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

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EMEA/CPMP/2347/03

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS
APRIL 2003 PLENARY MEETING
MONTHLY REPORT

The Committee for Proprietary Medicinal Products (CPMP) held its 92nd plenary meeting from 23 – 25 April 2003.

The CPMP Chairman, Dr Daniel Brasseur, welcomed the participation of Prof. Juris Pokratnieks, observer from Latvia, and Prof. János Borvendeg, observer from Hungary. A list of all nominated observers from the Accession Countries is provided in **Annex 6**.

Product related issues

Centralised procedures

The CPMP adopted 1 opinion on an initial marketing authorisation application at this meeting:

- A negative opinion on the initial marketing authorisation application for **Serostim** (somatropin), from Ares Serono, intended for the treatment of AIDS-related wasting syndrome. EMEA review began on 17 July 2001 and the opinion was adopted on 25 April 2003, with an active review time of 177 days.

  Serostim was designated an orphan medicinal product on 8 August 2000. The criteria for orphan designation mainly focus on the very low prevalence of a disease and are not the same as the criteria (quality, safety, efficacy) used in deciding whether a product should be granted a marketing authorisation. A summary of this opinion is available on the EMEA web site: http://www.emea.eu.int.

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

The Committee also gave a positive opinion to extend the indication for **Travatan** (travoprost), from Alcon Laboratories, for its use as first line therapy in patients with ocular hypertension or open-angle glaucoma. Travatan is currently indicated as second line treatment. Travatan was first authorised in the European Union in November 2001. Further information on this extension will be included in the public assessment report (EPAR) once the European Commission has taken its decision.

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 March 2003 is provided in **Annex 2.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 3**.

Referrals

The Committee concluded its Community-wide reviews for **Roaccutane** and associated invented names (isotretinoin) from Roche and generic products containing **isotretinoin** from Schering Health Care (Isotretinoin, Trivane, Scheritonin, Rexidal and Lurantal). The purpose of the referrals was to harmonise the product information for these products in all EU Member States, in order to avoid disharmony between the pregnancy prevention measures in place for the brand leader product (Roaccutane) and those proposed for the generic products. France made the referral to the EMEA in May 2002.

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The harmonised indications recommended by the Committee are for the products' use in severe forms of acne (i.e. nodular or conglobate acne or acne at risk of permanent scaring) that is resistant to standard therapy. Due to the risk of congenital defects, the Committee recommended a harmonised set of elements that should be included in all the nationally agreed risk management programmes. These should include measures to avoid risk of pregnancy exposure in women of child bearing potential.

The CPMP, having reviewed the evidence submitted by the Marketing Authorisation Holders/applicants, and having reassessed the benefit/risk profile of the **felodipine–containing medicinal products**, recommended the lifting of the suspension/granting of the Marketing Authorisations for the 5 and 10 mg tablets, and the maintenance of the suspension/non-granting of the Marketing Authorisations for the 2.5 mg tablets.

Other product related issues

The CPMP adopted a Public Statement on metabolic and cardiovascular complications ("Lipodystrophy") of antiretroviral combination therapy in HIV-infected patients. This followed a presentation made by the Oversight Committee in the February 2003 CPMP where the results of the collaborative work involving members from the MAHs, academia, patient organisations and the regulatory agencies in Europe (EMEA-CPMP) and the US (FDA) were discussed. The Public Statement (EMEA/CPMP/2383/03) is available on the EMEA web site (http://www.emea.eu.int).

The CPMP reviewed the safety of the centrally authorised **hexavalent vaccines**, **Hexavac** and **Infanrix Hexa**. The CPMP concluded that there was no change in the benefit/risk profile of these products and therefore did not recommend any changes to the present conditions of use. A separate Public Statement (EMEA/8519/03) is available on the EMEA web site (http://www.emea.eu.int). As with all centrally authorized medicines, the CPMP will continue to monitor these products closely in the light of any new information to be generated.

Invented Name Review Group

The Invented Name Review Group held its 37th meeting on 22 April 2003 and the conclusions of the group were subsequently adopted by the CPMP. The next meeting will take place on 19 May 2003. The second EMEA/EFPIA Workshop on Invented Names was held at the EMEA on 22 April 2003. During this Workshop, the EMEA gave an update on the Invented Name review procedure for centrally approved medicinal products and provided information on the latest activities of the Invented Name Review Group and its future challenges such as the Enlargement of the European Union.

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 7 – 8 April 2003. For further details, please see **Annex 4**.

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

The Blood Products Working Group (BPWG) meeting, chaired by Dr Manfred Haase was held on 6 – 7 February 2003. The Group discussed its ongoing work on Notes for Guidance and Core SPCs of blood products.

An Ad Hoc Expert Group on Revision of the Guideline on Excipients in the Package Leaflet meeting, chaired by Prof. Rolf Bass, was held on 21 March 2003. The Group discussed a summary and 'Consolidation' of the work done at the last meeting in February 2003 with an emphasis on the proposed warning statements for specific excipients under certain conditions as defined in the Annex of the revised Guideline.

