

CMDh SUMMARY OF ACTIVITIES 2010

*Doc. Ref.: CMDh/199/2011
January 2011*

1. INTRODUCTION

2010 was the fifth full year of operation of the Coordination Group for Mutual Recognition and Decentralised Procedures – human (CMDh), set-up in accordance with Directive 2001/83/EC for the examination of any question relating to marketing authorisation of a medicinal product in two or more Member States, in accordance with the Mutual Recognition Procedure (MRP) or the Decentralised Procedure (DCP).

The CMDh is composed of one representative per Member State, including Norway, Iceland and Liechtenstein and an observer from the European Commission. The list of the CMDh Members, together with the respective professional qualifications, has been published on the Heads of Medicines Agencies website. The CMDh cooperates closely with the Heads of Medicines Agencies for human medicines.

2. GENERAL INFORMATION

2.1. MAIN MEETINGS

The CMDh met 11 times in 2010. The meetings were chaired by Mrs. Truus Janse-de Hoog, who was re-elected Chairperson of the CMDh in November 2008 for a second term of three years. In addition, two informal CMDh meetings were held in 2010: in Madrid, Spain and in Bruges, Belgium. The April meeting was mainly held via teleconference due to travel disruptions caused by a volcanic ash cloud.

During the Spanish and Belgian presidencies of the Council of the European Union, the vice-Chairpersons were Mrs. Luisa Garcia-Vaquero and Mrs. Sophie Colyn respectively.

Following the monthly plenary meetings, press releases including statistics, adopted documents and information on the applications referred to the CMDh were published on the Heads of Medicines Agencies website.

A list of new and revised CMDh documents and Questions & Answers developed and published by the CMDh in 2010 is included as an Annex to this document.

2.2. CMDh SUBGROUPS

In order to support the CMDh in its activities and to facilitate the collaboration with the European Medicines Agency (EMA) and CMDv on topics of common interest, CMDh members are involved in the following working groups:

- Joint CMDh/EMA subgroup on Paediatric Regulation (10 meetings in 2010);
- Joint CMD/EMA subgroup on variation regulation (7 meetings in 2010);
- Joint CMDh/Pharmacovigilance working party working group (6 meetings in 2010);
- Working Party on the Future of CMDh (5 meetings and 2 teleconference in 2010);
- PSUR worksharing working group (5 meetings and 1 teleconference in 2010);
- CMDh subgroup on harmonisation of SmPC (3 meetings in 2010);
- Joint CMDh/GCP Inspectors subgroup (2 meetings in 2010);
- Communication Tracking System (CTS) working group in charge of the MRP and DCP tracking system (5 meetings in 2010).

In 2010, the CMDh has identified the need to create an ad-hoc group on ASMF assessment to discuss the feasibility and practical organisation of a worksharing procedure for the assessment of Active Substance Master Files (ASMF), in collaboration with the EMA, the EDQM and the Quality Working Party. The ad-hoc group on ASMF assessment has met 5 times in 2010.

In addition and in order to prepare the implementation of the adopted pharmacovigilance legislation, the CMDh has created a specific subgroup that held its first meeting in December 2010.

The activities of the various subgroups are reflected in the 2010 CMDh activities presented under section 5.

2.3. OTHER COLLABORATIONS

In 2010, the CMDh had representatives in the following working groups set up by the EMA or HMA

- EMA/HMA group on transparency
- HMA task force on resources
- Patients' and Consumers' working party
- Healthcare professionals working group
- SmPC advisory group
- TIGes

3. WORKPLAN 2010 - Summary

In the CMDh workplan for 2010 the following priorities were established:

- To achieve the active participation of all members of the group;
- To achieve the active participation of all Members States in worksharing procedures;
- To contribute to a successful implementation of variation Regulation (EC) No 1234/2008;
- To implement a risk-based assessment in MRP/DCP and for type II variations to contribute to a truly mutual recognition;
- To continuously improve of the decentralised procedure;

- To adapt to the new tasks of CMDh as foreseen in the new legislative proposals on “Strategy to better Public Health by strengthening and rationalising EU Pharmacovigilance”;
- To implement e-CTD in MRP and DCP;
- To use available tools for remote meeting in order to increase experts’ attendance and participation in Break-out discussions and save resources;
- To further discuss the development of CTS in cooperation with HMA to ensure that CTS is ready to support new developments in electronic communications and exchange of information between all MS on applications in DCP and MRP;
- To improve the MRI –Product Index layout and format.

In addition, it was agreed to increase transparency, further reduce national requirements and increase interactions with CMDv.

Established priorities are reflected in the activities of CMDh and associated subgroups in 2010.

4. CMDh ACTIVITIES IN 2010

4.1. ORGANISATIONAL MATTERS

Calendars with dates of plenary meetings and timetables for relevant procedures have been published on the Heads of Medicines Agency website.

In 2010, the CMDh has adopted a Best Practice guide on Organisational and Administrative issues for internal use giving guidance to current and new CMDh members and NCA staff on how to work in and with the group and establishing standards for an efficient way of communication between all involved parties. An Action Plan for Remote Meetings has been appended to the Best Practice Guide in order to ensure that important discussion will still take place monthly in case of transport (or other) disruption preventing Members to physically attend the meetings.

In order to increase the efficiency of the CMDh and to prepare for future tasks foreseen in new legislative proposals on pharmacovigilance, the CMDh discussed with the Heads of Medicines Agency the importance of a strong mandate for CMDh members. In its Strategy Paper for 2011-2015 adopted in October 2010, the HMA has announced that CMD members will have a strong mandate for decision making to achieve a common harmonised view and ensure implementation of agreements in each NCA. The CMDh has also advised the HMA to appoint alternate CMDh members in order to share the workload and broaden the competences of CMDh. Article 27(2) of Directive 2001/83/EC as amended by Directive 2010/84/EU provides for alternates appointment.

The European Medicines Agency has supported the Chairperson, the CMDh and the related subgroups in their activities.

The secretariat has kept track of the expiry dates of nominations of CMDh members, whilst the Member States have been responsible for sending in renewals and new nominations in due time.

The CMDh secretariat was also in charge of answering the questions received through the HMA website or addressed to the European Medicines Agency in relation to the MRP and DCP, in liaison with the CMDh Chairperson.

4.2. IMPLEMENTATION OF THE VARIATION LEGISLATION

With the input of the joint CMD/EMA subgroup on variation Regulation including representatives from CMDh, CMDv and EMA, the CMDh has successfully implemented the procedure for requests for recommendation on classification of unclassified variations and the procedure for variation worksharing (respectively Article 5 and Article 20 of Variation Regulation (EC) No 1234/2008). For worksharing variations involving centrally authorised products, the CMDh has worked in close collaboration with the European Medicines Agency.

Related templates have been adopted by the CMDh and published on the Heads of Medicines Agencies website. The MRP/DCP Communication and Tracking System used by NCAs has been further developed to support the new variation procedures.

The joint CMD/EMA subgroup on variation Regulation has met regularly to constantly create or revise guidance documents (Best practice guide for the submission and processing of variations in the MRP, explanatory notes on the variation application form) and Questions and Answers on variations to provide Marketing Authorisation Holders with up-to-date information reflecting the experience gained with the variation legislation.

