European Medicines Agency
Evaluation of Medicines for Human Use

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

The Committee for Medicinal Products for Human Use (CHMP) held its June plenary meeting from 26-28 June 2006.

The CHMP Chairman welcomed Dr. Laitinen-Parkkonen as the new CHMP alternate from Finland.

Centralised procedure

Initial applications for marketing authorisation

The CHMP adopted a positive opinion on an initial marketing authorisation application at this meeting:

- **Exjade** (Deferasirox), from Novartis Europharm Ltd, for the treatment of chronic iron overload due to blood transfusions. EMEA review began on 18 May 2005 with an active review time of 197 days.

The CHMP adopted a negative opinion on an initial marketing authorisation application for a similar biological medicinal product at this meeting:

- **Alpheon** (recombinant human Interferon-alfa-2a), from BioPartners GmbH, due to major quality concerns and to differences identified between Alpheon and the reference product Roferon-A in the quality and clinical comparability exercise. Alpheon was intended for the treatment of chronic hepatitis C. EMEA review began on 21 June 2004 with an active review time of 204 days.
  A separate question and answer document is available.

Summaries of opinion for these medicinal 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.

Extensions of indication and other recommendations

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

- The Committee adopted a positive opinion for the extension of indication for **DatSCAN** ([123 I] ioflupane), from GE Healthcare Limited, to extend its indication to help differentiate probable dementia with Lewy bodies from Alzheimer's disease. DatSCAN, a diagnostic agent, was first authorised in the European Union on 27 July 2000. It is currently indicated in the diagnosis of patients with clinically uncertain Parkinsonian syndromes, to help differentiate essential tremor from Parkinsonian syndromes related to idiopathic Parkinson´s disease, multiple system atrophy and progressive supranuclear palsy.

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- The Committee also adopted a positive opinion for the extension of indication for **Keppra** (levetiracetam), from UCB S.A., to extend its indication to monotherapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 16 years of age with newly diagnosed epilepsy. Keppra was first authorised in the European Union on 29 September 2000. It is currently indicated as adjunctive therapy in the treatment of partial onset seizures or myoclonic seizures in patients suffering from epilepsy

Summaries of opinions for these two products are available and can be found here.

The Committee also adopted a positive opinion on a "line extension" application (under the optional scope) (in accordance with Annex II of Commission Regulation (EC) No. 1085/2003).

Safety update

The EMEA has reviewed cases of intracranial haemorrhage associated with the use of Aptivus (tipranavir). Following this preliminary review the CHMP has asked the marketing authorisation holder (Boehringer Ingelheim International GmbH) to change the product information of Aptivus to add safety information concerning intracranial bleeding.

Lists of Questions

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

Consultation procedure on an ancillary substance in a medical device

The Committee also adopted a positive opinion on human serum albumin in the context of its use as ancillary medicinal substance in **GIII Series for In Vitro Fertilisation** from Vitrolife Sweden AB. The applicant/Notified Body for the consultation procedure is Det Norske Veritas Certification AS. EMEA review began on 26 October 2005 with an active review time of 174 days.

Withdrawals

The European Medicines Agency acknowledged the decision of Skye Pharma PLC to withdraw its application for an extension of the marketing authorisation for the medicinal product **DepoCyte** (cytarabine), which is currently indicated for the intrathecal treatment (injection into the space between the lining of the spinal cord and brain) of lymphomatous meningitis. In its official withdrawal letter, the company stated that it decided to withdraw the application for the extension of the marketing authorisation to include the treatment of solid tumour neoplastic meningitis because the Committee considered that the data provided would not allow a conclusion to be drawn on a positive benefit-risk balance.
A separate question and answer document will be made available after the next meeting of the CHMP on 24-27 July 2006.

Detailed information on the centralised procedure

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

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 May 2006 CHMP plenary meeting are provided in **Annex 4**.

