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

CPMP/651/97
25 July 1997

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 29th plenary meeting on 22-23 July 1997. The CPMP welcomed Prof. Miguel Forte from Portugal as a new member who succeeds Prof. Henrique Luz-Rodrigues.

An overview of applications is given in Annex I and II.

Centralised Procedures

The Committee adopted by consensus a positive opinion on a centralised application for a biotechnology product (Part A) for enzyme replacement therapy in patients with type I Gaucher's disease.

The Committee adopted by consensus *9* positive opinions for centralised type II variations and *10* positive opinions for centralised type I variations following the type II procedure.

Since the CPMP meeting in June 1997, the European Commission has granted a marketing authorisation for Cystagon (mercaptamine) for the treatment of nephropathic cystinosis, Orlaam (levacetylmethadol) for substitution maintenance treatment of opiate addiction, Revasc (desirudin), an anti-thrombotic agent and NeoRecormon (epoetin beta), an antianaemic agent (see Annex III).

Eleven applications forthcoming in the centralised procedure within the next 6 months have been attributed to Rapporteurs and Co-Rapporteurs.

Scientific Advice

The CPMP adopted by consensus one scientific advice following a specific and justified request presented to the Committee earlier by the pharmaceutical company.

ICH

Report was made to the CPMP on the results achieved at ICH Steering Committee & Expert Working Group meeting and the ICH4 conference in Brussels on 14-18 July 1997. (Overview of ICH Guidelines Status is given in Annex IV). Successful conclusion of the first phase of the tripartite International Harmonisation process were greeted. EMEA/CPMP will continue to provide technical support to future ICH activities (finalisation of guidelines, maintenance work, initiation of work for new topics). The CPMP validated the adoption by the ICH Steering Committee of the M3 guideline "Timing of Non-clinical Safety Studies in Relation to Clinical Trials". The CPMP also discussed the new topic M4, "Common Technical Document" (CTD).

Discussion/adoption of ICH4 guidelines by the CPMP for implementation or dissemination to interested parties is foreseen for the September meeting.

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Working Parties

The CPMP heard reports from its Quality, Biotechnology, Safety, Efficacy and Pharmacovigilance Working Parties.

The following documents were adopted:

- Note for guidance on inclusion of anti-oxidants and anti-microbial preservatives in medicinal products (CPMP/QWP/115/95). This provides guidance on the information to be included in applications for marketing authorisations concerning substances used as antioxidants and anti-microbial preservatives for coming into operation within 6 months.

- Note for guidance on medicinal products in the treatment of Alzheimer's Disease (CPMP/EWP/553/95) for coming into operation within 6 months. This guideline focuses mainly on the symptomatic treatment of Alzheimer's disease. It should be recognised that the symptomatic treatment of Alzheimer's disease is still a developing area of research in which experience is still accruing on the use of assessment scales and the possible need for them to be modified.

The following documents were released for 6 months consultation:

Note for guidance on plasma derived medicinal products (CPMP/BWP/269/95). This provides updated guidance on the information on the manufacture and control of plasma derived medicinal products to be included in applications for marketing authorisations.

Prof. R. Bass
Head of Human Medicines Evaluation Unit

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

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ANNEX I to **CPMP - July 1997**
Press Release

ICH Topics (* progress at ICH4)

Efficacy

E1A	The extent of population exposure to assess clinical safety (CPMP/ICH/375/95)	Step 5
E1B	Prospective and retrospective studies of databases on population exposure	Step 1
E2A	Clinical safety data management: definitions and standards for expedited reporting (CPMP/ICH/377/95)	Step 5
E2B*	**Clinical safety data management: data elements for transmission of individual case safety reports (CPMP/ICH/287/95)**	**Step 4**
E2C	Clinical safety data management: periodic safety update reports for marketed drugs (CPMP/ICH/288/95)	Step 4
E3	Clinical study reports: structure and content (CPMP/ICH/137/95)	Step 5
E4	Dose response information to support drug registration (CPMP/ICH/378/95)	Step 5
E5	Ethnic factors in the acceptability of foreign clinical data (CPMP/ICH/289/95)	Step 3
E6	Good clinical practice: consolidated guideline (CPMP/ICH/135/95) [incl. former topics E6A: Addendum onstigator's brochure and E6B: Addendum on essential documents}	Step 5
E7	Studies in support of special populations: geriatrics (CPMP/ICH/379/95)	Step 5
E8*	**General considerations for clinical trials (CPMP/ICH/291/95)**	**Step 4**
E9*	**Statistical principles for clinical trials (CPMP/ICH/363/96)**	**Step 3**
E10	Choice of control group in clinical trials (CPMP/ICH/364/96	Step 1

