

Report from the CMD(h) meeting held on 21st, 22nd and 23rd July 2008

CMD(h)/EMEA Sub-Group on Paediatric Regulation

Applicants are reminded that applications for marketing authorisation, in respect of medicinal products which are not authorised in the Community, submitted as of 26 July 2008 will only be regarded as valid if they include either the results of all studies performed and details of all information collected in compliance with an agreed paediatric investigation plan (PIP) OR a decision of the EMEA granting a product-specific or a class waiver OR a decision of the EMEA granting a deferral.

This requirement does not apply to medicinal products authorised or applied for under Article 10 – Generics, Hybrids, Similar biologicals, Article 10a – Well-established use, Articles 13 to 16 – Homeopathic medicinal products or Articles 16a to 16i – Traditional herbal medicinal products of Directive 2001/83/EC, as amended.

The CMD(h) has agreed, in an initial phase until experience is gained by National Competent Authorities on check of compliance with paediatric investigation plans, to request the Paediatric Committee, when validating an application, to assess compliance of the application for Marketing Authorisation with the agreed paediatric investigation plan concerned, as foreseen in Article 23(2) of Regulation (EC) No 1901/2006.

The CMD(h) would, therefore, like to advise Applicants to consider requesting the Paediatric Committee to assess compliance of the application for Marketing Authorisation with the agreed paediatric investigation plan, prior to submitting an application for marketing authorisation.

The CMD(h) has agreed to extend the deadline for comments on the procedural guidance to facilitate the submission of paediatric data according to Article 46 of the Paediatric Regulation until 5th September 2008. Any comments on the procedural guidance should be submitted to the attention of the CMD(h) secretariat (H-CMDhSecretariat@emea.europa.eu).

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 the agreed criteria, for discussion at the September Sub-Group meeting. The Group agreed also to consider differences in information on pregnancy and lactation and to take into account patients' perspectives when considering differences in SPCs between MSs.

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.

Sub-Group on Variation Regulation

The CMD(h) has set up a Sub-Group together with the CMD(v) and the EMEA, to take forward the various activities arising from the revision of the Variation Regulation.

The first meeting of the Sub-Group focused on the main tasks for the Sub-Group, including proposed actions and deadlines. These include the development of several procedures needed by the Variation Regulation, e.g. recommendation on classification of unforeseen variations, update of the CMD(h) referral SOP, work sharing procedure, etc.

The mandate and objectives of the Sub-Group, participants and frequency of meetings were also discussed.

Referrals to CMD(h) in the first semester of 2008 – Statistical information

The CMD(h) has agreed to publish statistical information on the applications referred/concluded by the CMD(h) in the first semester of 2008, addressing referrals to CMD(h) per type of procedure (MRP vs DCP), per type of product, per legal basis, per therapeutic area, per grounds and per outcome. This information will be published on the CMD(h) website under ‘Statistics’.

Working Group on Validation issues/National requirements

Further to the work carried out by the Working Group on Validation issues/National requirements, the CMD(h) has agreed on the following documents that will be published on the website:

- Common grounds seen for delaying Day 0 Renewals
- Updated table with additional data requested for new applications in the mutual recognition and decentralised procedures.

EU Work sharing procedure – Change in qualitative and quantitative composition of rubber stoppers of West Pharmaceutical Services

The CMD(h) has concluded a work sharing procedure which concerns the replacement of a rubber elastomer component – polyisobutylene by halogenated butyl rubber, which is the main rubber component of the elastomers. The proposed change does not concern a specific marketing authorisation, but the rubber is used for the manufacture of vial and plunger stoppers that form part of the immediate packaging material to a wide range of medicinal products.

The CMD(h) has agreed to follow a Type I, no. 29 variation for chemical medicinal products approved via MRP/DCP and a 30 days Type II variation for medicinal products not fulfilling the conditions of Type I, no. 29, i.e. sterile and biological medicinal products. All the other conditions and documentation requirements of Type I no. 29 should be fulfilled.

