29 September 2014
EMA/HMPC/441024/2014
Procedure Management and Business Support Division

Committee on Herbal Medicinal Products (HMPC)

Minutes of the 30 June-1 July 2014 meeting

FINAL

30 June 2014, 14:00 – 19:00, room 3A, *plenary*
1 July 2014, 09:00 – 13:00, room 3A, *plenary*
(Visit to 30 Churchill place on 1 July 2014, 19:00)

Chair: Werner Knöss

- **Health & Safety Information**

In accordance with Agency policy, delegates are to be shown a slide show with health and safety and emergency information and procedures. This is to be displayed at the start of this meeting using the Crestron system as delegates are entering the meeting room. In addition, the meeting secretariat is to draw the delegates' attention to the slideshow and point out the nearest fire exit(s), which are marked where the room has two or more exits. Should there be an evacuation during the meeting staff will guide delegates out of the building via the nearest fire exit.

- **Declaration of conflict of interests**

In accordance with the Agency's Policy and Procedure on the handling of conflicts of interests, participants in this meeting are asked to declare any conflict of interests on the matters for discussion (in particular any changes, omissions or errors to the already declared interests).
Discussions, deliberations and voting will take place in full respect of the restricted involvement of Scientific Committee members and, where relevant, experts attending the plenary meeting, as announced by the Scientific Committee secretariat at the start of the meeting.

- No new or revised conflict of interests was declared and no restriction in the involvement of members in relation to agenda topics was identified.

- **Note on access to documents**

Some documents mentioned in the agenda/minutes cannot be released at present within the framework of Regulation (EC) No 1049/2001 on access to documents because they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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I. Introduction	
I.1 Agenda, minutes	
I.1.1 Agenda of 30 June-1 July 2014 HMPC meeting - timetable, for order of topics *For adoption*	Adopted
I.1.2 Minutes of 5-6 May 2014 HMPC meeting *For adoption*	Adopted
I.2 Legislation and regulatory affairs	
I.2.1 Validation of the BSS - assessment of reliability and implications for specific monographs - draft assessment report - letter dated 18 Dec 2013 - response with attachments received on 30 April 2014 - list of additional data/literature - positions from Rapporteurs *For discussion*	Report: HMPC Chair After additional evaluation of quantitative aspects (reliability) the HMPC confirmed that the BSS can be useful to show therapeutic benefit in reduction of severity of symptoms of acute bronchitis from a clinical and statistical point of view. Despite shortcomings of a retrospective validation it represents an alternative for specific scales that have not been designed yet. Rapporteurs for relevant monographs were asked to check consequences for the assessment to be presented at the MLWP September meeting.
The Chair and Rapporteurs summarised the history and their position based on requested additional data following concerns expressed by some members on the reliability of the score and an extensive debate on clinical and statistical relevance. Upon this confirmation on the possibility to use BSS in principle to investigate some symptoms of bronchitis in absence of more suitable scales, Rapporteurs will check the relevance for the specific assessment of herbal substances and eventual changes to be introduced in AR, LoR with possible impact on the monographs to initiate a revision in line with the Reflection paper EMA/HMPC/326440/2007 Rev.2 (reasons and timelines for revision of final Community herbal monographs and Community list entries).	
I.3 Questions raised by HMPC members	
I.3.1 New QRD template for THMPs in mutual recognition and decentralised procedures - email *For discussion*	Small group to draft a problem statement with key issues and objectives for the next ORGAM DG meeting (8 Sep) as basis for coordination with QRD group.
It was now decided that ORGAM DG should be involved from the very beginning. Some issues regarding the monograph template and the public information on the status of a monograph vis-à-vis SmPC and labelling were raised and should be taken into account.	
I.4 Questions raised by companies	
I.5 Referral procedures	
II.Co-ordination issues	

