

Report from the CMD(h) meeting held on 12th and 13th November 2007

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

Marketing Authorisation Holders are reminded to use the excel templates without changes for submission of the line listings and of the wording of the SmPC (4.1 and/or 4.2) for medicinal products with paediatric use. The excel templates are published on the CMD(h) website, under 'Paediatric data assessment' in editable versions.

The templates and the respective declarations should be sent to each Competent Authority(ies) where the medicinal products are authorised in electronic format only and copied to the EMEA (paedstudies@emea.europa.eu).

A list of addresses to be used for the submission of paediatric information for each Competent Authority has been published on the CMD(h) website, under 'Contact Points'.

EU Work sharing Project – Assessment of paediatric data

The Marketing Authorisation Holder for the medicinal product Losec (omeprazole), involved in the EU work sharing project – assessment of paediatric data, is requested to submit, within 60 days of the finalisation of the procedure, i.e. by 31st December 2007, a national Type II variation to implement the agreed text for inclusion in the SPC.

CMD(h) meeting with representatives of Interested Parties

The CMD(h) held a meeting on 12 November 2007 with representatives of AESGP, EFPIA and EGA.

The topics discussed were the following:

- The revised Decentralised Procedure Standard Operating Procedure, which will be published on the website;
- A report from the activities of the Working Group on Validation issues/National requirements, addressing the on-going & planned activities of the working group;
- Experience with consultation with target patient groups and recommendations for bridging;
- Experience with national implementation following MRP/DCP (new applications, variations, renewals). Applicants are requested to submit high quality translations of the product information, to facilitate national approval following MRP/DCP;
- Member States' resources in the Mutual recognition and Decentralised procedures. Interested Parties were advised to try to use more Member States as Reference Member State and to avoid double booking of time slots for submission of applications.

A report from the meeting will be published on the website, for transparency reasons.

Working Group on Validation issues/National requirements

The CMD(h) has agreed on a template for a cover letter for new applications submitted through the MRP/DCP, prepared by the Working group on Validation issues/National requirements.

The template for the cover letter will be published on the website.

Informal CMD(h) meeting, 25-26 October 2007, Lisbon, Portugal

The CMD(h) convened for an Informal meeting on 25th and 26th October 2007 in Lisbon, Portugal, held as part of a programme of events organised under the Portuguese Presidency of the Council of the EU, in parallel to the informal CHMP and COMP meetings.

The main topics discussed at the meeting included a joint session with the CHMP, to discuss outcome of referrals to the CHMP and the links between the CMD(h) and EMEA Committees and Working Parties, information on the on-going work to revise the NfG on investigation of bioavailability and bioequivalence, the implementation of the Paediatric Regulation and, in particular, of a tracking system for paediatric studies submitted according to Articles 45 and 46. The CMD(h) discussed also MSs experiences with national

implementation following MRP/DCP, addressing the time for receipt of national translations following the end of MRP/DCP and for granting of the marketing authorisation by National Competent Authorities. There was also a presentation on the various telematics projects.

Change in the name of a medicinal product prior to granting a marketing authorisation

The CMD(h) has agreed a Q&A to address how to handle a change in the name of a medicinal product between finalisation of a MRP or DCP and the granting of a national marketing authorisation.

Applicants are advised to discuss with the particular Member State whether a change in the name of the medicinal product can be handled as part of the national implementation process or if a MRP variation has to be followed. The mutually recognised English package leaflet should be updated with the name of the medicinal product in that particular MS.

CMD(h) Guidance for Marketing Authorisation Holders for the Pharmacovigilance System and Risk Management Plan in the Mutual Recognition and Decentralised Procedures

The CMD(h) and the PhVWP have agreed a document aimed at providing specific guidance for the RMS and CMS on the submission of data related to the Pharmacovigilance system and Risk Management Plans (RMP) and how these are assessed during MRP and DCP.

This guidance document should be read in conjunction with Volume 9A of The Rules Governing Medicinal Products in the European Union, Part 1, Chapter 2 'Requirements for Pharmacovigilance Systems, Monitoring of Compliance and Pharmacovigilance Inspections' and Chapter 3 'Requirements for Risk Management Systems.'

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 25.10.2007.

Name of the product in the RMS	Hararamizid	Lerimamed
Active substance	ramipril HCTz	
Pharmaceutical form	Tablet	
Procedure number	DK/H/1073/001-002/MR	DK/H/1176/001-002/MR
CMS	CZ, DE, HU, IT, SI	BG, CY, CZ, LT, LV, RO, SK
Legal basis	Art 10.1 Dir 2001/83/EC - Generic	
Grounds for referral to CMD(h)	Referral was raised by a CMS on grounds of bioequivalence issues regarding acceptance limits of 90% confidence intervals. The applicant was asked to justify the positive risk/benefit ratio of the generic product Ramipril/Hydrochlorothiazide (Hararamizid, Lerimamed) and its essential similarity with the reference product with respect to the NfG on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98) and Questions & Answers on the Bioavailability and Bioequivalence Guideline (CHMP/EWP/40326/06).	
Day 60	25.10.2007	
Outcome	After having reviewed the response to the LoQ submitted by the company and the following RMS' AR, the referring CMS accepted to issue a marketing authorisation.	

