European Medicines Agency
Evaluation of Medicines for Human Use

17 March 2006
CHMP/70961/2006 Rev.1

COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
FEBRUARY 2006 PLENARY MEETING
MONTHLY REPORT

The Committee for Medicinal Products for Human Use (CHMP) held its February plenary meeting from 20 – 23 February 2006.

The Chairman on behalf of the Committee welcomed Dr. G. Aislaitner, as a new alternate CHMP Member from Greece replacing Pharm M. Avgerinos. The Committee expressed its thanks and appreciation to Pharm M. Avgerinos for his work in both the CPMP and CHMP in the past years.

Centralised procedure

Initial applications for marketing authorisation

The CHMP adopted positive opinions on six initial marketing authorisation applications at this meeting:

- **Duotrav** (travoprost/timolol maleate), Alcon Laboratories. Duotrav is an eye-drops solution, intended for the decrease of intraocular pressure in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues. EMEA review began on 18 May 2005 with an active review time of 196 days.
- **Evoltra** (clofarabine), Bioenvision Limited. Evoltra is indicated for the treatment of acute lymphoblastic leukaemia in paediatric patients. EMEA review began on 16 August 2004 with an active review time of 209 days. Evoltra is the **twenty-fifth orphan-designated medicinal product** to receive a positive CHMP opinion.
- **M-M-RVAXPRO** (measles, mumps and rubella vaccine (live)), Sanofi Pasteur MSD. M-M-RVAXPRO is a vaccine intended for prophylaxis against measles, mumps and rubella. EMEA review began on 21 June 2004 with an active review time of 193 days.
- **Preotact** (parathyroid hormone), Nycomed Danmark ApS. Preotact is intended for the treatment of osteoporosis in postmenopausal women at high risk of fractures. EMEA review began on 14 March 2005 with an active review time of 224 days.
- **Tygacil** (tigecycline), Wyeth Europa Ltd. Tygacil is intended for complicated skin and soft-tissue infections and complicated intra-abdominal infections. EMEA review began on 24 January 2005 with an active review time of 182 days.
- **Valtropin** (somatropin), BioPartners, a similar biological medicinal product. Valtropin contains somatropin, a growth hormone produced by recombinant DNA technology, and is indicated for the treatment of growth disturbance and growth-hormone deficiency. Valtropin is similar to Humatrope (somatropin), the reference medicinal product already authorised in the EU. EMEA review began on 19 July 2004 with an active review time of 179 days.

Summaries of opinion for these medic inal products are available on the EMEA website: http://www.emea.eu.int. Further information will be included in the European Public Assessment Report (EPAR) once the European Commission has granted final approval.

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The CHMP adopted a negative opinion on one initial marketing authorisation application at this meeting for:

- **Atryn** (recombinant antithrombin alfa), Genzyme Europe. Atryn was intended to be used for the prophylaxis of deep-vein thrombosis and thromboembolism in patients with congenital antithrombin deficiency undergoing surgery. EMEA review began on 23 February 2004 with an active review time of 207 days. A question-and-answer document has been published and can be found here.

Extensions of indication and other recommendations

The Committee adopted positive opinions on the extension of indication of medicinal products that are already authorised in the European Union:

- **Erbitux** (cetuximab) from Merck KGaA, to extend its indication to add the treatment of locally advanced squamous cell cancer of the head and neck in combination with radiation therapy. Erbitux was first authorised in the European Union on 29 June 2004 and is currently approved for the treatment of metastatic colorectal cancer.

- **Sifrol** (pramipexole) and **Mirapexin** (pramipexole), from Boehringer Ingelheim International GmbH, to extend their indication to add symptomatic treatment of moderate to severe idiopathic restless legs syndrome. Sifrol was first authorised in the European Union on 14 October 1997 and Mirapexin on 23 February 1998. Both are currently approved for the treatment of signs and symptoms of advanced idiopathic Parkinson's disease.

- **Enbrel** (etanercept), from Wyeth Europe Ltd, to include an alternative dosing regimen of 50 mg once weekly, which will allow treatment of ankylosing spondylitis and psoriatic arthritis to be added as new indications in Enbrel 50 mg. Enbrel was first authorised in the European Union on 3 February 2000 and is currently approved for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and plaque psoriasis.

Summaries of opinion for all these products are available and can be found here. Further information will be included in the EPAR once the European Commission has granted final approval.