II.1 General co-ordination issues	
II.2 Co-ordination with CHMP	
II.3 Co-ordination with SAWP	
II.4 Co-ordination with SWP	
II.4.1 Assessment of estragole and alkenyl benzenes - draft discussion paper - status report - presentation - letter to SWP Chair - HMPC PS on the use of HMPC cont estragole *For discussion*	HMPC noted coordination progress with SWP via CHMP. Rapporteur to draft revised public statement for discussion at the HMPC September meeting.
The committee noted the ongoing evaluation of HMPC specific questions at SWP and presentation of the case by the HMPC observer. After SWP response the document EMEA/HMPC/137212/2005 will be revised for public consultation in line with the previously presented rationale. Once the draft is published, coordination with EFSA was encouraged given the presence of estragole in food products.	
II.4.2 Revision on Public Statement on the use of herbal medicinal products containing pulegone and menthofuran - discussion paper toxicological assessment - comments received during May written procedure - draft revised public statement - letter to SWP Chair - presentation - menthae piperitae aetheroleum - monograph *For discussion*	Rapporteur: O. Pelkonen, J. Wiesner HMPC noted initiated coordination for follow-up within the network as necessary. Rapporteurs together with HMPC Chair to modify and further develop the draft revised public statement according to response from SWP for distribution among HMPC members by 10 September. HMPC members to send comments to the Rapporteur by 19 September for finalisation of the revised public statement.
Comments during written procedure were welcomed and had been introduced in the discussion paper. It became apparent that beside pre-clinical data few other new data are available and that consequences have to be more specifically communicated. The HMPC Chair informed that confirmation of the toxicological approach and threshold calculations by SWP was seen as essential before further action. A revised public statement (PS) had been drafted and included in communication to SWP alongside specific questions. The Rapporteur and observer at SWP had presented the case, however, the topic had been postponed and is expected to be discussed at the next SWP virtual meeting. Members were requested to check their national situation as regards products and pharmacovigilance signals and to comment on the draft revised PS to be further developed in particular as regards conclusions. The PS and coordination consequences will be discussed at the HMPC September meeting considering also the presence of pulegone containing products in other product categories. The systematic revision of the Mentha monographs will be continued at MLWP as scheduled with final modifications possible according to the HMPC discussion on pulegone.	

II.5 Co-ordination with PDCO	
II.6 Co-ordination with PRAC	
II.7 Co-ordination with PCWP	
II.8 Co-ordination with HCPWP	
II.9 Co-ordination with Medical Writers	
II.10 Co-ordination with COMP	
II.11 Co-ordination with CMDh	
II.12 Co-ordination with Eur. Com.	
II.13 Co-ordination with EFSA	
III. Organisational matters	
III.1 Organisational Matters Drafting Group	
III.1.1 Virtual ORGAM DG meeting to be held on 13 May 2014 - meeting report *For information*	Report: ORGAM DG Chair HMPC noted progress with regard to MO+LE template and CTD guideline revision as well as postponement of the June meeting. In addition to ongoing tasks the cross-check of the QRD template with HMPC monographs and standard herbal product information was requested (see I.3.1).
Three topics had been on the agenda of the ORGAM DG. A first step in the revision of the guideline EMA/HMPC/71049/2007 as regards points 2.5 and 2.7 had been performed by the Rapporteur and discussed by ORGAM DG. Changes in 2.4/2.6 were given to the Co-Rapporteur and the new ORGAM member in order to benefit from experience with non-clinical data. Draft revised MO+LE templates had been discussed and transferred to the MLWP. The review of the revision practice in particular as regards LEs was introduced and Rapporteurs appointed for discussion in September.	
III.2 Working methodology	
III.2.2 Nomination of co-opted members - procedure for nomination co-opted members for HMPC, 12 Nov 04 - Overview of expertise available in the HMPC *For discussion*	Report: HMPC Chair No changes were proposed for areas of expertise most required for the HMPC (Clinical pharmacology, Paediatric medicine, Experimental/non-clinical pharmacology, Toxicology, General and family medicine). Members to (re-)nominate co-opted members (Clinical pharmacology, Experimental/non-clinical pharmacology, General and family medicine) for election at the HMPC September meeting. HMPC secretariat to distribute Overview of expertise according to current membership for update among HMPC members.

