4 April 2016
EMA/HMPC/252822/2016
Procedure Management and Committees Support Division

# Committee on Herbal Medicinal Products (HMPC)

## Minutes for the meeting on 1-2 February 2016

Chair: Werner Knöss – Vice-Chair: Marisa Delbó

1 February 2016 14:00 – 19:00, 2F

2 February 2016 09:00 – 17:00, 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 this document is considered commercially confidential or sensitive and therefore not disclosed.

Of note, this 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 agenda 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).

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# 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).

Resignation: Gabriela Duchajová, Slovakian member terminated her membership as of 1 February 2016. New nomination awaiting.

Olavi Pelkonen, co-opted member for toxicology did not renew his mandate ending 10 March 2016. The HMPC Chair and members expressed high gratitude for his work for the HMPC, MLWP and as SWP observer since 2005 with Rapporteurship on several guidance documents and profound input on herbal substance assessments by other Rapporteurs. See also 5.1.2.

## 1.2. Adoption of agenda

HMPC agenda for 1-2 February 2016

**Outcome:**
Adopted

## 1.3. Adoption of the minutes

HMPC minutes for 23-24 November 2015

**Outcome:**
Adopted

# 2. European Union herbal monographs and list entries

## 2.1. Report on MLWP activities

### 2.1.1. Report from the MLWP November 2015 meeting

Report: MLWP Chair
**Action:** for information
Document: Draft minutes for the MLWP meeting on the 24–26 Nov 2015

### 2.1.2. Proposal for call of scientific data

- Boldi folium

Report: MLWP Chair
**Action:** for discussion

**Outcome:**
Endorsed. Boldi folium monograph not on 2016/2017 work plan for revision, but MLWP supported systematic review according to Rapporteur's recommendation.

### 2.1.3. Appointment of Rapporteurs and Peer-reviewers

- Revision

Herbal substance: Salviae officinalis folium and Salviae officinalis aetheroleum

**Outcome:**
HMPC endorsed Peer-reviewer as proposed by MLWP.

- Current Rapporteur Distribution

Document: Presentation

- Appointment of possible rapporteurship for non-MLWP members

Documents: MLWP work plan 2016; Presentation revision priorities

**Outcome:**
Members from Croatia, Latvia and Norway expressed interest in taking over Rapporteurship for the revision of monographs. France will give an update in April.
To be discussed at MLWP for endorsement at the HMPC April meeting.

### 2.1.4. Public statement – proposals for minor corrections

- Salviae officinalis aetheroleum

**Action:** for adoption
Document: PS

**Outcome:**
Adopted

During the systematic review of Salviae folium the AR and the LoR were updated including the limits on thujone in line with the HMPC PS EMA/HMPC/732886/2010. No new data were identified to change the view of the MLWP/HMPC expressed in the PS that explains why a monograph on Salviae aetheroleum is not established. Minor changes were introduced.

See also 2.3.2

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

### 2.2.1. Monograph on Equiseti herba and supporting documents

**Action**: for adoption
Documents: MO, AR, LoR, references: 95/127

**Outcome:**
Final revised monograph and supporting documents with changes in AR adopted by majority vote (21 out of 24). Norway expressed a favourable position.
Divergent opinion: E. van Galen, L. Anderson, M. Delbò

Questions were raised on the posology specified in the monograph vis-à-vis the AR as well as on the content of secondary pharmacodynamics. No justified need for changes was found. Divergent opinions referred to the wording of the indication as regards the increase in amount of urine (not considered demonstrated based on long-standing use), the use in adolescents for the traditional indication, or the inclusion of two traditional preparations using 'sweet wine' with no further specification as an extraction solvent.

### 2.2.2. Monograph on Valerianae aetheroleum and supporting documents

**Action**: for adoption
Documents: MO, AR, LoR, references: 156/156

**Outcome:**
Final revised monograph and supporting documents adopted by majority vote (25 out of 27). Norway expressed a favourable position.

Divergent opinion: L. Anderson, Z. Biro-Sandor

Divergent views referred to concerns regarding the use of the essential oil in adolescents.