The CMDh has agreed Article 5 requests for recommendation on classification of variations and the outcomes (19) have been published on the CMDh website. Rapporteurs for Article 5 requests are chosen in turn from a list with all Member States so that the workload is fairly spread. A rapporteur of the human side is also appointed for Article 5 requests addressed to CMDv.

The CMDh has met twice with the trade associations to discuss, among other, the implementation of variation Regulation (EC) No 1234/2008 (see under “Meeting with interested parties”) and has communicated with Industry through two joint DIA/EMA/CMDh conferences.

Some CMDh and EMA representatives met informally with EC in November 2010 to discuss questions that have arisen with the experience gained with the updated legislation on variations.

Since the entry into force of Regulation (EC) No 1234/2008, the CMDh is entitled to examine in the first instance disagreements occurring during the assessment of type II variations if related to products approved through MRP/DCP. No variation was referred to the CMDh in 2010.

Statistical information regarding variations can be found in annual statistics published on the CMDh website.

4.3. IMPLEMENTATION OF THE PAEDIATRIC LEGISLATION

The CMDh/EMA Sub-group on Paediatric Regulation met 10 times in 2009, to organise the work-sharing for the assessment of paediatric studies submitted according to Articles 45 and 46, including the development of guidance documents on Articles 45 & 46.

The CMDh has started 4 waves of worksharing for the assessment of paediatric studies submitted in accordance with Article 45 of Regulation (EC) No 1901/2006. The list of active substances included in the different waves as well as public assessment reports containing the final agreed texts for inclusion in Summary of Product Characteristics and Package Leaflet have been published on the Heads of Medicines Agencies website.

The CMDh has also coordinated assessment of paediatric studies submitted in accordance with Article 46 of Regulation (EC) No 1901/2006 submitted to the EMA and public assessment reports have been published.

In order to have more Member States involved in the worksharing procedures for the evaluation of paediatric studies submitted according to Articles 45 and 46 of the Paediatric Regulation, the rapporteurship has been widely distributed amongst Member States. Nearly all Member States participated.

With the input of the joint CMDh/EMA subgroup on Paediatric Regulation, the CMDh has adopted revised guidance documents that have been published on the Heads of Medicines Agencies:

- The templates for public assessment reports following Articles 45 and 46 procedures as well as the Best Practice Guides on Article 45 and 46 worksharing procedures have been revised to reflect the updated variation Regulation.
- The “Recommendations for implementing Commission Decisions following an Art. 29 Application under the Paediatric Regulation” have been updated to streamline the transfer of national procedures to Mutual Recognition procedures, to strengthen the procedure of implementation of the compliance statement and to reflect the updated variation Regulation.

A workshop for assessors was held in July with the aim to exchange experiences and have better understanding of the worksharing procedures. The “Recommendations on submission and assessment in paediatric worksharing” were updated to reflect the outcome of the workshop.

The Joint CMDh/EMA subgroup on Paediatric Regulation has met with trade associations in September 2010 to discuss the implementation of Regulation (EC) No 1901/2006 (experience with Art. 45/46 worksharing, the outcome of the paediatric assessors’ workshop, experience with Art. 29 procedures and the compliance statement).

4.4. IMPROVEMENT OF MRP AND DCP

The CMDh worked on the improvement of the MR and DC procedures, based on the input provided by the CMDh Working Party on the Future of CMDh, HMA TF on resources in MRP/DCP and in close collaboration with HMA and Interested Parties. Main discussions on improvement aimed at facilitating slot allocation, reducing delays before start of the procedures, increasing transparency on clock-stop duration and reducing national phases of the procedures.

4.4.1. Slot allocation for new DCP applications

- The difficulties faced by applicants and NCA with regards to timeslots and possible remedies have been discussed with interested parties. A common portal for EU submission will be discussed.
- For transparency reasons, the CMDh has published on its website information on national timeslot booking system and recommendations for request to act as RMS as well as links to NCA websites where more detailed information can be found.

4.4.2. Validation

- Member States have worked on the reduction of country-specific requirements for submission of new procedures, variations and renewals. Remaining requirements have been published on the CMDh website for transparency reasons.
- The CMDh has updated the country-specific requirements for e-submissions of new applications, variations and renewals and published Questions and Answers and a Best

- The CMDh has updated the common grounds for invalidation/delaying validation for new applications and variations that have been published on the CMDh website together with a template for RMS to collect validation issues raised by CMS and to provide the applicant with clear guidance on whether or not the issue would prevent the procedure from starting a new application
- Divergent regulatory interpretations between MS leading to invalidation/delayed validation of procedures have been discussed at CMDh plenary meeting and remaining issues have been brought to the attention of the European Commission for discussion with the Notice to Applicant group. Discussions within NtA group will continue in 2011.

4.4.3. Assessment

- In order to foster the mutual recognition by CMS of the assessment done by RMS, a feedback form on assessment report has been developed for CMS to give feedback to RMS on the quality of the assessment report circulated. This feedback form has been used by Member States since November 2009 for a one year pilot phase that has been further prolonged by HMA to November 2011.
- A multidisciplinary ad-hoc group on ASMF assessment including QWP, EMA, CMDv and EDQM has been created and has started to discuss the organisation of worksharing procedures for ASMF assessment as well as requirements for a tracking system. In order to prepare for the worksharing, a template for ASMF Assessment Reports has been created separately from the Day 70 Quality Assessment Reports.
- Clock stop durations have been discussed with interested parties. The CMDh has agreed on a revised Best Practice Guide on MRP/DCP including new rules on clock-stops to improve the transparency and predictability the process for applicants. Measures have been put in place for clock-stop monitoring and analysis of reasons for delayed restart of procedures.
- In order to avoid unnecessary referrals, member states have been encouraged to bring disagreements to the attention of the CMDh at an early stage and to use the experience gained with referrals to avoid repeated discussions.
- The CMDh has agreed to give the applicant the possibility to present their view in front of the CMDh in case the RMS is negative although the procedure cannot be referred to CMDh in that case. In 2010, one applicant requested an oral hearing at CMDh and was heard.

4.4.4. National implementation phase

A questionnaire has been circulated to Member States with the objective to get an overview of the different practices with regards to the national step of the procedures and to identify reasons for delayed implementation. Discrepancies between MS have been identified that will need to be further discussed.

4.4.5. Self-medication sector

The CMDh has discussed with the self-medication sector trade association specific issues faced by the companies with MRP and DCP.

The CMDh has made recommendations to HMA in order to make MRP/DCP more attractive for this sector. Practical measures still have to be developed in collaboration with industry and agreed by HMA.

