



21 November 2000
CPMP/2901/00 corr

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 65th plenary meeting from 14 to 16 November 2000.

Centralised Procedures¹

The Committee adopted:

- Two positive opinions by consensus on centralised marketing authorisation applications relating to two active substances (one Part A and one Part B).
- One positive opinion under exceptional circumstances on a “line extension” application (in accordance with Annex II of the Commission Regulation (EC) No 542/95 as amended) by consensus relating to one active substance (Part B).
- One positive opinion by consensus for a centralised type I variation following a type II procedure relating to one active substance (Part A).
- Thirteen positive opinions by consensus for centralised type II variations:
 - One related to an extension of the indication.
 - Nine related to SPC/PL updates and
 - Three related to pharmaceutical aspects.
- Following an appeal procedure, one positive opinion by consensus on a centralised marketing authorisation application relating to one active substance (Part B).
- One positive opinion by consensus following the annual re-assessment of Ferriprox (deferiprone) (Part B). Ferriprox is indicated for the treatment of iron overload in patients with thalassemia major for whom deferoxamine therapy is contra-indicated or who present serious toxicity with deferoxamine therapy. The CPMP recommended that the marketing authorisation for this medicinal product should remain "under exceptional circumstances".
- One positive opinion by consensus on the renewal of a marketing authorisation relating to one active substance (Part A).
- Six lists of questions on centralised marketing authorisation applications related to five active substances (four Part A and one Part B) and one list of questions for a line extension application (in accordance with Annex II of the Commission Regulation (EC) No 542/95 as amended) related to one active substance (Part B).

Since the October 2000 CPMP meeting, the Committee noted the withdrawal of one application (Part B) from the centralised procedure.

The Committee heard three oral presentations from applicants concerning ongoing procedures.

The Committee heard one oral presentation from a Marketing Authorisation Holder concerning their failure to comply with fundamental pharmacovigilance obligations within the EU. 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. The Committee discussed the general problem of

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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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compliance of Marketing Authorisation Holders with pharmacovigilance obligations and agreed that this was a matter of public health importance. The Committee considered that, in future, fundamental failures to meet such obligations may have to be publicized. Recommendations for improving communication on pharmacovigilance will be discussed at the EMEA workshop on transparency on 23^d November 2000 and subsequently submitted to the Management Board for decision at its December 2000 meeting.

An overview of centralised applications is given in Annex I.

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

Scientific Advice

The Committee adopted the following scientific advice letters:

Product	Indication(s)	Topic
Chemical Substance	Treatment of pulmonary hypertension	New Scientific Advice request on clinical programme
Biological Substance	Treatment of viral diseases such as Hepatitis C	New Scientific Advice request on clinical programme
Chemical Substance	Treatment of small cell lung cancer and non-small cell lung cancer	New Scientific Advice request on clinical programme
Biological Substance	Treatment of frailty in the elderly	New Scientific Advice request on clinical programme
Biological Substance	Measles, mumps and rubella vaccine	New Scientific Advice request on quality, safety and clinical programmes
Biological Substance	Selective Estrogen Receptor Modulator to be associated with estrogen in hormone replacement therapy	New Scientific Advice request on pharmaceutical programme
Biological Substance	Selective Estrogen Receptor Modulator to be associated with estrogen in hormone replacement therapy	Follow-up Scientific Advice request on pre-clinical and clinical programmes
Chemical Substance	Treatment of HIV-1 infected adults	New Scientific Advice request on pre-clinical programme
Chemical Substance	Treatment of chronic neuropathic pain	New Scientific Advice request on clinical programme

The Committee accepted eleven new requests from companies for scientific advice. Co-ordinators were appointed and three Scientific Advice oral explanations took place on ongoing Scientific Advice requests.

Referrals

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

Following a referral under Article 12 initiated by Belgium in October, 1999, the CPMP reviewed the safety and efficacy of Sibutramine containing medicinal products and after considering the commitment from the Marketing Authorisation Holder to perform a further clinical trial, adopted an opinion by majority vote, recommending the maintenance of the marketing authorisations with amendments to the Summary of Product Characteristics.

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.

Quality Working Party

The Committee adopted the updated workplan for the QWP 2000-2001 (CPMP/QWP/583/99 rev.5).

