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

23 December 2003
EMEA/CPMP/6016/03

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
16-17 DECEMBER 2003 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 99th plenary meeting from 16-17 December 2003.

This was the last meeting of the 2001-2003 mandate of the Committee for Proprietary Medicinal Products. The first meeting of the Committee's next mandate will be on 20-22 January 2004, at which time the Committee will hold elections for its chair and vice-chair.

Product related issues

Centralised procedures

The CPMP adopted one opinion on an initial marketing authorisation application at this meeting:

- A positive opinion on the marketing authorisation application for **Photobarr** (porfimer sodium), from Axcan International Pharma BV, intended for the treatment of high-grade dysplasia in patients with Barrett's oesophagus. EMEA review began on 20 May 2002 and the opinion was adopted on 17 December 2003, with an active review time of 197 days.

  Photobarr was designated an orphan medicinal product on 6 March 2002 and is the **fifteenth orphan medicinal product** to receive a positive CPMP opinion.

A summary of the opinion is available on the EMEA web site: http://www.emea.eu.int

The Committee also adopted an opinion recommending the suspension of the Marketing Authorisation of **Forcaltonin 100IU solution for injection** (recomb. salmon calcitonin), from Unigene UK Limited, as the company could not identify an authorised manufacturer to ensure the quality of the product. The opinion will be reviewed after one year or as soon as all relevant information on the authorised manufacturer has been provided to the Committee.

The Committee also adopted 3 Lists of Questions (Part B) on initial Marketing Authorisation Applications and 4 Lists of Questions (2 Part A and 2 Part B) on "line extension" applications (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 post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 2**. No Commission Decision was granted since the CPMP plenary meeting in November 2003.

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Invented Name Review Group

The Invented Name Review Group held its 44th meeting on 15 December 2003, and its conclusions were subsequently adopted by the CPMP.

Accessing Countries National Competent Authorities were requested in August 2003 to review the list of all the Invented Names for human medicinal products accepted/going through the centralised procedure or to be shortly submitted for evaluation. On this issue the EMEA received comments/objections from most National Competent Authorities. As a further action the EMEA will contact individual companies and Accession Countries National Authorities in order to highlight the objections raised and to seek their resolution.

The next meeting of the Invented Name Review Group is scheduled to take place on Monday 19 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 01-02 December 2003. For further details, please see **Annex 3**.
- Documents prepared by the CPMP Working Parties and Ad Hoc Groups adopted during the December 2003 CPMP meeting are listed in **Annex 4**.

Organisational Matters

The 28th CPMP Organisational Matters meeting (**ORGAM)** took place on Monday 15 December 2003, 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** and several Guidelines, Notes for Guidance, Concept Papers and Points to Consider (see **Annex 4**).

  The **Note for Guidance on comparability of medicinal products** containing biotechnology-derived proteins as active substance - annex on non-clinical and clinical issues (CPMP/3097/02) was discussed by the Group and subsequently adopted by the CPMP. This Note for Guidance will be published on the EMEA website (see **Annex 4**).

  The **Note for Guidance on the scientific data requirements for** a **Plasma Master File** (PMF) (CPMP/BWP/3794/03) and the Note for Guidance on the scientific data requirements for a **Vaccine Antigen Master File** (VAMF) CPMP/BWP/3734/03) were discussed by the Group and subsequently adopted by the CPMP. These Notes for Guidance will be published on the EMEA website early in January 2004 (see **Annex 4**).

- **EudraVigilance Status Report,** which identified implementation issues for the conduct of pharmacovigilance in the EU. This topic will be further discussed at the January 2004 meeting.

Upcoming meetings following the December 2003 CPMP meeting

- The next CPMP Organisational Matters meeting is scheduled to take place on Monday 19 January 2004.
- The 100rd plenary meeting of the CPMP will be held from 20-22 January 2004.

PROCEDURAL ANNOUNCEMENTS

- **New submission dates**

  New submission dates for full applications and variation applications will be published beginning of January 2004 on the EMEA website

- **Confidentiality agreements between the EMEA and the New Members States in view of the EU Enlargement**

  As announced in recent CPMP Monthly Reports, the EMEA recommends Applicants to submit their applications (Module 1 and 2) to the Contact Points of the New Member States.
  Please note that confidentiality agreements are in place between the EMEA and the Accession Countries' National Agencies.
  In addition the Accession Countries' CPMP Observers have signed personal confidentiality agreements with the EMEA.

- **Translations of the product information in the 9 accession country languages**

  In view of the upcoming enlargement of the EU and the fact that Commission Decision Annexes as of May 2004 will have to contain the 9 additional accession country languages, applicants are advised that for all new applications (including Extensions) for which an Opinion will be adopted in January 2004, translations of SPC, labelling and PL will also have to be provided in the 9 accession country languages.

