

Report from the CMDh meeting held on 16th, 17th and 18th November 2009

New variation regulation – transition period

Applicants are reminded that variation Regulations (EC) No 1234/2008 will apply to submissions as of 1st January 2010. Applicants have to make sure that **all** national competent authorities involved in the procedure will receive the applications submitted according to Regulation (EC) No 1084/2003 before 1st January 2010.

A Question & Answer will be published on the CMDh website to address the transition period and answer general questions in relation with the implementation of Regulation (EC) No 1234/2008.

In order to ease the transition, the CMDh **strongly recommends** not to submit any variation intended to be handled according to Regulation (EC) No 1084/2003 after 15th December 2009.

Electronic submissions

The HMA has endorsed the proposal from CMDh to handle the national translations outside of e-CTD in order to simplify the use of e-CTD format in Mutual Recognition and Decentralised Procedures. This will be incorporated in the coming update of the CMDh BPG for eCTD in MRP and DCP.

CMDh recommendations regarding the use of Certificates of Suitability (CEPs) and Active Substance Master Files in module 3 of dossiers of biological substances of non-recombinant origin

The European Directorate for the Quality of Medicines (EDQM) published on 22.10.09 its decision to exclude from the scope of the Certification Procedure, the products that have been classified as “other biological substances” by the CMDh. (See EDQM website link: <http://www.edqm.eu/site/News-General-Information-164.html>)

A list of these other biological substances is available on the CMDh website: http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/procedural_guidance/Compilation_Biological_Active_Substance_non-recombinant_origin.pdf.

Further to this publication by EDQM, the CMDh has agreed on the following **recommendations**:

a) Applicants are requested to submit full data on the Module 3 for new applications for Marketing Authorisation for medicinal products containing these biological substances. Existing CEPs for these substances can be included in the dossiers but should not be used as replacement of the relevant data in the corresponding sections of Module 3.

b) In the case of already authorised medicinal products containing a CEP as replacement of the relevant data in the corresponding section of Module 3 that intend to use the Mutual Recognition Procedure (MRP) or the repeat use MRP, applicants should liaise with the Reference Member State for inclusion of the relevant data in the module 3 prior to the start of the procedure.

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The reasoning behind this decision is that for biologicals the characterisation and determination of the quality of these products requires not only a combination of physico-chemical and biological testing, but also extensive knowledge over the production process and its control.

Applicants are also reminded that Active Substance Master Files (ASMF) are not applicable to biological medicinal products (See CMDh website: <http://www.hma.eu/215.html>).

Cyproterone acetate and the risk of meningiomas

The CMDh has endorsed the PhVWP report on cyproterone acetate and the risk of meningiomas and recommends the implementation of the PhVWP wording for the SmPC and PL for all products containing cyproterone acetate.

The following timetable has been agreed by the CMDh and PhVWP for implementation of agreed SmPC and PL changes:

15 January 2010	Variation applications requested through CMDh
15 March 2010	Variation applications submitted by MA holders
15 May 2010	Variation applications approved by RMS

The PhVWP recommended SmPC and package leaflet wording will be published on the CMDh website, under “Product information, PhVWP recommendations”.

Phenytoin-induced Stevens-Johnson syndrome (SJS) in association with HLA-B*1502 allele in individuals of Thai or Han Chinese origin

The CMDh has endorsed the PhVWP report on the increased risk of developing SJS in individuals of Thai and Han Chinese origin when treated with phenytoin and recommends the implementation of the wording for the SmPC and PL for all products containing phenytoin.

The agreed changes in the SmPC and PL should be implemented commencing from January 2010 according to timescales notified by the RMS and national competent authorities.

The PhVWP recommended SmPC and package leaflet wording will be published on the CMDh website, under “Product information, PhVWP recommendations”.

Adverse events to be included in the Product Information of HMG CoA Reductase Inhibitors

Applicants are reminded that the CMDh has recommended the implementation of the PhVWP agreed wording for the SmPC and PL for all HMG CoA reductase inhibitor containing products and that the agreed changes in the SmPC and PL should be implemented rapidly commencing from the end of October 2009 according to timescales notified by the RMS and national competent authorities.

The PhVWP recommended SmPC and package leaflet wording will be published on the CMDh website, under “Product information, PhVWP recommendations”.

EU Work-sharing Article 45 of the Paediatric Regulation – Public Assessment Reports

The CMDh has agreed on public assessment reports for paediatric studies submitted in accordance with Article 45 of the Paediatric Regulation for glucosamine, lisinopril, amlodipine and felodipine including a recommendation for the text to be included in the SmPC and package leaflet. The public assessment reports will be published on the CMDh website, under “Paediatric Regulation, Assessment reports”.

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Marketing Authorisation Holders of medicinal products with the same active substances and pharmaceutical forms are requested to include this information in their SmPCs and package leaflets within 90 days of publication of the public assessment reports, in accordance with the Best Practice Guide – Article 45, EU Work-sharing procedure.

Meeting between the CMDh and Interested Parties

The CMDh met with Interested Parties on Monday 16 November 2009 to discuss member states' resources in MRP/CDP and the contribution of CMDh to the HMA taskforce on resources, the status of the implementation of electronic submissions in member states, proposals to amend the SOP on DCP and the implementation of the new variation regulation.

All presentations will be published on the CMDh website under "About CMDh", "Contact with Representative Organisations".

Joint Pharmacovigilance working party and CMDh working group on PSUR worksharing

PhVWP and CMDh have adopted a Best Practice Guide for work sharing concerning the assessment of PSURs of products for which an EU harmonised virtual birth date and related harmonised data lock point have been agreed.

PhVWP and CMDh have also adopted a Guidance document for marketing authorisation holders on submissions of PSURs under the EU PSUR work sharing scheme.