4.4.6. Generic-specific issues

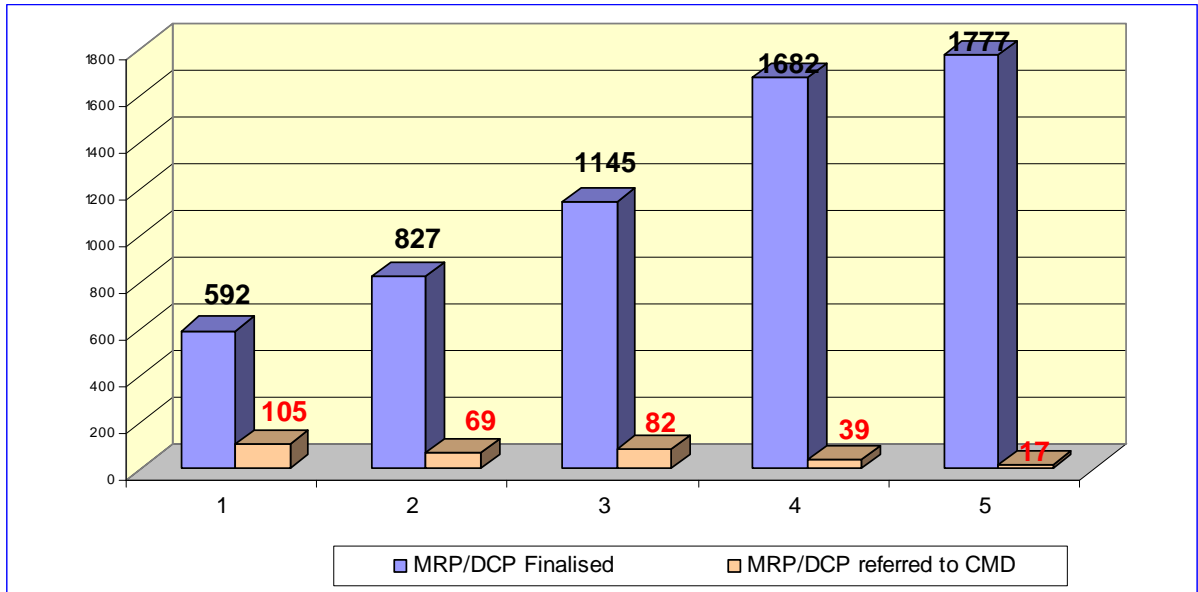
- The CMDh and the EMA have continued to exchange information on generic applications in order to ensure consistency of the assessments and to make a better use of available resources. CMDh members are cooperating with EMA on the elaboration of a Best Practice Guide for exchange of information between the Agency and Member States on generics in order to further improve circulation of information and to organise for early discussions of common issues.
- A question and answer on the choice of reference medicinal products has been revised and published on the CMDh website to give further guidance to the applicant and avoid validation issues.
- In order to avoid lengthy discussions related to generic products name during the national implementation phase, the Question and Answer on naming of generics referring to centrally authorised products has been reviewed and published on the CMDh website.

4.5. REFERRALS to CMDh (Article 29(1) of Directive 2001/83/EC)

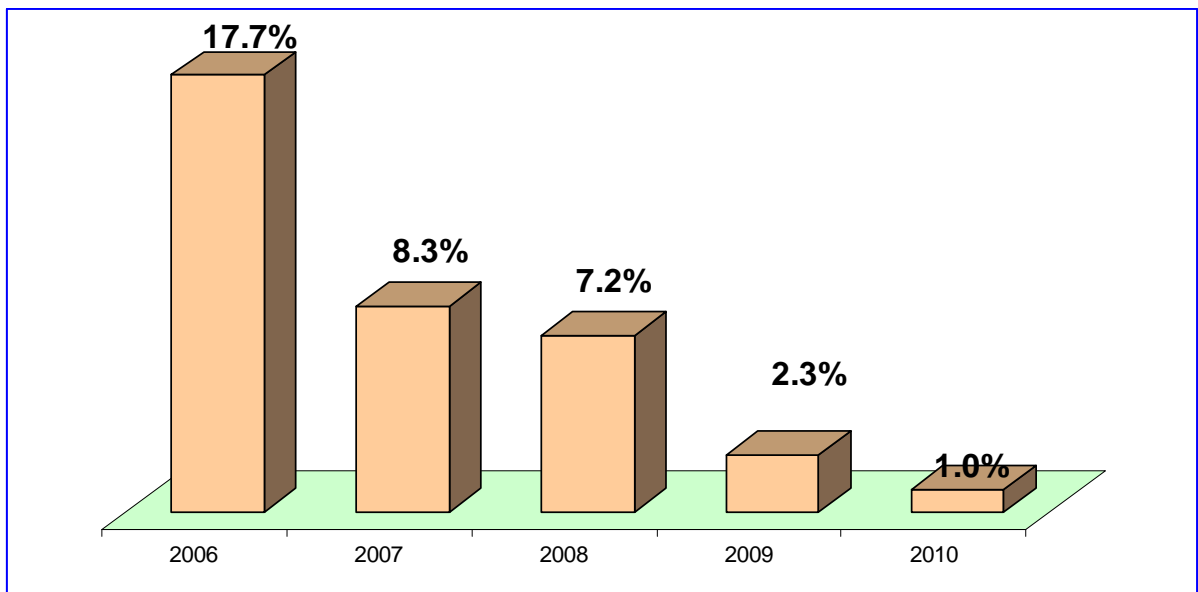
The 60 days referral procedure was introduced in 2005 with Directive 2001/83/EC to enforce a harmonised outcome in the Mutual recognition phase of MRP and DCP. The procedure has to be initiated by the RMS if one or more of the CMS in the procedure is of the opinion that there is potential serious risk of public health (PSRPH) with the granting of the marketing authorisation.

The number of referrals to the CMDh in the first years was relatively high, reflecting the different positions of Member States in 2005. After several years the percentage of procedures that has been referred to the CMDh has decreased. Especially the number of referrals in DCP is low.

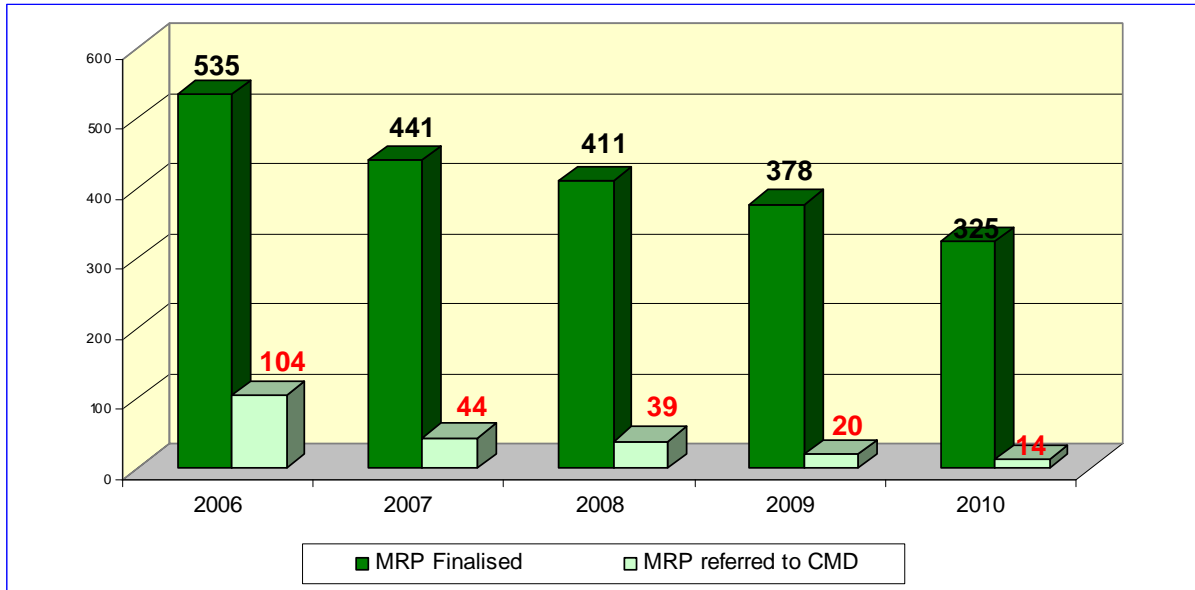
Finalised MR/DC Procedures vs. MR/DC Procedures referred to the CMDh since 2006