Referral procedures

- The Committee finalised arbitration procedures for generic medicinal products containing **doxazosin**, concluding that the benefit-risk profile of these medicines is beneficial in the agreed indications and that a marketing authorisation should be granted. Doxazosin-containing medicines are approved in a number of EU Member States for the treatment of essential hypertension and symptomatic treatment of benign prostatic hyperplasia. The medicinal products concerned were: **Cardoreg** 4 mg prolonged release tablets (doxazosin as mesylate), from Pharmcom Oy, **Doxagamma** 4 mg prolonged release tablets (doxazosin as mesylate), from Generics UK Limited, **Doxastad** 4 mg prolonged release tablets (doxazosin), from Stada Arzneimittel, **Doxazosin Retard "Arrow"** 4 mg prolonged release tablets (doxazosin as mesylate), from Arrow Generics Ltd, **Doxazosin Retard "Winthrop"** 4 mg prolonged release tablets (doxazosin as mesylate), from Winthrop Pharmaceuticals UK Ltd. The procedures were initiated under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) due to concerns regarding differences in the release profile of the reference product and the generic versions. Arbitrations under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) are initiated by one or more Member States in cases where an agreement cannot be reached in the context of the mutual recognition procedure.

- The Committee started an arbitration procedure under Article 29 of the Community code on human medicinal products (Directive 2001/83/EC as amended) for the generic medicinal product **Ciprofloxacine Kabi** (ciprofloxacin hydrogen sulphate), from Fresenius Kabi. The procedure was initiated by the United Kingdom with a view to harmonise the summary of product characteristics across the European Union regarding the dosages used to treat complicated urinary tract infections.

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 12-14 June 2006. For further details, please see **Annex 5**.

Documents prepared by the CHMP Working Parties adopted during the June 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 June 2006 CHMP plenary meeting:

- The 24th meeting of the CHMP will be held at the EMEA on 24-27 July 2006.
- The next Invented Name Review Group meeting will be held at the EMEA on 24th July 2006.
- The ninth CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised Procedures) will be held at the EMEA on 24-25 July 2006.

Organisational matters

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

- The Guideline on the procedural aspects and dossier requirements for the consultation to the EMEA by a notified body on an ancillary medicinal substance used in a medical device (EMEA/401993/2005). Such guideline was released for 3 months public consultation. The Committee adopted the corresponding application form (EMEA/434094/2005) for these requests.
- The initiation of CHMP Working parties' consultation in preparation of a future revision of the SPC Guideline.
- Discussions on the best utilisation of Co-opted PhVWP Members' Expertise in the EU Regulatory System.

EMEA Implementation of the New EU Pharmaceutical Legislation

The eighteenth CHMP/EMEA Implementation Task Force (CEITAF) meeting took place on Monday 26 June 2006.

The following Guideline was adopted by the CHMP and will be published on the EMEA website:

- Guideline on procedures for re-examination of CHMP opinions.

Initial discussions took place on the following topic:

- CHMP Renewal Assessment Report template.

The last CHMP/EMEA Implementation Task Force (CEITAF) meeting will take place on Monday 24th July 2006. Thereafter Review Implementation topics will be followed up within the ORGAM (Organisational matters) meeting.

PROCEDURAL ANNOUNCEMENT

- Bulgaria and Romania accession to the EU

In view of the upcoming EU enlargement with the accession of Bulgaria and Romania as of the 1st of January 2007 (tbc) EMEA has launched on 30th November 2005 the second phase of the Pre-accession linguistic review process (PALC II). This procedure aims at facilitating phasing-in of Commission Decisions related to the EU centralised procedure, in order to avoid delays of supply of relevant medicinal products in the 2 new Member States after enlargement and to prevent circulation of such products with sub-standard quality translations with potential public health concerns.

So far the number of submitted products through PALC II is far less than anticipated considering that 1st of October 2006 is the last scheduled submission date through this process.

The EMEA would like to emphasize that the availability of Bulgarian and Romanian Product Information will be an essential requirement to proceed with ongoing regulatory activity for existing centrally approved products and/or new applications after the accession date.

Therefore, pharmaceutical companies are urged to submit the required translations in order to ensure successful and timely completion of PALC II for all their centrally authorised products.

Relevant practical guidance on the phasing-in of Commission decisions will be published next month.

