

Report from the CMD(h) meeting held on 18th, 19th and 20th June 2007

Sub-group meeting on Harmonisation of SPCs

There was a meeting of the Sub-Group on harmonisation of SPCs, mainly to consider the proposals from Member States for products for which a harmonised SPC should be drawn up.

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, taking into account the proposals from all Member States, in accordance with Article 30(2) of Directive 2001/83/EC, as amended.

Meeting with EGA on Work-sharing for patient consultation

At the informal CMD(h) meeting held in Bonn, 7-8 May 2007, the CMD(h) endorsed, in principle, a proposal from EGA for a work-sharing initiative for patient consultation and agreed to set up a Working Group to take this initiative forward and to have contacts with Interested Parties.

This Working Group held a meeting with EGA on 19 June 2007 to further discuss the proposal for a work-sharing initiative for patient consultation across Europe.

The CMD(h) encourages Industry to participate in this Industry led work-sharing initiative and agreed to develop guidance to support extending use of test results to related products, consistent with agreed principles in previously published guidance.

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

There was a meeting of the Sub-Group on Paediatric Regulation, mainly to consider the action points identified at the meeting held on 21 May 2007 with representatives of Interested Parties and the comments received on the Q&A document addressing the submission of Paediatric studies according to Articles 45 and 46 of the Paediatric Regulation.

The Sub-Group will finalise the Q&As in July 2007, together with a procedure and template for Marketing Authorisation Holders to inform National Competent Authorities of the medicinal products with a Paediatric indication.

Decentralised Procedure – Member States Standard Operating Procedure

Further to the work carried out by the Working Group set up to evaluate the Decentralised Procedure and to consider the need for revision of the respective Standard Operating Procedure, the CMD(h) has agreed to publish the draft revised SOP for a one month period of public consultation.

Any comments on the draft revised SOP should be sent to the attention of the CMD(h) secretariat (sonia.ribeiro@emea.europa.eu) by 31 July 2007.

Recommendations on Multiple/Duplicate applications in Mutual Recognition and Decentralised Procedures

The CMD(h) has agreed a revised document 'Recommendations on Multiple/Duplicate applications in Mutual Recognition and Decentralised Procedures', to address both the Mutual Recognition and Decentralised Procedures and to structure the document into the following sections: General principles, Submission of duplicate applications, Sunset clause and Specific situations, which is aimed at improving the readability of the document.

Questions and Answers on the SOP - Disagreement in Procedures – Referral to CMD(h)

The CMD(h) has agreed a Q&A to clarify that in the situation where the RMS is negative but one or more of the CMS are positive on a decentralised procedure application, the application will be referred to the CMD(h) and the matters of disagreement will be discussed by the involved MSs.

Questions and Answers – Homeopathic medicinal products – Referrals to CMD(h)

The CMD(h) has agreed two Q&As to address the situation for homeopathic medicinal products (as defined in Article 14 of Directive 2001/83/EC, as amended) if no agreement could be reached at the end of a mutual recognition or decentralised procedure or at the end of a CMD(h) referral.

Questions and Answers – Guidance for Applicants on Biologicals

The CMD(h) has agreed Q&As to address the definition of biological medicinal products and how this definition is applied and special regulatory requirements for biologicals. The Q&As include a link to an overview of biological active substances of non-recombinant origin.

Change in the EU-Presidency

The June 2007 CMD(h) meeting was the last one under the German presidency of the EU. Portugal will take over the presidency in July 2007. Mrs. Marta Marcelino will be the Vice-Chairperson of the CMD(h), for the Portuguese 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 31.05.2007.

Name of the product in the RMS	Coxtral
Active substance	nimesulide
Pharmaceutical form	Gel
Procedure number	CZ/H/116/02/MR
CMS	EE, HU, LT, LV, PL, SK
Legal basis	Art 10.1 Dir 2001/83/EC - Generic
Grounds for referral to CMD(h)	The clinical documentation of the generic medical product Coxtral Gel 30 mg/g was considered insufficient to assess therapeutic efficacy of this product in the proposed SPC indications and to estimate the benefit/risk ratio. The clinical study of generic Coxtral Gel: “Analgesic and anti-inflammatory Efficacy and Tolerability of Topically Applied Nimesulide in Patients with acute Blunt Injury” is the clinical trial with parallel two groups design (first arm – Coxtral Gel, second arm - reference product). This two-arm design of above mentioned clinical study of Coxtral Gel do not meet the relevant requirements of ICH Harmonized Tripartite Guideline: Choice of Control Group in Related Issues in Clinical Trials E10 (CPMP/ICH/364/96).
Day 60	31.05.07
Outcome	Referred to CHMP for Arbitration

