



Report from the CMD(h) meeting held on 13th, 14th and 15th November 2006

CMD(h) meeting with representatives of Interested Parties

The CMD(h) held a meeting on 13 November 2006 with representatives of AESGP, EFPIA and EGA.

The topics discussed were the following:

- The Decentralised Procedure (DCP) and the Mutual Recognition Procedure (MRP), including communication of outcome of referrals in the CMD(h);
- The implementation of 'Usage patents' within the framework of the MRP/DCP;
- The experience with consultation with target patients groups;
- The implementation of e-CTD in the Decentralised and Mutual Recognition Procedures.

The CMD(h) has set up a working group to evaluate the Decentralised Procedure and to consider the need for revision of the Decentralised Procedure SOP.

Interested Parties were invited to send comments/proposals in relation to the Decentralised Procedure to the attention of the CMD(h) secretariat (sonia.ribeiro@emea.europa.eu) by 1 February 2007, for early consideration by the CMD(h).

The CMD(h) has also set up a working group to analyse validation issues and national requirements within the framework of the Decentralised and Mutual Recognition Procedures.

Guidance on Contacts with Representative Organisations

The CMD(h) has considered the comments received from Interested Parties on the Guidance on contacts with Representative Organisations and has agreed a final version that will be published on the website.

The CMD(h) would like to thank Interested Parties for the contribution on the CMD(h) Guidance document.

Functions of the CMD(h) Secretariat

The CMD(h) has agreed a document that details the functions of the CMD(h) secretariat, as set out in Article 16 of the CMD(h) Rules of Procedure, including the specific functions of the secretariat in relation to referrals to CMD(h) and contacts with Representative Organisations.

This document will be published on the website.

Enlargement of the European Union – 1st January 2007

The CMD(h) is currently reviewing the document 'Questions and Answers on MRP after the EU enlargement on 1 May 2004', to consider, where appropriate, the accession of Romania and Bulgaria to the EU on 1st January 2007.

The final document 'Questions and Answers on MRP&DCP after the EU Enlargement on 1 May 2004 & 1 January 2007' will be published with the December CMD(h) press release.

CMD(h) agreement regarding processing of generic applications when the generic product has more indications or fewer indications than the reference product in the CMS

With a view to avoiding referrals to the CMD(h) other than on the grounds of a potential serious risk to public health, the CMD(h) has agreed that a deviation in indications (more or fewer) in the generic product from the national reference product in the CMS is not considered to be, *per se*, an appropriate reason to refuse licensing a medicinal product and developed a paper regarding processing of generic applications when the generic product has more indications or fewer indications than the reference product in the CMS.

This interpretation is in line with the principle underlying the Commission communication on the Community marketing authorisation procedures for medicinal products (Official Journal C229, 22/7/1998) that concerned Member States should endeavour to recognise the assessment performed by the reference Member State, except where they have concerns as to the existence of a potential serious risk to public health.

The EMEA and CMD(h) review Europe-wide experience with user consultation in the readability testing of package leaflets

The EMEA and the CMD(h) organised, on 23 October 2006, a workshop on user consultation in the context of readability testing of package leaflets for medicines.

The aim of the workshop was to review and bring together experience and expertise of European regulators with readability testing of the package leaflet by target patient groups.

The workshop focused on the layout and design of a good package leaflet, the review of user testing reports and the assessment of justification for not performing user testing.

The press release from the workshop on user consultation is available on the EMEA website <http://www.emea.europa.eu/pdfs/general/direct/pr/45765806en.pdf>

EU Work sharing Project – Assessment of paediatric data

The Marketing Authorisation Holders for the following medicinal products, involved in the EU work sharing project - assessment of paediatric data, are requested to submit, within 60 days, a type II variation via the mutual recognition procedure, to implement the agreed text for inclusion in the SPC:

- Cosopt (dorzolamide hydrochloride and timolol maleate);
- Detrusitol/Detsel/Detrusitol SR/Protol SR (tolterodine tartrate);
- Zomig/Zomig Rapimelt/ Zomig Nasal (zolmitriptan)

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 27 October 2006.

