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

27 July 1998
CPMP/1342/98

PRESS RELEASE

The Committee for Proprietary Medicinal Products (CPMP) held its 40th plenary meeting from 21 July to 23 July 1998.

Centralised Procedures

The Committee adopted the following Opinions by consensus:

- Seven positive Opinions on Centralised Applications:
  - One positive Opinion was adopted relating to a Medicinal Product containing a new active substance (Part A), an immunomodulating agent, indicated for patients over 18 years with histologically proven chronic hepatitis.
  - One positive Opinion was adopted relating to a Medicinal Product containing a new active substance (Part A), a vaccine, indicated for the active immunisation of children against diphtheria, tetanus and pertussis.
  - Two positive Opinions were adopted relating to two Medicinal Products containing the same new fixed combination (Part B), an angiotensin II antagonist and a diuretic, indicated for the treatment of essential hypertension.
  - Three positive Opinions were adopted relating to three Medicinal Products containing the same new active substance (Part B), an angiotensin II antagonist, indicated for the treatment of essential hypertension.
- Thirteen positive Opinions on Applications in accordance with Annex II of the Commission Regulation 542/95:
  - One positive Opinion was adopted relating to an Application in accordance with Annex II of the Commission Regulation 542/95 (new pharmaceutical form) for an already Centrally Authorised Medicinal Product containing an antiviral for systemic use (Part B), indicated for the treatment of HIV-1 infected adult patients with advanced or progressive immunodeficiency.
  - Twelve positive Opinions were adopted relating to twelve Applications in accordance with Annex II of the Commission Regulation 542/95 (new pharmaceutical forms) for an already Centrally Authorised Medicinal Product containing a recombinant insulin analogue (Part A), indicated for the treatment of diabetes mellitus.
- Two positive Opinions for Centralised type I Variations following the Type II procedure.
- Seven positive Opinions for Centralised type II Variations.

Since the CPMP meeting in June 1998 the Committee noted the withdrawal of one Centralised Application (Part A).

Six Centralised Procedures have been started after validation (Part B), including two double applications for the same new active substance.

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Switchboard: (+44-171) 418 8400 Fax: (+44-171) 418 8551
E_Mail: mail@emea.eudra.org http://www.eudra.org/emea.html

The Committee heard three Oral Presentations/Clarifications from Applicants.

Rapporteurs and Co-rapporteurs were assigned for eight Applications forthcoming in the Centralised Procedure within the next four months, two for Part A and six for Part B. A Rapporteur was also assigned for an Extension Application for an already Centrally authorised Medicinal Product (Part A).

An overview of Centralised Applications is given in Annex I.

Since the CPMP meeting in June 1998, the European Commission has granted a Marketing Authorisation for:

- Iscover and Plavix (Clopidogrel), indicated for the reduction of atherosclerotic events in patients with a history of symptomatic atherosclerotic disease

- Turvel and Trovan (Trovafloxacin), indicated for the treatment of various bacterial infections

- Turvel IV and Trovan IV (Alatrofloxacin), indicated for the treatment of various bacterial infections

- EchoGen (Dodecafluoropentane), indicated for ultrasound echocardiography investigations

See Annex II for details.

Scientific Advice

The Committee:

- Accepted five new requests for Scientific Advice as justified. Co-ordinators were appointed.

- Adopted six Scientific Advice by consensus on manufacturing, preclinical and clinical issues and development plans concerning six new products, two for Part A and four for Part B intended for:
    - treatment of patients presenting an acute or recent coronary syndrome and high risk patients with chronic coronary artery disease
    - treatment of chronic hepatitis C, chronic myeloid leukaemia and solid tumours
    - treatment of patients with hyper-phosphatemia associated with renal failure
    - treatment of diabetes mellitus
    - immunisation against invasive disease caused by Hemophilus Influenzae type B
    - treatment of chronic obstructive pulmonary disease

Working Parties, Ad Hoc Expert Groups and Organisational Matters.

Given the impact of the delay of the fee reform on EMEA resources, the CPMP meeting of August 1998 was cancelled and a number of Working Party meetings had to be postponed until 1999.

The CPMP heard reports from its Quality, Biotechnology, Safety and Efficacy Working Parties and from the Ad Hoc Expert Working Groups on Blood Products and Update of Guidance on SPCs.

