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

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CPMP/3926/01

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
11-13 DECEMBER 2001 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 77th plenary meeting from 11-13 December 2001.

Product related issues

Centralised procedures

The CPMP adopted four positive Opinions by consensus (one Part A and three Part B) on initial marketing authorisation applications:

- For **Dynepo** (epoetin delta) from Aventis Pharma SA, France, indicated for the treatment of anaemia in patients with chronic renal failure. Review by the EMEA began on 26 September 2000 and the opinion was adopted on 13 December 2001, with an active review time of 206 days. For further details, please see the published Summary of Opinion (CPMP/3745/01).
- For the double application **Arixtra** (fondaparinux) from Sanofi Synthelabo and **Quixidar** (fondaparinux) from NV Organon indicated for the prevention of venous thromboembolic events (VTE) in patients undergoing major orthopaedic surgery of the lower limbs such as hip fracture, major knee or hip replacement surgery. Review by the EMEA began on 1 March 2001 and the opinion was adopted on 13 December 2001, with an active review time of 205 days. For further details, please see the published Summaries of Opinion (CPMP/2727/01 and CPMP/3988/01).
- For **Vfend** (voriconazole) from Pfizer Limited, indicated for the treatment of invasive aspergillosis, *Candida and Scedosporium* spp. and *Fusarium* spp. infections. Review by the EMEA began on 28 November 2000 and the opinion was adopted on 13 December 2001, with an active review time of 203 days. For further details, please see the published Summary of Opinion (CPMP/3699/01).

The CPMP adopted eleven positive opinions by consensus on "line extension" applications (in accordance with Annex II of Commission Regulation (EC) No 542/95 as amended) related to two active substances (one Part A and one Part B).

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 November 2001 is provided in **Annex 2**. The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Referrals

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

A referral for Arbitration under Article 7(5) of Commission Regulation (EC) No 541/95, as amended was initiated by Sweden and Germany on Genotropin from Pharmacia AS. A Rapporteur and Co-Rapporteur were appointed and the review procedure has been started.

Referral under Article 12 of Council Directive 75/319/EEC, as amended

Following a referral under Article 12 initiated by Germany in June 2000, the CPMP reviewed the efficacy and safety of Cisapride containing medicinal products and adopted an opinion by majority vote, recommending the maintenance of the marketing authorisations with amendments to the Summary of Product Characteristics restricting the use of these medicinal products. In addition, the marketing

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

authorisations will be subject to certain conditions such as inclusion of treated patients in clinical trials, safety studies or registry programmes.

Scientific Advice procedures

The CPMP was informed of the outcome of the discussions of the Scientific Advice Review Group (SciARG) meeting, which was held on Monday 10 December 2001. For further details, please see **Annex 4**.

Non-product related issues

CPMP Working Parties and Ad Hoc Groups

- Dr Frances Rotblat reported from the expert meeting on paediatric oncology of the Ad Hoc Group on Oncology held on 3 December 2001. Participants included national experts, members of the *ad hoc* Group in Oncology, the EORTC and representatives of European paediatric oncology research groups (SFOP, UKCCSG, GPOH, NL POG and the EORTC Children's Leukaemia Group). The group proposed that the current "*Note for guidance on evaluation of anticancer medicinal products in man (*CPMP/EWP/205/95 rev. 1) be extended to address paediatric oncology particularly in the field of Phase I methodology. Relevant sections of the guideline will be amended to address specific aspects in paediatric oncology development and requirements for marketing authorisation. It is expected that during the consultation phase of the revision of the guideline a meeting will be organised with industry and paediatric oncology groups. Also, preclinical paediatric anticancer models will be considered in view of a possible revision of the *Note for guidance on the pre-clinical evaluation of anticancer medicinal products* (CPMP/SWP/997/96). These actions as well as other initiatives will be co-ordinated in concert with the EWP, the SWP and the CPMP Paediatric Expert Group (PEG).
- Dr. Nilsson, chairman of the Ad Hoc HIV Expert Group on antiretroviral medicinal products, reported from the meeting held on 29 November 2001. The aim of the meeting was to discuss the problems of Anti-Retroviral Therapy (ART) in HIV infected patients with impaired liver function and especially HBV/HCV co-infection and immune-based therapies aimed to restore HIV-specific and/or general immunological competence.

  Furthermore the final Points to consider on the assessment of anti-HIV medicinal products (Appendix III on dual PI) (CPMP/602/95 rev. 3) was adopted by the CPMP during the plenary meeting and will be published on the EMEA website (see also **Annex 5**).

An overview of guidance documents adopted during the meeting or released for consultation to Interested Parties is attached as **Annex 5**.