The CMD(h) has prepared a public assessment report, further to the EU work sharing procedure that will be published on the CMD(h) website.

Marketing Authorisation Holders should refer to the work sharing procedure when submitting the corresponding variation applications in the Member States.

Implementation of warnings on antiepileptics and suicidal behaviour

Further to the meeting of the PhVWP and CMD(h) with representatives of EFPIA and the MAHs for products authorised nationally and through MR/DC procedures on 25th June 2008, to discuss the proposals to update section 4.4. of the SPC for all antiepileptics to include a class warning about the risk of suicidal thoughts and behaviour and of the proposed implementation plan, the following timetable has been agreed by the CMD(h) and PhVWP for implementation of warnings on suicidal thoughts and behaviour for antidepressants:

15 September 2008	Variation applications requested by NCAs
15 October 2008	Variation applications submitted by MA holders
15 January 2009	Variation applications approved by NCAs
15 April 2009	Updated PLs into new production batches

The agreed SPC and package leaflet wording and communication documents, including a key statement and a Q&A document will be published on the CMD(h) website, under ‘Pharmacovigilance, PhVWP recommendations’.

Carbamazepine related Stevens Johnson Syndrome and association with HLA-B*1502 – Plan for implementation of agreed SPC (sections 4.2 and 4.4) and package leaflet changes

Further to the PhVWP report to CMD(h) on carbamazepine related Stevens Johnson Syndrome and association with HLA-B*1502, agreed by the PhVWP in June 2008, the CMD(h) agreed to follow the same timetable for the implementation of the changes to the product information, as the one agreed for the implementation of warnings on antiepileptics and suicidal behaviour, i.e.:

15 September 2008	Variation applications requested on the CMD(h) website
15 October 2008	Variation applications submitted by MA holders
15 January 2009	Variation applications approved by NCAs
15 April 2009	Updated PLs into new production batches

The agreed SPC and package leaflet wording will be published on the CMD(h) website, under ‘Pharmacovigilance, PhVWP recommendations’.

Please note that for the above mentioned variations to implement the recommendations from the PhVWP, Marketing Authorisation Holders are not required to submit supporting information and the variations will be accepted by Member States Competent Authorities without further assessment or amendment.

Information on applications referred to the CMD(h) 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 CMD(h), Day 60 and outcome of the procedure, for the referrals to the CMD(h) finalised on 03.07.2008 will be available on the table with information on all applications referred to the CMD(h), published under ‘CMD(h)-Referrals’.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **33** Mutual Recognition Procedures were finalised during the month of June 2008. **4** Mutual Recognition Procedures were referred to CMD(h) in this period. There were **no** Mutual Recognition Procedures referred to CHMP in this period.

The status as of 30th June 2008 of procedures under Mutual Recognition is as follows:

Year	New applications finalised ¹	New applications in process	Referred to CMD(h)	Agreement reached in the CMD(h)		Withdrawn during CMD(h) referral	Applications referred to CHMP	
				For procedures referred in 2007	2008		For procedures referred to CMD(h) in 2007	2008
2008	202	115	27	7	9	1	2	1

20 Mutual Recognition Procedures (regarding **43** products) started in June 2008. The categories of these procedures are as follows:

19 abridged applications, including **3** multiple and **5** repeat use applications.

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

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 new procedures started in June 2008 related to **1** full dossier, **17** generic and **2** hybrid applications.

All of these procedures consisted of chemical substance products.

19 of these procedures related to prescription-only medicinal products and **1** procedure related to a non-prescription medicinal product in the reference Member State².