- MAHs are reminded that for Type IA/B variations affecting the Annexes of a EU Commission Decision (Annex A, Annex I, II and III), the updated Annexes are considered as part of the supporting documentation for the proposed variation and should be submitted together with the variation application. In case they are not submitted together with the variation application or they are incorrect the EMEA will deem the application invalid.
For detailed information on the submission of the updated Annexes please consult the EMEA post authorisation guidance (http://www.emea.eu.int/htms/human/postguidance/q08.htm)

- Criteria for Rapporteur/Co-Rapporteur appointment: Principles, objective criteria and methodology

Following the adoption of the Paper on the "CHMP Rapporteur /Co-Rapporteur appointment: Principles, objective criteria and methodology" by the CHMP at its May 2006 plenary meeting and the procedural announcement at the May 2006 CHMP Monthly Report, this Paper is now published on the EMEA website. A link to the document can be found here.

- The CHMP agreed to replace the August 2006 plenary meeting by written procedures to be established for certain ongoing applications.

Mutual Recognition procedure and Decentralised procedures-Human

The CHMP noted the report from the eighth CMD(h) (Co-ordination Group for Mutual Recognition and Decentralised procedures-Human) held on 26-27 June 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]	**13**	**4**	**0**	**12**	**3**	**7**	**39**	**529**
Positive opinions[3]	**13**	**2**	**0**	**4**	**0**	**6**	**25**	**351[4]**
Negative opinions[5]	**1**	**0**	**0**	**2**	**0**	**0**	**3**	**10[6]**
Withdrawals prior to opinion	**2**	**1**	**0**	**1**	**0**	**2**	**6**	**105**
Marketing authorisation granted by the Commission	**17**	**0**	**0**	**7**	**0**	**3**	**27**	**338**

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[6]	**1**	**5**
PMF	**1**	**8**
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] 351 positive Opinions corresponding to 278 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] 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 JUNE 2006 CHMP MEETING IN RELATION TO ACCELERATED ASSESMENT PROCEDURES

Substance	Intended indications(s)	Accelerated Assessment Requests	
		Accepted	Rejected
Chemical	Treatment of paroxysmal nocturnal hemoglobinuria	X	

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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)	331	3771
Type II Variations (positive opinions)	315	2497
Type II Variations (negative opinions)	0	7
Annex II Applications (positive opinions)	10	137
Annual Re-assessment (positive opinions)	16	N/A
Opinion for renewals of conditional MA's (positive opinions)	0	0
5 Year Renewals (positive opinions)	35	N/A

Opinions for Type II Variation applications	
Number of Opinions	**Outcome**
2 Extensions of indication	2 Positive opinions
39 SPC changes	39 Positive opinions
15 Quality changes	15 Positive opinions

Opinions for Annual Re-Assessment applications		
Name of Medicinal Product (INN) MAH	**Outcome**	**Comments**
Foscan (temoporfin) Biolitec Pharma Limited	Positive Opinion adopted	The Marketing Authorisation will remain under Exceptional Circumstances
Orfadin (nitisinone) Swedish Orphan International AB	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**
Ketek (telithromycin) Aventis Pharma S.A	Positive Opinion adopted	Additional 5-year renewal
Levviax (telithromycin) Aventis Pharma S.A	Positive Opinion adopted	Additional 5-year renewal
Twinrix adult (comb Hep A and B vaccine) GlaxoSmithKline Biologicals S.A	Positive Opinion adopted	Unlimited validity
Twinrix paediatric (comb Hep A and B vaccine) GlaxoSmithKline Biologicals S.A	Positive Opinion adopted	Unlimited validity

ANNEX 3 TO CHMP MONTHLY REPORT JUNE 2006

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

Invented Name	Tysabri
INN	natalizumab
Marketing Authorisation Holder	Pharma International Ltd
Proposed ATC code	L04AA23
Indication	TYSABRI is indicated as single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following patient groups: Patients with high disease activity despite treatment with a beta-interferon (see 5.1); Patients with rapidly evolving severe relapsing remitting multiple sclerosis (see 5.1).
CHMP Opinion date	27.04.2006
Marketing Authorisation Date	27.06.2006

