



Report from the CMD(h) meeting held on 29th and 30th May 2006

Sub-group meeting on Harmonisation of SPCs

There was a meeting of the Sub-Group on harmonisation of SPCs, to discuss the proposals from Member States for products for which a harmonised SPC should be drawn up.

The Group agreed to prepare the rationale for selection of the products to be included in the list for SPC harmonisation, addressing each of the agreed criteria, for discussion at the July sub-group meeting.

The CMD(h) Sub-Group on harmonisation of SPCs will continue its work with a view to laying down a list of medicinal products for which a harmonised SPC should be drawn up, in accordance with Article 30(2) of Directive 2001/83/EC, as amended.

Interpretation and Member States Recommendation for Applications submitted according to Article 10 when the strength and/or pharmaceutical form of the Reference medicinal product differs between RMS/CMS(s)

The CMD(h) has updated the above mentioned Recommendation, in line with the new legal references in the revised pharmaceutical legislation and to consider generic/hybrid applications submitted via the decentralised procedure.

The legal basis for the applications where the strength and/or pharmaceutical form of the Reference medicinal product differs between RMS/CMS(s) should be Article 10 of Directive 2001/83/EC, as amended.

The Applicant should tick in the application form either Article 10.1 or 10.3, depending on whether the strength and/or pharmaceutical form of the reference medicinal product is or not authorised in the MS where the application is made.

Applicants are reminded to inform the RMS in due time if different sections of Article 10 will be used.

Applicant's response document in Mutual Recognition and Decentralised Procedures

The CMD(h) has updated the above mentioned document, to consider the response documents to be submitted in the mutual recognition procedure and decentralised procedure, including the referral to the CMD(h) for the 60 days procedure and to address the submission of new proposals for the labelling and package leaflet.

Harmonisation of labelling and package leaflet in parallel to a repeat-use MRP – End of transitional period

The CMD(h) has agreed that from the 1st November 2006 separate applications will not be accepted for the harmonisation of the labelling and package leaflet of a medicinal product in parallel to a repeat-use MRP. After this date the revised pharmaceutical legislation must be applied and the harmonisation of the labelling and package leaflet of a medicinal product should be achieved before the start of the repeat-use MRP.

Consultation with target patients groups for the package leaflet

Applicants are reminded that the submission of the results of consultation with target patient groups, in accordance with Article 59(3) of Directive 2001/83/EC, as amended, or justification for its absence is required with the submission of applications for marketing authorisation via the mutual recognition procedure. Failure to address the matter may result in Member States deeming the application invalid.

For applications submitted via the decentralised procedure this is also a requirement and failure to comply could lead to invalidation of the application; however, within the decentralised procedure there is an additional possibility that applicants may make use of the 'clock stop' period to undertake consultation with target patients groups and therefore it may be possible for the matter to be addressed within the procedural timeframe.

For further information on the timing of user consultation, submission and assessment within the evaluation procedure in the mutual recognition or decentralised procedure, please refer, respectively, to the Best Practice Guide for the Mutual Recognition Procedure and to the Decentralised procedure – Member States SOP, available on the Heads of Medicines Agencies website.

Information on MR procedures for new active substances

A mutual recognition procedure for a medicinal product containing carbetocin has been finalised on 8 March 2006. Please find below information on the Invented name, INN, MAH, Indication, Procedure number and Day 90.

Invented Name (RMS)	Pabal solution for injection 100 micrograms in 1 ml
INN	Carbetocin
Marketing Authorisation Holder	Ferring Pharmaceuticals Ltd
Indication	Prevention of uterine atony following delivery of the infant by Caesarean section under epidural or spinal anaesthesia.
Procedure number	UK/H/0838/001/MR
Day 90	08.03.2006

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 2 May 2006.

Name of the product in the RMS	TerbiLich 250mg
Active substance	terbinafine
Pharmaceutical form	tablet
Procedure number	DE/H/0555/01
CMS	BE, PT
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic
Grounds for referral to CMD(h)	Different interpretation of the available clinical and toxicological data with regard to the inclusion of paediatric indications to the product information.
Day 60	02.05.06
Outcome	Agreement reached not to extend the current product information and to await the outcome of the evaluation of paediatric data for terbinafine in the current ongoing Paediatric Worksharing Project of the HMA. Further regulatory actions – if deemed necessary – will include all medicinal products with terbinafine as active substance.