### 2.2.3. List Entry and Monograph on Valerianae radix and supporting documents

**Action**: for adoption
Documents: MO, LE, AR, LoR, OoC, references: 156/156

**Outcome:**
List entry and supporting documents adopted by majority vote (20 out of 27) for transmission to the Eur. Commission for final adoption. Norway expressed a favourable position.
Divergent opinion: E. S. Leinonen, G. Calapai, I. Chinou, L. Anderson, M. Delbò, U. Mockler, W. Dymowski.

Final revised monograph and supporting documents with changes in monograph and assessment report adopted by majority vote (22 out of 27). Norway expressed a favourable position.

Divergent opinion: G. Calapai, L. Anderson, M. Delbò, S. Girotto, U. Mockler

Members discussed the appropriateness of the use in adolescents, which was not considered acceptable by some because treatment should be under medical supervision in this age group. Also the relatively high ethanol content of some preparations was mentioned. Others emphasised the long-standing use of products on the market without safety issues. The

difference in extrapolation possibilities as regards safety versus efficacy in TU or WEU was reiterated. All divergent opinions on the **LE** referred to the use in adolescents plus a concern regarding the inclusion of a traditional preparation using sweet wine as solvent.

From experiences in European procedures the posology in the WEU part of the **monograph** was modified to avoid ambiguity. General issues were raised regarding monograph revision and strength/posology calculations summarised from multiple products on the market. The lack of knowledge on the mechanism of action and the content of monograph section 5.1 were discussed. Divergent opinions referred to insufficient data to support WEU for all age groups or particularly for adolescents, concerns regarding unsupervised use of products by adolescents for the traditional indication, and inclusion of a traditional 'sweet wine' preparation.

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

### 2.3.1. Monograph on Harpagophyti radix and supporting documents

**Action**: for adoption
Documents: MO, AR, LoR, references: 57/110

**Outcome:**
Draft revised monograph and supporting documents adopted by consensus for 3 months public consultation.

### 2.3.2. Monograph on Salviae officinalis folium and supporting documents

**Action:** for adoption
Documents: MO, AR, LoR, references: 61/65

**Outcome:**
Draft revised monograph and supporting documents adopted by consensus for 3 months public consultation.

The HMPC Chair reminded MLWP and Rapporteurs that documents for adoption should be clean and not contain manifold comments unless these have still to be discussed at the Committee.

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

### 2.4.1. Monograph on Pistacia lentiscus (mastix) and supporting documents

Rapporteur: I. Chinou; Peer-reviewer: M. Delbò
**Action**: for adoption
Documents: MO, AR, LoR, references: 66/71

**Outcome:**
Final monograph and supporting documents adopted by majority vote (23 out of 27). Norway expressed a favourable position.

Divergent opinion: J. Wiesner, E. Attard, S. Bager, R. Länger

Discussion and divergent opinions referred to the inconsistent evidence for traditional use according to criteria set out in 2001/83/EC as presented in the AR and usually applied for HMPC monographs establishment and national procedures (e.g. specified strength/posology for 30 years as per indication; cautious use of data from clinical trials and combination products).

### 2.4.2. Monograph on Ricini oleum and supporting documents

Rapporteur: C. Purdel; Peer-reviewer: B. Kroes
**Action**: for adoption
Documents: MO, AR, LoR, references: 63/79

**Outcome:**
Final monograph and supporting documents with changes in monograph adopted by majority vote (24 out of 27). Norway expressed a favourable position.

Divergent opinion: E. Van Galen, L. Anderson, U. Mockler

Discussion and divergent opinions referred to the available evidence to support well-established use as well as considerations that safer alternative stimulant laxatives are available and preferred in this indication, whilst Ricini oleum as a laxative is regarded obsolete in current clinical practice and may cause excessive irritation of the colon and violent purgation.

### 2.4.3. List entry and Monograph on Sideritis herba and supporting documents

Rapporteur: I. Chinou; Peer-reviewer: B. Kroes
**Action**: for adoption
Documents: MO, LE, AR, LoR, references: 36/36

**Outcome:**
List entry and supporting documents adopted by majority vote (26 out of 27). Norway expressed a favourable position. Divergent opinion: W. Dymowski.