BIOTECHNOLOGY WORKING PARTY

The following documents were adopted during the May CPMP and are now released to the public:

- Position Paper on viral safety of oral poliovirus vaccine (OPV) (CPMP/BWP/972/98)
- Report on the selection of an additional influenza vaccine strain for 1998/1999 (CPMP/BWP/921/98)

The following documents were adopted for coming into operation in January 1999:

- Note for Guidance on plasma-derived medicinal products (CPMP/BWP/269/95, Rev.2)
- Note for Guidance on pharmaceutical and biological aspects of combined vaccines (CPMP/BWP/477/97)

SAFETY WORKING PARTY

The following document was adopted for coming into operation in January 1999:

- Note for Guidance on pre-clinical evaluation of anticancer medicinal products (CPMP/SWP/997/96)

EFFICACY WORKING PARTY

Two Concept Papers addressing clinical investigation of medicinal products for the treatment of amyotrophic lateral sclerosis (CPMP/EWP/565/98) and evaluation of diagnostic agents (CPMP/EWP/1119/98) were agreed and CPMP Points to Consider will now be drafted.

The following document was adopted:

- Points to Consider on clinical investigation of medicinal products used in the treatment of osteoarthritis (CPMP/EWP/784/97)

The following document was released for six months' consultation:

- Note for Guidance on clinical evaluation of new vaccines (CPMP/EWP/463/97)

AD HOC WORKING GROUP ON BLOOD PRODUCTS

The proposed mandate (CPMP/1489/98) and workplan (CPMP/BPWG/1488/98) were adopted.

ICH

A CPMP/ICH Preparatory Meeting for the ICH Steering Committee and Expert Working Groups' Meeting in Tokyo, 30.8. - 4.9.1998, was held on the Monday preceding the CPMP Meeting. This was to discuss the development of EU positions and progress with EFPIA.

Mutual Recognition

The CPMP noted the report from the Mutual Recognition Facilitation Group (MRFG) meeting held on 20 July 1998, which is circulated together with this Press Release (Annex III).

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

CENTRALISED APPLICATIONS TO THE EMEA

	Part A	Part B	Total
Scientific Advice	29	38	67

	Part A	Part B	Total*
Applications submitted since 1 January 1995	56	106	162
Withdrawn	5	13	18
Opinions given by the CPMP	30	59	89
Marketing Authorisations granted by the Commission	26	43	69**

	Part A	Part B	Total
Variations type I	90	117	207
Variations type II	32	51	83
Extensions	23	4	27

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

** 89 Opinions corresponding to 68 substances

*** 69 Marketing Authorisations corresponding to 66 substances

ISCOVER*

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

On 15 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Iscover, which contains clopidogrel. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 25 March 1998. The Marketing Authorisation Holder responsible for this medicinal product is Bristol-Myers Squibb Pharma EEIG.

Clopidogrel, the active ingredient in Iscover tablets, belongs to a group of medicines called antiplatelet medicinal products. Platelets are very small structures, smaller than red or white blood cells, which clump together during blood clotting. By preventing this clumping, antiplatelet medicinal products reduce the chances of blood clots forming.

Iscover is indicated for the reduction of atherosclerotic events (myocardial infarction, stroke, death due to vascular causes) in patients with a history of symptomatic atherosclerotic disease defined by ischaemic stroke (from 7 days until less than 6 months), myocardial infarction (from a few days until less than 35 days) or established peripheral arterial disease.

Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

This indication is based on the results of one comparative international multicentre clinical trial (the "CAPRIE" study, Clopidogrel versus acetyl salicylic acid in patients at risk on ischaemic events) involving 19185 patients, comparing clopidogrel with acetyl salicylic acid (ASA). The results showed that clopidogrel at a dose of 75 mg once daily significantly reduced the incidence of new ischaemic events compared to acetyl salicylic acid (325 mg once daily). The slight but statistically significant difference of clopidogrel over acetyl salicylic acid was mainly related to patients enrolled due to peripheral arterial disease.

Clopidogrel was well tolerated, having a safety profile comparable to ASA, but with a better gastrointestinal tolerability. Only rash, purpura and diarrhoea were reported with a higher frequency with clopidogrel but were rarely severe.

The CPMP, on the basis of efficacy and safety data submitted considered that Iscover showed adequate evidence of efficacy and a satisfactory safety profile, and therefore recommended that the Marketing Authorisation should be granted.

PLAVIX*

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

On 15 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Plavix, which contains clopidogrel. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 25 March 1998. The Marketing Authorisation Holder responsible for this medicinal product is Sanofi Pharma Bristol-Myers Squibb SNC.

Clopidogrel, the active ingredient in Plavix tablets, belongs to a group of medicines called antiplatelet medicinal products. Platelets are very small structures, smaller than red or white blood cells, which clump together during blood clotting. By preventing this clumping, antiplatelet medicinal products reduce the chances of blood clots forming.

