** (simvastatin) and associated product names from Merck Sharp & Dohme. The purpose of the referral was to harmonise the divergent marketing authorisations for these products in the European Union. The CPMP concluded that there is a positive benefit/risk balance for the product's use in hypercholesterolaemia (treatment of primary hypercholesterolaemia or mixed dyslipidaemia, as an adjunct to diet, when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate; treatment of homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate) and in cardiovascular prevention (reduction of cardiovascular mortality and morbidity in patients with manifest atherosclerotic cardiovascular disease or diabetes mellitus, with either normal or increased cholesterol levels, as an adjunct to correction of other risk factors and other cardioprotective therapy). The European Commission initiated the referral in November 2002 under Article 30 of the Community Code on human medicines.

Non-product related issues

CPMP Working Parties and Ad Hoc

- The CPMP was informed of the outcome of the discussions of the Scientific Advice Working Group (SAWG) meeting, which was held on 07-08 January 2004. For further details, please see **Annex 3**.
- Documents prepared by the CPMP Working Parties and Ad Hoc Groups adopted during the January 2004 CPMP meeting are listed in **Annex 4.**

Organisational Matters

The 29th CPMP Organisational Matters meeting (ORGAM) took place on Monday 19 January 2004, chaired by Mr T. Humphreys, Head of the EMEA Regulatory Affairs and Organisational Support Sector. During the meeting the following principle topics were presented/discussed:

- Issues related to **CPMP Working Parties/Ad Hoc Working Groups** (Guidelines, Notes for Guidance and Position Papers) (see **Annex 4**).
- Follow-up discussion on **section 4.1** (Therapeutic indications) **versus section 5.1** (Pharmacodynamic properties) of the Summary of Product Characteristics (SPC). Proposals on the review of the NTA SPC Guideline regarding section 4.1 versus the information provided in section 5.1 were presented and agreed at the CPMP plenary meeting. These proposals will be implemented in the ongoing revision of the NTA Guideline on the SPC
- BWP and QWP guidance on the assessment of **"similarity" with Orphan Medicinal products** in respect of the molecular structural features for the purpose of Article 8 of Regulation (EC) No. 141/2000. Once adopted by the Committee the proposals will be forwarded to the European Commission for consideration in the drafting of a procedural Guideline on similarity of Orphan Medicinal Products.
- A revised EMEA Policy on the **Handling of Conflicts of Interests** for CXMP Members was presented to the ORGAM and CPMP plenary meeting. Introductory meetings for EMEA staff, CXMP and CXMP Working Parties Members are being organised. A final discussion on this issue will take place at the March 2004 EMEA Management Board meeting.
- A follow-up discussion on the EudraVigilance Status Report, which identified implementation issues in the EEA took place. The CPMP's viewpoint on these implementation issues will be forwarded to the EU Heads of Agencies for further discussion and optimum resolution of this topic.

Meetings with Interested Parties

A meeting between the EMEA, the CPMP and EUCAST Chairmen was held on 15 December 2003. At this meeting a procedure for collaboration on setting of EU harmonised antimicrobial breakpoints was discussed. A formalisation of this collaboration is foreseen.

Upcoming meetings following the January 2004 CPMP meeting

- The 101st plenary meeting of the CPMP will be held from 24-26 February 2004.
- The next CPMP Organisational Matters meeting will be held on Monday 23 February 2004.
- The next NRG meeting is scheduled to take place on Monday 23 February 2004.
- The next CPMP Gene Therapy Expert Group (Chairperson Dr K. Cichutek) will meet on 26-27 February 2004 at the EMEA.
- The Informal CPMP meeting will take place on April 29th - 30th in Dublin, Ireland.

PROCEDURAL ANNOUNCEMENTS

- **New submission dates**

  New submission dates for Full Applications, Type II Variations, Renewals and Annual Re-Assessments are published on the EMEA website (http://www.emea.eu.int/htms/human/presub/q25-2.htm).

- **Dossier requirements for CPMP Members**

  Applicants/MAHs are reminded to respect the dossier requirements (paper and electronic version) when submitting centralised applications to CPMP Members and Accession countries contact points. An updated table is provided on the EMEA website (http://www.emea.eu.int/htms/human/presub/q23-2.htm).

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on Monday 19 January 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

ANNEX 1 to CPMP Monthly Report January 2004

EMEA CENTRALISED PROCEDURES

	1995 - 2003	2004	Overall Total
Scientific Advice	367	7	374
Follow-up to Scientific Advice	60	0	60
Protocol Assistance	30	1	31
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	0	2	2	407
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	22	55	77	0	0	0	77
Positive CPMP opinions[2]	99	172	271	0	2	2	273[3]
Negative CPMP opinions[4]	2	5	7	0	0	0	7[5]
Marketing authorisations granted by the Commission	91	164	255	0	0	0	255[6]

	1995-2003			2004			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	771	1505	2276	1	11	12	2288
Positive opinions, variations type II	583	697	1280	12	14	26	1306
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	49	56	105	0	1	1	106

[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] 15 positive opinion corresponding to 15 Orphan Medicinal Products
[3] 273 positive opinions corresponding to 209 substances
[4] In case of appeal, the opinion will not be counted twice
[5] 7 negative opinions corresponding to 6 substances (2 of these negative opinions correspond to 2 Orphan Medicinal Products)
[6] 255 marketing authorisations corresponding to 193 substances

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

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
3 Extension of indication	3 Positive opinions
13 SPC changes	13 Positive opinions
10 Quality changes	10 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Glivec (imatinib mesilate) Novartis Europharm Ltd	Positive opinion	Marketing Authorisation to remain under exceptional circumstances.