Invented Name	Evoltra
INN	clofarabine
Marketing Authorisation Holder	Bioenvision Limited
Proposed ATC code	L01BB06
Indication	Treatment of acute lymphoblastic leukaemia (ALL) in paediatric patients who have relapsed or are refractory after receiving at least two prior regimens and where there is no other treatment option anticipated to result in a durable response. Safety and efficacy have been assessed in studies of patients ≤ 21 years old at initial diagnosis (see section 5.1).
CHMP Opinion date	23.02.2006
Marketing Authorisation Date	29.05.2006

Invented Name	Acomplia
INN	rimonabant
Marketing Authorisation Holder	Sanofi-aventis
Proposed ATC code	Not yet assigned
Indication	As an adjunct to diet and exercise for the treatment of obese patients (BMI $\geq$ 30 kg/m^2), or overweight patients (BMI > 27 kg/m^2) with associated risk factor(s), such as type 2 diabetes or dyslipidaemia (see section 5.1).
CHMP Opinion date	27.04.2006
Marketing Authorisation Date	19.06.2006

Invented Name	RotaTeq
INN	rotavirus vaccine, live, oral
Marketing Authorisation Holder	Sanofi Pasteur MSD
Proposed ATC code	Not yet assigned
Indication	RotaTeq is indicated for the active immunisation of infants from the age of 6 weeks for prevention of gastroenteritis due to rotavirus infection (see section 4.2).
CHMP Opinion date	27.04.2006
Marketing Authorisation Date	27.06.2006

Invented Name	Avaglim
INN	Rosiglitazone/glimepiride
Marketing Authorisation Holder	SmithKline Beecham plc
Proposed ATC code	Not yet assigned
Indication	AVAGLIM is indicated in the treatment of type 2 diabetes mellitus patients who are unable to achieve sufficient glycaemic control on optimal dosage of sulphonylurea monotherapy, and for whom metformin is inappropriate because of contraindication or intolerance.
CHMP Opinion date	27.04.2006
Marketing Authorisation Date	27.06.2006

Invented Name	Zimulti
INN	rimonabant
Marketing Authorisation Holder	Sanofi-aventis
Proposed ATC code	Not yet assigned
Indication	As an adjunct to diet and exercise for the treatment of obese patients (BMI $\geq$ 30 kg/m^2), or overweight patients (BMI > 27 kg/m^2) with associated risk factor(s), such as type 2 diabetes or dyslipidaemia (see section 5.1).
CHMP Opinion date	27.04.2006
Marketing Authorisation Date	19.06.2006

Invented Name	Baraclude
INN	entecavir
Marketing Authorisation Holder	Bristol-Myers Squibb Pharma EEIG
Proposed ATC code	J05AF10
Indication	Baraclude is indicated for the treatment of chronic hepatitis B virus (HBV) infection in adults with compensated liver disease and evidence of active viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis. This indication is based on clinical trial data in patients with HBeAg positive and HBeAg negative HBV infection, nucleoside naive patients and patients with lamivudine-refractory hepatitis B (see sections 4.4 and 5.1).
CHMP Opinion date	27.04.2006
Marketing Authorisation Date	26.06.2006

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

Active substance	**Sponsor/applicant**	**EU Designation Number & Date of Orphan Designation**	**Designated Orphan Indication**
Nelarabine (Atriance)	Glaxo Group Limited	EU/3/05/293 16/06/2005	Treatment of acute lymphoblastic leukaemia
Bosentan (Tracleer)	Actelion Registration Limited	EU/3/03/139 17/03/2003	Treatment of systemic sclerosis (scleroderma)

PRE-AUTHORISATION: SCIENTIFIC ADVICE AND PROTOCOL ASSISTANCE EMEA CENTRALISED PROCEDURES

	1995 - 2005	2006	Overall Total
Scientific Advice	558	76	634
Follow-up to Scientific Advice	94	13	107
Protocol Assistance	107	26	133
Follow-up to Protocol Assistance	26	3	29
	775	**2124**	**903**

