

Report from the CMD(h) meeting held on 10th and 11th December 2007

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

The CMD(h) and the EMA have agreed on additional Q&As to clarify the submission of paediatric studies according to Article 45 of the Paediatric Regulation.

Marketing Authorisation Holder are reminded to fill in the line listing agreed by the CMD(h) and the EMA for all their authorised medicinal products and to submit it together with the declaration (Annex I) to each Competent Authority(ies) where the medicinal products are authorised in electronic format only, with a copy to the EMA (paedstudies@ema.europa.eu), by 26 January 2008.

CMD(h) Standard Operating Procedure – Disagreement in Procedures – Referral to CMD(h)

The CMD(h) has agreed a revised SOP to clarify that it is possible to close the procedure earlier than Day 60, if agreement is reached. In these cases the RMS shall ensure that all CMSs have been provided the opportunity to state their final view until the end of the given timeline.

The CMD(h) has also clarified in the SOP that the updated assessment report, following the submission of the response document by the Applicant, and the comments from the CMSs on the response document will be shared by the RMS with the Applicant.

Variation Assessment Reports Templates

The CMD(h) has revised the Type II variation templates for the preliminary and final assessment reports, mainly to include a table of contents, to update the section 'Administrative information' and to include a section on product information, to clarify whether the harmonisation of the package leaflet and labelling is part of the variation procedure or if the package leaflet and labelling have been previously harmonised or not.

Change in the EU-Presidency

The December 2007 CMD(h) meeting was the last one under the Portuguese Presidency of the Council of the European Union. Slovenia will take over the presidency in January 2008. Mrs. Sabina Zalar will be the Vice-Chairperson of the CMD(h), for the Slovenia Presidency of the Council of the European Union.

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 22.11.2007.

Name of the product in the RMS	Atorvatyrol 10, 20, 40 & 80mg Atorvac 10, 20, 40 & 80mg Atorvastatin "Hexal" 30 & 60mg Atorvapharm 10, 20, 40 & 80mg Atorvis 10, 20, 40 & 80mg
Active substance	atorvastatin
Pharmaceutical form	Film-coated tablet
Procedure number	AT/H/0158/001-004/DC AT/H/0159/001-004/DC AT/H/0159/005-006/DC AT/H/0160/001-004/DC AT/H/0161/001-004/DC
CMS	AT/H/0158/01-03/DC: CZ, DK, EE, EL, ES, FI, LT, LV, NO, PL, PT, SK AT/H/0158/04/DC: CZ, DK, EE, ES, FI, LT, LV, NO, PL, PT, SK AT/H/0159/01-02/DC: DK, ES, HU, IE, PL AT/H/0159/03-04/DC: DK, ES, HU, IE, PL, SI

	AT/H/0159/05-06/DC: HU, IE AT/H/0160/01-04/DC: CZ, EE, ES, HU, LT, LV, PL, SK AT/H/0161/01-04/DC: ES
Legal basis	AT/H/0158/01-04/DC AT/H/0159/01-04/DC Art 10.1 Dir 2001/83/EC - Generic AT/H/0160/01-04/DC AT/H/0161/01-04/DC AT/H/0159/05-06/DC Art 10.3 Dir 2001/83/EC - Hybrid
Grounds for referral to CMD(h)	Referral was raised on grounds of bioequivalence issues regarding predefined widening of the acceptance limits of 90% confidence intervals for Cmax of the metabolite to 70-143%. The applicant was asked to provide a comprehensive justification of why a widening of the acceptance range of the 90% CI for Cmax is acceptable, specifically addressing clinical efficacy and safety consequences of an increased or decreased maximum concentration of the metabolite.
Day 60	22.11.2007
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 a predefined widened 90% CI limit for Cmax of the metabolite. Following a discussion, no consensus could be reached to solve this issue. Accordingly, these applications were referred to CHMP for arbitration.

Name of the product in the RMS	Fentanyl HPC 25, 50, 75 & 100 ug/h Transdermales Pflaster
Active substance	fentanyl
Pharmaceutical form	Transdermal patch
Procedure number	DE/H/1045/001-004/MR
CMS	BG, CZ, EE, HU, LT, LV, PL, RO, SK
Legal basis	Art 10.1 Dir 2001/83/EC - Generic
Grounds for referral to CMD(h)	Concerns were raised about a potential increased skin irritancy score of Fentanyl HPC transdermal patch in comparison to the originator's product. The concern was based on a statistically driven explanation.
Day 60	22.11.2007
Outcome	The member states agreed on the fact that no indication of clinical relevance in regard to safety and efficacy could be concluded from the skin irritancy data provided.