  For other procedures, translations of SPC, labelling and PL will have to include the additional 9 languages as from the following dates:

Procedure	Submission
Type IA/IB Variations	As of April 2004
Type II Variations (30-day TT)	As of February 2004
Type II Variations (60/90-day TT)	After Opinion, as of February 2004
Renewals	As of January 2004
Marketing Authorisation Transfers	As of February 2004

More detailed guidance on this process and requirements will be made available in January 2004.

PROCEDURAL ANNOUNCEMENTS cont.

- **Commission Decisions on Type II variations and Standing Committee procedure**

  Marketing Authorisation Holders are reminded that, according to Art. 6 of Commission Regulation (EC) No 1085/2003, Commission Decisions on Type II variations shall be adopted without a Standing Committee procedure. Consequently, there will be no further revision of the translations of the product information in relation to Type II Variation procedures after Day +20 following adoption of the Opinion.

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 15 December 2003. For further details, please see **Annex 5.**

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This CPMP Monthly Report and other documents are available on the Internet at the following address: http://www.emea.eu.int

The EMEA Executive Director, EMEA Staff and CPMP Members

wish everybody a

MERRY CHRISTMAS AND A HAPPY NEW YEAR 2004!

ANNEX 1 to CPMP Monthly Report December 2003

EMEA CENTRALISED PROCEDURES

	1995 - 2002	2003	Overall Total
Scientific Advice	302	65	367
Follow-up to Scientific Advice	50	10	60
Protocol Assistance	13	17	30
Follow-up to Protocol Assistance	4	5	9

	1995-2002			2003			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	127	239	366	6	32	38	404
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	20	53	73	2	2	4	77
Positive CPMP opinions[2]	92	155	247	7	17	24	271[3]
Negative CPMP opinions[4]	1	4	5	1	1	2	7[5]
Marketing authorisations granted by the Commission	88	146	234	3	16	19	253[6]

	1995-2002			2003			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	585	1132	1717	186	366	552	2269
Positive opinions, variations type II	405	511	916	178	186	364	1280
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	44	44	88	5	12	17	105

[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] 271 positive opinions corresponding to 207 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] 253 marketing authorisations corresponding to 191 substances

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

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
0 Extension of indication	N/A
9 SPC changes	9 Positive opinions
16 Quality changes	16 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Agenerase (amprenavir), GlaxoSmithKline	Positive opinion	All specific obligations stated in the CPMP opinion dated 29 June 2000 have been fulfilled. There are no remaining grounds to keep the Marketing Authorisation under exceptional circumstances.

Opinion for Renewal applications		
Name of Medicinal Product (INN) **MAH**	**Outcome**	**Comments**
Emadine (emedastine) Alcon Laboratories (UK) Ltd	Positive opinion	---

ANNEX 3 to CPMP Monthly Report December 2003

OUTCOME OF THE DECEMBER 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				
Chemical	Prevention of organ rejection	**X**						**X**	
Chemical	Treatment of prostate cancer	**X**						**X**	
Chemical	Treatment of chronic iron overload				**X**			**X**	
Chemical	Treatment of dyslipidemia in patients with type 2 diabetes			**X**				**X**	
Chemical	Treatment of acute bleeding of gastric and duodenal ulcers	**X**						**X**	

SA: Scientific Advice

PA: Protocol Assistance

In December 2003, the above-mentioned 3 Scientific Advice letters, 1 Follow-up Scientific Advice letter and 1 Follow-up Protocol Assistance letter were adopted.
The Committee accepted 5 Initial Scientific Advice Requests and 4 Initial Protocol Assistance Requests.

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

BIOTECH WORKING PARTY

Reference number	Document	Status
CPMP/BWP/1571/02 rev. 1	Position Statement on the Quality of water used in the production of vaccines for parenteral use	Adopted
CPMP/BWP/2758/02	Note for Guidance on Pharmaceutical aspects of the product information for human vaccines	Adopted
CPMP/BWP/3794/03	Note for Guidance on the scientific data requirements for a Plasma Master File (PMF)	Adopted. To be published on the EMEA website early in January 2004.
CPMP/BWP/3734/03	Note for Guidance on the scientific data requirements for a Vaccine Antigen Master File (VAMF)	Adopted. To be published on the EMEA website early in January 2004.
CPMP/BWP/3207/00 /Rev1	Guideline on Comparability of Medicinal Products containing Biotechnology-Derived Proteins as Active Substances: Quality issues	Adopted

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/788/01	Note for Guidance on Clinical Investigation of Medicinal Products for the treatment of migraine	Adopted
CPMP/EWP/556/95 rev. 1	Points to Consider on Clinical Investigation of Medicinal Product other than NSAIDs for treatment of rheumatoid arthritis	Adopted
CPMP/EWP/1875/03	Points to Consider on the Clinical Requirements of modified release products submitted as a line extension of an existing Marketing Authorisation	Adopted