Opinion for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Infergen (interferon alfacon-1) Yamanouchi Europe B.V	Positive opinion	---
Regranex (becaplermin) Janssen-Cilag International B.V	Positive opinion	---
Zerene (zaleplon) Wyeth-Research (UK) Limited	Positive opinion	---
Sonata (zaleplon) Wyeth Europe Ltd	Positive opinion	---
Zenapax (daclizumab) Roche Registration Ltd	Positive opinion	---

OUTCOME OF THE JANUARY 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				
Biological	Prophylaxis of HPV infection	X						X	
Chemical	Treatment of Parkinson's disease	X					X	X	
Biological	Fabry disease				X			X	
Biological	Treatment of Multinodular goiter	X						X	
Chemical	Treatment of uraemic pruritus		X					X	
Chemical	Treatment of type 2 diabetes	X						X	
Chemical	Treatment of functional dyspepsia	X						X	
Chemical	Prevention of nausea and vomiting associated with highly emetogenic chemotherapy	X						X	
Chemical	Treatment of prostate cancer	X						X	

SA: Scientific Advice

PA: Protocol Assistance

In January 2004, the above-mentioned 7 Scientific Advice letters, 1 Protocol Assistance letter and 1 Follow-up Protocol Assistance letter were adopted.
The Committee accepted 3 Initial Scientific Advice Requests and 2 Initial Protocol Assistance Requests.

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

BIOTECH WORKING PARTY

Reference number	Document	Status
EMEA/CPMP/347/04	Guidance on Epidemiological data on blood transmissible infections (For inclusion in the Guideline on Scientific data requirements for a Plasma Master File (CPMP/BWP/3794/03))	Released for 3 months consultation

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/227/02	Guideline on Active Master File Procedure	Adopted. To be forwarded to CVMP for adoption prior to publication on the EMEA website.

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Report from the meeting held on 19 January 2004

General Issues

Update of the guidance document: Applications under annex II of Regulation (EC) N0 1084/2003 in Mutual Recognition Procedures Member States Recommendations
An updated version of the document has been adopted by the group and will be published on the website.

Document: Triggering of Mutual Recognition by Member States (article 18 of Directive 2001/83/EC) Member States' Standard Operating Procedure
The document, adopted by the group, will be published on the website.

MRFG expert group on the core SPC for HRT
The expert group met with the companies involved. A timetable for the next steps in the variation procedure was agreed by MRFG.

Liaison meeting with interested parties
A Liaison meeting with interested parties was held during the MRFG plenary session.

Meeting schedule
The next MRFG meeting will be held on 23 February 2004.

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

Mutual Recognition Monitoring

The MRFG noted that **76** new mutual recognition procedures were finalised during the month of December 2003, as well as **45** type I variations, **164** type IA variations, **46** type IB variations and **65** type II variations.

The status as of 31st December 2032 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
2003	529	135	2473	230	94	754*	5 N.A. and 3 Variations

*** the yearly figures of Procedures from type II variations finalised published last month were incorrect. The correct number was 689.**

The global status since 1st January 1995 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 IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CPMP
1995	10	16			17	1 N.A.
1996	84	49			73	1 N.A. and 1 variation
1997	146	101			163	1 N.A. and 1 variation
1998	182	339			222	1 N.A. and 4 variations
1999	228	671			301	2 N.A. and 2 variations
2000	306	1007			320	3 N.A. and 2 variations
2001	443	1487			474	1 N.A. and 3 variations
2002	420	2104			527	2 N.A. and 7 variations
2003	529	2473	230	94	754	5 N.A. and 3 variations
1995-2003	2348	8247	230	94	2851	17 N.A. and 23 variations

49 new procedures (regarding **104** products) started in December 2003. The categories of these procedures are as follows:

1 new active substance (first authorisation in the European Community after RMS approval).

9 known active substances (already authorised in at least one member state), of which **3** are classified as multiple applications and **1** is a repeat use.

35 abridged applications; including **18** multiple applications and **1** repeat use.

4 line extension applications.

The new procedures started related to **8** full dossiers, **31** generics, **4** bibliographic applications, **1** fixed combination and **5** for different use, route or dose.

The procedures consisted of **48** chemical substances and **1** biological-vaccine[1] .

49 of these procedures were prescription-only medicinal products in the reference Member State[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 December 2003

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (3)	11
DE (2)	14
DE (2)	1
DE (2)	12
DE (2)	3
DK (1)	1
DK (1)	2
FI (1)	6
FI (1)	1
FI (1)	1
FI (1)	10
FI (1)	6
IT (1)	6
IT (2)	1
NL (1)	16
NL (1)	5
NL (1)	1
NL (1)	3
NL (2)	3
SE (1)	9
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	1
SE (1)	3
SE (1)	1
SE (1)	1
SE (1)	1
SE (1)	2
SE (4)	7
SE (4)	4
SE (4)	1
SE (4)	1
SE (4)	1
SE (3)	1
SE (4)	1
SE (4)	1
SE (4)	1
SE (3)	1
SE (4)	1
SE (4)	2
UK (3)	9
UK (2)	1
UK (2)	1
UK (2)	1
UK (2)	1
UK (2)	7
UK (3)	11

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
UK (1)	5

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/