Report from the CMDh meeting held on 14-16 December 2015

Mandatory use of the electronic Application Form (eAF) from 1 January 2016

As earlier stated in the CMDh minutes and press release, the **eAF will be mandatory for all procedures in the EU** (Centralised procedure, MRP, DCP and by default National procedure), for Human and Veterinary products. This applies to all new Marketing Authorisation Applications, Renewals and Variations and is in line with the EU eSubmission Roadmap that can be found at the EMA eSubmission website.

In order to support this milestone, **a webinar session dedicated to Industry was held** providing information about where to find relevant documents, addressing the most common issues and workaround solutions faced by Industry when filling the forms. It also explained the support structure to be followed for business related queries for MRP/DCP/National applications and Centralised ones. The webinar has been recorded and the video file - including slides - is available via the following links: video and slides. Applicants are highly encouraged to consult it before submission of applications and also to regularly consult the eAF website to keep track of updated workarounds and other relevant information.

Furthermore, based on the high interest shown towards this training it is planned to organise a further training session and a follow-up Q&A session in the near future. The dates for these sessions will be announced on the eAF website.

Should you encounter any problems with the use of the electronic forms, any comments or change requests, these should be communicated to eaf@ema.europa.eu

Pharmacovigilance

CMDh positions following PSUSA procedure for only nationally authorised products

The CMDh, having considered the PSURs on the basis of the PRAC recommendations and the PRAC assessment reports, agreed by consensus on the variations of the marketing authorisations of medicinal products containing the following active substances:

- Amlodipine besilate/ramipril
- Carmustine (powder and solvent for solution for infusion)
- Influenza vaccine (surface antigen, inactivated)
- Ofloxacin (systemic use)
- Ofloxacin (topical use)

With regard to the outcome of the PSUSA procedure for the combination of amlodipine besilate/ramipril, further information on the implementation of a corresponding wording of the safety changes for the monocomponents and/or other combinations will be made available by the CMDh in due time.

Further information regarding the above-mentioned PSUSA procedures, including information on the implementation, will be published on the EMA website http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000620.jsp&mid=WC0b01ac0580902b8d

Outcomes of informal PSUR work-sharing procedures

The CMDh has adopted the conclusions of PSUR assessments for:

- Epirubicin
- Felbamate
- Folinic acid / (di)sodium folinate / calcium folinate / calcium levofolinate

- Gadopentetic acid dimeglumine
- Imipenem/cilastatin
- Labetalol
- Macrogol 4000 and combinations
- Mesalazine
- Nedocromil
- Paracetamol for infusion
- Quetiapine fumarate
- Ropinirole
- Strontium (89Sr) Chloride
- Tiagabine (hydrochloride)
- Tixocortol, Tixocortol/chlorhexidine

which may require changes to the product information or introduction of other risk minimisation measures.

The public summaries will be published on the CMDh website under "Pharmacovigilance, PSURs, Outcome of informal PSUR worksharing procedures".

MAHs of the products concerned should implement the outcome of the assessment by the appropriate variation or other procedure (as advised) within 90 days of publication.

Revision of the CMDh working document - Information to be submitted by the member state of the European reference medicinal product

The CMDh has agreed an updated version of the CMDh working document - Information to be submitted by the member state of the European reference medicinal product. The information to be provided has been further clarified and a clarification has been included that in case of concerns on the content of the originator dossier, these may not lead to a refusal of the generic application.
The revised document will be published on the CMDh website under "Procedural Guidance, Generics".

Revision of the Questions and Answers on QP declarat

The CMDh has agreed an updated version of the Q&As on QP declaration. The answers to question 5 and 6 have been further clarified.
The updated document will be published on the CMDh website under "Questions and Answers".

Regulation (EC) No 1234/2008 on variations

The CMDh has agreed an update of the Questions and Answers on variations. Question 3.8 has been updated to bring it in line with the outcome of the Art. 5 recommendation discussed in November 2015.
The updated document will be published under "Questions & Answers".

The CMDh has further agreed an update of the examples for acceptable and not acceptable groupings for MRP/DCP products. A general comment has been included that type IA or IAIN variations for the implementation of safety relevant changes may not be grouped together with type IB or type II variations as this would delay the implementation of the safety information. Further minor editorial changes have been included. The updated document will be published under "Procedural Guidance, Variation".

The CMDh has also agreed an update of the BPG (Chapter 4) for the processing of Type IB Minor Variations (Notifications) in MRP to clarify that an assessment report is generally not foreseen for the evaluation of type IB variations, except for ASMFs included in the ASMF worksharing procedure. The updated document will be published under "Procedural Guidance, Variation".