Name of the product in the RMS	Ciprofloxacin 2 mg/ml solution for infusion
Active substance	ciprofloxacin
Pharmaceutical form	Solution for infusion
Procedure number	UK/H/848/01
CMS	FI, NO, SE
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 (100mg twice daily) and considered that the maximum recommended daily dose (800mg) should be increased up to 1200mg daily.

	<p>Referring CMS consider that the experience of UTI posology of 200-400mg twice daily in a number of EU Member States, together with available published data from open post marketing studies, would justify amendment to the RMS approved posology (UTI).</p> <p>Furthermore, referring CMS were concerned that the SPC should include an optimal dosage regimen because, in their view, the RMS approved posology may risk sub-therapeutic dosing and lead to development of resistance.</p> <p>The RMS considered that the available information was insufficient to justify amendment to the posology and in the absence of data in favour or against the different options under discussion a consensus could not be reached.</p>
Day 60	02.05.06
Outcome	Referred to CHMP for arbitration.

Name of the product in the RMS	Estradiol 2mg film-coated tablets	
Active substance	estradiol	
Pharmaceutical form	Film-coated tablet	
Procedure number	NL/H/685/01	NL/H/686/01
CMS	DE, DK, EE, FI, FR, LT, LU, LV, SI, SK	CZ, DE, DK, EE, FI, LT, LV, SK
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic	
Grounds for referral to CMD(h)	The indication " <i>Prevention of osteoporosis in postmenopausal women at high risk of fractures who are intolerant or contraindicated for other medicinal products approved for the prevention of osteoporosis</i> " is beyond the indications approved for the reference product in one CMS.	
Day 60	02.05.06	
Outcome	Agreement reached. The procedure is finalised without the osteoporosis indication. The applicant commits to submit a type II variation to introduce this indication.	

Name of the product in the RMS	Modafinil 100mg Tablets	
Active substance	modafinil	
Pharmaceutical form	Tablet	
Procedure number	UK/H/834/01	
CMS	AT, BE, CZ, DE, DK, ES, IE, IT, NL, NO, PL, PT, SE, SK	
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic	
Grounds for referral to CMD(h)	<p>Concerns were raised on the GCP documentation for the bioequivalence study.</p> <p>Concerns were raised that the deletion of the indication for Obstructive sleep apnoea, which is authorised in some CMS, might result in inadequate information being provided to some patients.</p> <p>The applicant addressed all the concerns. Some changes were made to the Patient Information Leaflet.</p>	
Day 60	02.05.06	
Outcome	Agreement reached	

Name of the product in the RMS	Equasym 10, 20 and 30mg Capsules
Active substance	Methylphenidate hydrochloride
Pharmaceutical form	Capsule
Procedure number	UK/H/819/01-03
CMS	AT, BE, DK, FR, DE, EL, IS, IE, LU, MT, NO, NL
Legal basis	Article 10.1(a)(iii), last paragraph, Directive 2001/83/EC
Grounds for referral to CMD(h)	There were concerns that the once daily treatment with Equasym XL would not give sufficient therapeutic cover relative to the immediate release (IR) formulations. There were concerns that treatment with Equasym XL would provide less control of symptoms after the school day than a conventional twice daily regimen of IR methylphenidate and hence that patients using Equasym XL would be more likely to require additional IR methylphenidate to control ADHD, resulting in increased overall exposure to methylphenidate. There were concerns regarding initiating methylphenidate treatment with Equasym XL in the treatment of naive patients. Finally the applicant was requested to provide a risk management plan (RMP). The applicant addressed all the concerns. Some alterations were made to the Summary of Product Characteristics to clarify some of the above issues and a RMP has been agreed.
Day 60	02.05.06
Outcome	Agreement reached

Name of the product in the RMS	Metoprolol/Felodipin Yes	Metofelosan, Mefelof, Mefesan, Mefecur	Mefecomb
Active substance	felodipine/metoprolol tartrate		
Pharmaceutical form	Prolonged release tablet		
Procedure number	DK/H/853/01	DK/H/854, 884-6/01	DK/H/887/01
CMS	BE, DE, FI, LU	DE	DE, FI, LU
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic		
Grounds for referral to CMD(h)	Different interpretation of the submitted study to establish therapeutic equivalence.		
Day 60	02.05.06		
Outcome	Referred to CHMP for arbitration		

