

Report from the CMD(h) meeting held on 27th and 28th May 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.

For further information, please refer to Q&As 17, 18 and 19 of the Question and Answers document – Submission of Paediatric studies according to Articles 45&46 of the Regulation of the European Parliament and of the Council (EC) No 1901/2006, as amended and other paediatric information, published on the CMD(h) website.

Evaluation of the functioning of the CMD(h) – Questionnaire to Interested Parties

The CMD(h) agreed, as a priority for 2008, to evaluate the functioning of the CMD(h) and consider how further improvements in the operation of the Group can be achieved.

As part of this evaluation, the CMD(h) considers very important to collect the views of Interested Parties on the functioning of the CMD(h) and any comments/suggestions for improvement.

The CMD(h) has agreed a questionnaire, which will be sent to Trade Associations and published on the CMD(h) website.

Responses to the questionnaire should be sent to the CMD(h) Secretariat (H-CMDhSecretariat@emea.europa.eu) by 10th July 2008 coordinated, where possible, by Trade Associations.

Change of the Reference Member State

Marketing Authorisation Holders are reminded that a change of the Reference Member State cannot take place during pending procedures and, therefore, should ensure that all pending procedures (including variations and renewals) are finalised, in order to allow for a change of the Reference Member State.

For further information please refer to the CMD(h) Position on changing the Reference Member State, published on the CMD(h) website.

Informal CMD(h) meeting - Kranjska Gora, Slovenia

An informal meeting will be held in Kranjska Gora on 10-11 June 2008. The meeting will include a joint session with the CHMP to discuss experience on Article 29(4) referrals, how to increase transparency on outcome of referrals and the Paediatric Regulation. The CMD(h) will also discuss amongst other topics the role of the CMD(h) after revision of the Variation Regulation, the evaluation of the functioning of the CMD(h), validation issues and duration of clock-stops in the decentralised procedure.

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 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 referral to the CMD(h) finalised on 30.04.2008.

Name of the product in the RMS	Imazol Cream plus	Imazol Paste
Active substance	clotrimazole/hexamidine	clotrimazole
Pharmaceutical form	Cream	Cutaneous paste
Procedure number	DE/H/1013/001/MR	DE/H/1014/001/MR
CMS	AT, BE, BG, EE, HU, NL, PL, RO	AT, BE, EE, HU, NL, PL, RO
Legal basis	Art 10a Dir 2001/83/EC - Bibliographic	
Grounds for referral to CMD(h)	The applications have been referred to the CMD(h) on the claimed basis that there are neither published data nor submitted clinical studies to substantiate the clinical efficacy of the active substance or the combination of the active substances in the claimed indications. The claim of well established use is questionable.	
Day 60	30 th April 2008	
Outcome	There was an oral explanation by the Applicant and presentations made by the RMS and CMS. RMS as well as referring CMS presented their position on the acceptability of the presented data in the light of the claimed 'well established use' of the active substances in the sought indications. Agreement reached.	

Name of the product in the RMS	Salbutamol Easyhaler "Orion"
Active substance	salbutamol
Pharmaceutical form	Inhalation powder
Procedure number	DK/H/0125/001-002/E002
CMS	DK/H/0125/001/E002: AT, EL, FR, IT (1st wave) ES (2nd wave) CZ, EE, LT, LV, NL, SK (3rd wave) DK/H/0125/002/E002: AT, EL, IT (1st wave) ES (2nd wave) CZ, EE, LT, LV, NL, SK (3rd wave)
Legal basis	Art 10.3 Dir 2001/83/EC - Hybrid
Grounds for referral to CMD(h)	The procedure was referred to the CMD(h) due to potential serious risk to public health concerns on grounds that the design of the pivotal trials is not sensitive enough to prove therapeutical equivalence.
Day 60	30 th April 2008
Outcome	At the CMD(h) meeting, RMS, CMS and the applicant presented their view on the outstanding issues. No agreement was reached at the meeting or within the timeframe of the referral procedure. The objecting CMS was of the opinion that lack of assay sensitivity of the studies was of public serious health concerns. Referred to CHMP for arbitration.

