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

London, 30 January 2003
EMEA/CPMP/209/03

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
JANUARY 2003 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 89th plenary meeting from 20 – 23 January 2003.

Product related issues

Centralised procedures

No opinions were adopted on applications for marketing authorisation.

The Committee adopted 3 Lists of Questions (1 Part A and 2 Part B) and 2 List of Questions on "line extension" applications (Part B) (in accordance with Annex II of Commission Regulation (EC) No. 542/95, as amended).

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 2002 is provided in **Annex 2.** The post-authorisation centralised procedures finalized during this meeting are summarized in **Annex 3**.

Referrals

Referral under Article 7(5) of Commission Regulation (EC) No 541/95

The CPMP concluded its Community-wide review for medicinal products containing a fixed combination of **salmeterol and fluticasone propionate** (Seretide Diskus, Viani Diskus and associated product names) following an arbitration referral by Ireland in April 2002. This fixed combination is currently authorised through the mutual recognition procedure for the treatment of asthma. The referral relates to applications for a new indication to include chronic obstructive pulmonary disease (COPD). Based on the currently available information, the Committee considered that there is a positive risk/benefit balance for a restricted indication for the symptomatic treatment of patients with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy.

Referral under Article 29(2) of Directive 2001/83/EC (previously Article 10(2) of CD 75/319/EEC)

The CPMP began a Community-wide review for:

The generic product **Fluconazole Tiefenbacher** (fluconazole) from Tiefenbacher GmbH & Co. The arbitration referral by Germany relates to public health concerns over the use of the product in pregnancy and lactation and also to potential cardiac toxicity concerns. The application is currently under review in the mutual recognition procedure. The arbitration referral is made under Article 29 of the Community Code on human medicines.

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Referral under Article 30 of Directive 2001/83/EC (previously Article 11 of CD 75/319/EEC)

The Committee began Community-wide reviews for:

Coversyl (perindopril) and associated product names from Servier. The referral is part of the concerted action by EU regulatory authorities to harmonise the marketing conditions of a number of European brand leaders in major therapeutic areas. The referral is made by the European Commission under Article 30 of the Community Code on human medicines. The referral was not initiated as a result of any established safety or efficacy concern with this product.

Lopid (gemfibrozil) and associated product names from Pfizer. The referral is part of the concerted action by EU regulatory authorities to harmonise the marketing conditions of a number of European brand leaders in major therapeutic areas. The referral is made by the European Commission under Article 30 of the Community Code on human medicines. The referral was not initiated as a result of any established safety or efficacy concern with this product.

Invented Name Review Group

As announced at the October 2002 CPMP Monthly Report, the Invented Name Review Group (NRG) meetings in November 2002 and December 2002 were cancelled following the introduction of a contingency plan for meetings and related activities up to the end of 2002 (please see http://www.emea.eu.int/pdfs/human/press/pr/497902en.pdf. However, non-controversial issues emerging during this period (i.e. where there was no objection on invented name) were handled through a written procedure. The NRG held its 34th meeting on Monday 20 January 2003 and the conclusions of the group were subsequently adopted by the CPMP. A WHO representative came to the EMEA to update the NRG on the latest developments of WHO INN (International Nonpropriatary Names) programmes (http://www.who.int/medicines/organization/qsm/activities/qualityassurance/inn/orginn.shtml). The next NRG meeting is scheduled to take place on 17 February 2003.

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 13- 14 January 2003. For further details, please see **Annex 4**.

Documents prepared by the CPMP Working Parties and Ad Hoc Groups adopted during the January 2003 CPMP meeting are listed in **Annex 5**.

The Vaccines Expert Group (VEG) meeting, chaired by Dr Dobbelaer was held on 14 – 15 January 2003. The Group discussed amongst other topics the development of a "Note for Guidance (NfG) on Requirements for evaluation of new immunological adjuvants in vaccines". The development of this NfG was discussed in line with the CPMP "Concept paper on the development of a CPMP Note for Guidance on Requirements for the evaluation of new adjuvants in vaccines" (CPMP/BWP/6622/02), dated 25 April 2002. The next VEG meeting will take place on 20-21 March 2003. The VEG Work programme for 2003 was agreed and is available on the EMEA Website (http://www.emea.eu.int).

The Paediatric Expert Group (PEG) meeting, chaired by Dr Brasseur, was held on 24 January 2003. The main topics presented/discussed at this meeting will be summarized in the February 2003 CPMP Monthly Report.

The Ad Hoc Expert Group on Gene Therapy meeting, chaired by Prof. Chichutek, was held on 23-24 January 2003. The main topics presented/discussed at this meeting will be summarized in the February 2003 CPMP Monthly Report.

Upcoming meetings

The ICH Preparatory Meeting will take place in Brussels/Belgium on 28 January 2003.