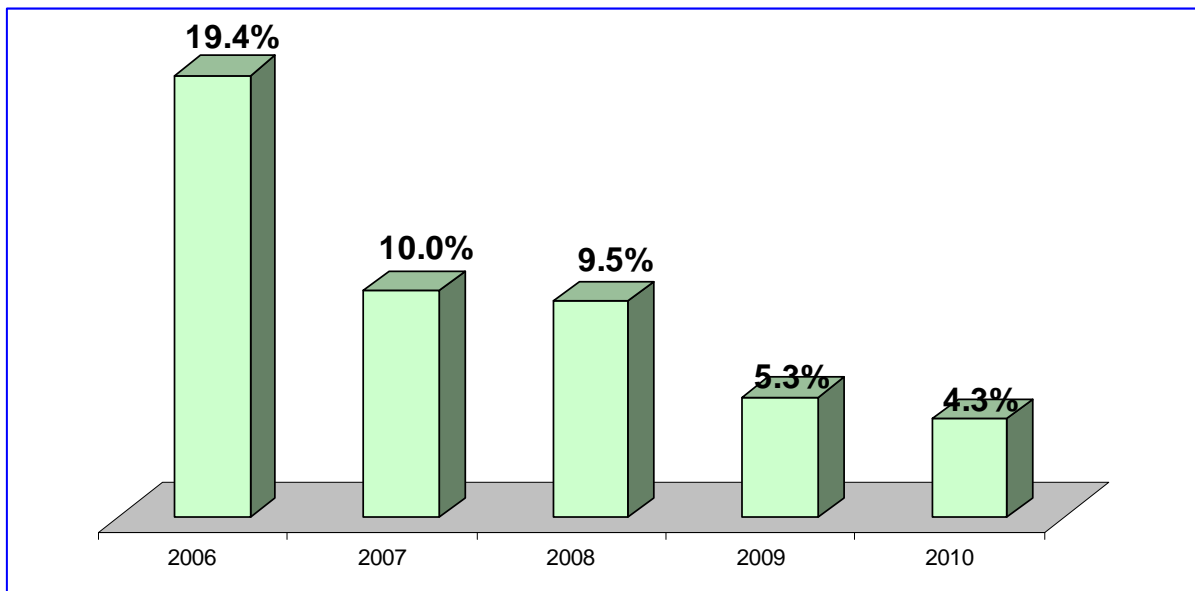
Percentage of MR/DC Procedures referred to the CMDh since 2006



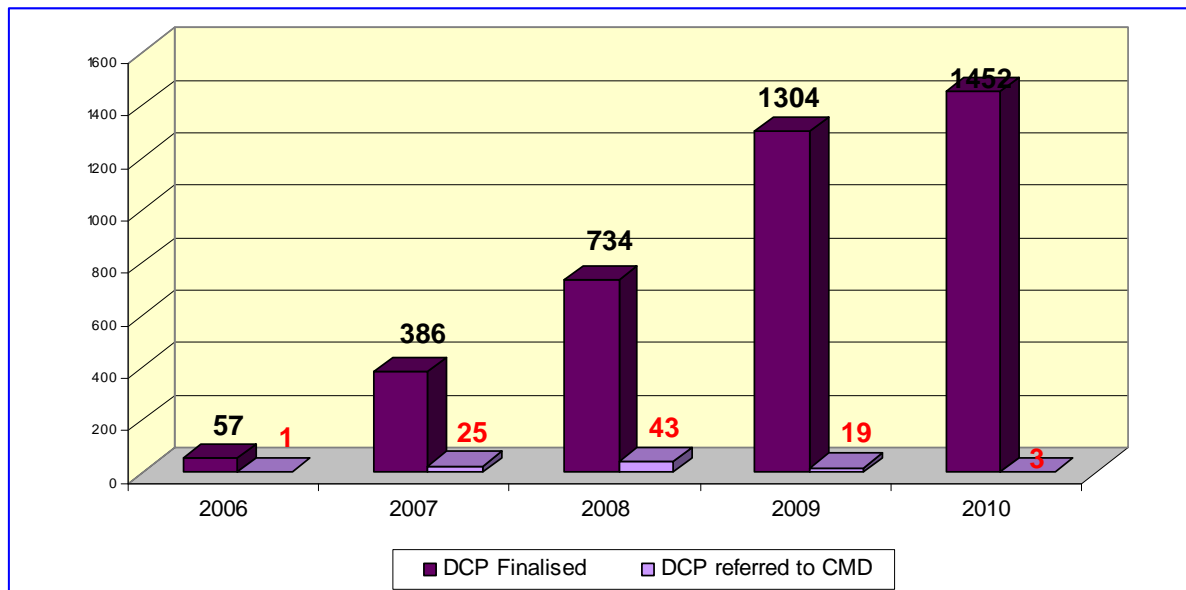
Finalised MRP vs. MRP referred to the CMDh since 2006



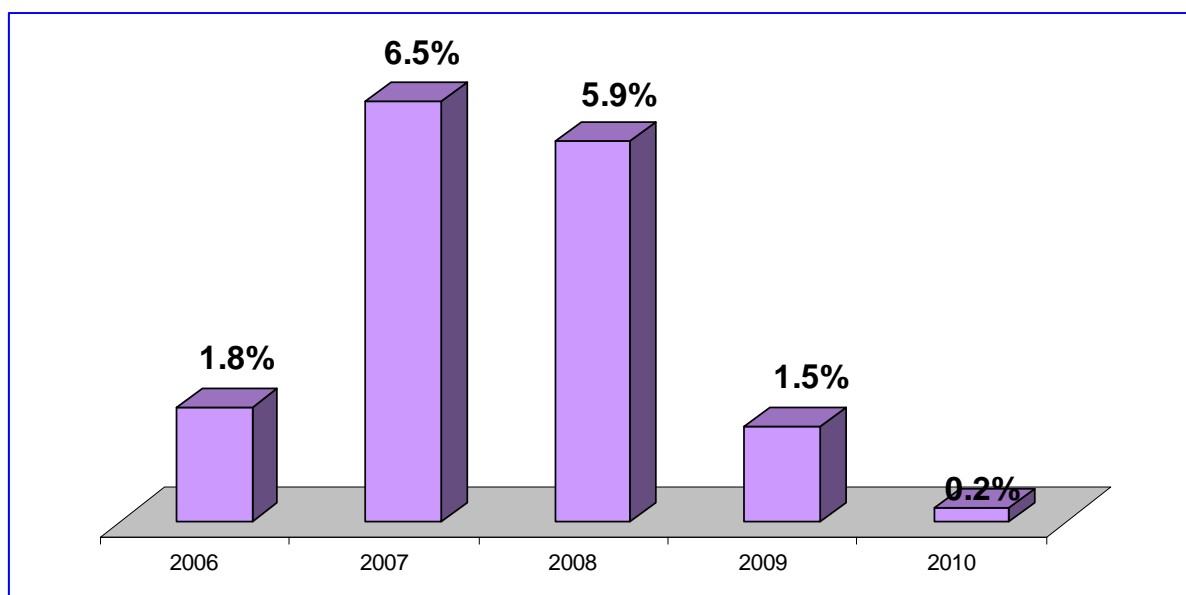
Percentage of MR Procedures referred to the CMDh since 2006



