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

18 December 2000
CPMP/4305/00

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 66th plenary meeting 12 to 14 December 2000.

This was the last meeting chaired by Prof. Jean-Michel Alexandre who has completed two CPMP mandate terms as Chairman since the establishment of the EMEA in 1995. All CPMP Members expressed their sincere gratitude for his excellent leadership and guidance provided during this period. They also warmly acknowledged his pivotal role in promoting an excellent spirit of collaboration between them which has resulted in the successful operation of the centralised procedure. Prof. Jean-Michel Alexandre thanked his fellow CPMP Members and experts for the excellence of their scientific contributions co-operation and achievements over the past years.

Centralised Procedures[1]

The Committee adopted:

- Five positive opinions by consensus on centralised marketing authorisation applications relating to five medicinal products (one Part A and four Part B). One of these opinions was adopted "under exceptional circumstances".
- Two positive opinions by majority vote on centralised marketing authorisation applications relating to one medicinal product (Part B).
- One positive opinion "under exceptional circumstances" by consensus, on a "line extension" application (in accordance with Annex II of the Commission Regulation (EC) No 542/95 as amended) relating to one active substance (Part B).
- Four positive opinions by consensus for a centralised type I variation following a type II procedure relating to two active substances (two Part A).
- Thirty two positive opinions by consensus for centralised type II variations:
  - Seven related to an extension of the indication.
  - Seventeen related to SPC/PL updates and
  - Eight related to pharmaceutical aspects.
- Three positive opinions by consensus following the annual re-assessment of:
  - Betaferon (interferon beta 1-b) (Part A), indicated for relapsing-remitting and secondary progressive multiple sclerosis.
  - Norvir (ritonavir) (Part B), indicated in combination with antiretroviral nucleoside analogue(s) for the treatment of HIV-1 infected patients with advanced or progressive immunodeficiency.

[1] Note for Editors:
Applicants may appeal any CPMP opinion, provided they notify the EMEA in writing of their intention to appeal within 15 days of receipt of the opinion.

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- Zeffix (lamivudine) (Part B), indicated for the treatment of adult patients with chronic hepatitis B and evidence of viral replication with decompensated liver disease or with histologically documented active liver inflammation and/or fibrosis.

The CPMP recommended that the marketing authorisations for the three above-mentioned products should no longer remain "under exceptional circumstances".

- Three lists of questions on centralised marketing authorisation applications related to two active substances (one Part A and one Part B).

Since the CPMP meeting in November 2000, the Committee noted the withdrawal of four applications related to one active substance (Part B) from the centralised procedure.

The Committee heard three oral presentations from applicants concerning ongoing centralised procedures as well as two oral presentations from Marketing Authorisation Holders, one on Pharmacovigilance issues and one concerning the company's failure to comply with fundamental GCP requirements. In the later case, the company committed itself to rectify the identified deficiencies within strict time lines. The EMEA, together with National Competent Authorities and the national inspection services, will closely monitor the company's compliance with these commitments.

An overview of centralised applications is given in Annex I.

For marketing authorisations granted by the European Commission since the last CPMP in November 2000, see Annex II.

Scientific Advice

The Committee adopted the following scientific advice letters:

Product	**Indication(s)**	**Topic**
Chemical Substance	Treatment of pancreatic carcinoma.	New Scientific Advice request on clinical programme.
Chemical Substance	Monotherapy in the treatment of adult patients with tonic-clonic seizures.	New Scientific Advice request on clinical programme.
Biological Substance	Measles, mumps + rubella vaccine.	New Scientific Advice request on clinical programme.
Chemical Substance	Treatment of eyes' external infections.	New Scientific Advice request on clinical programme.
Biological Substance	Treatment of muscular spasm, especially focal dystonias like blepharospasm or torticollis.	New Scientific Advice request on pharmaceutical, pre-clinical and clinical programmes.
Chemical Substance	Treatment of schizophrenia.	Follow-up Scientific Advice request on clinical programme.
Chemical Substance	Treatment of HIV-1 infected adults.	New Scientific Advice request on pharmaceutical programme.
Chemical Substance	Adequate relief of meal related upper stomach problems in patients with functional dyspepsia.	New Scientific Advice request on clinical programme.
Chemical Substance	Chronic constipation.	New Scientific Advice request on clinical programme.
Biological Substance	Rotavirus Vaccine.	New Scientific Advice request on pharmaceutical programme.