Final monograph and supporting documents adopted by consensus. Norway expressed a favourable position.

The HMPC Chair reminded that references should be provided by the Rapporteur and made available in MMD with the first discussion at MLWP after public consultation to allow all members access for their decision making.

Changes in the AR sections 2.2, 2.3, 4.4 (evidence and posology for traditional use and conclusions on efficacy) were requested to have correct conclusions and justify the content of the monograph.

The divergent view on the **LE** referred to insufficient evidence for any product with defined indication, strength and posology used in Europe throughout the period required by the legislation.

### 2.4.4. Monograph on Silybi mariani fructus and supporting documents

Rapporteur: O. Palomino; Peer-reviewer: W. Knöss
**Action**: for adoption
Documents: MO, AR, LoR, OoC, references: 114/195

**Outcome:**
Adoption postponed to April 2016 meeting.

According to the discussion and trend vote the majority of present members supporting the monograph as proposed by MLWP and according to the adopted draft was not sufficient for adoption.

Given the split view on the WEU indication it was agreed to prepare a TU and a TU/WEU option for the April meeting for decision and adoption.

Regarding availability of references see 2.4.3.

Members discussed the available evidence for WEU taking into account the Cochrane analysis, recommendations by professional societies but also endpoints and weaknesses in design and analysis of single studies with positive outcomes. The unique composition and strong history of the substance on the market lacking comparable alternatives was also taken into account. On the other side general concerns were raised for a traditional indication (no medical supervision) in this indication linked to hepatic diseases and alcohol abuse. Given the extensively clarified positions and exhaustive discussions at MLWP already, the final decision is to be taken at the HMPC April meeting.

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

### 2.5.1. Monograph on Origani majoranae herba and supporting documents

**Action**: for adoption
Documents: MO, AR, LoR

**Outcome:**
Draft monograph and supporting documents with a change in the monograph adopted by consensus for 3 months public consultation.

The available evidence for traditional use in particular in young children and linked safety concerns were discussed.

### 2.5.2. Public statement on Paeoniae radix rubra and supporting documents

**Action**: for adoption
Documents: PS, AR, LoR

**Outcome:**
Draft public statement and supporting documents adopted by consensus for 3 months public consultation.

Despite manifold use and publications, the available data were considered insufficient to establish a monograph. Specifics of the assessment were explained in particular the necessary distinction between P. radix rubra and P. radix alba - yet missing differentiation of both in most literature sources. Via public consultation it is intended to receive more data from Interested parties, NCAs, TCM research organisations or non-European regulatory bodies to eventually allow the monograph establishment for a substance used primarily in TCM.

### 2.5.3. Public statement on Paeoniae radix alba and supporting documents

**Action**: for adoption
Documents: PS, AR, LoR

**Outcome:**
Draft public statement and supporting documents adopted by consensus for 3 months public consultation.

See 2.5.2.

# 3. Referral procedures

None

# 4. Guidelines and guidance documents

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

None

## 4.2. Quality

### 4.2.1. Reflection paper on the use of new analytical methods in the quality control of herbal substances, herbal preparations and (traditional) herbal medicinal products

Report: QDG Chair
**Action:** for discussion
Document: Draft reflection paper

**Outcome:**
Members were invited to send comments to Rapporteurs, Q DG Chair and secretariat. The Reflection paper was returned to Q DG for discussion. Addition of state-of-the-art references and structural clarity as per methodology and regulatory purpose were requested. The document is scheduled for possible HMPC adoption in April 2016.

## 4.3. Regulatory

### 4.3.1. Revised CTD guideline on the use of CTD format for Registration Applications

Report: QDG Chair, ORGAM DG Chair
**Action**: for adoption
Documents: Revised CTD guideline (EMA/HMPC/71049/2007, Rev.2); OoC main text; OoC Appendix 2; SE comments on the Guideline on the use of CTD format for Registration Applications, 7 Dec 2015

**Outcome:**
Adoption postponed to April 2016. Members invited to send comments.

For final discussion at Q DG (Appendix 2) and main text changes (ORGAM) taking into account late SE comments.