Name of the product in the RMS	Ondansetron "BMM Pharma"
Active substance	ondansetron
Pharmaceutical form	Film-coated tablet
Procedure number	DK/H/1046/001-002/DC
CMS	EE, FI, LT, LV, NO, SE
Legal basis	Art 10.1 Dir 2001/83/EC - Generic
Grounds for referral to CMD(h)	A CMD(h) referral was raised due to bioequivalence issues. The potential serious risk to public health stated was that the applicant has not given a valid argument for the exclusion of subject No 8. Consequently, the test product and the reference product were not considered bioequivalent as the 90% CI for AUC0-t (79.39-102.66%) is outside the acceptable limits (80-125%).
Day 60	22.11.2007
Outcome	A new study was due to very exceptional grounds allowed during the referral procedure. The new study has not given any information on the reason for the finding for subject No 8. The majority of data (first study except subject No 8 and the new study) were however consistent with narrow confidence interval including unity for Cmax and AUC. MS involved have therefore found the product approvable. Agreement reached.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **28** Mutual Recognition Procedures were finalised during the month of November 2007. **4** Mutual Recognition Procedures were referred to CMD(h) in this period. **No** Mutual Recognition Procedure was referred to CHMP in this period.

The status as of 30th November 2007 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)		Withdrawn during CMD(h) referral	Applications referred to CHMP	
				For procedures referred in 2006	2007		For procedures referred to CMD(h) in 2006	2007
2007	404	179	39	25	26	1	9	6

26 Mutual Recognition Procedures (regarding **49** products) started in November 2007. The categories of these procedures are as follows:

3 known active substance (already authorised in at least one member state) applications;

22 abridged applications, including **2** multiple and **3** repeat use applications.

1 New Active Substance, which is a repeat-use application.

The new procedures started in November 2007 related to **1** full dossier, **22** generics and **3** bibliographic applications.

26 of these procedures consisted of chemical substances.

24 of these procedures related to prescription-only medicinal products and **2** to non-prescription medicinal products in the reference Member State¹.

Number of countries involved in the new applications in Mutual Recognition procedure started in November 2007.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	14
DE (1)	8
DE (1)	7
DK (1)	12
DK (2)	3
DK (2)	1
FI (4)	3
FR (1)	5
FR (1)	13
HU (1)	13
HU (1)	11
HU (3)	5
HU (3)	13
HU (3)	5
IE (1)	1
NL (3)	3
NL (1)	1
NL (3)	25

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 (3)	25
NO (1)	13
PT (1)	2
PT (3)	9
SE (2)	2
UK (1)	1
UK (2)	6
UK (2)	25

Decentralised Procedure

The CMD(h) noted that there were **50** Decentralised Procedures finalised during the month of November 2007 with a positive outcome. There was 1 Decentralised procedure withdrawn after Day 120. **No** Decentralised Procedures were referred to the CMD(h) in this period. **4** Decentralised Procedures were referred to the CHMP in this period.

The status as of 30th November 2007 of procedures under Decentralised Procedure is as follows:

Year	New applications finalised		New applications withdrawn ¹	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				2006	2007		2006	2007
2007	316	7	17	1150	21	1	11	3	--	6

82 Decentralised Procedures (regarding **195** products) started in November 2007. The categories of these procedures are as follows:

74 abridged applications, including **16** multiple applications.

7 known active substance applications.

1 New active substance.

The new Decentralised procedures started in November related to **74** generic, **1** bibliographic, **2** informed consent and **5** full dossiers.

80 of these procedures consisted of chemical substance applications and **2** biological blood products

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

Number of countries involved in the new applications in Decentralised procedures started in November 2007.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (6)	14
AT (6)	4
AT (6)	3
AT (2)	4
AT (2)	1
AT (2)	8
AT (2)	3

¹ After day 120 of the procedure.

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.

CZ (4)	17
DE (1)	9
DE (5)	15
DE (1)	9
DE (1)	12
DE (2)	1
DE (2)	1
DE (4)	1
DE (1)	2
DK (3)	5
DK (4)	4
DK (1)	17
DK (5)	12
DK (5)	12
DK (5)	4
DK (5)	1
DK (5)	1
DK (5)	1
DK (5)	1
DK (2)	1
FR (1)	23
FR (1)	6
NL (1)	26
NL (1)	5
NL (2)	1
NL (2)	2
NL (2)	4
NL (2)	1
NL (3)	2
NL (3)	4
NL (3)	7
NL (3)	13
NL (2)	6
NL (1)	10
NL (1)	2
NL (1)	1
NL (4)	4
NL (1)	5
NL (3)	1
SE (1)	22
SE (1)	3
SE (1)	3
UK (4)	7
UK (2)	3
UK (2)	19
UK (1)	19
UK (3)	25
UK (3)	20
UK (2)	24
UK (2)	19
UK (2)	8
UK (2)	9
UK 92)	22
UK (1)	1
UK (2)	6
UK (4)	14
UK (2)	23
UK (2)	5
UK (1)	5
UK (1)	7
UK (1)	17
UK (1)	1
UK (1)	16
UK (3)	1
UK (2)	16
UK (2)	6
UK (1)	4

UK (1)	16
UK (2)	1
UK (2)	1
UK (2)	4
UK (2)	11
UK (1)	1
UK (2)	7
UK (1)	5

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **576** type IA variations, **230** type IB variations and **172** type II variations were finalised during the month of November 2007. **31** renewals were finalised in this period.

The status as of 30th November 2007 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
2007	5237	2125	2031	359	8

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>