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

Final Scientific Advice Procedures

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Chemical	conditioning treatment prior to haematopoietic progenitor cell transplantation				X			X	
Chemical	treatment of malignant ascites			X				X	
Chemical	treatment of breast cancer			X				X	
Chemical	treatment of renal cell carcinoma	X						X	
Chemical	treatment of neutropenia in cancer patients			X				X	
Chemical	treatment of colorectal cancer	X						X	
Chemical	treatment of hypertension and resistant hypertension	X						X	

Substance	Intended indications(s)	Type of Request				Topic			
		New		Follow-up		Pharmaceutical	Pre-clinical	Clinical	Significant Benefit
		SA	PA	SA	PA				
Biological	treatment of distributive shock	X						X	
Chemical	treatment of hypertension and chronic renal disease in children	X						X	
Chemical	treatment of acute sensorineural hearing loss		X			X	X	X	
Biological	treatment of severe sepsis	X						X	
Chemical	conditioning treatment prior to haematopoietic progenitor cell transplantation				X			X	
Biological	prevention of gastro-enteritis due to rotavirus infection	X				X	X	X	
Biological	treatment of diabetes			X			X	X	
Chemical	treatment of urge incontinence	X						X	
Biological	treatment of melanoma stage 3 and 4	X				X	X	X	
Biological	treatment of Systemic Lupus Erythematosus	X				X	X	X	
Biological	treatment of AAT deficiency		X			X	X	X	X
Biological	treatment of ulcerative colitis	X						X	
Chemical	treatment of HIV/AIDS in the paediatric population	X				X		X	

SA: Scientific Advice
PA: Protocol Assistance

The above-mentioned 12 Scientific Advice letters, 5 Protocol Assistance letters and 3 Follow-up Scientific Advice letters were adopted at the 26-28 June 2006 CHMP meeting.

New requests for Scientific Advice Procedures

The Committee accepted 30 new Requests for which the procedure started at the SAWP meeting held on 12-14 June 2006. The new requests are divided as follows: 12 Initial Scientific Advice, 6 Follow-up Scientific Advice, 9 Initial Protocol Assistance and 3 Follow-up Protocol Assistance.

ANNEX 6 TO CHMP MONTHLY REPORT JUNE 2006

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

BIOLOGICS WORKING PARTY

Reference number	Document	Status[7]
CHMP/BWP/398498/2005	Guideline on viral safety evaluation of biotechnological investigational medicinal products	Released for 6 months consultation

GENE THERAPY WORKING PARTY

Reference number	Document	Status
CHMP/GTWP/60860/2006	Reflection Paper on Current Experience with Replication-Incompetent Retroviral Vectors	Adopted

SAFETY WORKING PARTY

Reference number	Document	Status
EMEA/CHMP/SWP/ 150115/2006	Guideline on Detection of early signals of drug-induced hepatotoxicity in non-clinical studies	Released for 6 months consultation
CPMP/SWP/5199/02 EMEA/CHMP/QWP/ 251344/2006	Guideline on the Limits of Genotoxic Impurities	Adopted

EFFICACY WORKING PARTY

Reference number	Document	Status
CHMP/EWP/185990/ 2006	Guideline on reporting the results of population pharmacokinetic analyses	Released for 6 months consultation
CHMP/EWP/147013/ 2006	Guideline on the Role of Pharmacokinetics in the Development of Medicinal Products in the paediatric Population	Adopted

[7] Adopted or release for consultation documents can be found at the EMEA website (under "What's new-recent publications" or under Human Medicines-Guidance documents").