Review procedure started

The Committee started a review for the centrally authorised vaccines **HBVAXPRO** (recombinant Hepatitis B virus small surface antigen (HBsAg)) and **Procomvax** (haemophilus influenzae b conjugate and Hepatitis B (recombinant) vaccine), both from Sanofi Pasteur MSD. The review, initiated at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004, is intended to assess the efficacy of the two products. HBVAXPRO and Procomvax share the same recombinant Hepatitis B component as Hexavac. The marketing authorisation of Hexavac is currently suspended due to concerns about long-term protection against Hepatitis B (for more information on Hexavac see press release and question-and-answer document with advice to patients and healthcare professionals published at the time of the suspension).
The Committee is now reviewing all available data to determine whether similar concerns would also apply to HBVAXPRO and Procomvax.
There is no immediate concern for children or adults vaccinated with these products. Further statements will be made as soon as the information becomes available.

Applications for marketing authorisation for orphan medicinal products

Details of those orphan medicinal products that have been subject of a centralised application for marketing authorisation since the January 2006 CHMP meeting are provided in **Annex 4**.

Lists of Questions

The Committee adopted four Lists of Questions on initial applications (two under the mandatory scope and two under the optional scope).

Detailed information on the centralised procedure

An overview of centralised procedures since 1995 is given in **Annex 1**. The list of medicinal products for which marketing authorisations have been granted by the European Commission since the CHMP plenary meeting in January 2006 is provided in **Annex 3.** The post-authorisation centralised procedures finalised during this meeting are summarised in **Annex 2**.

CHMP Working Parties

The CHMP was informed of the outcome of the discussions of the Scientific Advice Working Party (SAWP) meeting, which was held on 30 January -1 February 2006. For further details, please see **Annex 5**. Documents prepared by the CHMP Working Parties adopted during the January 2006 CHMP meeting are listed in **Annex 6**.

Invented Name Review Group (NRG)

Statistical information on the outcome of the checking of acceptability of proposed invented names for medicinal products processed through the centralised procedure is provided in **Annex 7.**

Upcoming meetings following the February 2006 CHMP plenary meeting:

- The 20th meeting of the CHMP will be held at the EMEA on 20-23 March 2006.
- The next Invented Name Review Group meeting will be held at the EMEA on 20 March 2006.
- The fifth CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) meeting will be held at the EMEA on 20-21 March 2006.
- An Expert Meeting on the revision of the core SPC and Note for Guidance for human normal Immunoglobulin for intravenous administration will be held at the EMEA on 5-6 July 2006.
- An Expert meeting on Factor VIII products and inhibitor development took place at EMEA on 28 February-2 March 2006.

Organisational matters

The main topics addressed during the February 2006 CHMP meeting related to:

- The Core group of the cardiovascular SAG (CVS); such a Core group was requested upon by the CHMP.
- The Peer review within the pre-authorisation phase of the centralised evaluation: A review of the last 6-month pilot phase of Peer Review (at day 100) of initial applications was presented to the Committee. The exercise was felt to be very positive providing a more effective compilation of the List of Question and it was therefore agreed to continue the pilot phase through 2006.
- The setting-up of a review and learning project group composed of EMEA/CHMP/PhVWP/CMD(h) representatives to monitor EU Risk Management Plans (RMPs)

implementation. The group aims to review all EU RMPs submitted from November 2005-June 2006 and provide a first overall report to the different Committees at the end of 2006.

- The identification of a EU network of Pharmacoepidemiology Centres on Pharmacoepidemiology and Pharmacovigilance in the Community, which is in line with the implementation of the EMEA Road Map and the European Management strategy. Further details of this project will be given at a later stage.

EMEA Implementation of the New EU Pharmaceutical Legislation

The fourteenth CHMP/EMEA Implementation Task Force (CEITAF) meeting took place on Monday 20 February 2006.

The following documents were adopted by the CHMP and have been **published for implementation** on the EMEA website:

- **"Sunset clause" provision** and **Actual Marketing and Cessation of Placing on the Market**

  together with an overview of external comments received and EMEA/CHMP Feedback/Action on each comment (http://www.emea.eu.int/pdfs/human/euleg/42440905en.pdf).