Organisational Matters

- The Tradename Ad Hoc Review Group (TRAHG) renamed invented Name Review Group (NRG) held its 24th meeting on Monday 10 December 2001 and the conclusions of the group were subsequently adopted by the CPMP. A workshop with Interested Parties was held on 11 December 2001 in order to present the invented Name Review procedure and discuss the *"Guideline on the acceptability of invented names for human medicinal products processed through the centralised procedure"* prior to its released in the next couple of months.
- The third meeting of the joint CPMP/Mutual Recognition Facilitation Group (MRFG) Working Group on the Harmonisation of Summary Product Characteristics (SPCs) chaired by Dr Tomas Salmonson took place on Monday 10 December 2001. For further details see MRFG Press Release (Annex 6).

PROCEDURAL ANNOUNCEMENT

The EMEA procedure for a simplified linguistic product information review process was presented to Industry on 11 December and companies are now advised that only the English language version of SPC, Labelling and Package Leaflet are to be submitted for new applications **as of January 2002**.

Detailed information on the new linguistic review procedure and its impact on ongoing procedures, will be published on the EMEA Website at the beginning of 2002.

EMEA ANNOUNCEMENT

Dr Agnès Saint Raymond has been appointed as EMEA Head of Sector of the Pre-authorisation Sector for Orphan Drug and Scientific Advice since 1 December 2001.

Mutual Recognition procedure

The CPMP noted the report from the MRFG which was held on 10 December 2001 (**Annex 6**). The December 2001 MRFG meeting was the last meeting under the Belgian Presidency. Spain will take over the Chairmanship as of January 2001 and Mrs Maria Luisa Garcia-Vaquero will be the next MRFG Chairperson.

The EMEA Executive Director, EMEA staff and CPMP Members wish everybody a MERRY CHRISTMAS and HAPPY NEW YEAR 2002

The 78th plenary meeting of the CPMP will be held from 15 to 17 January 2002.

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			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	74	122	196	14	44	58	254
Follow-up to scientific advice	15	11	26	5**	6	11	37

* Including two Protocol Assistance advice.
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	1995-2000			2001			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	97	182	279	23	33	56	335
Withdrawals	12	37	49	3	8	11	60
Positive CPMP opinions	64	112	176	13	19	32	208[1]
Negative CPMP opinions[2]	1	3	4	0	1	1	5[3]
Marketing authorisations granted by the Commission	56	95	151	15	28	43	194[4]

	1995-2000			2001			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	265	551	816	183	255	438	1254
Positive opinions, variations type II	159	224	383	126	138	264	647
Negative opinions, variations type II	0	2	2	1	4	5	7
Extensions (Annex II applications)	34	20	54	4	16	20	74

[1] 208 positive opinions corresponding to 162 substances
[2] In case of appeal the opinion will not be counted twice
[3] 5 negative opinions corresponding to 4 substances
[4] 194 marketing authorisations corresponding to 149 substances

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE NOVEMBER 2001 CPMP MONTHLY REPORT

Brand name	Travatan
INN	travoprost
Marketing Authorisation Holder	Alcon Laboratories (UK) Ltd
ATC code	S01EX
Indication	Decrease of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma who are intolerant or insufficiently responsive to another intraocular pressure lowering medication, as monotherapy or as adjunctive therapy.
CPMP Opinion date	26.07.2001
Date of Commission Decision	29.11.2001

OUTCOME OF THE DECEMBER 2001 CPMP MEETING IN RELATION TO CENTRALISED APPLICATIONS IN THE POST-AUTHORISATION PHASE

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
16 (SPC/PL update)	Positive by consensus
12 (Pharmaceutical Aspects)	Positive by consensus

Opinion for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Ferriprox (deferiprone) – Apotex	Positive by consensus	No longer under exceptional circumstances

Opinion for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Insuman (insulin human) – Aventis	Positive by consensus	-

OUTCOME OF THE NOVEMBER 2001 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	Metastatic colorectal cancer	**X**				**X**
Biological	Fabry Disease		**X**			**X**
Chemical	Type 2 diabetes		**X**			**X**

In December 2001, the above mentioned three final Scientific Advice letters were adopted. The Committee accepted three new requests and one follow-up request for Scientific Advice.

DOCUMENTS PREPARED BY THE CPMP WORKING PARTIES AND AD-HOC GROUPS ADOPTED DURING THE DECEMBER 2001 CPMP MEETING

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/609/96	Revision of the Note for guidance on Declaration of storage conditions for medicinal products in the product particulars and Active Substances	Released in December 2001 for 3 months consultation
CPMP/QWP/130/96	Note for guidance on Chemistry of the new Active Substance	Released in December 2001 for 6 months consultation

BLOOD PRODUCTS WORKING GROUP

Reference number	Document	Status
CPMP/BPWG/1089/00	Note for guidance on the Clinical investigation of plasma derived fibrin sealant products	Released in December 2001 for 6 months consultation
CPMP/BPWG/153/00	Core SPC for Plasma derived fibrin sealants	Released in December 2001 for 6 months consultation

EFFICACY WORKING PARTY

Reference number	Document	Status
CPMP/EWP/2863/99	Points to consider on adjustment for baseline covariates	Released in December 2001 for 3 months consultation

AD HOC HIV EXPERT GROUP ON ANTIRETROVIRAL MEDICINAL PRODUCTS

Reference number	Document	Status
CPMP/602/95 rev. 3	Points to consider on the assessment of anti-HIV medicinal products (Appendix III on dual PI)	Adopted in December 2001

AD HOC EXPERT GROUP ON PHARMACOGENETICS

Reference number	Document	Status
CPMP/3070/01 rev. 10	Revised position paper on terminology and pharmacogenetics	Released in December 2001 for 6 months consultation

Report from the meeting held on 10 December 2001

General issues

HFA 134a –IPACT 1 meta-analysis

The MRFG confirms that the outstanding concerns regarding the use of HFA 134a as a replacement propellant in metered dose inhalers have now been resolved.