Name of the product in the RMS	Anya	
Active substance	ethinylestradiol levonorgestrel	
Pharmaceutical form	Film-coated tablet	
Procedure number	FI/H/0665/001/MR	
CMS	BE, CY, DE, DK, EL, ES, FR, IE, IS, IT, LU, NL, NO, PT, SE, UK	
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) by four CMSs based on the insufficiently demonstrated contraceptive efficacy and safety of the product. Also the proposed SPC wording for inhibition of vaginal bleeding pattern was considered unacceptable.	
Day 60	25.10.2007	

Outcome	At the meeting the RMS introduced the unresolved issues. The Applicant made use of an oral hearing. The question on contraceptive efficacy combined with the bleeding pattern was considered as the most critical concern. No consensus was reached. The application was referred to the CHMP for arbitration.
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Name of the product in the RMS	Ipramol Steri-Neb 0.5mg / 2.5mg
Active substance	ipratropium bromide monohydrate
Pharmaceutical form	Nebuliser solution
Procedure number	IE/H/0163/001/E001
CMS	FI, NL, SE, UK (wave 1) AT, BE, DE, DK, EL, HU, IT, LU, LV, PL, PT, RO (wave 2)
Legal basis	Art 10.3 Dir 2001/83/EC - Hybrid
Grounds for referral to CMD(h)	A potential serious risk to public health was raised by a CMS in relation to concerns regarding the absence of therapeutic equivalence trials and the use of in vitro comparative studies to demonstrate the comparable efficacy and safety between Ipramol Steri-neb and the reference product.
Day 60	25.10.2007
Outcome	There was an oral explanation with the Applicant and presentations made by the RMS and CMS. Following discussion and taking into account the Revised Guideline on the Requirements for Clinical Documentation for Orally Inhaled Products (OIP) adopted at the October 2007 CHMP meeting for release for consultation, agreement was reached.

Name of the product in the RMS	Zuurstof medicinaal gasvormig Air Products
Active substance	oxygen
Pharmaceutical form	Medicinal gas
Procedure number	NL/H/0923/001/MR
CMS	CZ, DE, PT
Legal basis	Art 10(a) Dir 2001/83/EC - Bibliographic
Grounds for referral to CMD(h)	There was a concern with regard to the clinical evidence for the following indications: <ul style="list-style-type: none"> • Hyperbaric oxygen therapy: for the support treatment of blood circulation problems in skin transplants and skin reconstruction, and • Hyperbaric oxygen therapy: supporting treatment in cases of osteoradionecrosis
Day 60	25.10.2007
Outcome	At the CMD(h) meeting the RMS presented its view and the applicant's written response was discussed. The indications approved in another Mutual Recognition Procedure (SE/H/0607/001-002/MR, including DK, EE, FI, IS, LT, LV and NO) were also taken into account during the discussion. Following the discussion, agreement was reached to remove the indication 'Hyperbaric oxygen therapy: for the support treatment of blood circulation problems in skin transplants and skin reconstruction' because of the lack of adequate clinical data. It was also agreed to maintain the indication 'Hyperbaric oxygen therapy: supporting treatment in cases of osteoradionecrosis' as the established use of hyperbaric oxygen in daily clinical practice is considered to be of overriding importance, even though there is a lack of data from adequate clinical trials. Agreement was reached

Name of the product in the RMS	Alvesco 40, 80, 160 Inhaler
Active substance	ciclesonide

Pharmaceutical form	Pressurised inhalation, solution
Procedure number	UK/H/0699/001-003/E001
CMS	UK/H/699/01/MR: BE, DE, DK, EE, FI, HU, IE, IS, LT, LU, LV, NL, NO, PL, SE, SI, SK UK/H/699/01/E01: AT, BG, CY, ES, FR, IT, MT, PT UK/H/699/02-03/MR: BE, CZ, DE, DK, EE, EL, FI, HU, IE, IS, LT, LU, LV, NL, NO, PL, SE, SI, SK UK/H/699/02-03/E01: AT, BG, CY, ES, FR, IT, MT, PT
Legal basis	Art 8.3(i) Dir 2001/83/EC - Full dossier
Grounds for referral to CMD(h)	One CMS raised concern over the maximum approved dose with regard to severe asthma and the insufficiency of the available data to establish the optimal posology to control severe asthma.
Day 60	25.10.2007
Outcome	At the CMD(h) meeting, the RMS and referring CMS presented their position on this issue. There was discussion on the data provided to support the maximum dose in severe asthmatics at the CMD(h) meeting and up to Day 60 of the referral procedure. However, no agreement could be reached with the applicant on the necessary steps to take to solve the issue. As a result consensus was not reached in this repeat use MR procedure and accordingly, these applications were referred to CHMP for arbitration.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **32** Mutual Recognition Procedures were finalised during the month of October 2007. **1** Mutual Recognition Procedures was referred to CMD(h) in this period. **2** Mutual Recognition Procedure were referred to CHMP in this period.