Comments were mainly linked to the extensive texts copied from existing guidelines that potentially could be reduced to simple references to those guidelines in their current version. The differences between the guideline as such and the appendices including a 'mock up' as example with disclaimer were explained as well as the difference between Q&A and guidelines.

## 4.4. Report on HMPC Drafting Groups activities

### 4.4.1. Quality DG

Report: Q DG Chair
**Action:** for adoption
Document: Meeting report from Q DG meeting held on 9 Dec 2015

**Outcome:**
Adopted

HMPC welcomed Q DG plans to compile a written outcome of group discussions from the December 2015 assessors training for distribution to all participants. The tracking of follow up proposals as regards guidance / Q&A development/ revision and coordination with EDQM was necessary to guarantee the best possible outcome of such event.

The DG had discussed comments received on the revised herbal CTD guideline, mainly the new Appendix 2 'mock-up module 3'. Coordination topics with the CHMP QWP and with EDQM were discussed such as changes in Ph. Eur monographs affecting HMPC monographs, a proposal for an amendment of the Ph. Eur. herbal extracts monograph for clarification of the drug extract ratio ($DER_{genuine}$ versus $DER_{total}$), and status of the Ph. Eur. 13 A expert group activities as regards essential oils.

**Action:** for information
Document: Draft agenda for the Q DG meeting held on 11 Feb 2016

**Outcome:**
See 4.2.1 and 4.3.1.; final polishing of draft reflection paper and revised guideline on quality parts to be discussed at Q DG February meeting for transmission to HMPC for adoption in April 2016. No further topics were requested from HMPC.

### 4.4.2. ORGAM DG

Report: ORGAM DG Chair
**Action:** for adoption
Document: Meeting report from ORGAM DG meeting held on 10 Dec 2015

**Outcome:**
Adopted

Beside final amendments to the 2016 work plan, further discussion took place on the QRD template 'herbals' taking into account QRD group comments.

**Action:** for information
Document: Draft agenda for the ORGAM DG meeting held on 9 Feb 2016

**Outcome:**
See 4.3.1.: Document and late comments to be discussed for final adoption at HMPC April meeting.
See 5.2.3.: Documents to be finalised in direction of a HMPC suggestion how to use the standard QRD template for THMP (for endorsement by CMDh).

# 5. Organisational, regulatory and methodological matters

## 5.1. Mandate and organisation of the HMPC

### 5.1.1. Overview table of expertise of HMPC members and alternates

**Action:** for adoption
Documents:
Expertise of HMPC members 2014; Briefing note on competence and expertise of HMPC members and alternates; Annex B EMA recommendation on criteria for competence and expertise of new HMPC members and alternates

**Outcome:**
Endorsed. A sentence suggested by the HMPC Chair on the need for NCAs to provide nominated candidates with sufficient possibilities to contribute actively to committee work had been added. No further comments were received.

HMPC noted recommendation character of these documents that will in future accompany all calls for nomination for the HMPC in line with other scientific committees' practice.

### 5.1.2. Election of HMPC co-opted member (toxicology)

**Action:** for adoption
Documents: Request for nomination email 22 Oct 2015; Procedure for nomination co-opted members for HMPC; Nomination received

**Outcome:**
Prof. Heidi Foth (DE) elected by majority vote as co-opted member to the HMPC in the area of toxicology for a 3 year mandate starting 4 April 2016.

According to the call from October the active membership in MLWP (starting 5 April 2016) and possible observership at SWP (representing HMPC) was agreed.

### 5.1.3. Election of QDG Chair

**Action:** for adoption
Documents: QDG mandate; QDG waiting list; Croatian nomination of observer in HMPC and QDG; Candidature received

**Outcome:**
Dr. Linda Anderson elected by consensus as new Q DG Chair for a three year mandate starting 11 March 2016.

The HMPC thanked Dr. B. Kroes for 9 years of successful Chairmanship of the Quality DG representing an important HMPC subgroup to establish EU harmonised quality requirements and coordinate with Ph. Eur.