Plavix is indicated for the reduction of atherosclerotic events (myocardial infarction, stroke, death due to vascular causes) in patients with a history of symptomatic atherosclerotic disease defined by

* This text is the Abstract of the complete EPAR

ischaemic stroke (from 7 days until less than 6 months), myocardial infarction (from a few days until less than 35 days) or established peripheral arterial disease.

Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

This indication is based on the results of one comparative international multicentre clinical trial (the "CAPRIE" study, Clopidogrel versus acetyl salicylic acid in patients at risk on ischaemic events) involving 19185 patients, comparing clopidogrel with acetyl salicylic acid (ASA). The results showed that clopidogrel at a dose of 75 mg once daily significantly reduced the incidence of new ischaemic events compared to acetyl salicylic acid (325 mg once daily). The slight but statistically significant difference of clopidogrel over acetyl salicylic acid was mainly related to patients enrolled due to peripheral arterial disease.

Clopidogrel was well tolerated, having a safety profile comparable to ASA, but with a better gastrointestinal tolerability. Only rash, purpura and diarrhoea were reported with a higher frequency with clopidogrel but were rarely severe.

The CPMP, on the basis of efficacy and safety data submitted considered that Plavix showed adequate evidence of efficacy and a satisfactory safety profile, and therefore recommended that the Marketing Authorisation should be granted.

TURVEL*

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

On 8 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Turvel, which contains trovafloxacin. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 22 October 1997. The Marketing Authorisation Holder responsible for this medicinal product is Roerig Farmaceutici Italiana S.p.A.

The approved indications are for use in the treatment of community acquired pneumonia, nosocomial pneumonia, acute exacerbations of chronic bronchitis, acute sinusitis, complicated intra-abdominal infections and acute pelvic infections, salpingitis, uncomplicated gonococcal urethritis and cervicitis, chlamydial cervicitis, complicated skin and soft tissue infections. Detailed conditions for the use of this medicinal product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

The active substance of Turvel, trovafloxacin mesylate, is a synthetic broad spectrum fluoroquinolone antibacterial agent with *in vitro* activity against a wide range of Gram-negative and Gram-positive organisms, aerobes, anaerobes and atypical microorganisms at concentrations readily achieved in serum and tissues following administration of recommended doses. The bactericidal action results from interference with enzymes involved in the replication, transcription and repair to bacterial DNA and partitioning of the bacterial chromosome.

Clinical trials were designed to investigate the efficacy of trovafloxacin defined as at least equivalence with acceptable comparator medicinal products in the treatment of a range of infections. Over twelve thousand patients were investigated in the Phase II/III programme with over seven thousand patients receiving trovafloxacin or its prodrug alatrofloxacin (which is rapidly converted to trovafloxacin *in vivo*). Trovafloxacin appears to have a relatively low potential for phototoxicity, arthropathies and tendinitis with the most common adverse effects observed being dizziness or lightheadedness, headache and nausea. Compared to various other quinolones examined these events occurred more frequently with trovafloxacin while insomnia, diarrhoea and dyspepsia were reported more often with other quinolones.

The CPMP, on the basis of the efficacy and safety data submitted on Turvel considered that the risk/benefit assessment was sufficiently favourable to allow the granting of a Marketing Authorisation.

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TURVEL IV*

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

On 3 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Turvel IV, which contains alatrofloxacin. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 22 October 1997. The Marketing Authorisation Holder responsible for this medicinal product is Roerig Farmaceutici Italiana S.p.A.

The approved indications are for use in the treatment of community acquired pneumonia, nosocomial pneumonia, complicated intra-abdominal infections and acute pelvic infections and complicated skin and soft tissue infections. Detailed conditions for the use of this medicinal product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

Turvel IV contains alatrofloxacin mesylate, a prodrug of trovafloxacin, a synthetic broad spectrum fluoroquinolone antibacterial agent with *in vitro* activity against a wide range of Gram-negative and Gram-positive organisms, aerobes, anaerobes and atypical microorganisms at concentrations readily achieved in serum and tissues following administration of recommended doses. The bactericidal action results from interference with enzymes involved in the replication, transcription and repair to bacterial DNA and partitioning of the bacterial chromosome.