Quality

Q1A	Stability testing of new active substances and medicinal products (CPMP/ICH/380/95)	Step 5
Q1B	Stability testing: photostability testing of new active substances and medicinal products (CPMP/ICH/279/95)	Step 4
Q1C	Stability testing requirements for new dosage forms (CPMP/ICH/280/95)	Step 4
Q2A	Validation of analytical procedures: definition and terminology (CPMP/ICH/381/95)	Step 5
Q2B	Validation of analytical procedures: methodology (CPMP/ICH/281/95)	Step 4
Q3A	Impurities testing guideline: impurities in new active substances (CPMP/ICH/142/95)	Step 5
Q3B	Impurities in new medicinal products (CPMP/ICH/282/95)	Step 4
Q3C*	**Impurities: residual solvents (CPMP/ICH/283/95)**	**Step 4**
Q4	Harmonisation of pharmacopoeias	Step 1
Q5A	Quality of biotechnological products: viral safety evaluation of biotech-nological products derived from cell lines of human or animal origin (CPMP/ICH/295/95)	Step 4
Q5B	Quality of biotechnological products: analysis of the expression construct in cell lines used for production of r-DNA derived protein products (CPMP/ICH/139/95)	Step 4
Q5C	Quality of biotechnological products: stability testing of biotechnological/ biological products (CPMP/ICH/138/95)	Step 4
Q5D*	**Quality of biotechnological/ biological products: derivation and characterisation of cell substrates used for production of biotechnological/biological products (CPMP/ICH/294/95)**	**Step 4**
Q6A*	**Specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances(CPMP/ICH/367/96)**	**Step 2**
Q6B	Specifications: tests and procedures for biotechnological/biological products (CPMP/ICH/365/96)	Step 1

Safety

S1A	Guideline on the need for carcinogenicity studies of pharmaceuticals (CPMP/ICH/140/95)	Step 4
S1B*	**Carcinogenicity: testing for carcinogenicity of pharmaceuticals (CPMP/ICH/299/95)**	**Step 4**
S1C	Carcinogenicity: dose selection for carcinogenicity studies of pharmaceuticals (CPMP/ICH/383/95)	Step 5
S1C(R) *	**Addendum to 'Dose selection for carcinogenicity studies of pharmaceuticals': addition of a limit dose and related notes of pharmaceuticals (CPMP/ICH/366/95)**	**Step 4**
S2A	Genotoxicity: specific aspects of regulatory genotoxicity tests for pharmaceuticals (CPMP/ICH/141/95)	Step 5
S2B*	**Genotoxicity: a standard battery for genotoxicity testing of pharmaceuticals (CPMP/ICH/174/95)**	**Step 4**
S3A	Toxicokinetics: the assessment of systemic exposure in toxicity studies (CPMP/ICH/384/95)	Step 5
S3B	Pharmacokinetics: guidance for repeated dose tissue distribution studies (CPMP/ICH/385/95)	Step 5
S4*	**Duration of chronic toxicity testing in animal (rodent and non rodent toxicity testing (CPMP/ICH/300/95)**	**Step 2**
S5A	Reproductive toxicology: detection of toxicity to reproduction for medicinal products (CPMP/ICH/386/95)	Step 5
S5B	Reproductive toxicology: toxicity to male fertility (CPMP/ICH/136/95)	Step 5
S6*	**Preclinical safety evaluation of for biotechnology-derived pharmaceuticals (CPMP/ICH/302/95)**	**Step 4**