The Committee accepted seven new and two follow-up requests from companies for scientific advice. Co-ordinators were appointed and one Scientific Advice oral explanation took place on an ongoing Scientific Advice request.

Referrals

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

A procedure under Article 12 has been initiated by Austria. This procedure relates to the efficacy of medicinal products containing calcitonins for indications other than those previously included in the on-going Article 12 referral started in April 2000. A Rapporteur and a Co-Rapporteur were assigned.

Working Parties, Ad Hoc Expert Groups and Organisational Matters

The CPMP heard reports from its Quality, Biotechnology, Safety, Efficacy and Pharmacovigilance Working Parties and from the Ad Hoc Working Group on Blood Products.

Biotechnology Working Party

The CPMP/BWP explanatory note on "gelatin for use in pharmaceuticals" (EMEA/CPMP/4305/00) is annexed together with this press release (see Annex IV).

Safety Working Party

Reference number	Document	Status
CPMP/2278/00	CPMP Position paper on possible pre-clinical studies to investigate addiction and dependence/ withdrawal related to use of SSRIs.	Adopted in November 2000.
CPMP/SWP/4163/00	Concept paper on the Development of a CPMP Points to consider on the Need for reproduction toxicity studies in the development of human insulin analogues.	Adopted in December 2000.

Efficacy Working Party

Reference number	Document	Status
CPMP/EWP/QWP/1401/98	Note for guidance on the Investigation of bioavailability and bioequivalence.	Released for 3 months' consultation in December 2000.
CPMP/EWP/2747/00	Note for guidance on Co-ordinating investigator signature of clinical study reports.	Released for 6 months' consultation in December 2000.

Ad Hoc Working Group on Blood Products

Reference number	Document	Status
CPMP/BPWG/2220/99	Note for guidance on the Clinical investigation of plasma derived antithrombin products.	Released for 6 months' consultation in December 2000.
CPMP/BPWG/3226/99	Core SPC for Human plasma derived antithrombin.	Released for 6 months' consultation in December 2000.

Organisational Matters

The Committee was informed of the restructuring of the EMEA Human Medicines Evaluation Unit (see Annex III) and the following guideline was released for consultation:

Reference number	Document	Status
CPMP/2990/00	Guideline on the processing of renewals in the centralised procedure	Released for 3 months' consultation in December 2000

Upcoming Meetings

There will be an extraordinary CPMP meeting on the 11th and 12th January 2001 to discuss CPMP/EMEA organisational matters. The election of the new CPMP Chairperson and Vice-Chairperson will take place at the January 2001 CPMP plenary meeting on the 23 to 25 January 2001.

Mutual Recognition

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) held on 11 December 2000, which is circulated together with this Press Release (see Annex V).

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This Press Release and other documents are available on the Internet at the following address: http://www.eudra.org/emea.html

EMEA CENTRALISED PROCEDURES

	1995-1999			2000			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Scientific Advice	61	77	138	13	45	58	196
Follow-up to scientific advice	11	6	17	4	5	9	26

	1995-1999			2000			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Applications submitted	80	144	224	17	38	55	279
Withdrawals	12	26	38	0	11	11	49
Positive CPMP opinions	44	82	126	20	30	50	176[1]
Negative CPMP opinions[2]	1	3	4	0	0	0	4[3]
Marketing authorisations granted by the Commission	40	78	118	16	17	33	151[4]