CMDh Strategy to 2020

The CMDh wants to thank all external parties that have provided comments during the public consultation on the CMDh Strategy to 2020. The comments will be assessed over the coming weeks and taken into

account, where relevant, when updating the CMDh Strategy document. The CMDh will provide feedback to all contributions.

Pilots for merging and splitting of MRP/DCPs

The CMDh has agreed further details on the pilot projects for merging and splitting of MRP/DCPs. A document has been drafted summarising the background, scope, conditions and process for interested MAHs. It has been clarified that in the pilot only finalised MRP/DCPs can be included.
The document with further information will be published on the CMDh website under "Advice from CMDh".

CMDh/EMA Working Party on Paediatric Regulation

The CMDh has agreed a list of active substances for wave 29 of the worksharing for the assessment of paediatric studies submitted in accordance with Article 45 of the Paediatric Regulation.
Marketing Authorisation Holders will be requested to submit the paediatric studies to the appointed Rapporteur within one month of the request (i.e. by mid of February 2016).
The list of active substances included in wave 29 of the Article 45 worksharing procedure will be published on the CMDh website.

The CMDh has further agreed a revision of the "Recommendation for implementation of compliance statement for the agreed completed PIP" and the related "Template on compliance statement for the agreed completed PIP". Minor changes have been included in the documents, e.g. update of links to guidance documents and legislation. The updated documents will be published on the CMDh website under "Paediatric Regulation, Guidance documents".

The CMDh has also agreed an update of the template letter to be sent to MAHs to request the submission of Art. 45 data at the start of an Art. 45 worksharing procedure. MAHs will be asked to check before submission if the studies include paediatric subjects (0 up to 18 years) and if the studies have not already been submitted to an EU competent authority or evaluated through another regulatory procedure since submission of the Article 45 line listings.

EU Work-sharing Articles 45 & 46 of the Paediatric Regulation – Public Assessment Reports

The CMDh has agreed on public assessment reports for paediatric studies submitted in accordance with Article 46 of the Paediatric Regulation for Afluria (influenza virus), Seroxat (paroxetine), Lamictal (Dispers)/Lambipol (lamotrigine), Olmetec and related names (olmesartan) and Flixotide Evohaler and related names (fluticasone propionate).

Change in the Presidency of the Council of the European Union

The December 2015 CMDh meeting was the last one under the Luxembourg Presidency of the Council of the European Union. The Netherlands will take over the Presidency in January 2016. Mrs Kora Doorduyn-van der Stoep will be the appointed Presidency Vice-Chairperson of the CMDh during the Dutch Presidency of the Council of the European Union.

NEW APPLICATIONS

Mutual Recognition Procedure

The CMDh noted that **28** Mutual Recognition Procedures were finalised during the month of November 2015. **No** Mutual Recognition Procedures were referred to CMDh in this period**. No** Mutual Recognition Procedures were referred to CHMP in this period.

The status as of 30th November 2015 of procedures under Mutual Recognition is as follows:

Year	New applications finalised[1]	New applications in process	Referred to CMDh	Agreement reached in the CMDh		Withdrawn during CMDh referral		Applications referred to CHMP	
				For procedures referred in		For procedures referred in		For procedures referred to CMDh in	
				2014	2015	2014	2015	2014	2015
2015	**202**	**36**	**5**	**0**	**1**	**0**	**0**	**0**	**3**

20 Mutual Recognition Procedures (regarding **37** products) started in November 2015. The categories of these procedures are as follows:

- **11** abridged applications (including **10** repeat use procedure);

- **9** known active substance applications (including **8** repeat use procedures).

The Mutual Recognition Procedures started in November 2015 related to the following applications: **4** full dossier, **12** generic, **2** well-established use and **2** hybrid applications.

All procedures consisted of chemical substances.

18 of these procedures related to prescription-only medicinal products and **2** procedures related to non-prescription medicinal product in the reference Member State[2].

New applications in Mutual Recognition procedure started in November 2015:

Member State	Number of times involved in a procedure as RMS	Number of times involved in a procedure as CMS
Austria	1	6
Belgium		3
Bulgaria		3
Croatia		4
Cyprus		2
Czech Republic		3
Denmark	4	5
Estonia		3
Finland		4
France		8
Germany	4	6
Greece		2
Hungary		2
Iceland		2
Ireland		5
Italy	1	5
Latvia		1
Liechtenstein		
Lithuania		2
Luxembourg		2
Malta		
Netherlands	7	3
Norway		4

[1] Due to late database updates cumulative yearly figure differs from the monthly figures. Cumulative yearly figure includes late database updates on finalised procedures not captured in the monthly figures published in press releases. The applications referred to CHMP are included in the 'new applications finalised.'