The adaptation of the mandate of HMPC DGs in line with other drafting groups was announced. Given the current QDG membership, old 'waiting list' and request by HR, Members were invited to send nominations for active membership or observership at QDG to the HMPC secretariat for discussion at the HMPC April meeting.

### 5.1.4. Assessors Training, December 2015 – follow up

Report: QDG Chair
**Action:** for information
Documents: Presentations

**Outcome:**
The training including for the first time group discussions was considered a success to be pursued for future trainings.

HMPC welcomed QDG plans to compile a written outcome of group discussions from the December 2015 assessors training for distribution to all participants. Furthermore the tracking of follow up proposals as regards guidance / Q&A development/ revision and coordination with EDQM is necessary to guarantee the best possible outcome of such event.

Proposals for dates and topics for the assessors' training 2016 to be send to HMPC Chair, S. Bager (topic lead) and HMPC secretariat for discussion at the HMPC April meeting.

### 5.1.5. Strategic Review and Learning Meetings – organisational aspects

Report: HMPC Chair, E. V. Galen
**Action:** for discussion
Documents: Draft agenda, meeting 12-13 April 2016, Netherlands; Information from Slovakia and Malta

**Outcome:**
The first draft agenda of the meeting in Utrecht was briefly presented, while invites and updates will follow. Members were encouraged to contribute in particular to the strategic part on future tasks/structure of the HMPC.

HMPC members noted that no HMPC strategic meeting will be organised during the Slovakian Presidency second half 2016. The Slovak Agency is searching for another MS willing to host such meeting. Although to be decided by HMA, members to check at their NCAs.

The tentative date for the strategic meeting during the following Maltese EU presidency is 27/28 April 2017.

## 5.2. Coordination with EMA Scientific Committees or CMDh-v

### 5.2.1. Coordination with CHMP/SWP - Public statement on the use of herbal medicinal products containing pulegone/ menthofuran

Rapporteurs: O. Pelkonen, J. Wiesner
**Action:** for discussion
Documents: New data from interested parties, provided December 2015; Draft revised PS; Presentation

**Outcome:**
The new data were welcome as supporting the revised current views of HMPC and SWP as reported by the Rapporteur.

HMPC noted next discussion at SWP in mid-February. For possible finalisation at HMPC April meeting according to SWP/CHMP response.

### 5.2.2. Coordination with PDCO

- Report on relevant topics from PDCO meetings

Report: S. Girotto (observer)
**Action:** for information
Document: Presentation

**Outcome:**
HMPC observer clarified that the current extrapolation project focus is not directly related to herbal activities, thus, not requiring active HMPC participation.

With some extrapolations regularly discussed during monograph development, the HMPC Chairs' view to reflect on an appropriate herbal equivalent was agreed. S. Girotto (Rapporteur) to develop a draft paper for discussion at MLWP.

The committee discussed the specific background of the PDCO driven initiative. In view of models used that require hard pharmacological and clinical data from single active substances, concerns were raised towards any transfer attempts to traditionally used substances usually lacking such data. Nonetheless members reflected on common extrapolation discussions at MLWP/HMPC (minor quality differences, age groups, product use versus clinical data, *in vitro* and animal data extrapolation to human situations) that encourage to start an own initiative to pin down some general principles where possible.

### 5.2.3. Coordination with CMDh

Report: ORGAM DG Chair
**Action:** for discussion
Document: Draft Discussion paper on QRD templates for THMP

**Outcome:**
The preference of a 'standalone QRD template' for THMP in line with the QRD proposal was shared by most ORGAM members. HMPC agreed to an EMA secretariat proposal for a document with recommendations on the use of the QRD standard template for HMP/THMP in order to avoid unnecessary extension of the standard template with herbal specific instructions but also maintenance issues in case an extra template for herbals is created. To be finalised by ORGAM for the HMPC April meeting and coordination with CMDh thereafter.

