

**CO-ORDINATION GROUP FOR MUTUAL RECOGNITION AND  
DECENTRALISED PROCEDURES – HUMAN (CMD(h))**

**WORKPLAN 2009**

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**INTRODUCTION**

The Coordination Group for Mutual Recognition and Decentralised procedures – Human (CMD(h)) was set up under the revised EU pharmaceutical legislation for the examination of any question relating to the marketing authorisation of a medicinal product in two or more Member States, in accordance with the mutual recognition procedure (MRP) or the new decentralised procedure (DCP). The CMD(h) started its activities in November 2005.

The tasks and functioning of the group have been outlined in the Rules of Procedures, which were adopted by the Group and endorsed by the European Commission.

CMD(h) members are nominated for a period of 3 years, which is renewable. The group completed its first 3 year term in October 2008. Elections for the position of chairperson were held in the November meeting in 2008 and Mrs Truus Janse-de Hoog was elected for a new 3 years term.

The CMD(h) decided to evaluate the functioning of the group after its first 3 year term. A questionnaire on the functioning of the CMD(h) was sent to the members and interested parties. Results from this evaluation are included in the Workplan 2009, as well as continuing activities and scheduled work carried forward from workplan 2008.

Interested parties have raised their concerns on the availability of resources at the National Competent Authorities and the difficulties to find a RMS and book a ‘slot time’ for a new DCP.

HMA has set up a Taskforce on MRP/DCP resources to discuss how this can be improved. CMD(h) members are participating in this Taskforce and contributing, where possible.

In 2008 the number of applications for the Decentralised procedure has increased again. In order to plan resources at national level it is important to have more information in advance of numbers of applications and especially to anticipate on large numbers of applications for the same active substance when data exclusivity period has expired.

The percentage of applications referred to CMD(h) and CHMP in 2008 decreased slightly in comparison to 2007. In general, it is felt that referrals are a useful procedure to solve outstanding issues and to find agreement in discussions on matters of principle. There is an ongoing discussion on how to avoid ‘unjustified’ referrals and try to find agreement earlier during procedures. Information on the outcome of discussions in CMD(h) and CHMP on referred products is now available on CMD(h) website.

**PRIORITIES 2009**

For 2008 the CMD(h) agreed on priorities in the work plan. Some of the priorities are maintained for 2009.

For 2009 the following priorities have been defined:

- 1) Active participation of all members of the group. In order to create general consensus in the agreements reached and avoid repetition of discussions on the same topics, all CMD(h) members are encouraged to participate in scientific and regulatory discussions, also in applications in which they are not involved as RMS and CMS.
- 2) Active participation of all Member States in Worksharing procedures. Worksharing is a way to make the best use of available resources and avoid duplication in assessment of the same set of data. Worksharing has been agreed in the assessment of PSUR data, Paediatric data submitted in accordance with Art 45 and 46 of Paediatric regulation and some Variations.
- 3) Contributing to the HMA Taskforce on Resources MRP/DCP. CMD(h) shall concentrate on improvement of the booking system for DCP, Training and Workshops to exchange experience in acting as RMS.
- 4) Discuss how a 'Risk based assessment' can be implemented in MRP/DCP and contribute to a truly mutual recognition by elimination of parallel assessment by CMSs.
- 5) To contribute to a successful implementation of Paediatric Regulation and assess the data submitted in accordance with Art 45 and 46 in the agreed timeframes, having 4 waves of assessment each year for Art 45 procedures and an ongoing assessment of data submitted in accordance with Art 46 procedures.
- 6) To contribute to a successful implementation of the Variation Regulation with the help of the Variations subgroup and finalise the Guidance documents and Best Practice Guides in the agreed timelines.
- 7) To prepare for the new tasks of CMD(h) proposed in the new legislative proposals 'Strategy to better protect Public Health by strengthening and rationalising EU Pharmacovigilance'.
- 8) Increase transparency for industry on the outcome of referral discussions in CMD(h) and CHMP by publication of information and organisation of meetings with interested parties.
- 9) Reduction of national requirements. After the successful work of the validation Subgroup to reduce and harmonise national requirements HMA has been asked to reconsider the remaining national requirements.
- 10) Implementation of e-CTD in MRP and DCP: To discuss and provide guidance towards achieving the target timeline endorsed by HMA namely the acceptance by the NCA of paperless submissions using the eCTD as the format for submission of a MA by the end of 2009. In a transitional period Nees, according the defined standard, should also be accepted by NCA's. Close collaboration with the TIGes is necessary.
- 11) Implement use of Vitero (Virtual product discussions) to enhance expert participation and improve participation of experts in Break-out discussions. The CMD(h) will also initiate a pilot phase to expand the use of Vitero to CMD(h) Sub-groups.
- 12) Scientific Memory for outcome CMD(h) discussions on product related issues and regulatory questions.
- 13) Pandemic preparedness for National Competent Authorities as a follow up to the Workshop on pandemic plan. CMD(h) will discuss in particular how to process MRP and DCP applications and variations in the situation of a pandemic.