Revision of MRFG documents

The MRFG adopted the revision of the following documents that will be published on the Heads of Agencies Website:

- MRFG Best practice Guide for the Mutual Recognition Procedure
- MRFG Best practice Guide for the Reference Member State in the Mutual recognition Procedure
- Applicant's Response Document in Mutual Recognition

MRFG Frequently Asked Questions (FAQ)

The MRFG adopted the first statement, which will soon be published under FAQ on the Heads of Agencies Website.

Liaison meeting with interested parties

The MRFG plenary meeting was followed by a meeting with interested parties. The interested parties were updated on the ongoing work of the Joint CPMP/MRFG Working Group on Harmonisation of SPC's.

The meeting discussed the proposals in the Review 2001 for the decentralised procedure vs mutual recognition procedure highlighting the outstanding issues for which further clarification is sought.

In addition, the MRFG answered questions relating to the organisation of the MRFG documents on the Heads of Agencies website and the MR-Product Index.

Change in the EU-Presidency

The December MRFG meeting was the one last under the Belgian Presidency. Spain will take over the Chairmanship as of January 2002. Mrs Maria Luisa García-Vaquero will be the next chairperson. She should be contacted in future in case of any questions regarding the MRP.

Meeting schedule

The next MRFG meeting will be held on **14 January 2002**.

Joyeux Noël et Bonne Année!

Prettige Kerstdagen en Gelukkig Nieuwjaar!

Frohe Weihnachten und ein glückliches neues Jahr!

Merry Christmas and a Happy New Year!

ANNEX 1

Joint CPMP / MRFG Working Group on harmonisation of SPC's

The Joint CPMP / MRFG Working Group on Harmonisation of SPC's presented a detailed report on the progress of the SPC harmonisation project to the Heads of Agencies during their meeting on 29-30 November 2001 in Tournai. The Heads of Agencies decided that the project should continue on a case-by-case basis, in close collaboration with industry. A pre-referral dialogue should be started for a small number of medicinal products early 2002. During this pre-referral phase, companies would get the opportunity to propose a harmonised SPC in close collaboration with CPMP and EMEA. This should result in the selection of a smaller number of medicinal products. The Joint Group will report during the next Heads of Agencies meeting. This project will not interfere with national activities, meaning that both approvals or referrals remain possible on a national level.

Mutual Recognition Monitoring

The MRFG noted that 41 new mutual recognition procedures were finalised during the month of November 2001, as well as 164 type I and 44 type II variations.

The status as of 30th November 2001 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
2001	386	118	1346	236	428	235	1 N.A. 3 var.

23 new procedures (regarding 49 products) started in November 2001. The categories of these procedures are as follows (please note that one procedure has not been classified bu the RMS on the last three levels) :

9 known active substances (already authorised in at least one member state), including **3** multiple applications and **1** repeate use.

13 abridged applications including **1** multiple application and **4** repeate use.

1 line extension application.

The new procedures started this month relate to 1 full dossier, 18 generics and 3 for different use, route or dose.

The procedures consisted of 21 chemical substances and 1 biological – others[1].

17 of these procedures were prescription-only medicinal products in the reference Member State and 5 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 2001

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	2
DK (4)	9
DK (4)	10
DK (2)	1
DK (2)	1
DK (2)	6
DK (2)	1
DK (2)	1
DK (2)	1
DK (4)	3
ES (2)	1
IT (5)	2
NL (1)	3
NL (1)	3
NL (1)	2
NL (1)	4
NL (2)	10
NL (2)	1
SE (2)	1
SE (2)	1
UK (1)	3
UK (3)	13

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:

*Ms. Natacha **GRENIER***
Ministry of, Public Health
Pharmaceutical Inspectorate
Bd. Bischoffsheim 33, local 411
natacha.grenier@afigp.fgov.be
1000 BRUSSELS - BELGIUM

Phone: + 32 2 227 5516
Fax: + 32 2 221 0355
e-mail:

From 1st of January 2002:

*Ms. Maria Luisa **GARCIA VAQUERO***
Agencia Española del Medicamento
c/Huertas 75
28014 MADRID - SPAIN

Phone: + 34 91 596.40.40
Fax: + 34 91 596.40.74
e-mail: mgarciav@agemed.es

*Alternatively, you could visit the **MRFG web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*

http://heads.medagencies.org/