Multidisciplinary

M1*	**Standardisation of medical terminology for regulatory purposes**	**Vers. 2.0**
M2*	**The choice of electronic standards for the transfer of regulatory information**	
M3*	**Non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals (CPMP/ICH/286/95)**	**Step 4**
M4*	**Common Technical Document**	

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ANNEX II to **CPMP - July 1997**
Press Release

CENTRALISED APPLICATIONS TO THE EMEA

	CENTRALISED		TOTAL*
	Part A	***Part B***	
Applications submitted since 01.01.95	41	68	109
Withdrawn	0	7	7
Review ongoing	16	33	49
Opinions given by CPMP	25	28	53**
Marketing Authorization granted by Commission	22	21	43

* These figures include the 18 ex-concertation procedures submitted before January 1995 of which 14 have been authorised and 4 withdrawn before end 1996
** 53 opinions corresponding to 44 substances

	PENDING		FINAL		TOTAL
	Part A	***Part B***	***Part A***	***Part B***	
Variations type I	10	2	43	36	91
Variations type II	2	6	13	20	41
Scientific advice	7		35		42

Update 30 July, 1997

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ANNEX III to **CPMP - July 1997**
Press Release

Medicinal Product granted a Community Marketing Authorisation under the Centralised Procedure

Status: July 1997

oduct Brandname INN Part A/B	**Company** a) Name b) Origin	**Therapeutic Area** a) ATC b) Indication	**Presentation** a) Form b) Dose c) Number of Presentations	**EMEA/CPMP** a) Validation b) Opinion c) Active Time d) Clock stop	**Commission** a) Date of decision b) Date of notification c) OJ No.
Cystagon mocaptamine Part B	a) Orphan SARL b) FR	a) A16AA04 b) Nephropathic cystinosis	a) Capsule b) 50 mg, 150 mg c) 4 Presentations	a) 15.02.96 b) 19.02.97 c) 176 Days d) 181 Days	a) 23.06.97 b) c)
Orlaam levacetyl-methadol Part B	a) Sipaco International Lda. b) PO	a) N02AC b) Substitution maintenance treatment of opiate addiction	a) Aqueous solution for oral use b) 10 mg/ml c) 1 Presentation	a) 01.01.95 b) 22.01.97 c) 201 Days d) 487 Days	a) 01.07.97 b) c)
Revasc desirudin Part A	a) Novartis b) CH	a) BO1AX b) Antithrombotic	a) Powder for injection b) 15 mg c) 1 Presentation	a) 10.07.95 b) 19.03.97 c) 181 Days d) 398 Days	a) 09.07.97 b) c)
NeoRecormon epoetin beta Part A	a) Boehringer Mannheim b) DE	a) BO3XA b) Antianaemic	a) Powder for injection b) 500, 1000, 2000, 5000, 10.000, 50.000, 100.000 IU c) 24 Presentations	a) 01.11.95 b) 16.10.96 c) 209 Days d) 140 Days	a) 16.07.97 b) c)

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ANNEX IV to **CPMP - July 1997**
Press Release

London, 1 July 1997
CPMP/169/97

ORLAAM

International Non-proprietary Name (INN): **Levacetylmethadol**

On 1 July 1997, the European Commission issued a Marketing Authorisation valid for the entirety of the European Union for the medicinal product ORLAAM, which contains levacetylmethadol. This decision was based on the favourable opinion and on the assessment report adopted by the Committee for Proprietary Medicinal Products (CPMP) on 22 January 1997. The Marketing Authorisation Holder responsible for this medicinal product is Sipaco Internacional Lda., Portugal.

The approved indication is for the substitution maintenance treatment of opiate addiction in adults previously treated with methadone, as part of a comprehensive treatment plan including medical, social and psychological care. ORLAAM should be administered under the supervision of physicians with experience in addiction treatment and whenever practicable, in centers specialising in the treatment of drug addiction. ORLAAM is not intended for take home use. Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in this EPAR and is available in all European Union official languages.

The active substance of ORLAAM, levacetylmethadol is a synthetic opioid analgesic, structurally similar to methadone. Its pharmacological activity is qualitatively similar to morphine. In comparison to methadone which is administered daily, the main advantage with levacetylmethadol is its pharmacokinetic behaviour leading to a longer pharmacodynamic action and therefore allowing a three times weekly administration. The long-term drop-out of patients was comparable to that of methadone.

