25 September 2018
EMA/HMPC/672621/2018 **FINAL**
Inspections, Human Medicines Pharmacovigilance & Committees Division

Committee on Herbal Medicinal Products (HMPC)

Minutes for the meeting on 23-24 July 2018

Chair: Marisa Delbò Vice-Chair: Emiel van Galen

23 July 2018, 14:00 – 19:00, 2F

24 July 2018, 09:00 – 13:00, 2F

Health and safety information

In accordance with the Agency's health and safety policy, delegates are briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in the minutes is considered commercially confidential or sensitive and therefore not disclosed.

Of note, this minutes is a working document primarily designed for HMPC members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as 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).

Table of contents

1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

In accordance with the Agency's policy on handling of declarations of interests of scientific committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and based on the topics in the agenda of the current meeting, the Committee Secretariat announced that no restriction in the involvement of meeting participants in upcoming discussions was identified.

Participants in this meeting were asked to declare any changes, omissions or errors to their declared interests and/or additional restrictions concerning the matters for discussion. No new or additional interests or restrictions were declared.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure and as included in the list of participants. All decisions taken at this meeting were made in the presence of a quorum of members (i.e. 22 or more members were present in the room).

End of membership (UK): Sue Harris (alternate); End of mandate: 27 June 2018

New membership (Romania): Ligia Elena Dutu alternate; Start of mandate: 21 June 2018

1.2. Adoption of agenda

HMPC agenda for 23-24 July 2018

Time schedule for 23-24 July 2018

Outcome:
Agenda adopted. Point added 5.7.2.

Time schedule endorsed.

1.3. Adoption of the minutes

HMPC minutes for 04-05 June 2018

Outcome:
Minutes adopted.

Absence of committee members during voting for adoption of EU Herbal Monographs/ list entries always to be recorded.

2. European Union herbal monographs and list entries

2.1. Report on MLWP activities

2.1.1. Appointment of Rapporteurs and Peer-reviewers

Changes of Rapporteurs for MO review

Millefollii flos and Millefolii herba - Rapporteur
Phaseoli fructus (sine semine) – Co-Rapporteur

Outcome:
Endorsed.

2.1.2. Report from the MLWP June 2018 meeting

Report: MLWP Chair/MLWP Vice-Chair
Action: for information
Document: Draft minutes for the MLWP meeting on 05-07 June 2018

2.2. Revised EU herbal monographs and list entries for final adoption

2.2.1. Monograph on Curcumae longae rhizoma and supporting documents

Rapporteur: E van Galen, B Kroes; Peer-reviewer: M Delbò
Action: for adoption
Documents: MO, AR, LoR; References: 00/132

Outcome:

Adoption postponed to HMPC September meeting.

Before possible final adoption some corrections were requested in the AR mainly linked to references and details supporting the traditional use as well as the format of the LoR.

2.2.2. Monograph on Sennae folium and supporting documents

Rapporteur: W Knöss; Peer-reviewer: I Chinou
Action: for adoption
Documents: MO, AR, LoR, OoC; References: 173/217

Outcome:

Adoption postponed to HMPC September meeting.
Following the peer review, Rapporteur still to respond to comments and provide final clean documents for final adoption.

2.2.3. Monograph on Sennae fructus and supporting documents

Rapporteur: W Knöss; Peer-reviewer: I Chinou
Action: for adoption
Documents: MO, AR, LoR, OoC; References: 173/217

Outcome:

Adoption postponed to HMPC September meeting.
Following the peer review, Rapporteur still to respond to comments and provide final clean documents for final adoption.

2.3. Revised EU herbal monographs and list entries for public consultation

None

2.4. Reviewed EU herbal monographs and list entries for decision on revision

2.4.1. Monograph on Myrrhra (Commiphora molmol) and supporting documents

Action: for adoption
Document: Review outcome; References: 09/09

Outcome:

HMPC agreed with Rapporteurs position that no monograph revision is needed because no new data of relevance were detected that would change the content of the monograph.

The HMPC decided not to revise the monograph, assessment report and list of references on Myrrhra (Commiphora molmol).