PAEDIATRIC WORKING PARTY

Reference number	Document	Status
EMEA/181377/2006	Draft concept paper on the impact of brain immaturity when investigating medicinal products intended for neonatal use	Released for 3 months consultation
EMEA/207562/2006	Overview of comments received on the List of paediatric needs on Rheumatology	Adopted
EMEA/CHMP/234105/ 2005	Assessment of the paediatric needs - Rheumatology	Adopted
EMEA/224696/2006	Assessment of the paediatric needs – Supportive therapy in oncology	Released for 6 months consultation
EMEA/224688/2006	Assessment of the paediatric needs - Diabetes	Released for 6 months consultation
EMEA/224515/2006	Assessment of the paediatric needs - Migraine	Released for 6 months consultation

PHARMACOVIGILANCE WORKING PARTY (PhVWP)

Reference number	Document	Status
EMEA/CHMP/PhVWP/ 235910/2005	Guideline on Conduct of Pharmacovigilance for Medicines Used by the Paediatric Population	Adopted

INVENTED NAME REVIEW GROUP (NRG)

	June 2006			2006	
	Accepted	Rejected	Pending	Accepted	Rejected
Proposed invented names	15	14	15	62	88
Justification for retention of invented name *	4	4	3[1]	9	17

*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.

1 One justification request has been postponed from the June NRG meeting

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

Report from the CMD(h) meeting held on 26th and 27th June 2006

New Questions and Answers on the implementation of the new Legislation

The CMD(h) has agreed 3 new Q&As to address the possibility to follow the decentralised procedure for duplicate applications and extension applications of medicinal products authorised via the mutual recognition procedure and a Q&A to replace the document 'Simultaneous applications (Article 17 paragraph 2 of Directive 2001/83/EC) Member States standard operating procedure.'

Compliance with Articles 17 and 18 of Directive 2001/83/EC, as amended

Applicants are reminded that the use of the national procedure is strictly limited to the initial phase of the mutual recognition (granting of the marketing authorisation by the Reference Member State) and to medicinal products, which are not to be authorised in more than one Member State.

Any medicinal product which is to be placed on the market of more than one Member State has to be processed either by the decentralised procedure (where no marketing authorisation exists at the time of application) or by the mutual recognition procedure (where the medicinal product has already received a marketing authorisation at the time of application).

Where a Member State notes that a marketing authorisation application for the same dossier is being examined in another Member State or that a marketing authorisation has been granted for the same medicinal product in another Member State, the application will be rejected, unless it was **submitted via** the decentralised or mutual recognition procedure.

EU Work sharing procedure in the assessment of paediatric data - Best Practice Guide for the preparation of the Public Assessment Report

The CMD(h) has agreed on a draft best practice guide for the preparation of the public assessment report, within the framework of the EU work sharing procedure in the assessment of paediatric data.

The best practice guide addresses the structure and content of the paediatric public assessment report (PaedPAR). The PaedPARs for the medicinal products involved in the EU work sharing will be published on the Heads of Medicines Agencies website, within 60 days of the finalisation of the procedure.

Any comments on the draft best practice guide should be sent by 30 July, to the CMD(h) secretariat (sonia.ribeiro@emea.eu.int).

Best Practice Guide for the submission and processing of variations in the Mutual Recognition Procedure

The CMD(h) has agreed an updated best practice guide for the submission and processing of variations in the mutual recognition procedure, mainly to clarify that the Commission Regulation (EC) No 1084/2003 applies to changes to marketing authorisations granted via the new decentralised procedure.

Revision of the core SPC for trivalent influenza vaccines

The CMD(h) has agreed to publish a revision of the core SPC for trivalent influenza vaccines, for a one month public consultation period.

Any comments on the revised core SPC should be sent by 30 July, to the CMD(h) secretariat (sonia.ribeiro@emea.eu.int).

Low Molecular Mass Heparins (LMMHs) and Pancreatin – Biological medicinal products

The CMD(h) has agreed the view of the BWP that low molecular mass heparins and pancreatins should be considered biological medicinal products. Therefore, applications for marketing authorisation as generic medicinal products will not be accepted and should be submitted in accordance with Article 10 (4) of Directive 2001/83/EC, as amended – 'Similar biological application', with additional physico-chemical characterisation and clinical data.

Active substance master files (ASMF) are not applicable to biological medicinal products and while Certificates of Suitability (CEP) may be considered for these substances, they are not sufficient to replace Module 3S of the MAA dossier.