With respect to safety, levacetylmethadol shows an overall safety profile similar to that of opioid compounds. However, clinical data indicated that ORLAAM significantly prolonged the QT interval (ECG) in some patients. The clinical relevance of these findings is unclear. Therefore, additional comparative studies with levacetylmethadol and methadone should be performed, to evaluate the risk on cardiac conduction and repolarisation changes.

Despite the methodological deficiencies of the documentation of ORLAAM, the overall clinical data suggest that the efficacy and safety of ORLAAM is comparable to that of methadone in the substitution maintenance treatment of opiate addiction.

The CPMP, on the basis of the overall benefit/risk ratio considered that ORLAAM showed a satisfactory safety profile for the substitution maintenance treatment of opiate addiction in adults previously treated with methadone and therefore recommended that the Marketing Authorisation should be granted.

The European Agency for the Evaluation of Medicinal Products
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ANNEX V to **CPMP - July 1997**
Press Release

23 June 1997
CPMP/230/97

CYSTAGON

International Non-proprietary Name (INN): **Mercaptamine bitartrate**

On 23 June 1997, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product CYSTAGON, which contains mercaptamine bitartrate. This decision was based on the favourable opinion and on the assessment report adopted by the Committee for Proprietary Medicinal Products (CPMP) on 19 February 1997. The Marketing Authorisation Holder responsible for this medicinal product is Orphan Europe SARL.

The International Non-proprietary Name of the product is mercaptamine bitartrate whereas cysteamine bitartrate is the name currently used. The active substance of CYSTAGON, cysteamine bitartrate, is prescribed to manage nephropathic cystinosis, a rare inherited disorder characterised by the accumulation of cystine in some organs, such as kidneys. Cystine accumulation causes kidney damage and excretion of excess amounts of glucose, proteins and electrolytes. CYSTAGON is a medication that reacts with cystine to decrease its level in cells. Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in this EPAR and is available in all European Union official languages.

Clinical studies have demonstrated that cysteamine was effective in preventing degradation of renal function, improving survival and growth rate in patients with cystinosis.

The most common side effects of CYSTAGON include: nausea, vomiting, loss of appetite, fever, diarrhea, drowsiness, rash. Cases of the following have been reported: dehydration, high blood pressure, abdominal discomfort, effects on the nervous system (headaches, nervousness, depression, and rarely fits and hallucinations), allergic-type rash and effects on the kidney. CYSTAGON may cause anemia and leucopaenia and increases in liver enzymes. CYSTAGON may cause unpleasant breath and body odour.

Due to insufficient animal data and to the lack of human experience, the use of CYSTAGON is not recommended during pregnancy. The effect of untreated cystinosis on pregnancy is also unknown.

Despite deficiencies in the documentation provided, and considering the favourable benefit/risk ratio for this potentially effective drug intended for a fatal and very rare disease, the CPMP recommended that the Marketing Authorisation should be granted under exceptional circumstances. This implies that the Marketing Authorisation Holder will submit additional information on toxico-pharmacological and clinical aspects of this medicinal product. All additional data will be carefully monitored and reviewed by the CPMP.

The European Agency for the Evaluation of Medicinal Products
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ANNEX VI to **CPMP - July 1997**
Press Release

9 July 1997
CPMP/280/97

REVASC

International Non-proprietary Name (INN): **Desirudin**

On 9 July 1997, the European Commission issued a Marketing Authorisation valid for the entire European Union for the medicinal product Revasc, which contains desirudin. This decision was based on the favourable opinion and on the assessment report adopted by the Committee for Proprietary Medicinal Products (CPMP) on 19 March 1997. The Marketing Authorisation Holder responsible for this medicinal product is Ciba Europharm Ltd, United Kingdom.

The approved indication is for the prevention of deep venous thrombosis in patients undergoing elective hip and knee replacement surgery. Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in this EPAR and is available in all European Union official languages.