	1995-1999			2000			Overall Total
	Part A	**Part B**	**Total**	**Part A**	**Part B**	**Total**	
Variations type I	159	346	505	106	205	311	816
Positive opinions, variations type II	89	131	220	70	94	164	384
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	32	15	47	2	5	7	54

[1] 176 positive opinions corresponding to 136 substances
[2] In case of appeal the opinion will not be counted twice
[3] 4 negative opinions corresponding to 3 substances
[4] 151 Marketing Authorisations corresponding to 117 substances

Medicinal products granted a Community Marketing Authorisation under the Centralised Procedure since November 2000 Press Release

Brand name	Luveris
INN	Lutropin alfa
Marketing Authorisation Holder	Ares Sereno (Europe) Ltd.
ATC code	G03G
Indication	Stimulation of follicular development
Opinion receipt date	07/09/00
Date of Commission Decision	29/11/00

Brand name	NeoSpect
INN	depreotide
Marketing Authorisation Holder	Nycomed Imaging A/S
ATC code	V09IA05
Indication	For scintigraphic imaging of suspected malignant tumours in the lung.
Opinion receipt date	28/08/00
Date of Commission Decision	29/11/00

London, 18 December 2000
Doc. Ref: EMEA/CPMP/4305/00

Restructuring of the Human Medicines Evaluation Unit

As already announced in the EMEA Work Programme 2000 – 2001, the Human Medicines Evaluation Unit has been restructured by creating two operational Units, one dealing with pre-authorisation issues and the other with post-authorisation issues of medicinal products for human use.

Following the nomination of Mr. Noël Wathion as Head of Unit responsible for post-authorisation aspects (see EMEA Press Release dated 25 July 2000), Mr. Fernand Sauer, EMEA Executive Director, in consultation with his successor Mr. Thomas Lönngren, has decided on the appointment of Heads of Sector and Deputy Heads of Sector.

The following organigramme will be implemented as of 15 January 2001:

UNIT FOR THE PRE-AUTHORISATION EVALUATION OF MEDICINES FOR HUMAN USE	**UNIT FOR THE POST-AUTHORISATION EVALUATION OF MEDICINES FOR HUMAN USE**
[To be announced] *Head of Unit*	Noël WATHION *Head of Unit*
Sector for scientific advice and orphan drugs Patrick LE COURTOIS *Head of Sector*	***Sector for regulatory affairs and organisational support*** Anthony HUMPHREYS *Head of Sector*
Sector for quality of medicines John PURVES *Head of Sector*	***Sector for pharmacovigilance and post-authorisation safety and efficacy of medicines*** [Post vacant] *Head of Sector* Sabine BROSCH *Deputy Head of Sector*
Sector for safety and efficacy of medicines Isabelle MOULON *Head of Sector* Marisa PAPALUCA AMATI *Deputy Head of Sector*	

London, 18 December 2000
Doc. Ref: EMEA/CPMP/4305/00

GELATIN FOR USE IN PHARMACEUTICALS: EXPLANATORY NOTE[1] (13 December 2000) ON THE MANUFACTURE OF GELATIN IN RELATIONSHIP TO THE CPMP NOTE FOR GUIDANCE ON MINIMISING THE RISK OF TRANSMITTING ANIMAL SPONGIFORM ENCEPHALOPATHY VIA MEDICINAL PRODUCTS (CPMP/BWP/1230/98 rev 1)

The CPMP, in consultation with the trade organisations of the pharmaceutical industry (EFPIA) and the gelatin manufacturers (GME), have indicated that acid gelatin is still a necessary ingredient of some medicinal products.

Following the complementary approach developed in the CPMP Note for Guidance, proper sourcing of the starting material (bones) will render the gelatin acceptable if the following approach is adopted, such as sourcing bones from the following categories of countries (according to the classification made by the European Commission's Scientific Steering Committee, SSC):

- Category I and II countries for gelatin produced by the acid process,
- Category I, II and III countries for gelatin produced by the alkali process

This approach should be applied prospectively.