2.4.2. Monograph on Trigonellae foenugraeci semen and supporting documents

Action: for adoption
Document: Review outcome; References: 30/30

Outcome:

The HMPC agreed with the Rapporteur's position and decided by consensus to revise the monograph, assessment report and list of references on Trigonellae foenugraeci semen.

New safety-relevant non-clinical and clinical studies were detected.

2.5. EU herbal monographs, list entries and public statements for final adoption

None

2.6. EU herbal monographs, list entries and public statements for adoption for release for public consultation

None

2.7. EU herbal monographs, list entries and public statements - post finalisation

2.7.1. Monograph on Agni casti fructus and supporting documents

Action: for discussion
Documents: MO, AR, LoR; References: 109/98; Email correspondence dated 16 July 2018

Outcome:

HMPC noted general information on use of unpublished data according to provisions set out in document EMA/HMPC/1004/2006 Rev. 6 and potential changes in AR and monograph section 5.3 according to outcome of data owner consultation.

If the consent for use of unpublished data is obtained, additional data can be given in revised monograph and AR as presented by the Rapporteur. If no consent is obtained, no additional information should be included in the revised monograph/AR for publication and the wording of the existing documents kept in this respect.

2.7.2. Monograph on Pistacia lentiscus, resinum (mastix) and supporting documents (postponed)

3. Referral procedures

None

4. Guidelines and guidance documents

4.1. Non-clinical/clinical safety and efficacy and multidisciplinary

4.1.1. Public statement on the use of herbal medicinal products containing estragole

Action: for discussion
Documents: Draft revised PS, OoC; Comments from SE; SWP subgroup comments; Presentation

Outcome:

HMPC took note of SWP and SE comments and agreed by majority to follow largely the proposal by Rapporteur and MLWP. Remaining decisions regarding sensitive groups are to be taken at the HMPC September meeting for final adoption of the revised PS. Members invited to send comments by 11 September 2018.

HMPC discussed pros and cons of (a) the proposal by the Rapporteur/ MLWP and (b) the alternative proposed by one MS and supported by SWP experts. The Rapporteur presented consequences for products on the market and substances in HMPC monographs as well as uncertainties of food use estimates as starting point for calculation.

4.2. Quality

None

4.3. Regulatory / Procedural

4.3.1. Procedure for the review and revision of European Union herbal monographs and European Union list entries (EMA/HMPC/124695/2011 Rev.2)

Action: for adoption
Documents: Draft procedure; Review outcome template; OoC

Outcome:

Procedure adopted.

HMPC secretariat to publish documents on the EMA website and provide to all MLWP members.

Minor changes by ORGAM DG and EMA secretariat were presented and agreed.

The procedure is already followed for all reviews started in 2018, while revisions that had already started before can be finalised according to previous practice.

4.4. Report on HMPC Drafting Groups activities

4.4.1. Quality DG

Report: Q DG Chair

- Meeting report from Q DG virtual meeting held on 21 Jun 2018
  Action: for adoption
  Document: Meeting report
- Draft agenda for the Q DG virtual meeting to be held 06 Sep 2018
  Action: for information
  Document: Draft agenda

Outcome:

Meeting report was adopted.

HMPC took note of limited response to the Concept paper on new analytical methods. It was agreed to invite again Interested parties (IPs) for submission of data via meeting report and email (deadline 30 November) and clarify the topic with AESGP during the hearing at MLWP in September.

The standard practice and existing alert system for the newly published documents on the EMA website was discussed. IPs not used to the EMA system and included in the HMPC-recognised list of IPs (routinely alerted) may not always be aware of new documents and therefore a scarce feed-back is received.

Updates were given by the QDG Chair on the forthcoming virtual meeting in September.

HMPC noted also the adoption of the draft revised guidelines EMA/HMPC/201116/2005 Rev. 3 and EMA/HMPC/162241/2005 Rev. 2 by QWP, CHMP and CVMP without further changes for public consultation.