The active substance of Revasc, desirudin, is a synthetic analogue of hirudin and is manufactured by recombinant DNA technology, using a yeast cell as a vector. Hirudin is a natural anticoagulant found in the saliva of the European leech *Hirudo medicinalis.* Desirudin is a single-chain polypeptide consisting of 65 amino acids containing 3 disulphide bridges. The structure of desirudin is nearly the same as that of hirudin with the exception that it lacks a sulphate group on amino acid Tyr 65.

Clinical trials were designed to investigate dose ranging, the comparison of desirudin with unfractionated heparin and the comparison of desirudin with enoxaparin - a low molecular weight heparin. Efficacy was demonstrated in reducing the frequency of major thrombotic events (death, proximal deep venous thrombosis, pulmonary embolism); and the occurrence of other thromboembolic events. Studies showed that Revasc was more effective than unfractionated heparin and also more effective than enoxaparin in prophylaxis of thromboembolic disease after elective hip replacement surgery.

As with other anticoagulants, the most common adverse reactions observed during treatment were bleeding episodes. The results showed very similar haemorrhagic complications for desirudin, fractionated heparin and enoxaparin. The data from the studies demonstrated that bleeding at the site of injection, and wound haematoma, were slightly more frequent and slightly more profuse than with heparin or enoxaparin. At the dosage regimens used in clinical trials, desirudin did not induce major haemorrhagic complications. The small excess in bleeding is probably outweighed by the improvement in efficacy.

The CPMP, on the basis of the overall benefit/risk ratio, considered that Revasc showed a satisfactory safety profile and adequate evidence of prophylaxis of thromboembolic disease and, therefore, recommended that the Marketing Authorisation should be granted.

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

ANNEX VII to **CPMP - July 1997**
Press Release

16 July 1997
CPMP/910/96

NEORECORMON

International Non-proprietary Name (INN): **epoetin beta**

On 16 July 1997, the European Commission issued a marketing authorisation valid for the entirety of the European Union for the medicinal product NeoRecormon, which contains epoetin beta. This decision was based on the favourable opinion and on the assessment report adopted by the Committee for Proprietary Medicinal Products (CPMP) on 17 October 1996. The pharmaceutical company responsible for this medicinal product is Boehringer Mannheim GmbH.

The approved indications are for i) the treatment of chronic symptomatic renal anaemia, ii) prevention and treatment of anaemia in adult patients with solid tumours, treated with platinum-based chemotherapy iii) increasing the yield of autologous blood donation in patients with moderate anaemia and no iron deficiency if blood conserving procedures are not available or insufficient when a large volume of blood is required iv) prevention of the anaemia of prematurity in infants with a birth weight of 750 to 1500g and a gestational age of less than 34 weeks. Detailed conditions for the use of this product are given in Annex I of the CPMP Opinion, the Summary of Product Characteristics (SPC), which can be found in this EPAR and are available in all European Union official languages.

The active substance of NeoRecormon, epoetin beta, is produced by recombinant DNA technology and is found to be identical to the human erythropoietin in terms of protein sequence, biological activity and immunological reactivity. Its mechanism of action lies in the stimulation of red blood cells production (erythropoiesis).

Clinical trials were designed to investigate the efficacy of NeoRecormon in patients having the above mentioned indications. Clinical benefit was proven in different patient populations in terms of: increase of hematocrit and reticulocyte count, increase of autologous blood availability at the time of the elective surgery, shortening the period of anaemia after blood donation and reduction of blood transfusions, prevention of anaemia in premature babies, provided that epoetin beta therapy is accompanied by oral iron treatment.

The most frequent adverse reactions observed during treatment were cardiovascular events (mainly hypertension), upper and lower respiratory tract infections, changes in laboratory parameters such as hyperkaliemia and increase of liver enzymes, injection site reactions. The most frequent adverse events at withdrawal in the case of patients with renal failure were hypertension and shunt thrombosis.

The CPMP, on the basis of the overall benefit/risk ratio considered that NeoRecormon showed a satisfactory safety profile and therefore recommended that the Marketing Authorisation should be granted.