Both documents will be published on the Heads of Medicines Agencies website: <http://www.hma.eu/80.html>.

Working Party on the future of CMDh

Following the informal meeting held on 5th and 6th October 2009 in Uppsala, Sweden, the CMDh agreed to set-up a new working party to discuss the future of CMDh. The mandate of the new group will be published on the CMDh website, under CMDh subgroups/working groups.

Recommendation on submission dates for Applicants of the Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP)

The CMDh has adopted an updated recommendation on submission dates for Applicants of the Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP) in order to facilitate planning of submission dates for new applications in the DCP in 2010.

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

Information on the name of the product in the RMS, active substance, pharmaceutical forms, procedure number, CMS, legal basis, grounds for referral to CMDh, Day 60 and outcome of the procedure, for the referrals to the CMDh finalised on 29.10.2009 will be available on the table with information on all applications referred to the CMDh, published under "CMDh-Referrals".

NEW APPLICATIONS

Mutual Recognition Procedure

The CMDh noted that **33** Mutual Recognition Procedures were finalised during the month of October 2009. **5** Mutual Recognition Procedures were referred to CMDh in this period. There was **1** Mutual Recognition Procedures referred to CHMP in this period.

The status as of 31st October 2009 of procedures under Mutual Recognition is as follows:

Year	New applications finalised ¹	New applications in process	Referred to CMDh	Agreement reached in the CMDh		Withdrawn during CMDh referral	Applications referred to CHMP	
				For procedures referred in			For procedures referred to CMDh in	
				2008	2009	2008	2009	
2009	312	62	18	2	5	0	2	

5 Mutual Recognition Procedures (regarding **10** products) started in October 2009. The categories of these procedures are as follows:

4 abridged applications, including **1** multiple and **1** repeat use applications.

1 known active substance application.

The new procedures started in October 2009 related to **1** full dossier and **4** generic applications.

¹ Due to late database updates cumulative yearly figure differs from the monthly figures. Cumulative yearly figure includes late database updates on finalised procedures not captured in the monthly figures published in press releases. The applications referred to CHMP are included in the 'new applications finalised.'

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All of these procedures consisted of chemical substance products. All of these procedures related to prescription-only medicinal products in the reference Member State².

New applications in Mutual Recognition procedure started in October 2009.

Member State	Number of times involved in a procedure as RMS	Number of times involved in a procedure as CMS
Austria		2
Belgium		
Bulgaria		1
Cyprus		
Czech Republic		1
Denmark		
Estonia		1
Finland		
France		
Germany		2
Greece		1
Hungary		1
Iceland	1	2
Ireland		
Italy		1
Latvia		1
Lithuania		1
Luxembourg		
Malta		
Netherlands	2	2
Norway		
Poland		1
Portugal		2
Romania		1
Slovak Republic		1
Slovenia		1
Spain		
Sweden	2	2
United Kingdom		1

Decentralised Procedure1

The CMDh noted that there were **128** Decentralised procedures finalised with a positive outcome and **9** procedures finalised with a negative outcome. **1** Decentralised procedure was referred to the CMDh in this period. There were **3** Decentralised procedures referred to the CHMP in this period.

The status as of 31st October 2009 of procedures under Decentralised Procedure is as follows:

Year	New applications finalised ³	New applications withdrawn (After day 120)	New applications in process	Referred to CMDh	Agreement reached in the CMDh		Withdrawn during CMDh referral	Referred to CHMP	
					For procedures referred in 2008	2009		For procedures referred to CMDh in 2008	2009
2009	996	19	1707	18	8	8	0	1	7

116 Decentralised Procedures (regarding **211** products) started in October 2009. The categories of these procedures are as follows:

103 abridged applications, including **32** multiple applications.

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.

³ Due to late database updates cumulative yearly figure differs from the monthly figures. Cumulative yearly figure includes late database updates on finalised procedures not captured in the monthly figures published in press releases. This cumulative figure includes positive and negative procedures as well as those referred to CHMP.

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9 known active substance applications.

4 line extension applications.

The new Decentralised procedures started in October related to **76** generic, **5** full dossier, **5** bibliographic and **30** hybrid.

115 of these procedures consisted of chemical substance applications and **1** procedure consisted of a biological vaccine product.

107 of these procedures related to prescription-only medicinal products and **9** procedures related to non-prescription medicinal products in the reference Member State⁴.

New applications in Decentralised procedure started in October 2009.

Member State	Number of times involved in a procedure as RMS	Number of times involved in a procedure as CMS
Austria	2	29
Belgium		32
Bulgaria		22
Cyprus		11
Czech Republic	1	26
Denmark	6	41
Estonia	8	25
Finland		32
France	3	33
Germany	25	71
Greece		16
Hungary		19
Iceland		9
Ireland	3	23
Italy		33
Latvia		20
Lithuania		23
Luxembourg		22
Malta		5
Netherlands	19	47
Norway	2	28
Poland		39
Portugal	2	28
Romania		21
Slovak Republic		22
Slovenia		9
Spain		37
Sweden	9	43
United Kingdom	36	54

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMDh noted that **523** type IA variations, **263** type IB variations and **242** type II variations were finalised during the month of October 2009. **64** renewals were finalised in this period. There were **no** procedures referred to the CHMP in this period.

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.

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The status as of 31st October 2009 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	Applications referred to CHMP
2009	5865	3015	2503	462	5

All documents mentioned in this press release can be found at the CMDh website under the heading *Press Releases*.

Information on the above mentioned issues can be obtained from the chair of the CMDh or from the CMDh Secretariat:

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*Or you could visit the **CMDh website** at:*

<http://www.hma.eu/cmdh.html>