The following documents were agreed by the CHMP and will be published at the EMEA website for external consultation:

- **Guideline on procedures for re-examination of CHMP opinions** (released for 4 weeks external consultation)
- **Reflection paper on publication of withdrawals** (released for 4 weeks external consultation)

The following documents were agreed by the CHMP and will be transmitted to the European Commission:

- **Guideline on monitoring of compliance with pharmacovigilance regulatory obligations and pharmacovigilance inspections** : this guideline will be incorporated in Volume 9A of the Notice to Applicants (NTA) after the consultation process which will done by the European Commission *via* their external website (under "News": http://pharmacos.eudra.org/F2/pharmacos/new.htm).

EU Biosimilar Activities

The CHMP adopted several guidelines on similar biological medicinal products containing biotechnology-derived proteins as active substance related to quality, non-clinical and clinical issues and product specific annexes (see details in Annex 6 of this report under BWP and BMWP). These guidelines will come into force in June 2006.

Overview of CHMP Working Parties published on EMEA website

The EMEA published on 6 March 2006 a new section of the EMEA external website providing overview of the CHMP working parties, scientific advisory groups and other related groups. The information can be found here.

PROCEDURAL ANNOUNCEMENT

NEW PUBLISHED EMEA TIMELINES TO ANSWER LISTS OF QUESTIONS /LISTS OF OUTSTANDING ISSUES

Further to external consultation the CHMP adopted a revised "policy" document on "Time allowed for applicants to respond to questions and issues raised during the assessment of new Marketing Authorisations in the Centralised Procedure" (EMEA/75401/2006 Rev.1) which is aimed to provide applicants with clarifications as to how long applicants may take to address questions/issues between Day 120-121 (after adoption of the list of questions) and Day 180-181 (after adoption of the List of Outstanding issues). Details of this policy are outlined in the document. This policy will be applicable as of March 2006 for any new application submitted to the EMEA . The information can be found here.

Mutual Recognition and Decentralised procedures-Human

The CHMP noted the report from the fourth CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 20-21 February 2006. For further details, please see **Annex 8**.

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This CHMP Monthly Report and other documents are available on the Internet at the following address: http://www.emea.eu.int

PRE-AUTHORISATION: MARKETING AUTHORISATION APPLICATIONS

Activity	Dec 2005/2006[1]							1995 onwards
	Optional Scope			Mandatory scope			Total	Overall total
	NAS	Significant innovation	Interest of Patients	Biotech	Indications	Orphans		
Applications for MA submitted[2]	**2**	**4**	**0**	**5**	**3**	**2**	**16**	**506**
Positive opinions[3]	**4**	**0**	**0**	**3**	**0**	**2**	**9**	**335[4]**
Negative opinions[5]	**1**	**0**	**0**	**1**	**0**	**0**	**2**	**9[6]**
Withdrawals prior to opinion	**1**	**1**	**0**	**0**	**0**	**2**	**4**	**103**
Marketing authorisation granted by the Commission	**8**	**0**	**0**	**1**	**0**	**1**	**10**	**321**

PRE-AUTHORISATION: SCIENTIFIC SERVICES

Activity (submissions)	Dec 2005/2006	1995 onwards
Compassionate use applications	**0**	**0**
Art. 58 applications	**0**	**2**
Consultation for medical devices[7]	**0**	**4**
PMF	**2**	**10**
VAMF	**0**	**0**

[1] Starting point for operation of the new eligibility criteria to the centralised procedure
[2] Number of accelerated reviews requested and number of accelerated reviews granted (3/0)
[3] Subdivided by conditional and exceptional (0/0)
[4] 335 positive Opinions corresponding to 264 substances
[5] In case of Re-examination under Art. 9(2) of Regulation (EC) No. 726/2004, the opinion will not be counted twice.
[6] 9 Negative Opinions corresponding to 8 substances
[7] Consultation in accordance with Council Directive 93/42/EEC concerning medical devices as amended by Directive 2000/70/EC as regards medical devices incorporating stable derivates of human blood or plasma and Directive 2001/104/EC

OUTCOME OF THE FEBRUARY 2006 CHMP MEETING IN RELATION TO ACCELERATED ASSESMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Biological	Treatment of anaemia for patients on haemodialysis		X
Chemical	Treatment of cancer		X
Biological	Prophylaxis of Influenza infection	X	

The above-mentioned 3 requests for accelerated assessment were submitted in January and February 2006 and the Committee's conclusions were adopted at the 20 – 23 February 2006 CHMP meeting. The respective applicants were informed accordingly of the justification and details will be made available in the CHMP AR and the concerned medicinal products EPARs.