Mutual Recognition Facilitation Group
Report from the meeting held on 16 June 1997

The MRFG noted that 11 new mutual recognition procedures have been finalised recently as well as 11 type I and 30 type II variations.
The status as of 16 June 1997 of procedures under mutual recognition is as follows:

Year	New applications finalised	New applications in process	Type I variations finalised	Type I variations pending	Type II variations finalised	Type II variations pending	Arbitrations referred to CPMP
1997	48	37	50	12	65	41	2

Since 12 May for 8 new applications the procedures have been started with the following characteristics:

New active substance[1]	Line extensions[2]	Fixed combinations	Generics	Herbal products[3]	OTC[4]	Others[5]
0	4	1	2	1	0	0

1. When in one of the involved Member States it concerns a new active substance according to the definition in the Notice to Applicants Part IIA;
2. Line extensions are those applications which extend a range of products, e.g. an additional strenght, or a new pharmaceutical form from the same Marketing Authorisation Holder;
3. In this category products are classified as herbals when the RMS has considered them as herbal product;
4. In this category products are classified as OTC products when the RMS has approved it for OTC use, although the legal status is not part of the Mutual Recognition Procedure;
5. When the product is not classified in the previous six categories.

Each application can be classified in only one category.

Number of countries involved in the started procedures since 12 May 1997:

Reference Member State (number of products involved in the procedure)	Number of CMS involved in the procedure
BE (2)	14
BE (2)	12
DE (3)	10
NL (1)	5
SE (1)	2
SE (1)	2
UK (1)	12
UK (2)	12

The validation time will be provided when EUDRATRACK is fully operational.

General issues

- A first draft for a protocol for Break-out sessions was discussed.
- A MRFG-meeting will be organised on 19 August 1997 for break-out sessions.
- The chairmanship of the MRFG for the following six months will be divided between The Netherlands and United Kingdom.

Mutual Recognition Facilitation Group
Report from the meeting held on 21 July 1997

The MRFG noted that 19 new mutual recognition procedures have been finalised recently as well as 1 type I and 6 type II variations.
The status as of 21 July 1997 of procedures under mutual recognition is as follows:

Year	New applications finalised	New applications in process	Type I variations finalised	Type I variations pending	Type II variations finalised	Type II variations pending	Arbitrations referred to CPMP
1997	67	36	51	14	72	47	2

Since 16 June for 24 new applications the procedures have been started with the following characteristics:

New active substance[1]	Line extensions[2]	Fixed combinations	Generics	Herbal products[3]	OTC[4]	Others[5]
7	6	1	3	1	0	6

1. When in one of the involved Member States it concerns a new active substance according to the definition in the Notice to Applicants Part IIA;
2. Line extensions are those applications which extend a range of products, e.g. an additional strenght, or a new pharmaceutical form from the same Marketing Authorisation Holder;
3. In this category products are classified as herbals when the RMS has considered them as herbal product;
4. In this category products are classified as OTC products when the RMS has approved it for OTC use, although the legal status is not part of the Mutual Recognition Procedure;
5. When the product is not classified in the previous six categories.

Each application can be classified in only one category.

Number of countries involved in the started procedures since 16 June 1997:

Reference Member State (number of products involved in the procedure)	Number of CMS involved in the procedure
BE (2)	14
BE (2)	11
DE (4)	11
DK (1)	8
DK (1)	7
FR (1)	7
FR (1)	12
IR (2)	6
NL (3)	4
SE (1)	4
SE (1)	4
SE (1)	12
UK (1)	6
UK (2)	3
UK (1)	13
UK (3)	7
UK (2)	1
UK (1)	7
UK (3)	3
UK (1)	11
UK (4)	14
UK (4)	8
UK (1)	14
UK (2)	14

The validation time will be provided when EUDRATRACK is fully operational.

General issues

- In the September press release a table will be included of all the procedures and Member States involved since January 1995.
- All Member States agreed on the protocol for Break-out sessions (enclosed)
- The MRFG decided not to accept substantial new data for Part II during the procedure.
- A standard validation letter was agreed upon. This letter will be used by the Member State when there are problems in the validation of the application. The letter will be forwarded to the Marketing Authorisation Holder and the Reference Member State.