Name of the product in the RMS	Indapamid 'Ratiopharm'	Indapamid 'CT'	Mapemid
Active substance	indapamide		
Pharmaceutical form	Prolonged release tablet		
Procedure number	DK/H/954/01/DC	DK/H/955/01/DC	DK/H/956/01/DC
CMS	AT, DE, ES, FR, LU, PL, UK	DE	AT, DE, ES, FR, PL, UK
Legal basis	Art 10.1 Dir 2001/83/EC - Generic		
Grounds for referral to CMD(h)	Bioequivalence had not been sufficiently demonstrated under all relevant conditions.		
Day 60	31.05.07		
Outcome	There was consensus in CMD(h) that the applications were non-approvable. According to the current guidelines, bioequivalence (BE) after single-dose administration under fasting conditions as well as BE after single-dose administration under high-fat, fed conditions should be demonstrated before authorisation. Therefore, the results of these crucial investigations should be available in the dossier submitted to the authorities - post-approval commitments are not considered		

	acceptable. The applicants have withdrawn the applications in all MS.
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Name of the product in the RMS	Bisoprolol HCTZ Teva 2.5, 5, 10/6.25 mg
Active substance	bisoprolol HCTZ
Pharmaceutical form	Film-coated tablet
Procedure number	FR/H/307/01-03/DC
CMS	EE, HU, LT, LV, UK
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 the fact that the bioequivalence of the test product to an adequate comparator had not been demonstrated and the validity of the analytical technique was not certain.
Day 60	31.05.07
Outcome	Results from new bioequivalence studies were submitted by the applicant against an adequate comparator including new analytical methods. Agreement was reached before the CMD(h) meeting.

Name of the product in the RMS	Moapar
Active substance	triptorelin embonate
Pharmaceutical form	Powder and solvent for suspension for injection
Procedure number	SE/H/663/01/MR
CMS	BE, DE, DK, FI, FR, NL, NO, 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 one CMS on the basis of scarcity of scientific data from clinical studies that could support the proposed indication: <i>‘Moapar is indicated for the reversible reduction of testosterone to castrate levels in order to decrease sexual drive in adult men with sexual deviations’</i> but suggested the following: <i>‘Moapar is indicated for the reversible reduction of testosterone to castrate levels when it is presumed necessary’</i> . This wider indication was not acceptable to other CMS, nor to the RMS nor to the Applicant. One CMS suggested to limit the indication to ‘men with severe sexual deviations’, which was supported by other CMS. The RMS and other CMS considered that profound lowering of testosterone to castrate levels could be used as a surrogate endpoint for reducing sexual drive in adult men with severe sexual deviations. There is no evidence that lowering of testosterone to castrate levels will affect the sexual inclination, whereas at least limited evidence support that sexual drive is reduced also in men with sexual deviations, thereby reducing the frequency of possibly offensive sexual acts. This was considered a reasonable justification for the applied indication.
Day 60	31.05.07
Outcome	Before the CMD(h) meeting, the request for referral was conditionally withdrawn by the objecting CMS and all CMSs could agree on the proposed indication. It should be pointed out that data from clinical studies in men with severe sexual deviation was, indeed, limited. The main reasons for the scarcity of data that could have provided a better scientific basis for the application include, lack of reliable clinical endpoints, difficulties in standardizing the sexually deviant status, difficulty in follow-up and reporting of endpoints that are criminal acts, such as sexual offence.

Name of the product in the RMS	Aridol
Active substance	mannitol
Pharmaceutical form	Inhalation powder, hard capsule
Procedure number	SE/H/711/01/MR

CMS	BE, DE, DK, EL, ES, FI, FR, IE, IT, NL, NO, PT, UK
Legal basis	Art 8.3(i) Dir 2001/83/EC – Full dossier
Grounds for referral to CMD(h)	Potential serious risk to public health was raised by two Concerned Member States due to issues related to the diagnostic value and interpretation of the test, the indication, differential diagnoses and the influence of anti-asthmatic medications. Furthermore, the clinical study was criticised as not having followed the PtC on the evaluation of diagnostic agents. A further clinical study was requested.
Day 60	31.05.07
Outcome	At the CMD(h) meeting the RMS and the Applicant presented their view on the product. A post approval commitment was discussed. A clinical study has been conducted in US recently; however the results are not ready. It was agreed that the study protocol and a new revised SPC (minor revisions) should be circulated after the meeting. At day 60 of the procedure agreement was achieved that the medicinal product can be authorised. The Applicant committed to conduct a study to demonstrate the clinical usefulness of Aridol in untreated patients suspected of having asthma according to guidelines. The results of the US study will be submitted for assessment and if it does not fulfil the requirements, the Applicant agreed to perform another study with the appropriate design.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMD(h) noted that **59** new Mutual Recognition Procedures were finalised during the month of May 2007. **No** Mutual Recognition Procedures for new applications were referred to CMD(h) in this period. **1** Mutual Recognition Procedure for new applications was referred to CHMP in this period.