ANNEX 2 TO CHMP MONTHLY REPORT FEBRUARY 2006

POST-AUTHORISATION: TYPE I AND II VARIATIONS, ANNEX II, RENEWALS AND ANNUAL RE-ASSESSMENT APPLICATIONS

Activity	2006	Overall total 1995 onwards
Type I Variations (positive notifications)	81	3510
Type II Variations (positive opinions)	84	2266
Type II Variations (negative opinions)	0	7
Annex II Applications (positive opinions)	5	132
Annual Re-assessment (positive opinions)	5	N/A
Opinion for renewals of conditional MA's (positive opinions)	0	0
5 Year Renewals (positive opinions)	12	N/A

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
3 Extensions of indication	3 Positive opinions
21 SPC changes	21 Positive opinions
25 Quality changes	25 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Xigris (drotrecogin alfa (activated)) Eli Lilly Nederland B.V	Positive Opinion adopted	The Marketing Authorisation will remain under Exceptional circumstances
Zavesca (miglustat) Actelion Ltd	Positive Opinion adopted	The Marketing Authorisation will remain under Exceptional circumstances

Opinion for renewals of conditional MA's		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
N/A	**N/A**	**N/A**

Opinions for 5 Year Renewal applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
SonoVue (sulphur hexafluoride) Bracco International B.V.,	Positive Opinion adopted	Unlimited validity
Starlix (nateglinide) Novartis Europharm Ltd	Positive Opinion adopted	Unlimited validity
Trazec (nateglinide) Novartis Europharm Ltd	Positive Opinion adopted	Unlimited validity
Targretin (bexarotene) Ligand Pharmaceuticals Ltd,	Positive Opinion adopted	Unlimited validity
Vaniqa (eflornithine) Shire Pharmaceutical Contracts Ltd	Positive Opinion adopted	5-year renewal
Zometa (zoledronic acid) Novartis Europharm Ltd	Positive Opinion adopted	Unlimited validity

MEDICINAL PRODUCTS GRANTED A COMMUNITY MARKETING AUTHORISATION UNDER THE CENTRALISED PROCEDURE SINCE THE JANUARY 2006 CHMP MONTHLY REPORT

Invented Name	Macugen
INN	pegaptanib sodium
Marketing Authorisation Holder	Pfizer Ltd.
Proposed ATC code	S01XA17 (temporary)
Indication	Treatment of neovascular (wet) age-related macular degeneration (AMD).
CPMP Opinion date	15.09.2005
Marketing Authorisation Date	31.01.2006

Invented Name	Neupro
INN	rotigotine
Marketing Authorisation Holder	Schwarz BioSciences GmbH
Proposed ATC code	N04BC09
Indication	Treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease as monotherapy (i.e. without levodopa).
CPMP Opinion date	14.12.2005
Marketing Authorisation Date	15.02.2006

Invented Name	Rotarix
INN	Live human rotavirus RIX4414
Marketing Authorisation Holder	GlaxoSmithKline Biologicals
Proposed ATC code	J07BH01
Indication	Indicated for the active immunisation of infants from the age of 6 weeks for prevention of gastro-enteritis due to rotavirus infection
CPMP Opinion date	14.12.2005
Marketing Authorisation Date	21.02.2006

OVERVIEW OF DESIGNATED ORPHAN MEDICINAL PRODUCTS THAT HAVE BEEN THE SUBJECT OF A CENTRALISED APPLICATION FOR MARKETING AUTHORISATION: UPDATE SINCE THE JANUARY 2006 CHMP MEETING

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
Dasatinib (Sprycel)	Bristol-Meyers Squibb Pharma EEIG	EU/3/05/338 23/12/2005	Treatment of acute lymphoblastic leukaemia
Dasatinib (Sprycel)	Bristol-Meyers Squibb Pharma EEIG	EU/3/05/339 23/12/2005	Treatment of chronic myeloid leukaemia

OUTCOME OF THE FEBRUARY 2006 CHMP MEETING IN RELATION TO SCIENTIFIC ADVICE PROCEDURES

EMEA CENTRALISED PROCEDURES

	1995 - 2005	2006	Overall Total
Scientific Advice	558	24	582
Follow-up to Scientific Advice	94	6	100
Protocol Assistance	107	13	120
Follow-up to Protocol Assistance	26	1	27
	785	**44**	**829**