## **ORGANISATIONAL MATTERS**

The meeting calendar and relevant procedure dates have been published on CMD(h) website.

The secretariat is keeping track of the expiry dates, whilst the Member States are responsible for sending in renewals or new nominations in time.

## **REFERRALS**

The percentage of applications referred to the CMD(h) in 2008 is lower than in the previous years.

The percentage of applications referred to the CMD(h) is approximately 10% for MRP and 6% for DCP. Approximately 23% of the referrals finalised by the CMD(h) in 2008 were referred to the CHMP.

The CMD(h) considers that the percentage of CMD(h) referrals can still be further reduced. Especially in the Decentralised procedure, discussions in the CMD(h) could start earlier around the clock stop. This will allow all the Member States to give their views in the scientific discussions earlier and discuss potential options to come to consensus. After the training on the use of Vitero the RMS can organise teleconferences to discuss different views between CMS(s) and RMSs earlier in the procedure.

It is important that the CMD(h) will continue to be a platform for scientific discussions, if there are different views between the Member States. The CMD(h) should also discuss different standards in assessment and stimulate harmonised interpretation of Guidelines. Cooperation with the CHMP Working parties (Quality, Safety, Efficacy, and Pharmacokinetic Sub-group) has been successful in answering general questions and giving further clarification on Guidelines. This cooperation is very important in developing a harmonised approach also between different procedures (CP, MRP, DCP) and keeping informed on new developments that are considered to be 'state of the art'. This will help to avoid future referrals, but also to agree on common standards in assessment of dossiers.

The recommendations formulated to reduce the numbers of referrals in 2007 and 2008 are still valid for 2009:

- The results of agreements reached in the CMD(h) should be applied in the assessment of new applications. There is still the need for a Scientific Memory of the CMD(h) where the outcome of discussions can be stored and made accessible for all national experts;
- General questions are sent to CHMP Working Parties and agreements should be followed;
- Discussion in Working Parties on the update of Guidelines and training of assessors;
- Start discussions between Member States earlier in the procedures and involve CMD(h) earlier in the discussions;
- The commitment of all the National agencies to follow the agreements made in the CMD(h).

## **WORKING GROUPS**

The following permanent or ad hoc Working groups are in place.

### CTS Working Group (Hum+Vet)

The tracking system in CTS for paediatric applications in accordance with Art 45 and 46 of the Paediatric Regulation will be in place Q 1 2009.

### SPC harmonisation

A new list of products for SPC harmonisation in 2009 will be sent to the European Commission. On CMD(h) websites an overview is published of ongoing and finalised Art 30 referrals with a link to the Commission decision. CMD(h) will mention finalised referrals in their press release and encourage harmonisation of SPC's of products with the same active substance that are already on the market.

### Joint CMD(h)-PhVWP Working Group

The agreed procedure on Interactions on safety warnings agreed in PhVWP will be followed and regular meetings of the working group are foreseen in 2009.