Name of the product in the RMS	IG VENA
Active substance	human normal immunoglobulin
Pharmaceutical form	Solution for infusion
Procedure number	IT/H/0130/01/MR
CMS	AT, DE, EL, ES, PL, PT
Legal basis	Art 8.3(i), Directive 2001/83/EC – Full dossier
Grounds for referral to CMD(h)	A concerned member state raised doubts on the existence of sufficient evidence on the viral safety of this product with respect to non-enveloped viruses, as the safety of the product relies exclusively on the partitioning process. Though the effectiveness of this process is acknowledged, the introduction of a specific second step for non-enveloped viruses has been requested, and its absence has been considered as a major concern.
Day 60	27.10.06
Outcome	As the major objection was based mainly on a national interpretation of the relevant Guideline, it was agreed that IG Vena should be regarded as safe and that this product does not carry any potential serious risk to public health.

Name of the product in the RMS	Tobrineb	Actitob
Active substance	tobramycin	
Pharmaceutical form	Nebuliser solution	
Procedure number	IT/H/0132/01/MR	IT/H/0133/01/MR
CMS	AT, CZ, DE, EL, ES, FR, HU, IE, NL, PL, PT, SK, UK	DE, ES, FR, PT, UK
Legal basis	Article 10.3, Directive 2001/83/EC – Hybrid	
Grounds for referral to CMD(h)	One CMS suggested a direct comparison versus an active comparator.	

Day 60	27.10.06
Outcome	Agreement reached. Consensus was reached on the Applicant's post-approval commitment to perform the requested study.

Name of the product in the RMS	Prexige/Frexocell/Stellige/Hirzia 100, 200 & 400mg
Active substance	lumiracoxib
Pharmaceutical form	Tablet
Procedure number	UK/H/887-890/01-03/MR
CMS	UK/H/887: AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IS, IE, IT, LT, LU, LV, MT, NL, NO, PL, PT, SE, SI, SK UK/H/888: AT, DE, EL, IT, PT, SI UK/H/889: BE, DE, ES, IE, IT, PL, PT UK/H/890: DE, IT, PT
Legal basis	Article 8.3, Directive 2001/83/EC – Full dossier
Grounds for referral to CMD(h)	Several CMS considered that the safety and efficacy of lumiracoxib was not established in all indications sought and proposed that the indications be limited to osteoarthritis. There was also debate regarding the duration of treatment. The indication “relief of dental pain or pain after dental surgery” was not acceptable to referring CMSs.
Day 60	27.10.06
Outcome	At CMD(h) meeting the RMS presented their view and the main points for discussion. The company was subsequently invited for an oral hearing. The majority opinion at CMD (h) was that the indication for treatment of osteoarthritis of knee and hip would be acceptable with the proviso that the treatment should be for the shortest duration and with the lowest dose. The dental pain indication and with it the 200 and the 400mg strength tablets were withdrawn. The applicant agreed to a commitment to provide an appropriate Risk Management Plan in consultation with PhVWP. Agreement was reached based on the revised SPC and post approval commitment provided by the applicant regarding the Risk Management Plan.

Name of the product in the RMS	Imodium Plus Caplets
Active substance	loperamide / simeticone
Pharmaceutical form	Tablet
Procedure number	UK/H/0241/02/MR
CMS	BE, DE, DK, ES, FI, FR, IE, LU, NL, NO, PT, SE
Legal basis	Art 10b, Directive 2001/83/EC - Fixed combination
Grounds for referral to CMD(h)	Serious public health concerns were raised with regard to the lack of adequate proof of comparable bioavailability and problems in data collation together with inconsistencies in the analyses of bioequivalence studies presented by the applicant.
Day 60	27.10.06
Outcome	At the CMD(h) meeting the RMS presented its view and the company was invited for an oral hearing. The general opinion of CMD(h) was that the grant of a marketing authorisation was appropriate even though strict bioequivalence with the authorised chewable tablets used as the comparator had not been demonstrated. This is a locally acting product on the gut wall and a pharmacodynamic study would have been more