Substance	**Intended indications(s)**	**Type of Request**				**Topic**			
		New		**Follow-up**		**Pharmaceutical**	**Pre-clinical**	**Clinical**	**Significant Benefit**
		SA	**PA**	**SA**	**PA**				
Chemical	Unverricht-Lundborg disease		X			X	X	X	X
Chemical	Schizophrenia in children and adolescents	X						X	
Chemical	Bipolar disorder in children and adolescents	X						X	
Chemical	Schizophrenia	X					X	X	
Chemical	Thrombotic events in patients suffering from acute coronary syndromes			X				X	
Chemical	Atrial fibrillation	X						X	
Chemical	Hyperlipidemias	X						X	
Chemical	Pulmonary arterial hypertension		X				X	X	X
Chemical	Pulmonary hypertension		X				X	X	X
Chemical	Advanced (metastatic or unresectable) well-differentiated carcinoid tumor and pancreatic neuroendocrine tumor	X						X	
Chemical	Gastric cancer		X				X	X	X
Chemical	Hormone-refractory prostate cancer			X				X	
Chemical	Non-small cell lung cancer			X				X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	Muckle-Wells Syndrome, Familial Cold-associated Auto-inflammatory Syndrome, Polyarticular Juvenile Idiopathic Arthritis, Systemic-onset Juvenile Idiopathic Arthritis, and adult Rheumatoid Arthritis	X				X	X	X	
Biological	Shiga-toxin producing bacterial infection.		X			X	X	X	X
Biological	Parenteral nutrition for patients in hypercatabolic and/or hypermetabolic states	X				X			
Biological	Paroxysmal nocturnal haemoglobinuria				X			X	
Chemical	Stage 3 and 4 chronic kidney disease	X					X	X	
Chemical	Wegener's granulomatosis		X					X	X
Chemical	Osteoarthritis			X				X	
Chemical	Chronic inflammatory pain (non-neuropathic pain)	X							
Chemical	Cushing's syndrome secondary to ectopic ACTH secretion		X					X	X
Chemical	Symptomatic relief of diabetic gastroparesis and the improvement of gastric motility	X						X	
Chemical	Aid in smoking cessation and for preventing relapse in smokers who have quit.	X						X	
Chemical	Chronic hepatitis C	X					X	X	
	Total	**13**	**7**	**4**	**1**				

SA: Scientific Advice

PA: Protocol Assistance

The above-mentioned 13 Scientific Advice letters, 7 Protocol Assistance letters, 4 Follow-up Scientific Advice letters and 1 Follow-up Protocol Assistance letters were adopted at the 20-23 February 2006 CHMP meeting.

The Committee accepted 13 Initial Scientific Advice Requests, and 2 Initial Protocol Assistance Requests started at the meeting that took place on 30 January – 1 February 2006.

DOCUMENTS PREPARED BY THE CHMP WORKING PARTIES ADOPTED DURING THE FEBRUARY 2006 CHMP MEETING

BIOLOGICS WORKING PARTY

Reference number	Document	Status
EMEA/CHMP/BWP/49348/2005	Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: Quality issues	Adopted

WORKING PARTY ON SIMILAR BIOLOGICAL (BIOSIMILAR) MEDICINAL PRODUCTS (BMWP)

Reference number	Document	Status
CHMP/BMWP/9437/2006	Concept Paper on Guideline on Comparability of Biotechnology-derived medicinal products after a change in the manufacturing process – non-clinical and clinical issues	Released for 3 months consultation
CHMP/BMWP/246511/2005	Concept paper on guideline on immunogenicity assessment of therapeutic proteins	Released for 3 months consultation
CHMP/BMWP/31329/2005	Annex to guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues - guidance on similar medicinal products containing recombinant granulocyte-colony stimulating factor	Adopted
CHMP/BMWP/32775/2005	Annex to guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues - guidance on similar medicinal products containing - recombinant human soluble insulin	Adopted
CHMP/BMWP/42832/2005	Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues	Adopted
CHMP/BMWP/94528/2005	Annex to guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues - guidance on similar medicinal products containing - somatropin	Adopted