Reference number	Document	Status
CPMP/QWP/2820/00 EMEA/CVMP/815/00	Note for guidance on Specifications: Test procedures and acceptance criteria for herbal drugs, herbal drug preparations and herbal medicinal products	Released for 4 months' consultation in November 2000
CPMP/QWP/2819/00 EMEA/CVMP/814/00	Note for guidance on Quality of herbal medicinal products	Released for 4 months' consultation in November 2000
CPMP/QWP/2845/00	Note for guidance on Requirements for pharmaceutical documentation for pressurised metered dose inhalation products	Released for 6 months' consultation in November 2000

Biotechnology Working Party

Reference number	Document	Status
CPMP/BWP/3326/99	Concept paper on the Development of a Points to consider on Xenogeneic cell therapy	Adopted in November 2000
CPMP/BWP/2571/00	Points to consider on the Reduction, elimination or substitution of thiomersal in vaccines	Released for 3 months' consultation in November 2000

Efficacy Working Party

Reference number	Document	Status
CPMP/EWP/785/97	Concept paper on the Evaluation of drugs for the treatment of the irritable bowel syndrome	Adopted in November 2000
CPMP/EWP/1119/98	Points to consider on the Evaluation of diagnostic agents	Released for 3 months' consultation in November 2000
CPMP/EWP/566/98 rev 1	Note for guidance on Clinical investigation of medicinal products in the treatment of epileptic disorders	Adopted in November 2000
CPMP/EWP/714/98	Note for guidance on Clinical investigation of medicinal products for the treatment of peripheral arterial occlusive disease	Released for 6 months' consultation in November 2000

ICH

A report on the ICH Steering Committee and ICH5 Conference (4-11 November 2000) was presented to the CPMP.

The following ICH guidelines which reached step 4 during the Steering Committee in San Diego were adopted for implementation by June 2001:

Reference number	Document
CPMP/ICH/2736/99 (rev. of CPMP/ICH/380/95)	Q1AR: Stability testing guidelines: Stability testing of new active substances and medicinal products
CPMP/ICH/539/00	S7A: Safety pharmacology studies for human pharmaceuticals

The following ICH guideline which reached step 2 during the Steering Committee in San Diego was released for consultation by March 2001:

Reference number	Document
CPMP/ICH/4104/00	Q1D: Bracketing and matrixing designs for stability testing of drug substances and drug products

The following ICH guidelines have been agreed by the Steering Committee and were adopted for release for information:

Reference number	Document
CPMP/ICH/286/95 (modification)	M3 modification: Non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals
CPMP/ICH/136/95 (modification)	S5B modification: Reproductive toxicology: Toxicity to male fertility
CPMP/ICH/287/95 (modification)	E2B modification: Data elements for transmission of individual case safety reports

The Committee has been informed on the final documents, which will be implemented by the European Commission at a later stage:

Reference number	Document
CPMP/ICH/2887/99	M4: Common Technical Document (CTD)
CPMP/ICH/4106/00	Q7A: Good Manufacturing Practice guide for active pharmaceutical ingredients

Organisational Matters

Reference number	Document	Status
CPMP/328/98 rev 2	Revised CPMP guidance paper on Acceptance of tradenames for medicinal products processed through the centralised procedure	Released for 4 months' consultation in November 2000

The EMEA has written to the Marketing Authorisation Holders of centrally authorised medicinal products reminding them that demonstration of compliance with the TSE guideline is required by the Annex to Council Directive 75/318/EEC as amended by Commission Directive 99/82/EEC, if the medicinal product contains or uses in its manufacture materials covered by the scope of the TSE guideline. Where demonstration of compliance is required for centrally authorised products the Pharmaceutical Committee has agreed two procedures. These are described in the CPMP briefing document: *'Implementing the amendment to the Annex of Council Directive 75/318/EEC: Demonstration of compliance with the CPMP-TSE guideline'* (CPMP/BWP/2962/99) which is published on the DG Enterprise-Pharmaceuticals & Cosmetics WebSite (<http://dg3.eudra.org/pharmacos/docs/Doc2000/TSEnov99.pdf>).

Upcoming meetings

The Committee noted that a EMEA workshop on transparency will be held on 23 November 2000. Topics to be addressed include communication on CPMP opinions as well as post-marketing communication, including pharmacovigilance.

The Committee also noted that a public meeting on certification for TSE risk products, organised by the European Department for the Quality of Medicines (EDQM), will be held on 11 January 2001 in Strasbourg.

Mutual Recognition

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) held on 13 November 2000, which is circulated together with this Press Release (Annex III).

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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	12	39	51	189
Follow-up to scientific advice	11	6	17	4	4	8	25

	1995-1999			2000			Overall Total
	Part A	Part B	Total	Part A	Part B	Total	
Applications submitted	80	144	224	17	35	52	276
Withdrawals	12	26	38	0	7	7	45
Positive CPMP opinions	44	82	126	19	24	43	169 ¹
Negative CPMP opinions²	1	3	4	0	0	0	4 ³
Marketing authorisations granted by the Commission	40	78	118	15	16	31	149 ⁴

	1995-1999			2000			Overall Total
	Part A	Part B	Total	Part A	Part B	Total	
Variations type I	159	346	505	89	187	276	781
Positive opinions, variations type II	89	131	220	56	76	132	352
Negative opinions, variations type II	0	2	2	0	0	0	2
Extensions	32	15	47	2	3	5	52