Name of the product in the RMS	Mifegyne
Active substance	mifeprestone
Pharmaceutical form	Tablet
Procedure number	FR/H/0137/001/E002
CMS	AT, BE, DE, DK, EL, ES, FI, NL (1st wave) LU (2nd wave) IT, PT, RO, HU (3rd wave)
Legal basis	Art 8.3(i) Dir 2001/83/EC – Full dossier
Grounds for referral to CMD(h)	The procedure was referred to the CMD(h) due to the fact that in one Member State, the combined medicinal product (prostaglandin containing product) needed to ensure the safe and effective use of Mifegyne in two claimed indications is not authorised.
Day 60	30 th April 2008
Outcome	At the CMD(h) meeting the RMS presented its view and the applicant's written response was discussed. There was a discussion on whether this product could be approved in the claimed indications in the particular situation where the combined product is not authorised.

	The CMD(h) accepted the withdrawal of the application in the disagreeing Member State, on the basis that the issue raised was not considered as a potential serious risk to public health. Agreement reached.
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Name of the product in the RMS	Perindopril Ranbaxy 8 mg
Active substance	perindopril
Pharmaceutical form	Tablet
Procedure number	NL/H/0977/003/DC
CMS	BE, CZ, EE, FI, HU, LT, LV, PL, SK, UK
Legal basis	Art 10.1 Dir 2001/83/EC - Generic
Grounds for referral to CMD(h)	There was a concern with regard to the extrapolation of results from the bioequivalence study with the 4mg strength in support of the marketing authorisation application of the 8 mg strength.
Day 60	30 th April 2008
Outcome	At the CMD(h) meeting the RMS presented its view and the applicant's written response was discussed. The question on whether perindopril has linear pharmacokinetics will be put forward to the PK subgroup of the EWP. Agreement reached. The CMD(h) took account, in the discussion, of an on-going bioequivalence study with the 8 mg strength.

Name of the product in the RMS	Yaz 24+4	Ethinylestradiol/Drospirenon 24+4
Active substance	drospirenone / ethinylestradiol	
Pharmaceutical form	Film-coated tablet	
Procedure number	NL/H/1269/001/MR	NL/H/1270/001/MR
CMS	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, IE, IS, IT, LT, LV, MT, NO, PL, PT, RO, SE, SI, SK, UK	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, IE, IS, IT, LT, LU, LV, MT, NO, PL, PT, RO, SE, SI, SK, UK
Legal basis	Art 8.3(i) Dir 2001/83/EC – Full dossier	
Grounds for referral to CMD(h)	There was a concern with regard to the indication 'treatment of moderate acne vulgaris only in women seeking oral contraception'.	
Day 60	30 th April 2008	
Outcome	At the CMD(h) meeting the RMS presented its view and the applicant's written response was discussed. The applicant made use of an oral hearing. A discussion was held whether this indication could be acceptable. The indication was removed and information on the study results on acne vulgaris was placed in section 5.1 of the SPC. Agreement reached.	

Name of the product in the RMS	Hyderm
Active substance	hydrocortisone
Pharmaceutical form	Cream
Procedure number	SE/H/0619/001/MR
CMS	DK, FI
Legal basis	Art 10.1 Dir 2001/83/EC - Generic
Grounds for referral to CMD(h)	The procedure was referred to the CMD(h) due to potential serious risk to public health concerns on grounds that there was a need to introduce additional contraindications, warnings and adverse events in sections 4.3, 4.4. and 4.8 of the SPC.
Day 60	30 th April 2008
Outcome	The applicant circulated revised product information taking into account some of the concerns raised and provided a justification for not including the remaining concerns raised. Agreement was reached before the CMD(h) meeting.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **52** Mutual Recognition Procedures were finalised during the month of April 2008. **2** Mutual Recognition Procedures were referred to CMD(h) in this period. **1** Mutual Recognition Procedure was referred to CHMP in this period.

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

Year	New applications finalised	New applications in process	Referred to CMD(h)	Agreement reached in the CMD(h) For procedures referred in		Withdrawn during CMD(h) referral	Applications referred to CHMP For procedures referred to CMD(h) in	
				2007	2008		2007	2008
2008	138	146	12	7	7	--	2	1

40 Mutual Recognition Procedures (regarding **69** products) started in April 2008. The categories of these procedures are as follows:

6 known active substance (already authorised in at least one member state) applications, including **2** repeat use applications.

30 abridged applications, including **7** multiple and **8** repeat use applications.

4 line extension applications, including **2** repeat use applications.

The new procedures started in April 2008 related to **4** full dossier, **25** generic, **1** bibliographic, **1** fixed combination and **9** hybrid applications.

These procedures consisted of **39** chemical substance products and **1** biological blood product.