For 3 of 5 current co-opted members the mandate has expired and elections will take place in September. Following confirmation of the areas of expertise required for the HMPC tasks, candidates should be nominated, according to the HMPC RoP, the existing procedure and in analogy to other committees providing the necessary information (also if-renewed). In this context the committee agreed that an old overview of expertise available should be updated by the secretariat to current membership and redistributed to everybody for completion.	
III.2.3 Organisation of an assessors' training in 2014 for 20 participants - agenda *For discussion*	Report: HMPC Chair Supported by: R. Länger, H. Neef, I. Chinou HMPC agreed to main outline. Suggested speakers, discussion leaders and members (willing to give a presentation in session II or III) to confirm principle availability to HMPC Chair by 21 July 2014. All members to suggest specific questions or problems to be discussed by 11 August 2014.
The committee agreed in principle on an exchange of experiences between monograph/guideline users at NCAs and members of HMPC/MLWP producing those guidelines. The HMPC Chair proposed a stepwise further development of the agenda for the training in November. The next version (expected in August) to be distributed by the secretariat including further information on administrative aspects (participation, nomination, re-imbursement).	
III.2.4 Move to new EMA offices in July 2014 - presentation *For information*	
HMPC members were reminded that the next meeting will take place at the new premises but not Westferry circus anymore. A first possible visit of the new facilities was offered for the 01 July evening.	
III.2.5 Survey 'Uptake of traditional use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States' (2013 data) - status report *For discussion*	HMPC noted publication of the main 2013 data (EMA/322570/2011 Rev. 4) at the EMA website.
The secretariat thanked the contact points of all MS for providing the raw data. The received information could be completed and was summarised and published. Main features of current registrations across MS were presented. The committee noted in particular a newly increased number of registrations in 2013 in comparison to 2012 and the high portion of combination products registered in 2013 (over 50% of registrations) but also a high diversity among member states. A more detailed analysis may be presented at the next informal meeting of the HMPC.	
III.2.6 HMPC work plan and input for EMA work programme 2015 - presentation - current work programmes HMPC, MLWP, Q DG, ORGAM DG *For discussion*	HMPC, MLWP, ORGAM and Quality DG Chairs to liaise for draft 2015 work programmes to be discussed at HMPC September meeting. HMPC secretariat to inform members on cross agency activities to collect proposals for future Agency work programme and road map. Chairs and HMPC members to suggest HMPC long

	term projects and deliverables beside core-task for further consideration.
A first overview on the new approach as regards the agency work programme and committee work plans was presented giving the main ideas and features. A harmonised approach among committees work plans feeding into the Agency work programme (annual basis) under involvement of the Scientific coordination board is planned. As a first step the HMPC Chair will liaise with the Chairs of the drafting groups and the MLWP to check the status of existing work programmes and review future activities. After information by the secretariat on the latest status regarding process and format, members are invited to provide suggestions for discussion at the HMPC September meeting in order to agree on first proposals. A requested more detailed discussion on activities, deliverables and reporting with the distinction between core-business and other activities will follow.	
IV. Quality	
IV.1 Quality Drafting Group	
IV.1.1 Meeting report from Q DG meeting held on 18 June 2014 *For adoption*	Report: Q DG Chair Adopted
The Q DG Chair presented the main outcome of the June meeting. A reflection paper on benzene in extracts is expected to be completed and presented for the next HMPC meeting. Some progress has been made with the module 3 mock-up as appendix for the herbal CTD guideline EMA/HMPC/71049/2007. A set of Q&A had been finalised as well as comments to EDQM as regards fresh herbal drug quality requirements. Furthermore general quality issues currently discussed at QWP were on the agenda to identify relevance of new guidelines for HMP.	
IV.1.2 Q&A on herbal substances that do not contain an assay in the Ph.Eur. monograph. *For adoption*	For inclusion into Quality Q and A document (EMEA/HMPC/41500/2010) Adopted
IV.1.3 Q&A on herbal preparation that do not contain an assay in the Ph.Eur. monograph. *For adoption*	For inclusion into Quality Q and A document (EMEA/HMPC/41500/2010) Adopted
IV.1.4 Q&A on declaration of DER and extraction solvent in case of fresh herbal substances *For adoption*	For inclusion into Quality Q and A document (EMEA/HMPC/41500/2010) Adopted
IV.1.5 Q DG comments on EDQM monograph on fresh herbal drugs *For adoption*	Agreed for transmission to EDQM secretariat.
IV.2 European Pharmacopeia	
IV.2.1 Report from EDQM Expert Group 13A meeting held on 2-3 June 2014 - group 13A summary of decisions *For discussion*	EDQM: M. Bald HMPC Observer: I. Chinou HMPC noted summary of decisions and monographs currently at different stages of development/publication. Upon information by EDQM secretariat HMPC secretariat to inform HMPC members on previously commented revised Ph. Eur. monograph on herbal drug extracts (plus

