



## **Report from the CMD(h) meeting held on 26<sup>th</sup> and 27<sup>th</sup> 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](mailto: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](mailto: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.

<b>Name of the product in the RMS</b>	Loratadine 10mg Tablets
<b>Active substance</b>	loratadine
<b>Pharmaceutical form</b>	Tablets
<b>Procedure number</b>	UK/H/829/01/MR
<b>CMS</b>	FR
<b>Legal basis</b>	Article 10.1, Directive 2001/83/EC - Generic
<b>Grounds for referral to CMD(h)</b>	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.
<b>Day 60</b>	09.06.06
<b>Outcome</b>	Agreement reached

<b>Name of the product in the RMS</b>	Ciprofloxacin Kabi 100mg/50ml	Ciprofloxacin Kabi 200mg/100ml, 400mg/200ml
<b>Active substance</b>	ciprofloxacin	
<b>Pharmaceutical form</b>	Solution for infusion	
<b>Procedure number</b>	NL/H/695/01/MR	NL/H/695/02-03/MR
<b>CMS</b>	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
<b>Legal basis</b>	Art 10.1, Directive 2001/83/EC - Generic	
<b>Grounds for referral to CMD(h)</b>	<p>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.</p> <p>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.</p>	

	In the absence of data in favour or against the different options under discussion a consensus could not be reached.
<b>Day 60</b>	09.06.06
<b>Outcome</b>	Referred to CHMP for arbitration

<b>Name of the product in the RMS</b>	Lamotrigine 25, 50, 100, 200mg Tablets	Lamotrigine 2, 5, 25, 50, 100, 200mg Dispersible Tablets
<b>Active substance</b>	lamotrigine	
<b>Pharmaceutical form</b>	Tablets	Dispersible Tablets
<b>Procedure number</b>	UK/H/835/01-04/MR	UK/H/836/01-06/MR
<b>CMS</b>	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
<b>Legal basis</b>	Art 10.1, Directive 2001/83/EC - Generic	
<b>Grounds for referral to CMD(h)</b>	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.	
<b>Day 60</b>	09.06.06	
<b>Outcome</b>	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 31<sup>st</sup> 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.

**Report from the CMD(h) meeting held in June 2006**

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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<sup>2</sup>.

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.
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Number of countries involved in the new applications in Mutual Recognition procedure started in May 2006.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
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 31<sup>st</sup> May of procedures under Decentralised Procedure 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	--	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<sup>3</sup>.

**All** of these procedures were prescription-only medicinal products in the reference Member State<sup>4</sup>.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
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 31<sup>st</sup> 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/>**