Finalised DCP vs. DCP referred to the CMDh since 2006



Percentage of Decentralised Procedures referred to the CMDh since 2006



Oral explanations

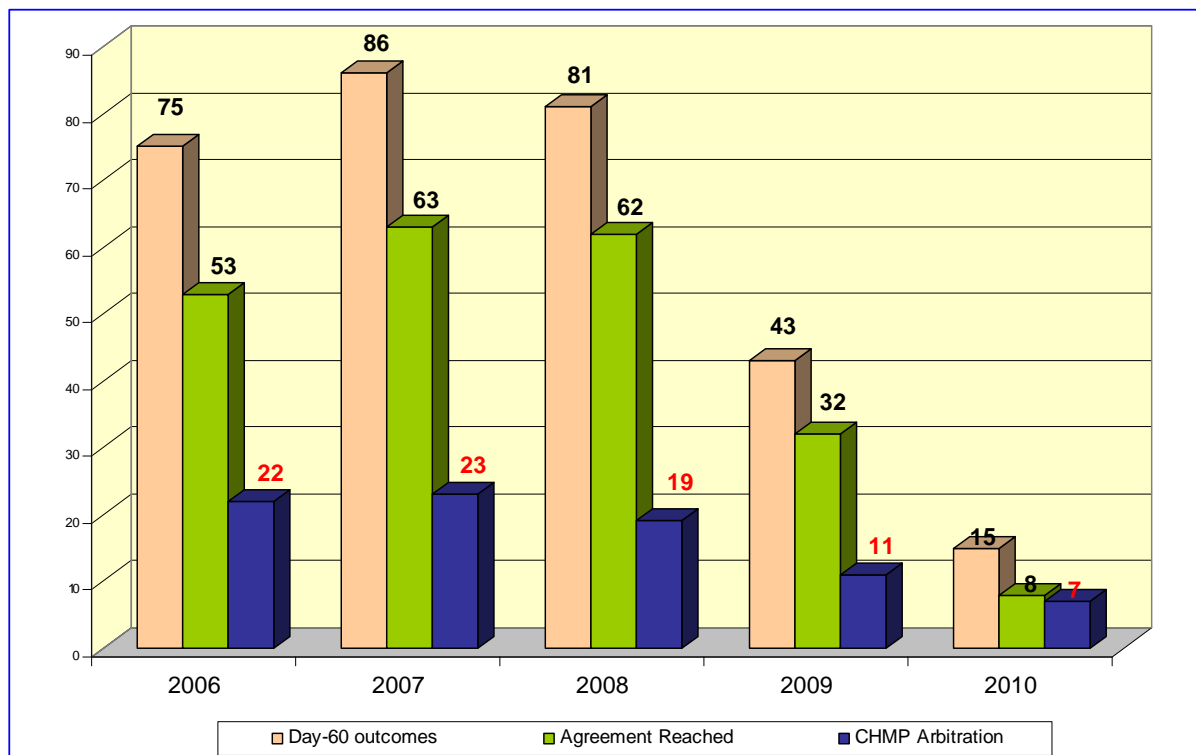
The number of oral explanations from Applicants with the CMDh in 2010 (5) has decreased by 50% in comparison with the previous year (10). This is mainly due to the reduced overall number of referrals.

Outcomes at Day 60

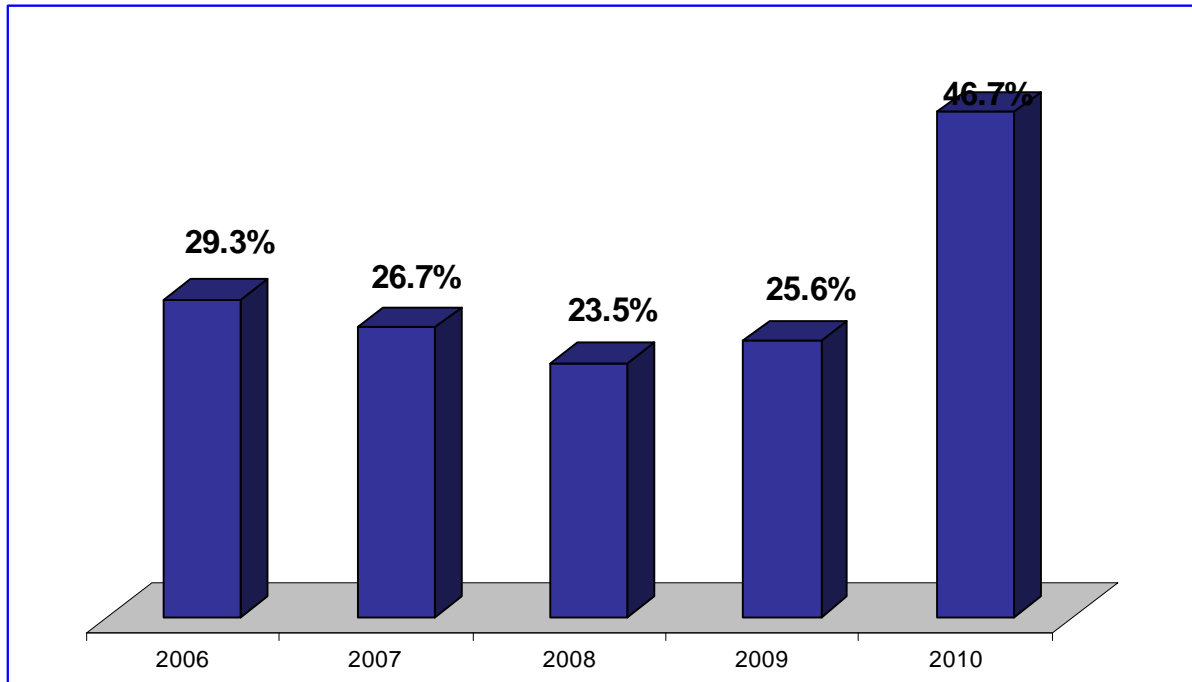
In 2010 in 8 procedures agreement was reached in the CMDh (including withdrawals), while 7 procedures were referred to CHMP (including duplicates).

The Members of the CMDh shall use their best endeavours to reach agreement on the action to be taken. In 2010, 47% of applications referred to CMDh could not find consensus.

MRPs/DCPs referred to CMDh (outcome in 2010) vs. Agreement reached (incl. withdrawals)/CHMP Arbitration



Percentages of Arbitrations to CHMP at Day 60 of CMDh referral procedures, since 2006



In 2010, Member States not involved in the referrals have actively participated to the discussions and several experts who could not be physically present have attended the discussions on referrals through teleconference.

In view of future tasks and workload of the CMDh, the Working Party on the Future of CMDh has discussed how to optimise the referral procedure and make better use of CMDh as a platform for scientific discussions to ensure a consistent approach in the assessment of similar substances.

More statistical information regarding referrals can be found in annual statistics published on the CMDh website.

4.6. HARMONISATION OF SmPC

The CMDh Sub-group on harmonisation of SmPC, set up in view of the role of the Co-ordination group to lay down a list of products for which a harmonised SPC should be drawn up, met 3 times in 2010 to draw up a list of products for SmPC harmonisation.

After public consultation, the CMDh has adopted a list of 4 products for SPC harmonisation, in accordance with Article 30(2) of Directive 2001/83/EC, as amended, which has been published on the CMDh website.