Clinical trials were designed to investigate the efficacy of trovafloxacin defined as at least equivalence with acceptable comparator medicinal products in the treatment of a range of infections. Over twelve thousand patients were investigated in the Phase II/III programme with over seven thousand patients receiving alatrofloxacin (which is rapidly converted to trovafloxacin *in vivo*) or the oral form trovafloxacin mesylate. Trovafloxacin appears to have a relatively low potential for phototoxicity, arthropathies and tendinitis with the most common adverse effects observed being dizziness or lightheadedness, headache and nausea. Compared to various other quinolones examined these events occurred more frequently with trovafloxacin while insomnia, diarrhoea and dyspepsia were reported more often with other quinolones.

The CPMP, on the basis of the efficacy and safety data submitted on Turvel IV considered that the risk/benefit assessment was sufficiently favourable to allow the granting of a Marketing Authorisation.

TROVAN*

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

On 3 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Trovan, which contains trovafloxacin. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 22 October 1997. The Marketing Authorisation Holder responsible for this medicinal product is Pfizer Limited.

The approved indications are for use in the treatment of community acquired pneumonia, nosocomial pneumonia, acute exacerbations of chronic bronchitis, acute sinusitis, complicated intra-abdominal infections and acute pelvic infections, salpingitis, uncomplicated gonococcal urethritis and cervicitis, chlamydial cervicitis, complicated skin and soft tissue infections. Detailed conditions for the use of this medicinal product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

The active substance of Trovan, trovafloxacin mesylate, is a synthetic broad spectrum fluoroquinolone antibacterial agent with *in vitro* activity against a wide range of Gram-negative and Gram-positive organisms, aerobes, anaerobes and atypical microorganisms at concentrations readily achieved in serum and tissues following administration of recommended doses. The bactericidal action results from interference with enzymes involved in the replication, transcription and repair to bacterial DNA

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and partitioning of the bacterial chromosome.

Clinical trials were designed to investigate the efficacy of trovafloxacin defined as at least equivalence with acceptable comparator medicinal products in the treatment of a range of infections. Over twelve thousand patients were investigated in the Phase II/III programme with over seven thousand patients receiving trovafloxacin or its prodrug alatrofloxacin (which is rapidly converted to trovafloxacin *in vivo*). Trovafloxacin appears to have a relatively low potential for phototoxicity, arthropathies and tendinitis with the most common adverse effects observed being dizziness or lightheadedness, headache and nausea. Compared to various other quinolones examined these events occurred more frequently with trovafloxacin while insomnia, diarrhoea and dyspepsia were reported more often with other quinolones.

The CPMP, on the basis of the efficacy and safety data submitted on Trovan considered that the risk/benefit assessment was sufficiently favourable to allow the granting of a Marketing Authorisation.

TROVAN IV*

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

On 3 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product Trovan IV, which contains alatrofloxacin. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 22 October 1997. The Marketing Authorisation Holder responsible for this medicinal product is Pfizer Limited.

The approved indications are for use in the treatment of community acquired pneumonia, nosocomial pneumonia, complicated intra-abdominal infections and acute pelvic infections and complicated skin and soft tissue infections. Detailed conditions for the use of this medicinal product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

Trovan IV contains alatrofloxacin mesylate, a prodrug of trovafloxacin, a synthetic broad spectrum fluoroquinolone antibacterial agent with *in vitro* activity against a wide range of Gram-negative and Gram-positive organisms, aerobes, anaerobes and atypical microorganisms at concentrations readily achieved in serum and tissues following administration of recommended doses. The bactericidal action results from interference with enzymes involved in the replication, transcription and repair to bacterial DNA and partitioning of the bacterial chromosome.

Clinical trials were designed to investigate the efficacy of trovafloxacin defined as at least equivalence with acceptable comparator medicinal products in the treatment of a range of infections. Over twelve thousand patients were investigated in the Phase II/III programme with over seven thousand patients receiving alatrofloxacin (which is rapidly converted to trovafloxacin *in vivo*) or the oral form trovafloxacin mesylate. Trovafloxacin appears to have a relatively low potential for phototoxicity, arthropathies and tendinitis with the most common adverse effects observed being dizziness or lightheadedness, headache and nausea. Compared to various other quinolones examined these events occurred more frequently with trovafloxacin while insomnia, diarrhoea and dyspepsia were reported more often with other quinolones.

The CPMP, on the basis of the efficacy and safety data submitted on Trovan IV considered that the risk/benefit assessment was sufficiently favourable to allow the granting of a Marketing Authorisation.