4.4.2. ORGAM DG

Report: ORGAM DG Chair

- Meeting report from ORGAM DG virtual meeting held on 18 Jun 2018
  Action: for adoption
  Document: Meeting report
- Agenda ORGAM DG meeting to be held on 04 Sep 2018
  Action: for information
  Document: Draft agenda

Outcome:

Meeting report was adopted.

Updates were given by the ORGAM Chair on the forthcoming virtual meeting in September.

The HMPC was informed on topics currently under discussion at the DG which included beside the finalisation of the review/revision procedure (see 4.3.1) work on update/

revisions of several templates and procedures older than 10 years according to the ORGAM DG work plan.

5. Organisational, regulatory and methodological matters

5.1. Mandate and organisation of the HMPC

5.1.1. Strategic Review and Learning Meetings

Austria Presidency meeting – Vienna, 15-17 Oct 2018
Action: for discussion
Document: Revised Draft Agenda; Invitation; Practical information

Outcome:

HMPC noted updates on content and practical information given by the Austrian member.

Members were invited to submit further proposals regarding draft agenda point 5.

5.2. Coordination with EMA Scientific Committees or CMDh-v

5.2.1. Scientific Coordination Board Meeting

Report: HMPC Chair
Action: for information
Documents: Minutes 03 May 2018; Agenda 16 July 2018; HMPC Chair remarks

Outcome:

HMPC noted updates given by the HMPC Chair regarding EMA regulatory science strategy and upcoming EU Telematics strategy Concept Paper.

The HMPC Chair presented her comments on the regulatory science strategy from a herbal perspective and first background information on the EU Telematics strategy Concept Paper which will be introduced to all committees in September.

5.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

None

5.4. Cooperation within the EU regulatory network

5.4.1. Coordination with the European Commission (postponed)

- Clarification of classification on Saccharomyces cerevisiae CBS 5926

5.4.2. Coordination with European Pharmacopoeia

- EDQM 13A expert group meetings
  Action: for information
  Document: SoD meeting 12/13 June
- EDQM 13B expert group meetings

Action: for information
Document: SoD meeting 25/26 April

- EDQM TCM expert group meetings
  Action: for information
  Document: SoD meeting 18/19 April
- EDQM PA working party
  Document: SoD meeting 24 April

Outcome:

HMPC noted summary of decisions (SoDs) and updates on 13A, 13B expert group activities and monographs adopted or in preparation at the Ph. Eur. commission given by the EDQM representative.

Some question regarding development or revision of specific monographs as well as the progress with the PA method development were clarified.

5.4.3. Understanding the training needs of NCA assessors involved in the work of the HMPC: Priority needs and plans for training 2018 – 2020 (postponed)

5.4.4. EMA Implementation Plan of the new medical device and in vitro diagnostic regulation

Action: for discussion
Documents: Presentation; Borderline manual; https://ec.europa.eu/docsroom/documents/29021/attachments/1/translations/en/renditions/nativegroup

Outcome:

HMPC noted information given by the EMA and highlighted the importance regarding the borderline HMP – MD and HMPC involvement – mainly on two work streams: 'substance-based medical devices' and 'borderline consultation'.

Objective and main features of the new regulation were introduced as well as the planned future role of EMA and committees on some subjects. These focus mainly on procedures and timelines applicable for substances used in products approved via centralised procedure, consultation on substance based medical devices, the interface between precision medicines and diagnostics and integral drug device combinations (CHMP, CAT, BWP, QWP).

The HMPC Rapporteur for the borderline HMP – MD pointed to previous examples and comments provided by the HMPC and informed that herbal-specific examples are still under discussion by an ad-hoc group on HMPs for the MEDDEV 2.1/3.

The HMPC should be updated on any relevant new developments for the opportunity to comment because many herbal products are marketed as medical devices.

5.5. Cooperation with International Regulators

5.5.1. EU – India/AYUSH communication

Document: Email correspondence dated 07 June 2018 to Dr Bangarurajan; AYUSH reply to EMA dated 27 June 2018; Email correspondence dated 18 July

Outcome:

HMPC noted the correspondence between EMA and AYUSH / India and updates given in preparation of the September meeting and the participation of AYUSH experts at HMPC/MLWP with focus on data availability on four Indian substances.