4.7. E-SUBMISSIONS

The CMDh has worked in close collaboration with the European Medicines Agency, HMA, and Industry on the implementation of electronic submission in the European Union and has gathered and regularly published new information and guidance documents related to e-submissions.

The CMDh Best Practice Guide on the use of eCTD in the MRP/DCP has been updated and published on the CMDh website to promote the use of e-CTD in MRP and DCP. In order to continue to discuss with Industry how electronic submissions for these procedures can be facilitated, a central email address for any comments about this guidance in relation to experience from its use in application procedures has been provided (to be coordinated by trade associations where possible).

The CMDh has agreed and published updated requirements for electronic submissions of new applications and for submissions of renewals and variations for MRP/DCP or national applications.

Questions and Answers on the use of e-CTD in MRP/DCP have been agreed and published on the CMDh website.

4.8. TRANSPARENCY AND COMMUNICATION

The CMDh has continued to publish on a monthly basis the outcome of CMDh referrals. Detailed statistical information were published in January and July 2010 on the applications referred to and concluded by the CMDh in 2010, according to Article 29(1) of Directive 2001/83/EC.

The CMDh is still closely collaborating with the CHMP with a view to publishing positions agreed at EU level on any questions of general interest.

In 2010, CMDh members have been actively involved the HMA/EMA group working on transparency in order to reach a common approach regarding requests for access to documents. In 2010, the CMDh has endorsed several of the documents prepared by this group.

In order to improve access to product information, the CMDh has agreed specifications for a more user-friendly version of the Product Index accessible through the CMDh website.

4.9. PHARMACOVIGILANCE

The joint CMDh/Pharmacovigilance WP Working Group has discussed issues of common interest to the CMDh and PhVWP, including the reports prepared by the PhVWP on safety related issues, the agreed wording for implementation in Summary of Product Characteristics and Package Leaflet of products concerned and proposed implementation plan, as foreseen in the document on interaction between PhVWP and CMDh. The CMDh has endorsed the PhVWP reports and has published the PhVWP recommended wording and implementation plan on the following:

- Propylthiouracil and the risk of serious liver injury
- Valproic acid and the risk of interactions with carbapenems
- Selective serotonin reuptake inhibitors (SRRIs) and tricyclic antidepressants (TCAs) and risk of bone fracture
- Selective serotonin reuptake inhibitors (SRRIs) and the risk for development of persistent pulmonary hypertension of the newborn (PPHN)
- Fluoxetine and risk of congenital malformations
- Isotretinoin and risk of erythema multiforme
- Rosuvastatin and higher incidence of diabetes melitus and glucose metabolism disorders in healthy individuals without hyperlipidemia
- Camphor-containing ointments and risk of unintended oral ingestion
- Isotretinoin for oral use and the risk of erythema multiforme, Stevens Johnson syndrome and toxic epidermal necrolysis
- Tamoxifen and the risk of variability in clinical response due to CYP2D6 genetic variants or when given with CYP2D6 inhibitors
- Alendronate and the risk of oesophageal cancer in patients with Barrett's oesophagus

In addition, the CMDh has adopted recommendations on the wording to be included in Summary of Product Characteristics and Package Leaflet of azithromycin-containing products regarding the contraindication of these products in patients with severe hepatic impairment with a timetable for implementation.

All agreed wordings have been published on the CMDh website.

4.10. INTERACTION WITH CMDv

The CMDh has work in close collaboration with CMDv and EMA in the subgroup on Variation Regulation and information on article 5 are regularly exchanged and published on the website. See under variations for further details.

Two joint CMDh/CMDv virtual meetings have been organised in June and December to discuss topics of common interest and documents have been exchanged between the two coordination groups along the year.

4.11. INTERACTION WITH EMA SCIENTIFIC COMMITTEES AND WORKING PARTIES

The CMDh has liaised regularly with EMA Scientific Committees and Working Parties and sent requests for scientific opinions and/or for interpretation of scientific guidelines or guidance documents, mainly arising from discussions for applications referred to the CMDh in case of disagreement between the involved MS in a MRP or DCP application.

CMDh Observers have continued to participate in the EMA/Human Scientific Committees WP with Patients' and Consumers' Organisations and in the EMA/CHMP Working Group with Health Care Professionals' Organisations.

4.12. INTERACTION WITH INTERESTED PARTIES

The CMDh has liaised regularly with representatives of interested parties through public consultation of CMDh documents and discussions of questions raised by Interested Parties.

The CMDh held two general meetings with trade associations in June and November 2010 to discuss the following topics

- Contribution of CMDh to the HMA Task Force on Resources;
- Member States' resources in MRP and DCP;
- Implementation of the variation Regulation (EC) No 1234/2008;
- Paediatric worksharing procedures;
- Implementation of outcome of article 30 referrals;
- Difficulties encountered by the self-medication sector with the Decentralised procedure.

In addition the joint CMDh/EMA subgroup on Paediatric Regulation held a meeting with trade associations in September focussing on the implementation of the paediatric legislation (see under "Implementation of the paediatric legislation").

CMDh representatives have given presentations and participated in panels at two joint DIA/EMA/CMDh conferences.

4.13. INTERACTION WITH HMA

The Chairperson of CMDh provides a progress report on a regular basis to HMA. The CMDh has sent comments on HMA Strategy paper II and proposals for implementation. The Chairperson of the Working Party on the Future of CMDh, in cooperation with the rapporteurs, gave a report on the several topics discussed in the group and endorsed by CMDh.

5. MRP/DCP STATISTICS

The number of new applications submitted in 2010 via MRP and DCP (1912) has increased by 15% compared to 2009. The number of new applications submitted in 2010 via MRP (313) has decreased by 4% compared to 2009. The number of new applications submitted in 2010 via DCP (1599) has increased by 15% compared to 2009.

The number of applications finalised via MRP and DCP (1777) in 2010 has increased by 6% compared to 2009. The number of new applications finalised via MRP (325) in 2010 has decreased by (14%) in comparison with 2009 while the number of applications finalised via DCP in 2010 has increased by 11%.

Statistical information on applications under the MRP and the DCP was provided by the EMA and presented in the monthly CMDh press releases.

More statistical information regarding referrals can be found in annual statistics published on the CMDh website.

	Total started in 2010*	Under evaluation in 2010*	Ended in 2010*	Referrals to CMDh in 2010**	Referrals to CHMP in 2010**
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New applications MRP (including Repeat Use)	313	53	325	14	5
New applications DCP	1599	1846	1452	3	2
Type-IA variations	6735	716	3027	N/A	N/A
Type-IB variations	8785	1112	3935	N/A	N/A
Type-II variations	4001	1796	2361	0	0