[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.

Member State	Number of times involved in a procedure as RMS	Number of times involved in a procedure as CMS
Poland		8
Portugal		4
Romania		3
Slovak Republic		4
Slovenia		3
Spain		7
Sweden	1	6
United Kingdom	2	5

Decentralised Procedure

The CMDh noted that **81** Decentralised procedures with positive outcome and **no** procedures with negative outcome were finalised during November 2015. **6** Decentralised procedures were withdrawn after day 120 in this period. **1** Decentralised Procedure was referred to the CMDh in this period. **No** Decentralised Procedures were referred to the CHMP in this period.

The status as of 30th November 2015 of procedures under Decentralised Procedure is as follows:

Year	New applications finalised[3]	New applications withdrawn[3] (After day 120)	New applications in process	Referred to CMDh	Agreement reached in the CMDh For procedures referred in		Withdrawn during CMDh referral For procedures referred in		Referred to CHMP For procedures referred to CMDh in	
					2014	2015	2014	2015	2014	2015
2015	**990**	**86**	**1348**	**8**	**3**	**3**	**0**	**2**	**1**	**1**

127 Decentralised Procedures (regarding **262** products) started in November 2015. The categories of these procedures are as follows:

- **91** abridged applications (including **14** multiple applications);
- **35** known active substance applications (including **11** multiple applications);
- **1** extension application.

The Decentralised Procedures started in November 2015 related to the following applications: **3** full dossier, **103** generic, **7** well-established use, **13** hybrid and **1** herbal traditional use application.

124 of these procedures consisted of chemical substances and **3** herbal applications.

118 of these procedures related to prescription-only medicinal products and **9** procedures related to non-prescription medicinal products in the reference Member State[4].

New applications in Decentralised procedure started in November 2015:

Member State	Number of times involved in a procedure as RMS	Number of times involved in a procedure as CMS
Austria	3	19
Belgium		21

[3] Due to late database updates cumulative yearly figure differs from the monthly figures. Cumulative yearly figure includes late database updates on finalised procedures not captured in the monthly figures published in press releases. For finalised procedures, this cumulative figure includes positive and negative procedures as well as those referred to CHMP.

[4] 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.

Member State	Number of times involved in a procedure as RMS	Number of times involved in a procedure as CMS
Bulgaria		13
Croatia		12
Cyprus		7
Czech Republic		16
Denmark	18	16
Estonia		12
Finland	4	16
France		32
Germany	13	45
Greece		8
Hungary	9	13
Iceland		6
Ireland	1	21
Italy		36
Latvia		12
Liechtenstein		
Lithuania		11
Luxembourg		23
Malta	3	6
Netherlands	30	16
Norway		9
Poland		19
Portugal	15	21
Romania		14
Slovak Republic		17
Slovenia		15
Spain	9	30
Sweden	6	18
United Kingdom	16	27

VARIATIONS AND RENEWALS

Mutual Recognition and Decentralised Procedures

The CMDh noted that **263** type IA variations, **232** type IB variations, **34** type II variations and **34** renewals were finalised during November 2015. **No** Type II variation, **no** variation worksharing, or renewal procedure was referred to the CMDh in this period. **No** type II variation procedure was referred to the CHMP in this period.

The status as of 30th November 2015 of variations and renewals under Mutual Recognition is as follows:

Year	Type IA variations finalised	Type IB variations finalised	Type II variations finalised	Variation work-sharing[5] finalised	Renewals finalised
2015	**2765**	**2481**	**332**	**262**	**655**

2015	Referred to CMDh	Agreement reached in the CMDh **For procedures referred in**		Withdrawn during CMDh referral	Applications referred to CHMP **For procedures referred to CMDh in**	
		2014	**2015**		**2014**	**2015**

[5] Finalised work sharing do not include work sharing involving centrally approved products coordinated by EMA

Type II	2	0	0	1	0	1
Worksharing	0	1	0	0	0	0
Renewal	0	0	0	0	0	0

Information on the above mentioned issues can be obtained from the chair of the CMDh or from the CMDh Secretariat:

Dr. Peter Bachmann
Bundesinstitut für Arzneimittel und
Medizinprodukte (BfArM)
Kurt-Georg-Kiesinger-Allee 3
D – 53175 Bonn, Federal Republic of Germany

Phone: + 49 228 207 4163
Fax: + 49 228 207 3452
E-mail: Peter.Bachmann@bfarm.de

CMDh Secretariat

E-mail: H-CMDhSecretariat@ema.europa.eu

*Or you could visit the **CMDh website** at:*

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