Name of the product in the RMS	Yasminelle	Belanette	Yasminelle 28
Active substance	Drospirenone, ethinyl estradiol		
Pharmaceutical form	Film-coated tablet		
Procedure number	NL/H/701/01	NL/H/702/01	NL/H/704/01
CMS	AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IS, IT, LV, LT, MT, NO, PL, PT, SK, SI, SE, UK	AT, BE, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IT, LV, LT, MT, NO, PL, PT, SK, SI, SE, UK	DK, ES, FR, NO, SE
Legal basis	Art 8.3 Dir 2001/83/EC - Full Dossier		
Grounds for referral to CMD(h)	The proposed package leaflet (PL) is not in accordance with the Directive 2001/83/EC, which states that "the package leaflet must be written and designed to be clear and understandable, enabling the user to act appropriately". The proposed PL is too long, repetitive and alarming for women, with too many details, which are not relevant and not always understandable for women. The text in the paragraph on liver tumours under section <i>Yasminelle and cancer</i> is not agreed, like the recommendations on the shift/delay of menstrual period.		
Day 60	02.05.06		
Outcome	Agreement reached. The MAH commits to perform user consultation in two Member States, amongst France.		

Name of the product in the RMS	Paroxetine Ranbaxy 20mg
Active substance	paroxetine
Pharmaceutical form	Film-coated tablet
Procedure number	DE/H/0574/01
CMS	BE, DK, ES, FI, IS, NL, NO, PT, SE, UK
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic
Grounds for referral to CMD(h)	The bioequivalence data submitted with the application have been regarded by CMS as not in agreement with the criteria given in the 'Note for Guidance on the Investigation of Bioavailability and Bioequivalence'.
Day 60	02.05.06
Outcome	Agreement reached following a scientific discussion at the CMD(h)-Meeting.
	The CMD(h) and the MS concerned have noted, that not all criteria mentioned in the 'Note for Guidance on the Investigation of Bioavailability and Bioequivalence' are fulfilled. However, due to the nature of the medicinal product, these deviations are not of clinical relevance and therefore not a risk to public health. The CMD(h) has agreed to forward questions with regard to the scientific methodology to the PK Study Group of the Efficacy Working Party of the CHMP for further discussion.

Name of the product in the RMS	Sumatriptan Basics 50/100 mg	Sumatriptan Basics F 50/100 mg	Sumatriptan Basics A 50/100 mg	Sumatriptan Basics B 50/100 mg
Active substance	Sumatriptan succinate			
Pharmaceutical form	tablet			
Procedure number	DE/H/0530/00 1-2	DE/H/0545/00 1-2	DE/H/0591/001-2	DE/H/0592/001-2
CMS	AT, BE, CZ, EE, EL, ES, IS, IT, LT, LU, LV, NL, PL, SI, SK, UK	DK, FI, NO, SE	AT, BE, ES, LU, NL, UK	DK, FI, NO, SE
Legal basis	Article 10.1(a)(iii), Directive 2001/83/EC - Generic			
Grounds for referral to CMD(h)	Non-GCP compliance of the submitted bioequivalence study.			
Day 60	02.05.06			
Outcome	Withdrawal of the marketing authorisation and applications in the RMS and CMS. No further actions were deemed to be necessary by the CMD(h), as the potential serious risk to public health raised was not related to the active substance, but to the specific medicinal products.			

INFORMAL CMD(h) MEETING HELD ON 18 AND 19 MAY 2006, VIENNA, AUSTRIA

The CMD(h) convened for an Informal Meeting on 18th and 19th May 2006 in Vienna, Austria, chaired by the CMD(h) Vice-Chair Christa Wirthumer-Hoche.

The Meeting was held as part of a programme of events organised under the Austrian Presidency of the EU, in parallel to the Informal CHMP and COMP.

- Joint meeting CHMP – CMD(h)

A joint meeting between the CHMP and CMD(h) took place in order to discuss the experience with CMD(h) referrals. A closer cooperation was agreed with regard to the update and interpretation of guidelines, in particular the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