**The numbers include multiple procedures as stated at 31 December 2010.*

***Referred renewals are excluded*

ANNEX

NEW DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of (last) revision	Title
CMDh/159/2010	Rev0	About CMDh-CMDh Reports	January 2010		Summary of CMDh Activities in 2009
CMDh/165/2010	Rev0	About CMDh-CMDh Workplan	January 2010		CMDh Workplan 2010
CMDh/166/2010	Rev0	About CMDh-Contact with Representatives-Organisations	January 2010		Minutes from the CMDh meeting with representatives of Interested Parties – 16th November 2009
CMDh/187/2010	Rev0	About CMDh-Contact with Representatives-Organisations	September 2010		Minutes from the CMDh meeting with representatives of Interested Parties – 21st June 2010
CMDh/196/2010	Rev0	Procedural Guidance-Application for MA	December 2010		Declaration form submission DDPS (Detailed Description Pharmacovigilance System) already approved by a competent authority (CA)
CMDh/164/2010	Rev1	Procedural Guidance-Variations	January 2010	February 2010	Implementation of New Variation Regulation in each Member State for Medicinal Products Authorised by purely national procedures
CMDh/171/2010	Rev7	Procedural Guidance-Variations	April 2010	December 2010	CMDh Recommendation for classification of unforeseen variations according to Article 5 of Commission Regulation (EC) No 1234/2008
CMDh/173/2010	Rev1	Procedural Guidance-Variations	May 2010	October 2010	Examples for acceptable and not acceptable groupings for MRP/DCP products

NEW DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of (last) revision	Title
CMDh/182/2010	Rev0	Procedural Guidance-Variations	August 2010		Timetables 2011 for request to CMDh for a recommendation on the classification of an unforeseen variation-Article 5 of Commission Regulation (EC) No.1234/2008
CMDh/197/2010	Rev0	Procedural Guidance-Variations	December 2010		Data requested for Variations and/or Renewal Applications in the MRP/DCP
CMDh/174/2010	Rev0	Procedural Guidance e-submissions	May 2010		Q&A on the use of e-CTD in MRP/DCP
CMDh/183/2010	Rev0	CMDh Referrals	August 2010		Overview of timetables 2011 – CMDh 60 day procedures for MPR/DCP Applications
CMDh/181/2010	Rev0	Templates-Application for Marketing Authorisation	July 2010		Validation on Application for Marketing Authorisation
CMDh/162/2010	Rev0	Templates-Variations	January 2010		Template of letter of intent for the submission of a work-sharing procedure
CMDh/168/2010	Rev1	Templates-Variations	March 2010	September 2010	Recommendation of the CMDh on the classification of an unforeseen on variations to the terms of the marketing authorisation
CMDh/185/2010	Rev0	Templates-AR-Paediatric Data	July 2010		Rapporteur's <Preliminary> <Final> Assessment Report for paediatric studies submitted in accordance with Article 45 of Regulation (EC) No1901/2006, as amended
CMDh/186/2010	Rev0	Templates-AR-Paediatric Data	July 2010		Rapporteur's <Preliminary> <Final> Assessment Report for paediatric studies submitted in accordance with Article 46 of Regulation (EC)

NEW DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of (last) revision	Title
					No1901/2006, as amended
CMDh/190/2010	Rev0	Templates-AR-DCP	September 2010		Template for the ASMF AR
CMDh/163/2010	Rev0	CMD Subgroups/Working groups-Subgroup on Paediatric Regulation	January 2010		Workplan 2010 on Paediatric Regulation
CMDh/179/2010	Rev0	CMD Subgroups/Working Groups-SPC Harmonisation	July 2010		Final list of products for SPC Harmonisation – 2010 in accordance with Article 30(2) of Directive 2001/83/EC, as amended
CMDh/194/2010	Rev0	CMD Subgroups/Working Groups-SPC Harmonisation	October 2010		Final list of products for SPC Harmonisation – 2010 in accordance with Article 30(2) of Directive 2001/83/EC, as amended
EMA/CMDh/416275/2010	Rev0	CMD Subgroups/Joint CMDh/PhVWP WG	June 2010		CMDh and PhVWP Best Practice Guide on communication and implementation of safety information
CMDh/175/2010	Rev0	CMD Subgroups/Working Groups-CTS WG	May 2010		Mandate for the CTS working group
CMDh/193/2010	Rev0	Product Information-CMDh Recommendations	October 2010		Azithromycin Containing Medicinal Products Severe Hepatic Impairment contraindication SmPC and Package Leaflet warning
CMDh/PhVWP/016/2010	Rev0	Product Information-PhVWP Recommendations	January 2010		PhVWP Report to CMDh on Propylthiouracil and reports of serious liver injury

NEW DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of (last) revision	Title
CMDh/PhVWP/017/2010	Rev0	Product Information-PhVWP Recommendations	January 2010		PhVWP Report to CMDh on Valproic acid and interaction with carbapenems
CMDh/PhVWP/018/2010	Rev 1	Product Information-PhVWP Recommendations	March 2010	June 2010	PhVWP Report to CMDh on Fluoxetine and the risk of Congenital Malformations
CMDh/PhVWP/019/2010	Rev 0	Product Information-PhVWP Recommendations	March 2010		PhVWP Report to CMDh on SSRIs, venlafaxine and mirtazapine And the risk of Persistent Pulmonary Hypertension in Neonates (PPHN)
CMDh/PhVWP/020/2010	Rev 0	Product Information-PhVWP Recommendations	March 2010		PhVWP Report to CMDh on SSRIs and TCAs and the risk of bone fractures
CMDh/PhVWP/021/2010	Rev 1	Product Information-PhVWP Recommendations	March 2010	July 2010	PhVWP Report to CMDh on Isotretinoin and the risk of erythema multiforme
CMDh/PhVWP/022/2010	Rev 0	Product Information-PhVWP Recommendations	June 2010		PhVWP Report to CMDh on Rosuvastatin and the risk of diabetes mellitus
CMDh/PhVWP/023/2010	Rev 0	Product Information-PhVWP Recommendations	July 2010		PhVWP Report to CMDh on ointments containing 400mg and over of camphor per package and risk of unintended oral ingestion
CMDh/PhVWP/024/2010	Rev 0	Product Information-PhVWP Recommendations	October 2010		PhVWP Report to CMDh on Tamoxifen and the risk of variability in clinical response due to CYP2D6 genetic variants or when given with CYP2D6 inhibitors
CMDh/PhVWP/025/2010	Rev 0	Product Information-PhVWP Recommendations	October 2010		PhVWP Report to CMDh on Alendronate and oesophageal cancer (use in patients with Barrett's oesophagus)

NEW DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of (last) revision	Title
CMDh/PhVWP/026/2010	Rev 0	Product Information-PhVWP Recommendations	November 2010		PhVWP Report to CMDh on Long-Acting Beta Agonists (LABAs) – Increased risk of exacerbation of asthma symptoms
CMDh/PhVWP/027/2010	Rev 0	Product Information-PhVWP Recommendations	December 2010		Risk of psychiatric adverse drug reactions to inhaled and intranasal corticosteroids and risk of non-psychiatric systemic adverse drug reactions to intranasal corticosteroids

NEW QUESTIONS & ANSWERS

Heading on website	Date of creation	Title
Procedural Guidance - eSubmissions	May 2010	Q&A on the use of eCTD in MRP/DCP
Questions & Answers – Generics and Usage Patents	May 2010	Q&A on the eligibility of a medicinal product authorised in a member state prior to its accession to the EU to serve as a reference medicinal product