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

### 5.3.1. Coordination with PCWP/HCPWP

Observer: S. Bager

- Training session for patients and consumers interested in EMA activities, 25 Nov 2015

**Action:** for information

- EMA PCWP meeting with all eligible organisations, 26 Nov 2015

**Action:** for information
Document: Minutes

**Outcome:**
No HMPC comments.

- Involvement of patients in HMPC activities

**Action:** for discussion
Document: Presentation

**Outcome:**
Proposals on possible patient involvement were presented starting first with feedback on the herbal AR summaries (English) generated by the Agency and endorsed by HMPC Rapporteurs.

Direct input on monograph development was discussed and practical considerations such as appropriate timing, group (MLWP or HMPC) and necessary background training to be further elaborated.

### 5.3.2. European Union reference date (EURD) list – update for herbal substances

Report: Z. Biro-Sandor
**Action:** for discussion
Document: Email communication on optional addition of herbal substance

**Outcome:**
Postponed to April 2016 meeting.

## 5.4. Cooperation within the EU regulatory network

### 5.4.1. European Pharmacopeia

- EDQM 13A expert group meeting to be held on 23-25 February 2016
  EDQM: M. Bald, U. Rose; HMPC Observer: I. Chinou
  **Action:** for information
- EDQM 13B expert group meeting held on 26-27 January 2016
  EDQM: M. Bald, U. Rose; HMPC Observer: B. Kroes (H. Neef)
  **Action:** for information
  Documents: Draft Agenda; Observer's report; Summary of discussion
- EDQM TCM expert group meeting held on 19-20 January 2016
  EDQM: M. Bald, U. Rose; HMPC Observer: R. Länger
  **Action:** for information
  Document: Summary of discussion

**Outcome:**
HMPC noted topics highlighted by the EDQM observer and the HMPC observer at the last 13B meeting including latest developments regarding essential oils, assay requirements, fresh drugs in the herbal drugs monograph. Beside recent monographs for Pharmeuropa or Ph. Eur. as outcome of 13A, 13B or TCM groups, comments on the planned HMPC Saccharomyces monograph by the live bio-therapeutics products group were announced.

The ongoing discussions on pyrrolizidine alkaloid analysis at 13B was emphasised given the HMPC public statement and recent findings on national markets (see 6.1.3). Also species changes for the Passiflora herba Ph. Eur. monograph may be checked for impact on the HMPC monograph. Assay requirement discussions initiated by TCM group are still under discussion at EDQM. HMPC members highlighted possible impact on quality guidelines and asked for an early opportunity to comment reminding that homogenous standards should be maintained independent from the origin of a herbal substance.

### 5.4.2. HMPC request to EDQM on modification herbal extract monograph

Report: QDG Chair
**Action:** for adoption
Documents: Request for revision herbal drug extracts; EDQM request form

**Outcome:**
Adopted. HMPC secretariat to transmit request to EDQM.

A proposal was made to clarify within the Ph. Eur. extract monograph $DER_{native}$ versus $DER_{total}$ (including excipients) and the use of the term DER without specification. Although some considered the corresponding Ph. Eur. information chapter as sufficient explanation the proposal was agreed to be submitted to avoid misunderstandings in the future.

### 5.4.3. European Commission - Report: Update on establishment of LE

**Action:** for discussion
Document: Presentation

**Outcome:**
HMPC noted Eur. Com. concerns regarding divergent opinions for new and revised LEs and appeal to apply diligence. The reasons not to accept a LE should be clearly linked to (safety) concerns specific for the LE (data missing and additionally required in a national application) vis-à-vis the TU part of the monograph. Opinions on revisions are views on the performed changes in previously adopted documents based on new data or even template adaptations but should not refer to or question all aspects of old decisions. EMA RA/legal support confirmed this as fundamental principle in all scientific committee decisions.

The Chair reminded that individual divergent opinions but also conclusions in ARs on the possibility to establish an LE should be as clear and transparent as possible (not always linked to availability of genotoxicity data). Furthermore he proposed that more clarity regarding the issues raised should be achieved within the review of MO/LE revision procedural documents as outlined in the HMPC, MLWP and ORGAM 2016 work plans.