	corresponding information chapter) as agreed by Ph. Eur. commission for publication in Ph. Eur. supplement 8.5.
IV.2.2 Report from EDQM Expert Group TCM meeting held on 5-6 June 2014 - group TCM summary of decisions *For discussion*	EDQM: M. Bald HMPC Observer: R. Länger HMPC noted summary of decisions and monographs currently at different stages of development/publication.
IV.2.3 Priority of herbal substances with a need of Ph. Eur. Monographs for submission to EDQM - priority list (EMA/HMPC/328288/2014) submitted 28/05/14 *For information*	HMPC proposal have been submitted to Ph. Eur. Commission and are taken into account for the upcoming work programme according to response from the member states. HMPC to consider similar exercise after one year taking into account Community monographs under preparation and rational for alignment between HMPC and Ph. Eur. monographs as provided previously by the Rapporteurs.
V. Safety & efficacy	
V.1 Report on MLWP activities	
V.1.1 Report on progress achieved Overview of status of MLWP assessment work *For discussion*	Report: MLWP Chair
V.1.2 Appointment for Rapporteurs and Peer-reviewer	HMPC agreed to the appointment or change of Rapporteurs and Peer reviewers.

Herbal substance	Rapporteur	Peer-reviewer
Arctii radix (M)		
Boldi folium (M)		
Caryophylii flos (PS)		
Caryophylii floris aetheroleum (M)		
Centaurii herba (M)		
Curcumae longae rhizoma (M)		
Equiseti herba (M)		
Hamamelidis folium et cortex aut ramunculus destillatum (M+LE)		
Hamamelidis cortex (M)		
Hamamelidis folium (M)		
Harpagophyti radix (M)		
Hippocastani cortex (M)		
Hippocastani semen (M)		
Orthosiphonis folium (M)		
Leonuri cardiacae herba (M)		
Mate folium (M)		
Polypodii rhizoma (M)		
Salicis cortex (M)		
Sideritis herba		
Taraxaci radix cum herba (M)		

Taraxaci folium (M)		
Thymi aetheroleum (M + LE)		
Trigonellae foenugraeci semen (M)		
Vitis viniferae folium (M + LE)		
Myrtilli fructus recens plus myrtilli fructus siccus (M)		

V.2 Community list entries transmitted to European Commission

V.3 Community herbal monographs for public consultation / final adoption after systematic review / revision

V.4 Community herbal monographs (post finalisation)

V.5 Community herbal monographs, Community list entries and public statements for adoption after public consultation

V.5.1 Monograph on Rosae flos (and supporting documents: AR, LoR, references 0/32) *For adoption*	Final monograph and supporting documents adopted by a majority vote (26 out of 27). NO expressed a favourable position. Divergent position: E. v. Galen

The package was adopted without changes. A proposal to reconsider the indication (irritation vis-à-vis inflammation) was not agreed. Available literature was provided.

V.6 Community herbal monographs, Community list entries and public statements for adoption for release for public consultation

V.6.1 Monograph on Capsici fructus (and supporting documents: AR, LoR, OoC) *For adoption/discussion*	Draft monograph and supporting documents adopted by consensus for release for public consultation until 31 October 2014.

The Rapporteur presented relevant background information and previous discussions on marketed herbal preparations, available data and specific considerations for WEU for locally applied and acting medicinal products as regards equivalence. A proposal for establishment of a WEU monograph was widely accepted with the caveats that depending on the specific preparation and product it should be clear that more data may be required and contact with the national agencies before starting a procedure is advised (national scientific advice). Thus the monograph contributes to a harmonised European view, while final issues can be sorted at individual national procedures. Scientific and procedural aspects as regards comparability such as chemical equivalence, bioequivalence and therapeutic equivalence as well as applicable guidelines, WEU criteria and previous communication with the Eur. Com. were discussed. It was agreed on a specific footnote and supportive information in the AR.

Other topics for discussion were some qualitative and quantitative comparisons of preparations (e.g. oleoresin) and in particular the duration of use taking into account experiences from products on the market and state of knowledge on the mechanism of action. Subsequently changes were introduced in monograph sections 4.2 in addition to sections 2 and 4.1.