The rules of procedure and the composition of the CPMP Therapeutic Advisory Groups (TAGs) (Oncology, Diagnostics and Anti-Infectives) were adopted by the Committee.

Upcoming meetings following the April 2003 CPMP plenary meeting:

- The next Ad Hoc Working Group on (pre) clinical comparability of Biotechnology products (Chairperson Dr P. Kurki) took place on 29 April 2003.
- The Informal CPMP meeting will be held on 5 - 6 May 2003 in Athens, Greece.
- The first EMEA / CPMP working group meeting with Patients Organisations will be held at the EMEA on 8 May 2003.

Organisational Matters

The 22nd CPMP Organisational Matters meeting took place on Tuesday 22 April 2003, chaired by Dr D. Brasseur. During the meeting the following principle topics were addressed:

- Follow-up discussion on the SPC Expert Group proposals on the content reflected in section 4.1 (Therapeutic indications) versus section 5.1 (Pharmacodynamic properties) of the SPC. These proposals will be considered in a future revision of the SPC Guideline.
- Discussion on CPMP internal organisational issues regarding the optimum links between ORGAM and CPMP meetings.
- Discussion on follow-up in monitoring the timing of the circulation of the Rapporteurs Assessment Reports to CPMP Members in the relevant steps of the centralised procedure, in order to ensure the optimum handling of centralised applications.
- Follow-up discussion on the revision of the Pharmacovigilance Working Party mandate.

The next CPMP Organisational Matters meeting is scheduled to take place on Monday 19 May 2003.

Mutual Recognition procedure

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 22 April 2003. For further details, please see **Annex 7.**

The 93rd plenary meeting of the CPMP will be held from 20 – 22 May 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 - 2000	2003	Overall Total
Scientific Advice	302	20	322
Follow-up to Scientific Advice	50	4	54
Protocol Assistance	13	4	17
Follow-up to Protocol Assistance	4	1	5

	1995-2002			2003			
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	127	239	366	2	12	14	380
Consultation for Medical Device[1]	0	1	1	0	0	0	1
Withdrawals	20	53	73	1	2	3	76
Positive CPMP opinions[2]	92	155	247	1	2	3	250[3]
Negative CPMP opinions[4]	1	4	5	1	0	1	6[5]
Marketing authorisations granted by the Commission	88	146	234	0	9	9	243[6]

	1995-2002			2003			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	585	1132	1717	56	184	240	1957
Positive opinions, variations type II	405	511	916	52	63	115	1031
Negative opinions, variations type II	1	6	7	0	0	0	7
Extensions (Annex II applications)	44	44	88	1	0	1	89

[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] 2 positive opinion corresponding to 2 Orphan Medicinal Product
[3] 250 positive opinions corresponding to 188 substances
[4] In case of appeal, the opinion will not be counted twice
[5] 6 negative opinions corresponding to 5 substances
[6] 243 marketing authorisations corresponding to 182 substances

ANNEX 2 to CPMP Monthly Report April 2003

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE MARCH 2003 CPMP MONTHLY REPORT

Invented Name	Valdyn
INN	valdecoxib
Marketing Authorisation Holder	Pharmacia Europe
ATC code	M01AH
Indication	Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea
CPMP Opinion date	22/07/2002

Invented Name	Bextra
INN	valdecoxib
Marketing Authorisation Holder	Pharmacia-Pfizer EEIG
ATC code	M01AH
Indication	Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea
CPMP Opinion date	22/07/2002

Invented Name	Kudeq
INN	valdecoxib
Marketing Authorisation Holder	Pfizer Limited
ATC code	M01AH
Indication	Symptomatic relief in the treatment of osteoarthritis or rheumatoid arthritis.Treatment of primary dysmenorrhoea
CPMP Opinion date	22/07/2002

Invented Name	Ytracis
INN	Yttrium(Y-90)
Marketing Authorisation Holder	CIS bio International
ATC code	V10X
Indication	Radiolabelling of carrier molecules, which have been specifically developed and authorised for radiolabelling with this radionuclide
CPMP Opinion date	21/11/2002

ANNEX 3 to CPMP Monthly Report April 2003

OUTCOME OF THE APRIL 2003 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 by consensus
21 SPC changes	21 Positive opinions by consensus
10 Quality changes	10 Positive opinions by consensus

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Ammonaps (phenylbutyrate) Orphan Europe SARL	Positive opinion by consensus	Marketing Authorisation to remain under exceptional circumstances
Neurobloc (botulinum toxin type B) Elan Pharma International Ltd	Positive opinion by consensus	Marketing Authorisation to remain under exceptional circumstances
Viread (tenofovir) Gilead Science International Limited	Positive opinion by consensus	Marketing Authorisation to remain under exceptional circumstances
Renagel (sevelamer) Genzyme B.V.	Positive opinion by consensus	Marketing Authorisation to remain under exceptional circumstances