¹ 169 positive opinions corresponding to 130 substances

² In case of appeal the opinion will not be counted twice

³ 4 negative opinions corresponding to 3 substances

⁴ 149 Marketing Authorisations corresponding to 115 substances

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

Brand name	Agenerase
INN	amprenavir
Marketing Authorisation Holder	Glaxo Group Ltd.
ATC code	J05AE05
Indication	Treatment of HIV infected adults and children.
Opinion receipt date	09/08/00
Date of Commission Decision	20/10/00

Brand name	Infanrix hexa
INN	Combined diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis virus, hepatitis B virus and Haemophilus type b vaccine.
Marketing Authorisation Holder	SmithKline Beecham Biological S.A.
ATC code	J07CA
Indication	Immunisation against haemophilus influenza, diphtheria, pertussis, tetanus, hepatitis B and poliomyelitis
Opinion receipt date	09/08/00
Date of Commission Decision	23/10/00

Brand name	Infanrix penta
INN	Combined diphtheria, tetanus, acellular pertussis, inactivated poliomyelitis virus and hepatitis B virus vaccine.
Marketing Authorisation Holder	SmithKline Beecham Biological S.A.
ATC code	J07CA
Indication	Primary and booster vaccination of infants against diphtheria, pertussis, tetanus, hepatitis B and poliomyelitis
Opinion receipt date	09/08/00
Date of Commission Decision	23/10/00

Brand name	Hexavac
INN	Purified diphtheria and tetanus toxoids, purified acellular pertussis components, HbsAg produced from recombinant strain of the yeast accharomyces cerevisiae, inactivated type 1, 2 and 3 poliovirus and haemophilus influenzae type b polysaccharide conjugated to tetanus protein.
Marketing Authorisation Holder	Pasteur Merieux MSD
ATC code	J07CA
Indication	Immunisation against diphtheria, pertussis, tetanus, hepatitis B, poliomyelitis and Haemophilus influenza
Opinion receipt date	09/08/00
Date of Commission Decision	23/10/00



Report from the meeting held on 13 November 2000

The MRFG noted that 76 new mutual recognition procedures were finalised during the month of October 2000, as well as 82 type I and 33 type II variations.

The status as of 31 October 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	259	60	799	78	263	135	2 N.A. and 2 variations

12 new procedures (regarding 18 products) started in October 2000. The categories of these procedures are as follows:

1 new active substance (first authorisation in the European Community after RMS approval) classified as multiple application.

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

9 abridged applications including **1** for an additional form or strength and **1** repeat use.

The new procedures started this month relate to 3 full dossiers, 8 generics, and 1 for different use, route or dose.

The procedures consisted of 11 chemical substances and 1 biological product¹.

11 of these procedures were prescription-only medicinal products in the reference Member State and 1 was Non-prescription (including OTC) medicinal product².

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 October 2000

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

General issues

TSE and Mutual Recognition Procedure

The MRFG has recommended the MAH to demonstrate the compliance with the TSE requirements by using the Model Declaration of compliance with the annex to Dir 75/318/EEC as amended by Dir 99/82/EEC relating to the application of the Note for Guidance on minimising the risk of transmission of animal spongiform encephalopathy agents via medicinal products.

For products approved through Mutual Recognition procedure the Member States agreed the following approach:

- Products listed in Annex I of the Model Declaration: It will not be necessary to start a type I variation. The RMS will check the information provided by MAH and will notify the receipt of the Ph.Eur. Certificates to CMS.
- Products listed in Annex II of the Model Declaration: the assessment of the submitted dossier will be performed through a type II variation procedure.
- Products listed in Annex III of the Model Declaration: no specific dossier is required.

For products authorised through national procedures, national requirements have to be followed.

Medicinal products containing milk derivatives, wool, and hair are excluded from the scope, provided that certain source criteria are met as specified in the updated version of the above-mentioned Note for guidance. In this case MAH will not need to provide any TSE documentation for such medicinal products.

Simplified handling of variations in MRP not related to a merger

A simplified handling for certain listed type I variations in MRP - not in connection with a merger - was adopted by the MRFG during the November meeting.

- Change of the brand name (Type I, No.2) where the approved brand name is different in the CMS. If the MAH wants to change the brand name after authorisation in more than one CMS, the submission of only one Type I variation per medicinal product (MA) will cover all different names and all different CMS.

If the brand name has to be changed during the MRP, no variation procedure is necessary.

- Change of the name and/or the address of a MAH (Type I, No.3) where the name and/or address is different in the CMS and the change is not to be considered as a transfer. In such cases also the submission of only one type I variation per medicinal product (MA) will cover all different CMS.

It has to be mentioned that fees remain under national considerations.

Renewal of influenza vaccines

The MRF agreed on the common European renewal date for all the influenza vaccines authorised via Mutual Recognition Procedure being **30 December 2002**. This would enable a more efficient processing of renewal procedure of this group of medicinal products. The date was set up by using the day 90 of the first mutually recognised influenza vaccine as a common European “birth date” for influenza vaccines.

Meeting schedule

The next MRFG meeting will be held on 11 December 2000.

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

<http://heads.medagencies.org/>