REVISED DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of last revision	Title
CMDh/020/2009	Rev4	Procedural Guidance-Application for MA	February 2009	March 2010	Links to NCA websites - National Recommendations for requests to act as RMS
CMDh/068/1996	Rev7	Procedural Guidance-Application for MA	October 1996	March 2010	Best Practice Guide for Decentralised and Mutual Recognition Procedures
CMDh/080/2005	Rev1	Procedural Guidance-Application for MA	July 2005	May 2010	Flow chart of the decentralised procedure and background note
CMDh/043/2007	Rev5	Procedural guidance-Application for MA	July 2007	August 2010	Additional data requested for new applications in the MRP/DCP
CMDh/070/1999	Rev3	Procedural Guidance-Application for MA	May 1999	September 2010	Informed consent applications in Mutual Recognition and Decentralised Procedures - Recommendations
CMDh/075/2007	Rev1	Procedural Guidance-Application for MA	July 2007	September 2010	Common grounds for invalidation/delaying validation
CMDh/079/2005	Rev5	Procedural Guidance-Application for MA	October 2005	November 2010	Recommendations on submission dates for Applicants of the Decentralised Procedure
CMDh/082/2002	Rev3	Procedural Guidance-Application for MA	October 2002	November 2010	Recommendations on submission dates for Applicants of the Mutual Recognition Procedure
CMDh/139/2009	Rev1	Procedural Guidance-Variations	April 2009	May 2010	Timetables 2010 for request to CMDh for a recommendation on the classification of an unforeseen variation-Article 5 of Commission Regulation (EC) No.1234/2008

REVISED DOCUMENTS

Document reference	Revision number	Heading on website	Date of creation	Dates of last revision	Title
CMDh/132/2009	Rev8	Procedural Guidance-Variations	December 2009	October 2010	Q&As for the submission of Variations according to the Commission Regulation (EC) 1234/2008
CMDh/133/2010	Rev4	Procedural Guidance-Variations	December 2009	October 2010	European Medicines Agency/CMDh explanatory notes on Variation Application Form (Human medicinal products only)
CMDh/094/2003	Rev11	Procedural Guidance-Variations	June 2003	November 2010	CMDh Best Practice Guides for the Submission and Processing of Variations in the Mutual Recognition Procedure
CMDh/095/2008	Rev1	Procedural Guidance-Variations	September 2008	December 2010	Position paper on common grounds seen for invalidation/delaying Day 0 for variations
CMDh/088/2006	Rev1	Procedural Guidance-Generics	January 2006	June 2010	Information to be submitted by the Member State of the European Reference Medicinal Product
CMDh/090/2003	Rev4	Procedural Guidance-Generics	January 2003	June 2010	CMDh Recommendation on Implementation of Article 30 Decisions for Generic Products
CMDh/097/2000	Rev4	Procedural Guidance-USR	June 2000	March 2010	Urgent Safety Restriction Member State Standard Operating Procedure
CMDh/084/2008	Rev2	Procedural Guidance-eSubmissions	April 2008	June 2010	CMDh BPG on the use of eCTD in MRP/DCP
CMDh/085/2008	Rev7	Procedural Guidance-esubmissions	January 2008	October 2010	Requirements on eSubmissions for New Applications within MRP, DCP or National procedures
CMDh/006/2008	Rev6	Procedural Guidance-esubmissions	December 2008	December 2010	Requirements on eSubmissions for Renewals and Variations within MRP, DCP or National procedures

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Document reference	Revision number	Heading on website	Date of creation	Dates of last revision	Title
CMDh/098/2005	Rev2	Procedural Guidance-Art 61.3 Procedure	October 2005	June 2010	CMDh Standard Operating Procedure - Procedure for Article 61(3) changes to patient information and the notification for product information amendment under Article 61(3) (not accompanying a variation change)
CMDh/101/2001	Rev5	Procedural Guidance-Post Referral Phase	September 2001	November 2010	Recommendation for Mutual Recognition Procedure after finalisation of an arbitration procedure with a positive decision by the EU-Commission
CMDh/138/2009	Rev2	Paediatric Regulation-Guidance Documents	March 2009	June 2010	BPG Article 46 - Paediatric Regulation EU worksharing Procedure
CMDh/037/2009	Rev3	Paediatric Regulation-Guidance Documents	September 2008	July 2010	BPG Article 45 of Paediatric Regulation (EU Worksharing procedure)
CMDh/019/2009	Rev2	Paediatric Regulation-Guidance Documents	February 2009	October 2010	Recommendations for implementing Commission Decisions following an Article 29 application under the Paediatric Regulation
CMDh/141/2009	Rev1	Paediatric Regulation-Guidance Documents	December 2009	October 2010	Recommendations on submission and assessment in paediatric worksharing
CMDh/124/2008	Rev4	Paediatric Regulation-Article 45 and previous Worksharing	May 2008	April 2010	List of active substances and agreed SPC wordings - EU Worksharing procedure in the assessment of paediatric data
CMDh/014/2008	Rev11	Paediatric Regulation-Article 45 and previous Worksharing	October 2008	September 2010	Worksharing on Art.45 - List of the active substances included in the work-sharing procedure

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Document reference	Revision number	Heading on website	Date of creation	Dates of last revision	Title
CMDh/151/2009	Rev4	Paediatric Regulation-Article 45 and previous Worksharing	December 2009	December 2010	List of Active Substances for which data has been submitted in accordance with Art.45 of the Paediatric Regulation
CMDh/104/2006	Rev2	CMDh Referrals	January 2006	March 2010	Annex - Guidance on Oral Explanations
CMDh/103/2005	Rev5	CMDh Referrals	October 2005	June 2010	CMDh Standard Operating Procedure Disagreement in procedures – Referral to CMDh (incl. annex Guidance on OE to CMDh)
CMDh/140/2008	Rev13	Product Information-Harmonisation of SPCs Article 30 referrals	October 2008	June 2010	Information on applications referred in accordance with Article 30(2) of Directive 2001/83/EC
CMDh/130/2005	Rev1	Product Information-Core SPC/PL	March 2005	December 2010	Core SPC for FDG Fludeoxyglucose
CMDh/021/2009	Rev2	Templates-AR-Paediatric Data	February 2009	July 2010	Assessment Report for paediatric studies submitted in accordance with Article 45 of Regulation (EC) No1901/2006, as amended
CMDh/022/2009	Rev2	Templates-AR-Paediatric Data	February 2009	July 2010	Assessment Report for paediatric studies submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended
CMDh/160/2009	Rev1	Templates-AR-DCP	September 2009	November 2010	Assessment Report Feedback Form
CMDh/198/2010		Templates-AR-DCP	2005	September 2010	RMS Day 70 Quality Preliminary Assessment Report

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Document reference	Revision number	Heading on website	Date of creation	Dates of last revision	Title
CMDh/191/2009	Rev1	Templates-AR-Renewals	June 2009	October 2010	Template of Preliminary Renewal AR
CMDh/167/2005	Rev7	Questions & Answers -CMDh Referrals	2005	June 2010	Q&As on the SOP – Disagreement in procedures - Referral to CMDh
CMDh/154/2007	Rev12	Contact Points	October 2007	April 2010	Contact addresses for the submission of Paediatric information in Member States
CMDh/156/2009	Rev12	Contact Points	February 2007	April 2010	Contact e-mail addresses for submission of electronic response documents during Mutual Recognition & Decentralised Procedures
CMDh/142/2006	Rev17	Contact Points	March 2006	April 2010	Contact addresses for Submission of Translations in Mutual Recognition and Decentralised Procedures
CMDh/143/2006	Rev18	Contact Points	February 2006	July 2010	Contact e-mail addresses for submission of electronic version of the responses to the list of questions for applications referred to the CMDh
CMDh/144/2000	Rev17	Contact Points	February 2008	September 2010	Compiled list of contact points for Advice on MRP and DCP