A Joint workshop of CPMP assessors, GCP Inspectors and EMEA Inspection Sector will be held on 11 March 2003.

The next Ad Hoc Expert Group on Pharmacogenetics meeting, chaired by Dr Abadie, will be held on 12 March 2003.

Meetings with Interested Parties

The 6th EMEA / IFAPP (International Federation of Associations of Pharmaceutical Physicians) Conference on Biotech products: "Current issues and comparability (non-clinical and clinical consideration" will be held at the EMEA on Friday 21 February 2003.

Organisational Matters

The 19th CPMP Organisational Matters meeting took place on Monday 20 January 2003, chaired by Dr D. Brasseur. During the meeting the following principle topics were addressed:

- In the framework of the establishment of an EMEA Risk Management Strategy, discussions on the EMEA's proposals for the future handling of safety concerns by the CPMP continued and focused on the post-authorisation phase. Further discussion on this topic will take place at the February 2003 plenary CPMP meeting.
- Opportunities to reinforce and increase the use of electronic tools during the review process of centralised applications were discussed. Further discussion will take place at future ORGAM meetings.

The next CPMP Organisational Matters meeting is scheduled to take place on Monday 17 February 2003.

PROCEDURAL ANNOUNCEMENT

Practical guidelines for the delivery of a MAA:
For health and safety reasons and in accordance with recognised safe lifting limits, the EMEA recommends practical guidelines for the delivery of an Marketing Authorization Application (MAA) dossier (for further details, please see **Annex 6**).

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 20 January 2003. For further details, please see **Annex 7.**

The 90th plenary meeting of the CPMP will be held from 18 – 20 February 2003.

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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

EMEA CENTRALISED PROCEDURES

	1995-2002			2003			Overall Total
	Part A	Part B	Total	Part A	Part B	Total	
Scientific Advice	97	205	302	3	4	7	309
Follow-up to Scientific Advice	23	27	50	-	1	1	51
Protocol Assistance	5	8	13	1	-	1	14
Follow-up to Protocol Assistance	3	1	4	-	-	-	4

	1995-2002			2003			
	Part A	Part B	Total	Part A	Part B	Total	
Applications submitted	127	239	366	0	3	3	369
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	20	53	73	0	0	0	73
Positive CPMP opinions	92	155	247	0	0	0	247[2]
Negative CPMP opinions[3]	1	4	5	0	0	0	5[4]
Marketing authorisations granted by the Commission	88	146	234	0	0	0	234[5]

	1995-2002			2003			Overall Total
	Part A	Part B	Total	Part A	Part B	Total	
Variations type I	585	1132	1717	18	43	61	1778
Positive opinions, variations type II	405	511	916	11	4	15	931
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	44	44	88	0	0	0	88

[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] 247 positive opinions corresponding to 185 substances
[3] In case of appeal, the opinion will not be counted twice
[4] 5 negative opinions corresponding to 4 substances
[5] 234 marketing authorisations corresponding to 175 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE DECEMBER 2002 CPMP MONTHLY REPORT

Invented Name	Carbaglu
INN	carglumic acid
Marketing Authorisation Holder	Orphan Europe
ATC code	A16AA05
Indication	Treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency
CPMP Opinion date	17.10.2002

Invented Name	Theryttrex
INN	yttrium(Y-90) chloride
Marketing Authorisation Holder	MDS Nordion
ATC code	Pending
Indication	Radiolabelling of carrier molecules, which have been specifically developed and authorised for radiolabelling with this radionuclide
CPMP Opinion date	17.10.2002

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

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
0 Extensions of indication	N/A
7 SPC changes	7 Positive opinions by consensus
8Quality changes	8 Positive opinions by consensus

Opinions for Annual re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Agenerase (amprenavir) GlaxoSmithKline	Positive opinion by consensus	Marketing Authorisation to remain under exceptional circumstances
Caspofungin MSD (caspofungin) Merck Sharp & Dohme	Positive opinion by consensus	Marketing Authorisation to remain under exceptional circumstances

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

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

Substance	Intended indications(s)	Topic				
		Type of Request		Pharma-ceutical	Pre-Clinical	Clinical
		New	Follow-up			
Biological	Renal cell carcinoma	**X**			**X**	**X**
Biological	Hepatitis C	**X**		**X**	**X**	**X**
Chemical	Diagnosis in liver ultrasonography	**X**				**X**
Chemical	Major depression	**X**				**X**
Chemical	Generalized anxiety disorders	**X**				**X**
Chemical	Postmenopausal osteoporosis, Paget's disease		**X**		**X**	
Biological	Renal cell carcinoma	**X** (Protocol Assistance)			**X**	
Biological	Degenerative spondylolisthesis	**X**				**X**
Chemical	Breast cancer	**X**		**X**	**X**	**X**

In January 2003, the above-mentioned 7 Scientific Advice letters, 1 Follow-up Scientific Advice letter and 1 Protocol Assistance letter were adopted. The Committee accepted 4 new Scientific Advice requests and 1 new Follow-up Scientific Advice request.