The group will work together and focus on fast and simple procedures for implementation of safety information in SPC and PL.

The ongoing project of synchronisation of PSUR submissions and work sharing will be followed and CMD(h) members will participate in the PSUR Taskforce.

### CMD(h)-EMEA Sub-group on Paediatrics

All paediatric data, submitted in accordance with Art 45 and 46 of the Paediatric Regulation, will be assessed in an EU Work sharing procedure. The Working Group has already provided Guidance to industry on format and type of data to be submitted. The group will follow the process and Work sharing procedure for data submitted according to Art 45 and Art 46 procedures. Priorities have been agreed and first wave of assessment of Art 45 procedures has started. The assessment will be done in waves of products agreed according to priorities. All Member States should contribute in the assessment of Art 45 and Art 46. In 2009 the worksharing procedure will be evaluated after the first 2 waves.

If appropriate meetings with interested parties can be arranged.

### CMD(h)-GCP Inspectors

This group was a new initiative to work closer together in the development of New Guidance papers. The group has met several times in 2008 and will continue in 2009. Most important topics for discussion are cooperation in inspections for MRP/DCP procedures, exchange of information between Inspectors and Regulators and a common approach with regard to outcome of GCP inspections of CRO's involved in conducting bioequivalence trials.

### Joint Subgroup on Variations

The subgroup will work together with CMD(h) and EMEA in order to come with harmonised proposals for Recommendations on unforeseen variations and Work sharing procedure.

A list of documents to be developed/revised by the Sub-group, to prepare for the implementation of the Variation Regulation is included as an Annex to the Work plan.

As an outcome from the questionnaires on the evaluation of the functioning of the CMD(h), the Group has agreed to publish the mandates and objectives for all its Sub-groups/Working groups.

### Cooperation with CMD(v)

In areas of common interest the CMD(h) will share information and seek cooperation with the CMD(v). This includes the organisation of joint CMD(h)-CMD(v) meetings.

Areas of particular common interest include the implementation of the Variation Regulation, generics policy, quality issues and information technology (website, CTS, regulatory scientific memory).

## **TRANSPARENCY**

### CMD(h) website

Updating of CMD(h) website was considered as one of the priorities in 2008 and this has been partly achieved. The work on improvement of CMD(h) website will continue in 2009.

CMD(h) has increased transparency, especially with regard to the information on reasons and outcome of CMD(h) referrals and CHMP referrals.

### MRI-Product Index

The CMD(h) will consider how to increase transparency of publication of public assessment reports (PARs) in the MRI-PI and improve the MRI-PI.

## **THE SECRETARIAT**

The support of CMD(h) secretariat is extremely important for the functioning of CMD(h). It includes amongst others organisation of the meetings, drafting Agenda and Minutes, follow –up actions, coordination of referrals and liaison with other committees and Working Parties.

**CMD(h) GUIDANCE DOCUMENTS**  
**To be developed/revised in 2009**

<b>Document</b>	<b>Action</b>	<b>Adoption/ Last Update</b>
<b>Contacts with Representative Organisations</b>		
Guidance on contacts with Representatives Organisations	Check need for update	November, 2006
<b>Transparency Measures</b>		
Position paper on transparency policy of the CMD(h)	Update	February, 2007
<b><u>CMD(h) Subgroups</u></b>		
<b>CTS Working Group (Hum + Vet)</b>		
Mandate of WG	New	
<b>Joint CMD(h)-PhVWP Working Group</b>		
Mandate of WG	New	
<b>CMD(h)/EMEA Sub-group on Paediatric Regulation</b>		
Mandate of Sub-group	New	
<b>CMD(h)-GCP Inspections Sub-group</b>		
Mandate of Sub-group	New	
<b><u>Procedural Guidance</u></b>		
<b>General Information</b>		