EFFICACY WORKING PARTY

Reference number	Document	Status
CHMP/EWP/6172/03	Guideline on the Clinical Evaluation of Medicinal Products Intended for Treatment of Hepatitis B	Adopted
EMEA/CHMP/EWP/372003/2005	Concept Paper on the development of the CHMP guideline on the evaluation of non-clinical and clinical data on the medicinal substances contained in drug-eluting (medicinal substance-eluting) coronary stents within the framework of a consultation procedure for combination products	Released for 6 months consultation

VACCINE WORKING PARTY (VWP)

Reference number	Document	Status
CHMP/VWP/7477/2006	CHMP Position paper on Thiomersal – Implementation of the warning statement relating to sensitisation	Adopted

NAME REVIEW GROUP (NRG)

	February 2006			2006	
	Accepted	Rejected	Pending	Accepted	Rejected
Proposed invented names	9	10	22	16	19
Justification for retention of invented name *	1	4	5	1	7

*In case of objections to the proposed invented name(s), the applicant may justify the retention of the proposed invented name using the relevant justification form available on the EMEA website.

Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human

Report from the CMD(h) meeting held on 20th and 21st February 2006

General Issues

CMD(h) Rules of Procedure

The European Commission has given a favourable opinion on the CMD(h) proposal for the Rules of Procedure for the Coordination Group for Mutual Recognition and Decentralised procedures – Human, as provided for in Article 27(3) of Directive 2001/83/EC, as amended.

The CMD(h) Rules of Procedure will be published on the website.

Role of the Vice-Chairperson of the CMD(h)

The CMD(h) has agreed on a document giving detailed instructions on the role of the Vice-Chairperson of the CMD(h), in accordance with Article 4(2) of the CMD(h) Rules of Procedure.

The document will be published on the website for information.

Functions and Tasks for the CMD(h)

Article 27 of Directive 2001/83/EC, as amended establishes the CMD(h) for the examination of any question relating to marketing authorisation of a medicinal product in two or more Member States in accordance with the Mutual Recognition and Decentralised procedures.

As this covers a variety of issues related to new applications, variations and renewals, the CMD(h) has agreed on a document to give further guidance on the functions and tasks for the CMD(h).

The document will be published on the website for information.

Procedure for adoption of lists of questions for Applications referred to the CMD(h) in accordance with Article 29(1) of Directive 2001/83/EC, as amended

In order to make optimal use of the 60 days timeline in case of disagreement between Member States in a particular mutual recognition or decentralised procedure, the CMD(h) has agreed to follow a written procedure for adoption of the lists of questions. The lists of questions will be sent to the Applicant by Day 10 of the Procedure. The timeframe for Applicants to prepare a response document will remain 15 days.

The CMD(h) will work with the new timelines for a pilot period of 6 months. Review of the CMD(h) SOP – Disagreement in Procedures – Referral to CMD(h) will be considered after finalisation of the pilot phase.

CMD(h) Position on changing the Reference Member State

The CMD(h) has updated the Position on changing the Reference Member State, to consider the new decentralised procedure and to clarify that a change of the RMS cannot take place during a pending procedure.It has also been agreed that the transfer of dossier/assessment reports and other relevant material to the new RMS should be done within 30 days. The new RMS will only be able to start new procedures when the requested information has been received.

E-mail addresses for submission of translations in Mutual Recognition and Decentralised procedures

The CMD(h) has agreed to publish a list of e-mail addresses for submission of translations in the mutual recognition and decentralised procedures.

Member States have agreed to accept text proposals for the SPC, PL and labeling in English with the submission of applications for marketing authorisation, type II variations and renewals in the MRP/DCP.

High quality translations of the agreed SPC, PL and labeling should be submitted at the latest 5 days after the end of the procedure.

For further information, please refer to Q&A 12 and 13 of the Questions and Answers document on the implementation of the new legislation, January 2006.

E-mail addresses for submission of electronic responses to the List of Questions for Applications referred to the CMD(h) in accordance with Article 29(1) of Directive 2001/83/EC, as amended

In view of the short timeframe for the procedure in the CMD(h) in case of disagreement between Member States in a particular MRP or DCP, the CMD(h) recommends the submission of the response to the list of questions in electronic format and has agreed to publish a list of e-mail addresses for this purpose.

Information on applications referred to the CMD(h) in accordance with Article 29(1) of Directive 2001/83/EC, as amended

The CMD(h) has finalised on 30 January 2006 the first application for marketing authorisation referred to the CMD(h) for the 60-days procedure.