DOCUMENT PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE JANUARY 2003 CPMP MEETING

SAFETY WORKING PARTY

Reference number	Document	Status
CPMP/SWP/2599/02	Position Paper on the non-clinical safety studies to support clinical trials with a single micro dose	Date of coming into operation: 01 July 2003

PROCEDURAL ANNOUNCEMENT

Practical guidelines for delivery of a MAA

(1) For health and safety reasons and in accordance with recognised safe lifting limits, an application dossier should be packed in boxes weighing no more than 15kgs each

(2) All boxes should be numbered by an indication of the dossier part or module inside with the box containing the cover letter and diskettes/CD-Roms clearly identified

(3) Very large dossiers of 10-15 boxes or more should be packed on pallets and delivered by truck with a tail lift unloading facility

(4) All dossiers are to be delivered to the following address:

EMEA Loading Dock

Ontario Way
(located at the rear of EMEA premises)
Canary Wharf
UK-London E14 4HB
(9:00 – 17:30 hours Monday to Friday)

We would be grateful if you could complete the information below for return by fax to +44 20 7418 8660 before shipment of your dossier to the EMEA.

Company name: …….

MAA/dossier name: ……...

No. of boxes: ……...

Estimated date of arrival: …….

In the event of queries, the EMEA mail/archive team will be pleased to assist:

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Report from the meeting held on 20 January 2003

General issues:

The following new documents will be published on the MRFG website:

- MRFG Recommendation on Implementation of Article 30 Decisions for Generic Products

MRP statistics 2002

Statistics regarding new applications in the MRP in the year 2002 according to the 5-level classification will be available on the Heads of Agencies Website by the end of January 2003.

Applications in CTD format in the MRP

Marketing authorisation holders are reminded that the CTD format will be mandatory for all applications which will be submitted after 1 July 2003.

Simultaneous applications for marketing authorisation in different Member States

If identical applications are submitted in different Member States, companies are strongly recommended to state this in the application form accordingly. Companies are reminded, that in such cases Article 17 paragraph 2 of Directive 2001/83/EC is applied. A relevant SOP is published on the Heads of Agencies Website (http://heads.medagencies.com/mrfg/docs/sops/sim_application.pdf) .

Meeting schedule

The next MRFG meeting will be held on 17 February 2003.

Annex 1

Joint CPMP/ MRFG working group on harmonisation of SPCs:

The group decided to start cooperation with EMACOLEX, to discuss future legislation concerning the harmonisation of SPCs.

On 7 January 2003 the European Commission triggered two new referrals. Pre-referral discussions will begin in February for four new products.

Mutual Recognition Monitoring

The MRFG noted that 46 new mutual recognition procedures were finalised during the month of December 2002, as well as 198 type I and 53 type II variations.

The status as of 31st December 2002 and for the period 1995–2002 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
2002	420	106	2104	224	527	223	2 N.A. and 7 variations

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 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
1995-2002	1819	5774	2097	12 N.A. and 20 variations

50 new procedures (regarding 111 products) started in December 2002. The categories of these procedures are as follows:

11 new active substances, including **2** repeate use.

12 known active substances (already authorised in at least one member state), including **3** multiple applications and **2** repeate use.

27 abridged applications including **10** multiple applications and **6** repeate use.

The new procedures started this month relate to 17 full dossiers, 16 generics, 6 bibliographic applications and 11 for different use, route or dose.

The procedures consisted of 49 chemical substances and 1 biological – blood product[1].

47 of these procedures were prescription-only medicinal products in the reference Member State and 3 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 December 2002

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (1)	1
BE (1)	5
DE (1)	2
DE (1)	14
DE (3)	16
DE (3)	5
DE (3)	14
DE (1)	16
DE (1)	1
DE (1)	1
DE (1)	16
DK (1)	4
DK (2)	5
DK (2)	1
DK (1)	3
DK (1)	4
DK (3)	5
DK (3)	5
DK (3)	1
DK (3)	1
DK (3)	1
ES (1)	5
FI (1)	3
FI (5)	2
FI (5)	1
FI (5)	1
FI (5)	9
FI (5)	2
FI (2)	3
FI (2)	1
FR (1)	9
FR (1)	3
FR (1)	5
IT (2)	1
NL (5)	9
NL (3)	16
NL (3)	2
NL (3)	6
NL (3)	2
NL (4)	11
SE (1)	11
SE (1)	11
SE (1)	11
SE (1)	8
SE (1)	16
UK (1)	12
UK (3)	1
UK (3)	1
UK (2)	4
UK (1)	1

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