Document	Action	Adoption/ Last Update
CMD(h) Position on changing the Reference Member State	Check need for update	February, 2006
CMD(h) Agreement on sunset clause and its application to marketing authorisations granted in more than one MS	Check need for update	December, 2006
<b>Application for Marketing Authorisation</b>		
Best Practice Guide for Decentralised and Mutual Recognition Procedures	Check need for update	May, 2007
Procedure for Automatic Validation of MR Procedures for New Applications	Check need for update	December, 2005
Best Practice Guide on Break-out sessions for Mutual Recognition and Decentralised Procedures	Update with experience on Vitero	July, 2006
Additional data requested for new applications in the MRP/DCP	Update annually	July, 2008
Common grounds for invalidation/delaying validation	Check need for update	July, 2007
<b>[DCP]</b> Decentralised procedure - Member States' SOP	Check need for update	November, 2007
<b>eSubmissions</b>		
CMD(h) BPG on the use of eCTD in MRP/DCP <i>(open for comments until end 2008)</i>	To be finalised following consultation	
<b>Generics in MRP and DCP</b>		
CMD(h) agreement regarding processing of generic applications when the generic has more indications or fewer indications than the reference product in the CMS	Check need for update	November, 2006

<b>Document</b>	<b>Action</b>	<b>Adoption/ Last Update</b>
Information to be submitted by the Member State of the European Reference Medicinal Product	Check need for update	February, 2007
Interpretation and Member States Recommendation for Applications submitted according to Article 10 when the strength and/or the pharmaceutical form of the reference medicinal product differs between RMS/CMS(s)	Check need for update	May, 2006
CMD(h) Recommendation on Implementation of Article 30 Decisions for Generic Products	Check need for update	January, 2006
<b>Variation Procedure</b>		
CMD(h) Best Practice Guides for the Submission and Processing of Variations in the Mutual Recognition Procedure	Update to comply with Variation Reg.	February, 2008 (Chapter 5)
Best Practice Guide – CMD(h) recommendations on unforeseen variations	New	
Best Practice Guide – Article 20 Worksharing	New	
<b>Urgent Safety Restriction</b>		
Urgent Safety Restriction Member State Standard Operating Procedure	Update to strengthen implementation aspects	December, 2005
<b>Consultation with target patient groups</b>		
Consultation with target patient groups – Meeting the requirements of Article 59(3) without the need for a full test recommendations for bridging	Check need for update	October, 2007
<b>Post referral phase</b>		
Recommendation for Mutual Recognition Procedure after finalisation of an arbitration procedure with a positive opinion by the CPMP and a positive decision by the EU-Commission	To be finalised following consultation	February, 2004

Document	Action	Adoption/ Last Update
<b><u>CMD(h) Referrals</u></b>		
CMD(h) Standard Operating Procedure Disagreement in procedures – Referral to CMD(h) (incl. <i>annex</i> Guidance on OE to CMD(h))	Update to comply with Variation Reg.	December, 2007
Recommendations to reduce the number of [unjustified] referrals	New	
<b><u>Paediatric Data Assessment</u></b>		
<b>Responsibilities from Paediatric Regulation</b>		
Best Practice Guide Art.46 – EU work sharing procedure	New	
Q&As on the Paediatric Regulation	Check need for update	November, 2008
<b><u>Product Information</u></b>		
<b>Core SPCs</b>		
Core SPC for Hormone Replacement Therapy	Update	February, 2004
Core SPC for FDG Fludeoxyglucose	Update	March, 2005
<b><u>Templates</u></b>		
<b>Variations</b>		
Cover letter for variations submitted through MRP/DCP	New	
Application forms for Annual updates and grouped variations	New	
<b><u>FAQs</u></b>		
[Advice from CMD(h)] Q&As on Requests for advice from CMD(h)	Check need for update	May, 2007

Document	Action	Adoption/ Last Update
[Referrals to CMD(h)]	Q&As on the SOP Disagreement in procedures – Referral to CMD(h)	Update to comply with Variation Reg. October, 2007
[Variations]	Q&As on the submission of variations according to Commission Regulation (EC) 1084/2003	Update to comply with Variation Reg. March, 2005