HMPC requirements in general and data gaps for substances specifically (previously assessed but not leading to a monograph; current call for scientific data for possible reconsideration) will be subject to meetings and points on HMPC and MLWP agendas.

5.6. Contacts of the HMPC with external parties and interaction with the Interested Parties to the Committee

5.6.1. Question on HMPC assessment and national monograph use

Report: HMPC Chair
Action: for adoption
Document: Draft response letter dated 25 January 2018; Hederae helicis folium MO, AR, LoR; Email correspondence dated 08 May 2018; Letter from Herbapol dated 21 December 2017; Supportive references

Outcome:

HMPC agreed to HMPC Chair proposal to dissociate (1) the response to the letter and (2) the possible reconsideration of the contraindication in children for Hedera in coordination with PRAC and/or PDCO.

For (1) letter to be finalised and send out with references in line with Hedera AR and LoR; for (2) to draft a discussion paper as basis for follow-up at the September HMPC meeting.

Previous decisions and current discussions on data requirements and precautionary principle should be considered.

5.7. Work plan

5.7.1. HMPC work plan 2018

Report: HMPC Chair
Action: for information
Document: Work plan 2018 – current status July 2018

- 1.3.2. Activity area: Forward planning and prioritisation
  Action: for discussion
  Document: Email correspondence from 16 July 2018

- 1.3.3. Activity area: Coordination on safety assessments of herbal constituents
  - Public statement on Contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids (PAs) (EMA/HMPC/328782/2016)
  - Reflection paper on Polycylic Aromatic Hydrocarbons

  Action: for discussion
  Documents: Presentation; EFSA statement June 2017: Risks for human health related to the presence of pyrrolizidine alkaloids in honey, tea, herbal infusions and food supplements

Outcome:

Updates were given on projects 1.3.2 and 1.3.3. and HMPC agreed to proposed next steps for follow-up in September (1.3.2 at ORGAM and 1.3.3 on PA at HMPC/MLWP) and November (1.3.3 PAH at subgroup and HMPC).

For project 1.3.2 (identification of new substances for assessment and implementation of a validation step before addition to HMPC work programme) the topic leader referred to the procedure revision and possible new template under development at ORGAM DG.

For project 1.3.3 (Coordination on safety assessments of herbal constituents) the outcome of two online meetings was presented and the way forward agreed on the 5 sub-points.

Priority will be given to the finalisation of the PS on estragole (see 4.1.1) and the follow-up on the 'PS on Contamination of herbal medicinal products/traditional herbal medicinal products with pyrrolizidine alkaloids (PAs) with the planned revision of PS EMA/HMPC/328782/2016 (end of transition period mid-2019) but also PS EMA/HMPC/893108/2011 with possible reconsideration of acceptable values according to newly available data (September HMPC and MLWP).

Next steps following the reflection paper on Polycylic Aromatic Hydrocarbons are planned for November HMPC.

The development of suitable toxicological models for the 'safe use of herbal substances/preparations in medicinal products in view of background exposure via food' is considered a long-term project (2 years) requiring coordination with EFSA. A first subgroup meeting is planned for September.

5.7.2. HMPC work plan 2019

Report: HMPC Chair
Action: for information
Document: presentation

The Chair invited HMPC members to submit comments on the proposal for essentials for the HMPC work plan 2019 preparation by 7 September 2018.

5.8. Planning and reporting

None

5.9. Legislation and regulatory affairs

5.9.1. WEU/Bibliographic application regarding Art. 10a Dir. 2001/83/EC for HMPs – Reference to other products

Report: HMPC Chair
Action: for discussion
Documents: Comments by EUCOPE received 14 May 2018; Draft response to EUCOPE dated 07 July 2018 Guideline on the assessment of clinical safety and efficacy; Regulatory Q&A

Outcome:

Rapporteur together with EMA will amend draft response letter according to the discussion for endorsement at HMPC September meeting.