V.6.2 Monograph on Eschscholziae herba cum flore (and supporting documents: AR, LoR) *For adoption*	Draft monograph and supporting documents adopted by consensus for release for public consultation until 31 October 2014.
V.6.3 Monograph on Matricariae aetheroleum	Draft monograph and supporting documents

(and supporting documents: AR, LoR) *For adoption*	adopted by consensus for release for public consultation until 31 October 2014.
The Committee welcomed the finalisation of the draft package. The Rapporteur was asked for final alignments between monograph and AR covering both M. flos and aetheroleum before publication for consultation. For use in children see M. flos below.	
V.6.4 Monograph on Matricariae flos (and supporting documents: AR, LoR) *For adoption*	Draft monograph and supporting documents adopted by consensus for release for public consultation until 31 October 2014.
The high number of preparations fulfilling TU criteria had been reviewed and merged where possible. Despite the unusual long posology section it was agreed to maintain the monograph standard structure for not causing confusion with users familiar to the standard template. Amendments in the monograph were performed following a discussion on acceptable use in children as regards different routes of administrations, preparations and available data versus general considerations for young age groups. The Rapporteur was asked for final alignments between documents before publication for consultation.	
V.6.5 Public statement on Picrorhizae kurroae rhizhoma (and supporting document: LoR) *For adoption*	Draft public statement and supporting LoR adopted by consensus for release for public consultation until 31 October 2014.
The draft public statement together with the draft List of references was adopted for public consultation aiming for more data allowing the establishment of a monograph.	
V.6.6 *Monograph on Pilosellae herba cum flore (and supporting documents: AR, LoR) *For adoption*	Draft monograph and supporting documents adopted by consensus for release for public consultation until 31 October 2014.
Further to update of the package to reduce amendments requested in May the monograph supporting documents were adopted.	
V.7 Community herbal monographs, Community list entries and public statements for discussion	
V.8 Guidelines	
VI. Other relevant business	
VI.1 Conferences, presentations & research projects	
VI.2 International cooperation, collaboration with non-EU regulatory authorities	
VI.3 Documents for information	
VI.3.1 Table of Decisions from HMPC meeting held on 5-6 May 2014	
VI.3.2 Meeting report from HMPC meeting held on 5-6 May 2014	http://www.ema.europa.eu/docs/en_GB/document_library/Committee_meeting_report/2014/05/WC500167583.pdf
VI.3.3 Draft agenda of MLWP meeting to be held on 2-3 July 2014	

VI.3.4 Table of Conclusions from MLWP meeting held on 6-8 May 2014	
VI.3.5 Draft Minutes from MLWP meeting held on 6-8 May 2014	
VI.3.6 Overview of status of HMPC assessment work – priority list	
VI.3.7 Inventory of herbal substances for assessment work – alphabetical order	
VI.3.8 Common names of herbal substances in all EU official languages	
VI.4 Any other information	
VI.4.1 Abbreviations in HMPC minutes	http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/11/WC500155666.pdf

List of participants

Chair of the HMPC	***Apologies***
Werner Knöss	Heidi Neef (BE)
	Evelin Saar (EE)
HMPC members	Niamh Curran (IE)
Reinhard Länger (AT)	Dace Kalke (LV)
Elena Mustakerova (BG)	Arturas Kažemekaitis (LT)
Ivan Kosalec (HR)	Jacqueline Genoux-Hames (LU)
Maria Stavrou (CY)	Barbara Razinger (SL)
Marie Heroutová (CZ)	Gioacchino Calapai (co-opted)
Steffen Bager (DK)	Tina Engraff (European Commission)
Eeva Sofia Leinonen (SF)	
An Lê (FR)	***HMPC alternate members***
Jacqueline Wiesner (DE)	Marje Zernant (EE)
Ioanna Chinou (GR)	Jacqueline Viguet Poupelloz (FR)
Zsuzsanna Biró-Sándor (HU)	Anna Cunney (IE)
Marisa Delbó (IT)	Baiba Jansone (LV)
Everaldo Attard (MT)	Erika Svedlund (SE) (via TC)
Emiel van Galen (NL)	Samo Kreft (SL)
Steinar Madsen (NO)	Burt Kroes (NL)
Wojciech Dymowski (PL)	Sue Harris (UK)
Ana Paula Martins (PT)	
Nadia Grigoras (RO)	**Observer**
Martina Hudecová (SK)	Saša Pilipović (Bosnia and Herzegovina)
Adela Núñez Velázquez (ES)	Melanie Bald (Conseil de l'Europe – via TC)
Per Claeson (SE)	Arianit Jakupi (Kosovo)
Linda Anderson (UK)	Merjem Hadjihamza (Macedonia)
Silvia Girotto (co-opted)	Jasmina Krlic (Montenegro)
Gert Laekeman (co-opted)	Dragan Djurovic (Serbia)
Olavi Pelkonen (co-opted)	
Maria Helena Pinto Ferreira (co-opted)	