Opinions for Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Mabthera (rituximab) Roche Registration Ltd	Positive opinion by consensus	---

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

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharma ceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Ankylosing Spondylitis	**X**						**X**	
Chemical	Type 2 diabetes			**X**				**X**	
Chemical	Osteoarthritis	**X**						**X**	
Chemical	Vascular Dementia and Parkinson's disease dementia			**X**				**X**	
Biological	Intra-operative photodynamic diagnosis of residual glioma		**X**						**X**
Chemical	Type 2 diabetes			**X**				**X**	

SA: Scientific Advice

PA: Protocol Assistance

In April 2003, the above-mentioned 2 Scientific Advice letters, 3 Follow-up Scientific Advice letters and 1 Protocol Assistance letter were adopted. The Committee accepted 6 Scientific Advice New Requests, 2 Follow-up Scientific Advice New Requests and 1 Protocol Assistance New Request.

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

QUALITY WORKING PARTY

Reference number	Document	Status
CPMP/QWP/450/03	Position Paper on Specifications for Class 1 and Class 2 Residual Solvents in Active Substances	Adopted
CPMP/QWP/2054/03	Annex II to Note for Guidance on Process Validation Guideline – Non Standard Processes	Released for 6 months' consultation
CPMP/QWP/609/96 rev. 1	Note for Guidance on Declaration of Storage Conditions: A: in the product information of medicinal products B: For Active Substances	Adopted

BIOTECH WORKING PARTY

Reference number	Document	Status
CPMP/BPWG/BWP/561/03	Joint BWP/BPWG Note for Guidance on Warning on transmissible agents SPCs and Package Leaflets for plasma-derived medicinal products	Released for 4 months' consultation

NOMINATED OBSERVERS FROM THE ACCESSION COUNTRIES

Czech Republic	Prof. Milan Smid
Cyprus	Dr Panayiota Kokkinou
Estonia	Dr Raul Kiivet
Hungary	Prof. János Borvendeg
Latvia	Prof. Juris Pokratnieks
Lithuania	Dr Vladas Volbekas
Malta	To be announced
Poland	Dr Waldemar Zielinski
Slovenia	Dr Vesna Koblar
Slovak Republic	Dr Pavel Svec

Report from the meeting held on 24 April 2003

General issues:

Processing of renewals in the post referral phase

Following an Article 30 or 31 referral, the MAHs are strongly recommended to select and contact an RMS immediately in order to plan the procedures ahead, inlcuding renewals and variations and resolve relevant issues.

Starting date of the data exclusivity period

The interpretation of the European Commission on this item is as follows:

The requirement for the use of 'essential similarity' is stated in Article 10.1 a) iii). It requires that the medicinal product, to which essential similarity is claimed, is authorised within the Community, in accordance with Community provisions in force, for not less than 6 years, respectively 10 years.

The starting date of the data exclusivity period is the date of the first approval in the European Union.

Therefore an application claiming Article 10.1. a) iii) can only be accepted after expiring of the data exclusivity time of 10 years. If the application is made only in Member States with 6 years exclusivity, than the 6 years have to be expired.

As the above mentioned laws are covering all EU Member States, the answer to the question – if a generic company can apply in respect to the 10 years data expired in a State before the EU 10 years exclusivity time is expired – is that the EU data exclusivity time has to be expired before a generic application can be submitted in an EU Member State.

Meeting schedule

The next MRFG meeting will be held on Monday 19 May 2003.

Mutual Recognition Monitoring

The MRFG noted that 49 new mutual recognition procedures were finalised during the month of March 2003, as well as 220 type I and 34 type II variations.

The status as of 31st March 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 I variations pending	Procedures from Type II variations finalised	Procedures from Type II variations pending	Arbitrations referred to CPMP
2003	104	85	545	329	109	297	1 N.A.

34 new procedures (regarding 87 products) started in March 2003. The categories of these procedures are as follows:

2 new active substances, classified as repeat use.

4 known active substances (already authorised in at least one member state), including 1 repeat use.

22 abridged applications including 5 multiple applications.

6 Line extension applications, including 2 repeat use.

The new procedures started related to 7 full dossiers, 24 generics, 2 bibliographic applications and 1 for different use, route or dose.

The procedures consisted of 32 chemical substances, 1 biological- blood product and 1 biological-other[1].

31 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 March 2003

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (2)	4
AT (2)	2
DE (2)	11
DE (4)	1
DE (1)	3
DK (3)	1
DK (1)	1
DK (1)	1
DK (2)	1
DK (4)	1
DK (3)	1
DK (3)	4
DK (3)	4
DK (3)	3
DK (2)	2
DK (1)	3
DK (2)	1
DK (4)	5
DK (3)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (4)	11
DK (4)	12
DK (4)	5
DK (4)	1
DK (3)	3
NL (1)	1
NL (3)	5
SE (2)	1
SE (1)	1
SE (2)	4
SE (2)	16
UK (3)	1
UK (4)	6
UK (1)	5
UK (2)	4

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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http://heads.medagencies.org/