Applicants are advised to seek scientific advice for these products, at EU or national level, until guidance is available.

Declaration from Qualified Person (QP) on Good Manufacturing Practice (GMP) compliance of Active Pharmaceutical Ingredient (API) Manufacturer

The CMD(h) agreed to accept, in case more than one manufacturing authorisation holder is involved, a single declaration signed by one QP that the active substance manufacturer(s) operate in compliance with the guidelines on GMP for starting materials, provided the following:

- The declaration makes it clear that it is signed on behalf of all the involved QPs;
- The arrangements are underpinned by a technical agreement, as described in Chapter 7 of the GMP Guide and the QP providing the declaration is the one identified in the agreement as taking specific responsibility for the GMP compliance of the active substance manufacturers. (These arrangements are subject to Inspection by the Competent Authorities).

Change in the EU-Presidency

The June 2006 CMD(h) meeting was the last one under the Austrian presidency. Finland will take over the presidency in July 2006. Ms Outi Hemmo will be the Vice-Chairperson of CMD(h), for the Finnish presidency of the Council of the European Union.

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

Please find below information on the Name of the products in the RMS, active substances, pharmaceutical forms, procedure numbers, CMS, legal basis, grounds for referral to CMD(h), Day 60 and outcome of the procedures, for the referrals to the CMD(h) finalised on 9 June 2006.

Name of the product in the RMS	Loratadine 10mg Tablets
Active substance	loratadine
Pharmaceutical form	Tablets
Procedure number	UK/H/829/01/MR
CMS	FR
Legal basis	Article 10.1, Directive 2001/83/EC - Generic
Grounds for referral to CMD(h)	The application was referred to CMD(h) as the company were unable to resolve all of the CMS concerns in relation to product quality during the 90 day procedure. Further clarification of data was provided during the referral to CMD(h) and consensus was reached.

Day 60	09.06.06
Outcome	Agreement reached

Name of the product in the RMS	Ciprofloxacin Kabi 100mg/50ml	Ciprofloxacin Kabi 200mg/100ml, 400mg/200ml
Active substance	ciprofloxacin	
Pharmaceutical form	Solution for infusion	
Procedure number	NL/H/695/01/MR	NL/H/695/02-03/MR
CMS	AT, CY, CZ, DE, EL, IT, PL, PT, SK, UK	AT, BE, CY, CZ, DE, DK, EL, ES, FI, HU, IT, PL, PT, SE, SK, UK
Legal basis	Art 10.1, Directive 2001/83/EC - Generic	
Grounds for referral to CMD(h)	The procedure highlighted differences in approved posology between national 'brand leader' SPCs. Specifically, the referring CMS objected to the RMS approved posology for urinary tract infections, UTI (200-400 mg twice daily) and considered that the maximum recommended daily dose (1200mg) should be decreased to 800mg daily. The referring CMS considered that the available information was insufficient to justify amendment of the posology. The other Member States were concerned that lowering the dose will result in a suboptimal dosage regimen. In their view, the lower dosing may risk sub-therapeutic dosing and lead to development of resistance. In the absence of data in favour or against the different options under discussion a consensus could not be reached.	
Day 60	09.06.06	
Outcome	Referred to CHMP for arbitration	

Name of the product in the RMS	Lamotrigine 25, 50, 100, 200mg Tablets	Lamotrigine 2, 5, 25, 50, 100, 200mg Dispersible Tablets
Active substance	lamotrigine	
Pharmaceutical form	Tablets	Dispersible Tablets
Procedure number	UK/H/835/01-04/MR	UK/H/836/01-06/MR
CMS	AT, BE, CZ, DE, DK, FI, HU, IE, IT, LT, NO, PL, PT, SE, SK	AT, BE, CZ, DE, DK, ES, FI, HU, IE, IT, LT, NL, NO, PL, PT, SE, SK
Legal basis	Art 10.1, Directive 2001/83/EC - Generic	
Grounds for referral to CMD(h)	The application was referred on the basis of the acceptability of the design and conduct of the comparative bioequivalence studies with reference to the Note for Guidance for claiming essential similarity of all strengths; the omission of an additional indication in the summary of product characteristics; agreement of safety information concerning use in pregnancy; and agreement of the patient information. Further clarification of data was provided and agreement of the SPC reached.	
Day 60	09.06.06	

Outcome	Agreement reached

Meeting schedule
The next CMD(h) meeting will be held on 24 and 25 July 2006.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **32** new Mutual Recognition Procedures were finalised during the month of May 2006. **3** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period. **7** Mutual Recognition Procedures for new applications were referred to CHMP in this period.