[1]This explanatory note should be considered as an appendix of the CPMP Note for Guidance on Minimising the risk of transmitting animal spongiform encephalopathy via medicinal products (CPMP/BWP/1230/98, rev 1) and will be integrated in this guidance at its next revision.

Report from the meeting held on 11 December 2000

The MRFG noted that 26 new mutual recognition procedures were finalised during the month of November 2000, as well as 82 type I and 33 type II variations.

The status as of 30th November 2000 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
2000	285	70	881	125	296	125	2 N.A. and 2 variations

37 new procedures (regarding 68 products) started in November 2000. The categories of these procedures are as follows:

3 new active substances (first authorisation in the European Community after RMS approval).

6 known active substances (already authorised in at least one member state), classified as **1** multiple application and **5** repeat use.

27 abridged applications including **12** multiple applications and **3** repeat use.

1 line extension application.

The new procedures started this month relate to 5 full dossiers, 4 bibliographic applications, 4 fixed combination, 18 generics, and 6 for different use, route or dose.

The procedures consisted of 37 chemical substances[1].

30 of these procedures were prescription-only medicinal products in the reference Member State and 7 were Non-prescription (including OTC) medicinal product[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 2000

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	3
DE (1)	3
DE (1)	3
DE (2)	15
DE (4)	13
DE (4)	13
DE (1)	14
DE (1)	14
DE (1)	14
DE (1)	1
DK(2)	6
DK(2)	1
DK(2)	2
DK(2)	2
DK(2)	1
DK(2)	1
DK(2)	1
DK(2)	1
DK(2)	8
FI (3)	8
FI (3)	8
NL (1)	2
NL (1)	1
NL (1)	1
SE (1)	2
SE (1)	2
SE (1)	1
SE (2)	14
SE (2)	15
UK (1)	5
UK (4)	3
UK (2)	3
UK (2)	3
UK (2)	3
UK (2)	1
UK (2)	1
UK (2)	1

General issues

Mutual Recognition Procedure – change in the timetable

Following the in-depth discussions on possible improvements in the Mutual Recognition Procedure, the MRFG agreed that in order to have more time for discussion between Member States within the procedure, CMS should send their comments to the RMS within 50 days (instead of 55 days). However, this additional time period is to be used by the Member States, not the applicant. Therefore the applicant shall still send his response report within the following 10 days. The MRFG agreed on a six- month trial period for MR-procedures for new applications starting between 1 January 2001 and 30 June 2001. The new amended timetable for Mutual recognition new applications is as follows:
Day 0: start of the procedure
Day 50: comments from the CMS
Day 60: applicant's response document to the RMS and CMS
Day 75: break out meeting, if necessary
Day 85: final position from the CMS
Day 90: end of the procedure

National administrative procedures in the Mutual Recognition Procedure

The MRFG conducted a survey among member states about the relevant National administrative procedures in Mutual Recognition. The main purpose of this exercise was to analyse the administrative procedures and exchange experiences between Member States. However, it was agreed that some general advice to applicants could be useful, and such advice will be published in the website.

TSE and Mutual Recognition Procedure

Any replacement in the excipient of a medicinal product with comparable excipient is to be considered as a type I variation (No. 4). This applies also to the replacement of an excipient from ruminant origin to the same excipient but from vegetable origin.

Change in the EU-Presidency

The December MRFG meeting was the last under the French Presidency. Sweden will take over the Chairmanship as of January 2000. Dr. Tomas Salmonson and Mr. Christer Backman will be the next chairmen. They should be contacted in future in case of questions regarding the MRP.

Meeting schedule

The next MRFG meeting will be held on 22 January 2001.

Joyeux Nöel et Bonne Année à Tous !

Merry Christmas and a Happy New Year!

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:*
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