Information on the above mentioned issues can be obtained by the presiding chair of the MRFG:

Mrs G.M. Janse-de Hoog
Medicines Evaluation Board in The Netherlands
Tel. 31-70-3407422

MUTUAL RECOGNITION FACILITATION GROUP
BREAK-OUT SESSION / MEETING PROTOCOL

1. INTRODUCTION

Meetings between representatives of Concerned Member States (CMS) and applicant companies seeking marketing authorisations can be a part of the operation of the Mutual Recognition Procedure (MRP). This document seeks to outline the protocol for the conduct of such meetings known as and referred to as a Break-out Session or Break-out Meeting.

2. OBJECTIVE OF BREAK-OUT SESSION

The two key objectives of the Break-out Session or Meeting are,

- to provide a structured forum for interaction between representatives from all the CMS with a view to enabling them through negotiation to find agreement on the detail of the Summary of Product Characteristics (SPC)
- to provide an opportunity for the applicant company to assist the assembled Member States in the process of finding agreement on the detailed content of the SPC.

3. PARTICIPANTS

The participants should normally include the Reference Member State (RMS) who should act as facilitator of the discussions, representatives from all CMS and from the applicant company. The RMS and CMS where possible should be represented by the relevant assessors of the application or the original dossier. The attendance would be determined by the issues which have been identified as requiring discussion. The applicant company should be represented by not more than five persons in total; a list of the names of proposed attendees representing the applicant should be sent to the RMS and the offices of EMEA. Other Member States with an interest or concern in the particular product, the active substance or the therapeutic area in question should be permitted to attend the meeting.

4. RESPONSIBILITIES

It is the responsibility of all the participants to be fully briefed on the outstanding issues and to be empowered to negotiate and to make decisions on behalf of their member state or applicant company.

In order to facilitate meaningful and productive discussions, the applicant should ensure that their 'consolidated response' has been received by all Concerned Member States (CMS). The response documents should be with the CMS not less than five days before the scheduled date for the next MRFG meeting.

It is the responsibility of the RMS to chair the meeting and to facilitate fair and open discussion without confrontation between CMS colleagues in the first instance, and with the applicant thereafter. It is also the responsibility of the RMS to prepare a brief summary of the meeting and its outcome after the conclusion of the meeting.

5. MEETING OUTLINE

The meeting should be conducted in three parts as follows,

- a clarifying discussion between member states,
- if needed the applicant will be asked to join the meeting and to react (respond) to outstanding issues. The company should not give general presentations,
- a wrap-up discussion between member states.

The RMS and CMS should meet at the designated time and place in order to have a preliminary discussion in an attempt to resolve, if possible, some or all of the outstanding issues and then to prioritise any remaining issues. An agreed approach to the questioning of the application should be informally defined by the member states before inviting the applicant into the meeting room.

The RMS should start by introducing the representatives of the member states present to the applicant company and invite the company to do likewise before the presentation.

The RMS should then identify the outstanding issues of concern to the applicant. If a direct discussion with the applicant is preferred the applicant will be invited to the meeting to give a brief comment in response to these highlighted issues. A time limit should be set for the applicant's presentation. The RMS should facilitate the questioning of the applicant by the CMS ensuring a fair and open discussion without confrontation between all those present. Upon completion of the questions and discussion the applicant should be informed that they will be notified in due course about any residual issues.

Following the departure of the applicant from the room the member states should then continue their discussions on the outstanding issues, with a view to trying to reach agreement where possible. Where it is not possible to reach full agreement between all CMS on the residual issues e.g. absence of one or more CMS from the meeting, these matters will be noted by the RMS for subsequent discussion with missing colleagues.

6. MEETING SUMMARY REPORT

A brief summary report of the break-out meeting should be prepared by the RMS as soon as possible after the meeting has finished as is technically possible. The report should be copied to the chairman of the Mutual Recognition Facilitation Group (MRFG), the Mutual Recognition liaison person at the European Medicines Evaluation Agency (EMEA) and all CMS whether present at the meeting or not.

A brief follow-up description on the final outcome of the negotiations at the break-out session should be given by the RMS to the MRFG at it's subsequent meeting.

Version 1.0 : July 1997