The status as of 31st May 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)	Agreement reached in the CMD(h)	Arbitrations referred to CHMP
2006	193	214	37 N.A.	20	14

60 Mutual Recognition Procedures (regarding **154** products) started in May 2006. The categories of these procedures are as follows:

4 new active substances (first authorisation in the European Community after RMS approval), of which 3 procedures were multiple applications.

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

43 abridged applications, including **22** multiple applications and **1** repeat use.

4 line extension applications.

The new procedures started in May related to **6** full dossiers, **44** generics, **1** fixed combination, **1** informed consent application, **1** hybrid application and **7** bibliographic applications.

The procedures consisted of **59** chemical substances and **1** biological vaccine product.

50 of these procedures were prescription-only medicinal products and **10** procedures related to non prescription (OTC) products in the reference Member State[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 May 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (1)	9
DK (2)	7
DK (2)	1
DK (1)	2
DK (7)	5
DK (7)	1
DK (5)	1

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (5)	3
DK (4)	1
DK (6)	1
DK (5)	1
DK (4)	1
DK (5)	1
DK (7)	4
DK (6)	1
DK (5)	1
DK (4)	1
DK (7)	1
DK (1)	1
EE (1)	24
FI (1)	17
FI (4)	9
FI (1)	1
FI (7)	9
FR (1)	2
FR (1)	9
FR (1)	4
FR (1)	2
FR (1)	3
FR (1)	8
NL (1)	6
NL (1)	1
NL (1)	1
NL (1)	4
NL (1)	1
NL (1)	1
NL (1)	11
NL (1)	5
NL (2)	1
NL (2)	3
NL (2)	9
NL (2)	1
NL (1)	2
NL (1)	5
NL (2)	1
NL (2)	1
NL (2)	1
NL (2)	3
NL (2)	1
NL (2)	7
NL (1)	4
SE (2)	7
UK (1)	12
UK (1)	1
UK (1)	13
UK (2)	19
UK (3)	27
UK (3)	6
UK (3)	7
UK (3)	3

Decentralised Procedure

The status as of 31st May of procedures under Decentralised Procedure is as follows:

Year	Procedures from New applications	Procedures from New applications	Procedures referred to	Agreement reached in the	Arbitrations referred to

	finalised	in process	CMD(h)	CMD(h)	CHMP
2006	--	158	--	--	--

31 Decentralised Procedures (regarding **49** products) started in May 2006. The categories of these procedures are as follows:

All of these applications were abridged applications, including **9** multiple applications.

The new Decentralised procedures started related to **27** generic applications and **4** hybrid applications.

The procedures consisted of **31** chemical substances[3].

All 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 May 2006.

Reference Member State (number of products involved in the procedure)	**Number of CMSs involved in the procedure**
DE (2)	7
DE (1)	1
DE (1)	9
DE (1)	1
DE (1)	1
DE (2)	8
DE (1)	3
DE (1)	12
DE (1)	19
DE (1)	1
DE (1)	3
DK (1)	7
DK (1)	1
DK (1)	6
DK (4)	3
DK (3)	11
DK (2)	3
NL (1)	19
NL (1)	9
NL (1)	10
NL (1)	1
NL (1)	11
NL (1)	1
NL (1)	12
NL (1)	3
NL (1)	1
SE (4)	10
SE (4)	11
SE (3)	2
UK (1)	4
UK (3)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **506** type IA variations, **244** type IB variations and **148** type II variations were finalised during the month of May 2006. **29** renewals were finalised in this period.

The status as of 31st May 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	1835	952	677	122	--

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/