	<p>appropriate to prove safety and efficacy for this line extension rather than a bioequivalence study. Nevertheless given the absence of local exposure biomarkers, bioequivalence studies have been accepted as a surrogate.</p> <p>In addition, the company has provided a commitment to undertake a post-authorisation comparative efficacy and safety study, and to provide other appropriate safety data on the use of the product in the UK and US in order to confirm clinical equivalence and the on-going risk-benefit evaluation of the product.</p> <p>CMD(h) reached a consensus agreement that because this application is for a line extension and both actives have a well known safety and efficacy profile there is no potential serious risk to public health. It must be recognised however that this case does not serve as precedent for post-hoc deviation from the relevant guidelines.</p>
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NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **79** new Mutual Recognition Procedures were finalised during the month of October 2006. **10** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period. None of the Mutual Recognition Procedures for a new application were referred to CHMP in this period.

The status as of 31st October 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	417	245	73 N.A.	39	19

54 Mutual Recognition Procedures (regarding **100** products) started in October 2006. The categories of these procedures are as follows:

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

4 new active substances, including **1** repeat use application.

45 abridged applications, including **29** multiple and **3** repeat use applications.

1 line extension application, which is a repeat use application.

The new procedures started in October related to **5** full dossiers, **46** generics, **1** fixed combination application and **2** bibliographic applications.

53 of these procedures consisted of chemical substance applications and **1** biological vaccine application.

51 of these procedures related prescription-only medicinal products and **3** procedures related to non-prescription medicinal products in the reference Member State¹.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
CZ (1)	1
DE (3)	4
DE (1)	1
DE (1)	11
DE (1)	12
DE (1)	27
DK (1)	5
DK (4)	22
DK (1)	1
FI (1)	1
FI (1)	4
FI (1)	1
FI (1)	3
FI (1)	10
FI (1)	1
FI (1)	6
FI (1)	2
FI (1)	1
FI (1)	1
FI (1)	1
FI (1)	1
FI (1)	5
FI (1)	9
FR (1)	4
NL (1)	1
NL (3)	9
NL (3)	7
NL (3)	1
NL (3)	1
NL (3)	4
NL (3)	1
NL (3)	1
NL (3)	5
NL (3)	8
NL (3)	1
NL (3)	9
NL (3)	1
NL (3)	1
NL (3)	1
NL (1)	1
NL (1)	1
NL (1)	1
NL (3)	3
SE (4)	4
SE (1)	16
SE (1)	1
SE (2)	3
SE (1)	8
UK (1)	8
UK (4)	5
UK (3)	1
UK (1)	5

¹ 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.

Decentralised Procedure

The CMD(h) noted that **4** new Decentralised Procedures were finalised during the month of October 2006.

The status as of 31st October 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	18	342	--	--	--

40 Decentralised Procedures (regarding **121** products) started in October 2006. The categories of these procedures are as follows:

39 abridged applications, including **14** multiple applications.

1 known active substance application.

The new Decentralised procedures started related to **30** generic, **9** hybrid and **1** bibliographic applications.

All of these procedures consisted of chemical substance applications.

These procedures related to **39** prescription-only and **1** non-prescription medicinal products in the reference Member State².

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (1)	1
AT (1)	1
AT (1)	1
DE (4)	12
DE (2)	4
DE (1)	4
DE (1)	23
DE (1)	1
DE (1)	1
DE (1)	1
DE (2)	15
DE (2)	5
DE (2)	1
DE (2)	1
DE (2)	1
DE (2)	1
DK (1)	5
DK (1)	2
DK (1)	2
DK (3)	5
DK (4)	5
DK (4)	2
DK (4)	1
DK (5)	10

² 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.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (2)	14
DK (1)	3
DK (11)	9
DK (5)	3
DK (1)	7
FI (11)	19
FI (10)	1
FI (11)	1
FI (2)	11
NL (2)	1
UK (1)	21
UK (3)	11
UK (3)	6
UK (3)	11
UK (4)	1
UK (2)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **366** type IA variations, **241** type IB variations and **180** type II variations were finalised during the month of October 2006. **29** renewals were finalised in this period.

The status as of 31st October 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	3690	1870	1531	293	--

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/>