SAFETY WORKING PARTY

CPMP/SWP/5958/03	Concept Paper on the development of a CPMP Note for Guidance on the non-clinical investigation of the dependence potential of medicinal products	Adopted

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/576/96 rev 1	Guideline on Stability Testing for applications for variations to a marketing authorisation	Adopted
CPMP/QWP/122/02 rev 1	Guideline on stability testing: Stability testing of existing active substances and related finished products	Adopted
CPMP/QWP/130/96 rev 1	Guideline on the chemistry of new active substances	Adopted
CPMP/QWP/609/96 rev. 2	Guideline on Declaration of Storage conditions: a) In the product information of medicinal products b) For active substances	Adopted
CPMP/QWP/6203/03	Guideline on Control of impurities of pharmacopoeial substances: Compliance with the European Pharmacopoeia general monograph "Substances for pharmaceutical use" and general chapter "Control of Impurities in substances for pharmaceutical use"	Adopted. To be forwarded to CVMP and for adoption prior to publication on the EMEA website.

AD HOC WORKING GROUP on (pre) clinical comparability of Biotechnology products

Reference number	Document	Status
CPMP/3097/02	Note for Guidance on comparability of medicinal products containing biotechnology-derived proteins as active substance - annex on non-clinical and clinical issues	Adopted

AD HOC WORKING GROUP on Xenogeneic and Cell Therapy

Reference number	Document	Status
CPMP/1199/02	Points to Consider on Xenogeneic Cell Therapy	Adopted

Report from the meeting held on 15 December 2003

General Issues

MRFG expert group on the core SPC for HRT

The expert group met on 15 December to take up the work of updating the core SPC. Good progress was made and a draft revised core SPC will be circulated to MRFG members and then posted on the MRFG website on Friday 19 December 2003.

Applicant's Response Document

An updated document was adopted and will be published on the website.

Core SPC for influenza vaccines

The harmonised core SPC for influenza vaccines was corrected to take into account the age range of the 'Note for Guidance on Harmonisation of Requirements for Influenza Vaccine'. The new revised text will be published on the website.

Change in the EU-Presidency

The December 2003 MRFG meeting was the last one under the Italian presidency. Ireland will take over the presidency in January 2004. Dr. Caitríona Fisher will be the next MRFG chairperson and she should be contacted in the future in case of any questions regarding the MRP.

Meeting schedule

The next MRFG meeting will be held on 19 January 2004.

Merry Christmas and a Happy New Year!
Καλά Χριστούγεννα και ευτυχισμένο το καινούριο έτος !!
Buon Natale e Felice Anno Nuovo!

Mutual Recognition Monitoring

The MRFG noted that **90** new mutual recognition procedures were finalised during the month of November 2003, as well as **126** type I variations, **66** type IA variations, **48** type IB variations and **62** type II variations.

The status as of 30 November 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 IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Arbitrations referred to CPMP
2003	453	176	2428	66	48	669	5 N.A.* and 3 Variations

*** the figures of arbitrations from New Applications published last month were incorrect. No new arbitrations from New Applications were referred to the CPMP during the month of October 2003.**

52 new procedures (regarding **110** products) started in November 2003. The categories of these procedures are as follows:

3 new active substances (first authorisation in the European Community after RMS approval), of which **1** is classified as repeat use.

7 known active substances (already authorised in at least one member state), of which **2** are classified as repeat use.

41 abridged applications; including **16** multiple applications and **2** repeat use.

1 line extension application.

The new procedures started related to **6** full dossiers, **29** generics, **5** bibliographic applications and **12** for different use, route or dose.

The procedures consisted of **47** chemical substances, **1** herbal medicinal product, **1** biological-other, **1** biological-vaccine, **2** biological blood products[1].

48 of these procedures were prescription-only medicinal products in the reference Member State and **4** were Non-prescription (including OTC) medicinal products[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 November 2003

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (2)	6
AT (1)	1
BE (2)	1
BE (2)	5
DE (1)	2
DE (1)	3

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (1)	3
DK (1)	9
DK (1)	1
DK (2)	10
DK (2)	1
DK (4)	1
ES (3)	1
ES (3)	1
ES (2)	2
ES (1)	2
FI (2)	6
FI (2)	1
FI (2)	2
FI (2)	2
FI (2)	2
FI (2)	2
FR (2)	16
IE (1)	1
IE (6)	4
NL (1)	1
NL (2)	1
NL (2)	1
NL (2)	1
NL (2)	2
NL (1)	10
NL (3)	2
NL (3)	9
NL (3)	2
NL (3)	1
NL (3)	4
NL (3)	11
NL (3)	1
NL (3)	1
NL (3)	1
NL (2)	2
NL (2)	2
NL (2)	2
NL (2)	1
NL (2)	2
NL (2)	2
SE (5)	5
SE (2)	1
UK (1)	10
UK (1)	10
UK (1)	9
UK (1)	15

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:

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http://heads.medagencies.org/