28 of these procedures related to prescription-only medicinal products and **12** procedures related to a non-prescription medicinal product in the reference Member State¹.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
CZ (1)	1
CZ (2)	21
CZ (1)	5
DE (1)	24
DE (1)	11
DE (1)	3
DE (1)	2
DK (4)	13
DK (3)	8
DK (3)	4
DK (3)	12
DK (1)	1
DK (2)	4
FI (1)	7
FR (1)	4
HU(3)	3
IT (1)	8
NL (1)	4

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.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
NL (2)	5
NL (2)	1
NL (1)	1
NL (2)	3
NL (1)	1
NL (2)	1
NL (1)	12
NL (3)	11
NL (3)	13
NL (3)	20
NL (1)	1
NO (3)	1
PT (1)	1
SE (1)	1
SE (1)	12
SE (1)	2
SE (1)	1
SE (1)	2
SE (1)	21
UK (1)	8
UK (4)	10
UK (1)	14

Decentralised Procedure

The CMD(h) noted that there were **74** Decentralised Procedures finalised with a positive outcome and **4** Decentralised Procedures finalised with a negative outcome during the month of April 2008. **1** Decentralised Procedure was referred to the CMD(h) in this period. There was **no** Decentralised Procedure referred to the CHMP in this period.

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

Year	New applications finalised		New applications withdrawn ²	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	220	4	1	1205	12	2	8	1	2	--

134 Decentralised Procedures (regarding **310** products) started in April 2008. The categories of these procedures are as follows:

121 abridged applications, including **25** multiple applications.

9 known active substance applications.

4 line extension applications, including **2** multiple applications.

The new Decentralised procedures started in April related to **114** generic, **2** bibliographic, **2** fixed combination, **8** hybrid and **8** full dossiers.

All of these procedures consisted of chemical substance applications.

133 of these procedures related to prescription-only medicinal products and **1** to a non-prescription medicinal product in the reference Member State³.

² After day 120.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (4)	8
AT (4)	8
AT (4)	10
AT (4)	8
AT (4)	12
AT (3)	1
AT (2)	1
AT (3)	1
AT (4)	2
AT (4)	2
BE (1)	2
CZ (1)	1
CZ (1)	1
CZ (1)	4
DE (4)	7
DE (1)	1
DE (3)	1
DE (3)	1
DE (3)	5
DE (2)	16
DE (5)	3
DE (3)	15
DE (2)	2
DE (2)	9
DE (1)	5
DE (3)	18
DE (3)	3
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	1
DE (3)	2
DE (3)	14
DE (3)	1
DE (5)	4
DE (4)	6
DE (4)	4
DE (1)	4
DE (1)	6
DE (4)	1
DE (4)	7
DK (2)	15
DK (2)	4
DK (2)	2
DK (4)	3
DK (4)	1
DK (4)	3
DK (4)	1
DK (4)	2
DK (4)	1
DK (4)	9
DK (4)	1
DK (2)	13

³ 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.

DK (2)	11
DK (2)	1
DK (2)	12
DK (2)	12
DK (2)	1
DK (1)	8
DK (1)	8
DK (1)	1
DK (2)	10
FI (2)	4
FI (1)	3
FR (1)	24
FR (1)	24
FR (1)	1
HU (4)	8
HU (4)	3
HU (4)	11
IE (1)	10
IT (1)	13
NL (3)	2
NL (1)	9
NL (1)	15
NL (1)	17
NL (2)	5
NL (3)	18
NL (3)	3
NL (3)	1
NL (3)	9
NL (3)	1
NL (10)	4
NL (1)	8
NL (1)	3
NL (1)	3
NL (1)	5
NL (1)	2
NO (2)	17
NO (1)	5
NO (2)	17
NO (2)	17
NO (2)	17
NO (2)	17
NO (2)	17
NO (2)	17
NO (2)	17
SE (1)	16
SE (1)	5
SE (1)	1
SE (1)	20
SE (1)	2
SE (3)	8
UK (1)	16
UK (1)	4
UK (1)	19
UK (1)	1
UK (3)	21
UK (1)	15
UK (1)	19
UK (1)	9
UK (2)	11
UK (1)	7
UK (1)	1
UK (1)	1
UK (1)	2
UK (1)	12
UK (1)	9
UK (1)	4
UK (1)	10

UK (1)	3
UK (1)	3
UK (2)	1
UK (2)	8
UK (2)	5
UK (1)	2
UK (1)	4
UK (1)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **611** type IA variations, **238** type IB variations and **421** type II variations were finalised during the month of April 2008. **30** renewals were finalised in this period. There was **no** procedure referred to the CHMP in this period.

The status as of 30th April 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	2098	848	916	126	--

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>