The status as of 31st May 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
2007	224	156	17 N.A.	35	1	12

36 Mutual Recognition Procedures (regarding **73** products) started in May 2007. The categories of these procedures are as follows:

6 known active substances (already authorised in at least one member state).

28 abridged applications, including **2** multiple and **6** repeat use applications.

1 new active substance, which is a repeat use application.

1 line extension application.

The new procedures started in May related to **5** full dossiers, **26** generics, **2** hybrid applications and **3** bibliographic applications.

These procedures consisted of **33** chemical and **3** biological vaccine substances.

32 of these procedures related to prescription-only medicinal products and 4 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 May 2007.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (1)	1
DE (1)	25
DE (3)	3
DE (1)	12
DE (1)	9
DE (1)	8
DE (1)	26
DK (5)	1
DK (7)	2
DK (2)	2
DK (2)	6
DK (2)	1
DK (2)	1
DK (2)	1
DK (2)	5
DK (2)	7
EE (1)	2
EE (3)	1
EE (1)	5
FI (2)	2
FI (1)	3
FR (1)	10
FR (1)	7
FR (1)	17
IE (1)	14
NL (2)	2
NL (1)	3
NL (4)	8
NL (4)	5
NL (1)	3
NL (1)	2
UK (3)	8
UK (3)	2
UK (3)	4
UK (2)	9
UK (2)	4

Decentralised Procedure

The CMD(h) noted that there were 42 new Decentralised Procedures finalised during the month of May 2007. There were 5 Decentralised Procedures referred to the CMD(h) in this period. There were 3 Decentralised Procedures withdrawn at day 210 during the month of May 2007.

The status as of 31st May 2007 of procedures under Decentralised Procedure is as follows:

Year	New applications finalised with		New applications withdrawn ¹	New applications in process	Referred to CMD(h)	Agreement reached in the CMD(h)	Withdrawn during CMD(h) referral	Applications referred to CHMP
	positive outcome	negative outcome						
2007	88	1	8	698	11	3	3	--

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.

¹ After day 120 of the procedure.

85 Decentralised Procedures (regarding **144** products) started in May 2007. The categories of these procedures are as follows:

76 abridged applications, including **18** multiple applications.

9 known active substance applications.

The new Decentralised procedures started in May related to **72** generic, **6** full dossier, **4** hybrid and **3** fixed combination applications.

84 of these procedures consisted of chemical substance applications and **1** biological blood product.

All 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 May 2007.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DE (2)	16
DE (2)	7
DE (3)	3
DE (1)	10
DE (3)	2
DE (2)	13
DE (1)	6
DE (1)	11
DE (1)	1
DE (1)	6
DE (1)	4
DE (1)	1
DE (1)	1
DE (1)	1
DK (3)	6
DK (3)	5
DK (2)	13
DK (1)	1
DK (1)	1
DK (2)	1
DK (2)	1
DK (1)	4
DK (1)	9
DK (1)	12
DK (1)	1
DK (1)	1
DK (1)	3
DK (1)	12
DK (1)	2
DK (1)	18
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	1
DK (1)	3
DK (1)	4
DK (1)	2
DK (1)	2
DK (1)	1
DK (2)	12
DK (2)	9

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.

Reference Member State (number of products involved in the procedure)	Number of CMSs involved in the procedure
DK (2)	2
DK (2)	1
DK (2)	1
DK (2)	1
ES (1)	1
FI (5)	7
FR (4)	24
FR (4)	18
FR (4)	3
HU (2)	8
NL (1)	6
NL (1)	15
NL (4)	4
NL (2)	3
NL (2)	1
NL (4)	4
NL (2)	3
NL (2)	3
NL (2)	5
NO (3)	11
NO (3)	1
SE (1)	11
SE (1)	2
SE (1)	11
SE (1)	4
SE (1)	8
SE (2)	18
SE (2)	3
SE (2)	1
SE (2)	1
SE (2)	1
SE (2)	1
UK (1)	9
UK (12)	22
UK (1)	1
UK (1)	11
UK (1)	2
UK (1)	2
UK (1)	1
UK (1)	1
UK (13)	1
UK (2)	1

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMD(h) noted that **497** type IA variations, **195** type IB variations and **161** type II variations were finalised during the month of May 2007. **19** renewals were finalised in this period. **2** Mutual Recognition Procedures for Type II variation applications were referred to CHMP in this period.

The status as of 31st May 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	2298	835	848	169	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>