Number of countries involved in the new applications in Mutual Recognition procedure started in June 2008.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
CZ (2)	1
DE (1)	2
DK (1)	7
DK (2)	3
FR (1)	13
FR (1)	18
LV (1)	4
NL (3)	10
NL (1)	20
NL (1)	4
NL (1)	4
NL (3)	6
NL (2)	1
NL (3)	5
SE (2)	7
SE (5)	9
SE (5)	2
SE (5)	3
UK (2)	9
UK (4)	12

Decentralised Procedure

The CMD(h) noted that there were **64** Decentralised Procedures finalised with a positive outcome during the month of June 2008. **3** Decentralised Procedures were withdrawn after day 120. **5** Decentralised Procedures were referred to the CMD(h) in this period. There were **no** Decentralised Procedures referred to the CHMP in this period.

The status as of 30th June 2008 of procedures under Decentralised Procedure is as follows:

Year	New applications finalised ³		New applications withdrawn ⁴	New applications in process	Referred to CMD(h)	Agreement reached in the CMD(h) For procedures referred in		Withdrawn during CMD(h) referral	Referred to CHMP For procedures referred to CMD(h) in	
	Positive outcome	Negative outcome				2007	2008		2007	2008
2008	365	4	4	1273	19	2	10	1	2	--

106 Decentralised Procedures (regarding **271** products) started in June 2008. The categories of these procedures are as follows:

100 abridged applications, including **31** multiple applications.

5 known active substance applications, including **1** multiple application.

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.

⁴ After day 120.

1 line extension application.

The new Decentralised procedures started in June related to **96** generic, **2** bibliographic, **5** hybrid and **3** full dossiers.

All of these procedures consisted of chemical substance applications.

102 of these procedures related to prescription-only medicinal products and **4** to non-prescription medicinal products in the reference Member State⁵.

Number of countries involved in the new applications in Decentralised procedures started in June 2008.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (1)	1
AT (1)	1
DE (1)	14
DE (1)	21
DE (5)	18
DE (5)	8
DE (5)	4
DE (5)	1
DE (5)	2
DE (5)	1
DE (5)	1
DE (5)	1
DE (5)	1
DE (5)	1
DE (10)	6
DE (6)	24
DE (1)	5
DE (1)	6
DE (4)	6
DE (4)	4
DE (4)	1
DE (4)	13
DK (2)	1
DK (2)	2
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	11
DK (2)	2
DK (2)	14
DK (2)	1
DK (2)	1
DK (2)	4
DK (2)	14
DK (2)	10
DK (2)	9
DK (4)	12
DK (4)	1
DK (4)	1
DK (2)	6
DK (2)	5
DK (4)	23
DK (4)	8
DK (4)	9
FI (1)	7
FR (1)	15

⁵ 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.

HU (6)	8
HU (6)	1
HU (1)	8
NL (4)	4
SE (3)	9
UK (2)	5
UK (1)	6
UK (1)	14
UK (1)	5
UK (1)	5
UK (2)	5
UK (4)	8
UK (4)	8
UK (4)	1
UK (4)	1
UK (4)	1
UK (1)	7
UK (1)	2
UK (2)	7
UK (1)	7
UK (1)	7
UK (1)	5
UK (1)	6
UK (1)	1
UK (1)	1
UK (1)	1
UK (2)	15
UK (2)	16
UK (2)	11
UK (2)	2
UK (2)	2
UK (2)	9
UK (1)	18
UK (1)	27
UK (1)	1
UK (2)	21
UK (2)	7
UK (2)	6
UK (2)	4
UK (1)	1
UK (1)	1
UK (1)	1
UK (2)	18
UK (1)	1
UK (3)	12
UK (2)	4
UK (2)	23
UK (3)	4
UK (4)	16
UK (4)	1
UK (4)	1
UK (4)	1
UK (2)	1
UK (1)	6
UK (1)	4
UK (1)	1
UK (1)	2
UK (1)	6

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **591** type IA variations, **236** type IB variations and **216** type II variations were finalised during the month of June 2008. **38** renewals were finalised in this period. There were **no** procedures referred to the CHMP in this period.

The status as of 30th June 2008 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
2008	3261	1289	1376	203	2

All documents mentioned in this press release can be found at the CMD(h) website 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:*

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