The scope of the questions and draft answers was discussed with respect to applicability to HMPC monograph development and the reference to other products and demonstration of similarity during national procedures. It was agreed that both the response and the option to reconsider the wording in the relevant Q&A need further discussion.

6. Any other business

6.1. Topics for discussion

None

6.2. Documents for information

6.2.1. HMPC

Table of Decisions from HMPC meeting held on 04-05 June 2018

Overview of expertise of members HMPC and subgroups

Meeting report from HMPC meeting held on 04-05 June 2018

Overview of status of HMPC assessment work – priority list

Inventory of herbal substances for assessment work

Abbreviations in HMPC agendas/minutes

Common names of herbal substances in all languages

6.2.2. MLWP

- Overview of status of HMPC/MLWP assessment work

6.2.3. ARSP

- English template
- English summaries for publication:
  - Pale coneflower root
  - Evening primrose
  - Pelargonium root

No comments were received on new herbal summaries for publication on the EMA website.

6.2.4. Other

- EU herbal monographs, list entries and public statements post adoption
  - Allii sativi bulbus: Scientific literature compilation and open questions; post adoption delays (MO, AR, LoR, OoC)
  - Cynarae: post adoption delays (MO, AR, LoR; Email correspondence from 17 July 2018)
- 6th Annual GP-TCM meeting at Royal Kew Gardens, London on 6 June – Symposium programme
- Paediatric Overview (2017 update)

6.2.5. Feedback on national experiences with HMPC monographs and guidelines

Rapporteur: R Laenger, A Assisi

- draft template
- summary feedback

6.2.6. Workshop on Pyrrolizidine Alkaloids, 12-13 September 2018 (see also 5.7.1.)

Report: HMPC Chair

Documents: Agenda; Registration form

Participants should give feedback at the HMPC September meeting.

6.2.7. Annual Meeting of International Regulatory Cooperation for Herbal Medicines (IRCH), WHO, 07-09 December 2018

Report: HMPC Chair

Document: Email correspondence from 10 July 2018

List of participants

List of participants including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 23-24 July 2018 meeting.

Name	Role	Member State or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Marisa Delbò	Chair	Italy	No interests declared	
Reinhard Länger	Member	Austria	No interests declared	
Iliana Ionkova	Alternate	Bulgaria	No interests declared	
Ivan Kosalec	Member	Croatia	No restrictions applicable to this meeting	
Darko Trumbetic	Alternate	Croatia	No interests declared	
Marie Heroutova	Member	Czech Republic	No interests declared	
Markéta Příhodová	Alternate	Czech Republic	No restrictions applicable to this meeting	
Eeva Sofia Leinonen	Member	Finland	No interests declared	
Jacqueline Wiesner	Member	Germany	No interests declared	
Ioanna Chinou	Member	Greece	No interests declared	
Zsuzsanna Bíróné Dr Sándor	Member	Hungary	No interests declared	
Rachel Cox	Alternate	Ireland	No interests declared	
Alessandro Assisi	Member	Italy	No interests declared	
Evita Skukauska	Member	Latvia	No interests declared	
Everaldo Attard	Member	Malta	No interests declared	
Emiel Van Galen	Member	Netherlands	No interests declared	
Wojciech Dymowski	Member	Poland	No interests declared	
Ana Paula Martins	Member	Portugal	No interests declared	
Raluca Iavorszky	Member	Romania	No interests declared	
Milan Nagy	Alternate	Slovakia	No interests declared	
Barbara Razinger	Alternate	Slovenia	No interests declared	
Adela Núñez Velázquez	Member	Spain	No interests declared	
Karin Erika Svedlund	Member	Sweden	No interests declared	
Malin Kyllikki Hobro Soderberg	Alternate	Sweden	No interests declared	
Linda Anderson	Member	United Kingdom	No interests declared	
Gert Laekeman	Co-opted member	Belgium	No interests declared	
Heidi Foth	Co-opted member	Germany	No interests declared	
Maria Helena Pinto Ferreira	Co-opted member	Portugal	No interests declared	
Melanie Bald	Observer – via TC	EDQM	No interests declared	