The application for Omeprazole, submitted in accordance with Article 10.1 (a)(iii) of Directive 2001/83/EC, was referred to the CMD(h) because potential serious health concerns were raised with regard to the available bioequivalence data for these specific formulations.

The Member States involved in the procedure were able to reach agreement on the authorisation of the medicinal product.

Please find below information on the Name of the product in the RMS, active substance, pharmaceutical form, procedure number, CMS, legal basis, grounds for referral to CMD(h), Day 60 and outcome of the procedure.

Name of the product in the RMS	Omeprazole 10mg, 20mg & 40mg Capsules
Active substance	Omeprazole
Pharmaceutical form	Gastro-resistant capsules
Procedure number	UK/H/799/01-03
CMS	AT, BE, CZ, DE, ES, EL, HU, LI, LU, NL, PL, PT, SK
Legal basis	Article 10.1 (a)(iii), Directive 2001/83/EC - Generic
Grounds for referral to CMD(h)	Different interpretation with regard to existing guidelines on the required bioequivalence data for the formulations
Day 60	30.01.2006
Outcome	Agreement reached

Meeting schedule

The next CMD(h) meeting will be held on 20th, 21st and 22nd March 2006.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **46** new Mutual Recognition Procedures were finalised during the month of January 2006. **8** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period.

The status as of 31st January of procedures under Mutual Recognition is as follows:

Year	Procedures from New applications finalised	Procedures from New applications in process	Procedures referred to CMD(h)	Arbitrations referred to CHMP
2006	46	111	8 N.A.	- -

16 Mutual Recognition Procedures (regarding **22** products) started in January 2006. The categories of these procedures are as follows:

1 new active substance classified as repeat use.

5 known active substances (already authorised in at least one member state).

9 abridged applications including **1** repeat use.

1 line extension application.

The new procedures started related to **2** full dossiers, **9** generics and **5** bibliographic applications.

The procedures consisted of **15** chemical substances and **1** Biological - Other[1].

15 of these procedures were prescription-only medicinal products in the reference Member State and **1** procedure was classified as 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 in Mutual Recognition procedure started in January 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	6
DK (1)	1
DK (4)	1
EE (2)	2
FR (1)	14
FR (1)	15
NL (3)	10
NL (1)	5
NL (1)	4
PT (1)	1
SE (1)	14
SE (1)	19
SE (1)	3
UK (1)	14
UK (1)	14
UK (1)	9

Decentralised Procedure

The CMD(h) noted that **21** new Decentralised Procedures (regarding **50** products) started in January 2006. The categories of these procedures are as follows:

18 abridged applications including **6** multiple applications.

3 known active substances (already authorised in at least one member state).

The new Decentralised procedures started related to **3** full dossiers, **14** generics and **4** for different use, route or dose.

The procedures consisted of **21** chemical substances[3].

21 of these procedures were prescription-only medicinal products in the reference Member State[4].

3. As considered by RMS.
4. In this category products are classified as prescription-only or Non-prescription (OTC) products as applied for in the RMS, although the legal status is not part of the Decentralised Procedure.

Number of countries involved in the new applications in Decentralised procedures started in January 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (4)	12
AT (4)	6
AT (4)	8
AT (4)	1
DE (3)	1
DE (3)	1
DE (1)	7
DE (1)	25
NL (3)	20
NL (3)	8
NL (3)	8
NL (1)	23
NL (3)	15
NL (1)	12
NL (1)	2
NL (1)	17
NL (1)	3
NL (1)	1
NL (3)	1
UK (1)	20
UK (4)	3

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **316** type IA variations, **163** type IB variations and **93** type II variations were finalised during the month of January 2006. **16** renewals were finalised in this period.

The status as of 31st January of variations and renewals under Mutual Recognition is as follows:

Year	Procedures from Type IA variations finalised	Procedures from Type IB variations finalised	Procedures from Type II variations finalised	Renewals finalised	Arbitrations referred to CHMP
2006	316	163	93	16	- -

All documents mentioned in this press release can be found at the CMD(h) website at the European Medicines Authorities Windows under the heading Press Releases.

Information on the above mentioned issues can be obtained from the chair of the CMD(h):

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*Or you could visit the **CMD(h) web site** at the EUROPEAN NATIONAL MEDICINES AUTHORITIES WINDOW:*

http://heads.medagencies.org/