The status as of 31st October 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	376	183	35	25	25	2	9	6

22 Mutual Recognition Procedures (regarding **44** products) started in October 2007. The categories of these procedures are as follows:

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

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

The new procedures started in October 2007 related to **3** full dossiers, **17** generics and **2** bibliographic applications.

20 of these procedures consisted of chemical substances and **2** biological blood products.

22 of these procedures related to prescription-only medicinal products in the reference Member State¹.

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.

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
AT (1)	1
CZ (3)	1
CZ (4)	2
DE (2)	15
DK (1)	11
FI (2)	2
FR (2)	1
NL (1)	4
NL (1)	2
NL (1)	8
NL (1)	12
NL (3)	11
NL (3)	1
NL (2)	15
NO (2)	1
NO (2)	1
PT (3)	19
PT (3)	8
PT (3)	9
SK (2)	2
UK (1)	13
UK (1)	12

Decentralised Procedure

The CMD(h) noted that there were **36** Decentralised Procedures finalised during the month of October 2007 with a positive outcome and **3** Decentralised Procedures with a negative outcome during this period. **No** Decentralised Procedure was referred to the CMD(h) or to the CHMP in this period.

The status as of 31st October 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	266	7	16	1073	21	1	10	3	--	2

117 Decentralised Procedures (regarding **215** products) started in October 2007. The categories of these procedures are as follows:

105 abridged applications, including **19** multiple applications.

8 known active substance applications.

4 Line extension applications.

The new Decentralised procedures started in October related to **104** generic, **2** bibliographic, **3** fixed combination, **2** informed consent and **6** full dossiers.

117 of these procedures consisted of chemical substance applications.

¹ After day 120 of the procedure.

117 of these procedures related to prescription-only medicinal products in the reference Member State².

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

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
BE (1)	1
BE (1)	2
CZ (1)	5
CZ (1)	9
DE (1)	1
DE (1)	1
DE (5)	2
DE (1)	2
DE (1)	1
DE (1)	1
DE (1)	1
DE (1)	1
DE (1)	4
DE (1)	7
DE (1)	12
DE (1)	11
DE (2)	2
DE (3)	6
DE (1)	1
DE (1)	1
DE (3)	10
DE (1)	3
DE (1)	10
DE (1)	4
DE (1)	1
DE (1)	7
DE (1)	3
DE (2)	1
DE (2)	3
DE (2)	3
DE (1)	8
DE (4)	11
DE (3)	1
DE (1)	1
DE (1)	1
DK (1)	10
DK (1)	1
DK (2)	10
DK(1)	3
DK (2)	9
DK (1)	9
DK (2)	6
DK (3)	2
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	3
DK (2)	5
DK (2)	5
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	11
DK (3)	2
DK (3)	2
DK (3)	2

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.

DK (1)	9
DK (1)	2
FI (1)	3
FR (2)	16
FR (1)	12
IT (1)	1
IT (1)	1
IT (1)	4
NL (2)	2
NL (1)	2
NL (3)	19
NL (3)	3
NL (3)	26
NL (3)	8
NL (3)	3
NL (3)	3
NL (2)	11
NL (1)	2
NL (4)	4
NL (2)	13
NL (2)	12
NL (2)	1
NL (2)	1
NL (2)	1
NL (2)	1
NL (4)	10
SE (2)	6
SE (1)	4
SE (1)	24
SE (4)	1
SE (4)	12
SE (4)	1
SE (3)	1
SE (3)	17
SE (3)	1
UK (2)	9
UK (1)	19
UK (1)	19
UK (2)	14
UK (2)	6
UK (2)	4
UK (2)	19
UK (1)	15
UK (1)	4
UK (1)	1
UK (1)	19
UK (1)	19
UK (1)	3
UK (2)	3
UK (2)	7
UK (2)	1
UK (2)	1
UK (2)	5
UK (1)	28
UK (3)	2
UK (1)	21
UK (1)	14
UK (1)	2
UK (4)	10

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **480** type IA variations, **205** type IB variations and **204** type II variations were finalised during the month of October 2007. **34** renewals were finalised in this period.

The status as of 31st October 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	4661	1895	1859	328	3

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