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ECHOGEN*

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

On 17 July 1998, the European Commission issued a Marketing Authorisation valid throughout the European Union for the medicinal product EchoGen, which contains dodecafluoropentane. This decision was based on the assessment report and the favourable opinion adopted by the Committee for Proprietary Medicinal Products (CPMP) on 25 March 1998. The Marketing Authorisation Holder responsible for this medicinal product is Sonus Pharmaceuticals Ltd.

The approved indication relates to the context of diagnostic ultrasound investigations, and EchoGen is indicated as a transpulmonary echocardiographic contrast agent for use in patients with suspected or established cardiovascular disease to provide opacification of cardiac chambers, enhance left ventricular border delineation with resulting improvement in wall motion visualisation. EchoGen should only be used in patients where the study without contrast enhancement is inconclusive. Detailed conditions for the use of this product are described in the Summary of Product Characteristics (SPC) which can be found in the EPAR and is available in all European Union official languages.

A total of 506 patients were enrolled in clinical studies in support of diagnostic efficacy; the majority (405) of these received the product as intended for marketing. The results of two reference controlled studies indicated acceptable contrast enhancement in the context of echocardiography investigations.

An updated safety evaluation based on 1128 patients concluded that the product was safe when used in accordance with the restrictions defined in the SPC. Specific patient populations with cardiac disease considered to be at special risk were studied and evaluated.

The active substance in EchoGen is dodecafluoropentane in the form of a liquid/liquid emulsion stabilised by a surfactant (PEG Telomer B). The product is supplied as a multicomponent kit containing a 5ml vial of a 2% w/v emulsion for intravenous injection. The dose for adults is 0.05 ml/kg (it is not intended for use in children). Contrast enhancement depends largely on physical aspects of the system as a whole, e.g. the number and size of ‘particles’ of the disperse phase, the physical state of the disperse phase itself, etc. A characteristic of this product is that the liquid microparticles must be manually ‘activated’ under reduced pressure to form gaseous microbubbles before administration to the patient. Equipment for doing this is included in the kit.

Precise activation/administration instructions and conditions relating to the safe and effective use of EchoGen are defined in the SPC .

The CPMP, on the basis of the efficacy and safety data submitted, considered that EchoGen showed adequate evidence of efficacy and a satisfactory safety profile and therefore recommended that the Marketing Authorisation should be granted.

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MRFG
Mutual Recognition Facilitation Group

Report from the meeting held on 20th July 1998

The MRFG noted that 22 new mutual recognition procedures have been finalised during the month of June 1998 as well as 19 type I and 32 type II variations.
The status as of 30th June 1998 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
1998	87	47	119	59	110	108	1 var.

12 new procedures (regarding 20 products) have been started in June 1998. The categories of these procedures are as follows:

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

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 strength, 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 new applications procedures in June 1998:

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	13
DK (1)	4
FI (2)	2
FR (1)	8
SE (3)	1
UK (2)	11
UK (1)	5
UK (1)	14
UK (3)	7
UK (1)	5
UK (2)	4
UK (2)	1

General issues

- The MRFG noted for the first time the finalised "Commission Communication on the Community Marketing Authorisation Procedure for Medicinal Products"(C98/2016).

- The group received a further report from its EudraTrack subgroup and noted that the EudraTrack system runs now satisfactorily. From the 1 st of October 1998 all the communications concerning procedural data between MSs will rely only on EudraTrack. Notwithstanding these positive aspects, the need of future enhancements has been considered.

- In order to give more detailed information on the types of applications, the MRFG started reclassifying the procedures. So far 17 former "others" have been reclassified. The issue of new sub-categories (i.e. blood products and vaccines) will be dealt with on an ongoing basis, and a first update is foreseen for the near future.

- The MRFG agreed that the automatic validation procedure has to be followed also for the type I variations for which type II procedure applies (Annex 1(A) Regulation EC/541/95). Furthermore, the MRFG agreed that, in line with Commission Regulation 1146/98, in case of Urgent Safety Restriction, Member States should refer to the RMS for further actions.

- The MRFG decided to put on its web site two documents:

  1. The content of the letter received from Prof. Rolf Bass listing the documentation relevant to MRPs (new applications and variations) to be sent to the EMEA by the applicants *(Annex I)*.

  2. Applicants Response Document in Mutual Recognition. The version 5, including comments from AESGP and Member States, has been adopted *(Annex II)*.

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

Dr. Christa Wirthumer-Hoche
Federal Ministry of Labour, Health and Social Affairs
Stubenring 1
A-1010 Vienna
Phone +43 1 711 72 4132
Fax +43 1 714 9222
E-mail: christa.wirthumer@bmg.gv.at

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

http://heads.medagencies.org/