- European Pharmacopoeia (EP) requirement for Influenza vaccines
Based on new requirements in the EP 5.3, the maximum amount of ovalbumin has to be stated in the labelling of the Influenza vaccines. This should be done until the end of June 2006 or if Companies are not ready with the new labelling, in order not to jeopardize seasonal flu vaccination, the national competent authorities will accept a change in the labelling later via a variation application. This approach was confirmed at the May CMD(h) meeting.
- Experience with DCP
The discussions on the decentralised procedure were mainly focussed on MS experience until day 105 of the procedure, in particular on communication between day 100 and 105, as there are no applications in the DCP finalised yet.
- Potential serious risk to public health
The Commission presented the final Guideline on “Potential serious risk to public health” which will be published on 5 June 2006 on the Commission website in Eudralex, Vol.1. The guideline will be translated into all national EU-languages. Annexed separately to the guideline there will be a list of examples of issues, which normally would not be considered as grounds for a ‘potential serious risk to public health’ and will be updated as experience is gained. This annex will be published in Eudralex, Vol.2C.
- Readability/ User testing
Different methods for user testing were discussed and MSs agreed to be flexible in accepting different testing methods. A valid interpretation and justification on the methods used, language tested, etc., should be provided by the Applicant.
The need for readability/user testing for already authorised medicinal products where significant changes are made to the package leaflet was also discussed and would be further considered by the CMD(h).

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **9** new Mutual Recognition Procedures were finalised during the month of April 2006. **2** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period. There has not been any Mutual Recognition Procedures for new applications referred to CHMP in this period.

The status as of 30th April 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	161	153	34 N.A.	11	7

48 Mutual Recognition Procedures (regarding **90** products) started in April 2006. The categories of these procedures are as follows:

1 new active substance, which is a repeat use.

8 known active substances (already authorised in at least one member state), including **1** repeat use.

37 abridged applications including **14** multiple applications and **3** repeat use.

2 line extension application, including **1** repeat use.

The new procedures started in April related to **8** full dossiers, **32** generics, **6** hybrid applications, **1** similar-biological application and **1** bibliographic application.

The procedures consisted of **46** chemical substances and **1** biological blood product and **1** biological vaccine product.

All of these procedures were prescription-only medicinal products in the reference Member State².

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 April 2006.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
CZ (2)	4
CZ (4)	5
CZ (3)	5
DE (1)	6
DE (2)	1
DE (1)	5
DE (1)	9
DE (4)	6
DK (1)	7
DK (4)	7
FI (2)	2
FI (1)	7
FI (1)	3
FI (1)	5
FI (1)	1
FI (1)	1
FI (1)	1
FI (1)	1
FI (2)	17
FI (2)	4
FI (2)	10
FI (2)	4
FI (2)	12
FI (1)	6
FR (1)	11
FR (1)	1
IT (1)	6
IT (4)	3
IT (1)	13
IT (1)	5
NL (1)	20
NL (3)	2
NL (3)	2
NL (2)	1
NL (2)	8
NL (2)	3
NL (3)	1
NL (3)	3
NL (2)	1
NL (2)	1
SE (4)	11
SE (1)	27
SE (1)	4
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	1

Decentralised Procedure

The status as of 30th April 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	--	121*	--	--	--

25 Decentralised Procedures (regarding **65** products) started in April 2006. The categories of these procedures are as follows:

24 abridged applications including **8** multiple applications.

1 known active substance (already authorised in at least one member state), which was an initial application.

The new Decentralised procedures started related to **1** full dossier and **24** generic applications.

The procedures consisted of **25** chemical substances³.

All of these procedures were prescription-only medicinal products in the reference Member State⁴.

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.

* The number of procedures from new applications in process for the months of January, February and March provided in previous press releases were incorrect. The correct numbers were 22 for January, 34 for February and 30 for March. This gives a total of 96 procedures in process as of 31 March 2006.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DK (6)	8
DK (3)	7
DK (3)	5
DK (1)	3
FR (3)	5
NL (2)	18
NL (2)	11
NL (2)	9
NL (2)	2
NL (3)	19
NL (3)	7
NL (3)	5
NL (3)	1
SE (3)	10
UK (3)	17
UK (3)	3
UK (2)	14
UK (1)	9
UK (1)	8
UK (1)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **337** type IA variations, **176** type IB variations and **109** type II variations were finalised during the month of April 2006. **16** renewals were finalised in this period.

The status as of 30th April 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	1329	708	529	93	--

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):

Mrs. Truus Janse-de Hoog

College ter Beoordeling van Geneesmiddelen

Kalvermarkt 53

NL – 2500 Den Haag , The Netherlands

Phone: + 31 70 356 74 08

Fax: + 31 70 356 75 15

E-mail: gm.janse@cbg-meb.nl

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

<http://heads.medagencies.org/>