### 5.4.4. European Commission – health claims for food products containing hydroxy anthracene derivatives

Report: HMPC Chair, L. Anderson
**Action:** for information
Documents: Email correspondence; HMPC letter to DG SANTE E4, 13 March 2014

**Outcome:**
While HMPC had re-emphasised the concerns raised in a letter 2 years ago, several other MS had also send comments to the Commission. Members were informed that the decision is still pending and of expected next steps.

The Commission was informed that new data of concern regarding e.g. Aloe are now being evaluated during the HMPC review/revision of several monographs on laxatives containing hydroxyanthracene derivatives.

### 5.4.5. EFSA – Guidance on health claims applications and Guidance on immune-GI-defence against pathogens

Report: HMPC Chair; Rapporteurs: G. Calapai; I. Kosalec; H. Pinto Ferreira
**Action:** for information
Documents: General scientific guidance for stakeholders on health claim applications; Outcome of a public consultation of the EFSA NDA Panel; Guidance on the scientific requirements for health claims related to the immune system, the gastrointestinal tract and defence against pathogenic microorganisms; Outcome of a public consultation of the EFSA NDA Panel

**Outcome:**
Postponed to April 2016 meeting.

**Post-meeting note (Chair):** Timelines for comments on EFSA documents are often rather short. If publications from EFSA are brought to the attention of the HMPC by delegates for further attention, they should be ideally accompanied by a distinct comment or raise defined questions, which could be evaluated by the nominated Rapporteurs if timelines are appropriate.

## 5.5. Cooperation with International Regulators

### 5.5.1. 8th Annual Meeting of IRCH held in Riyadh, Saudi Arabia, 1-3 December 2015

Report: HMPC Chair, HMPC Vice-Chair
**Action:** for information
Document: Agenda

**Outcome:**
HMPC noted feedback by participants. Minutes will be provided once available.

Participants informed that although some organisational and leadership issues remain, IRCH represents a good platform of real herbal experts. A grown global membership over the years and the best global representation provide good opportunities to promote the European model and achievements in this area. EMA should closely monitor the development. The next meetings are scheduled for India (2016) and eventually Germany (2017).

### 5.5.2. HMPC – International representation and cooperation – postponed

Report: HMPC Chair
**Action:** for discussion
Document: Draft proposal HMPC international cooperation

**Outcome:**
Postponed to April 2016 meeting.

### 5.5.3. 2nd Annual Complementary/Herbal Medicines Workshop in the margins of the 10th International Summit of Heads of Medicines Regulatory Agencies (ICMRA), Mexico City, 10 November 2015

Report: HMPC Chair
**Action**: for information
Documents: Minutes; Summary of action; Presentation

**Outcome:**
Feedback was provided from international affairs department.

HMPC was informed on the last small satellite meeting of the annual global medicines regulatory agencies summit. Usually driven by few agencies (e.g. TGA) it serves for exchange of information in a wider scope than herbal medicines regulation (e.g. regulation of other product types or also health practitioners) and is not attended by experts in the field. While attendance of an EMA herbal representative may not be justified on a regular basis, the next meeting in Interlaken (CH) could be attended by the HMPC Chair. The actual role and the relationship to other fora (IRCH, ICDRA) has not yet fully crystallised.

### 5.5.4. Confidentiality arrangements DG SANTE and EMA with international partners – Request by Swissmedic for observership MLWP

**Action**: for information

**Outcome:**
HMPC agreed to EMA proposal on Swissmedic observership at MLWP to promote the European model.

After an initial observation experience at a full MLWP meeting, objectives to observe the drafting of monographs at the working party could be identified with the Swiss counterpart. A limited test phase (e.g. one year) with clarified modalities on the 'observer only' status as practised in other groups was proposed.

### 5.5.5. Health Canada request

**Action**: for information
Document: Email, 27 Jan 2016

**Outcome:**
No objections were raised to distribute the request from those non-European partners with a confidentiality agreement in place within the network (for information and own NCA follow up) in cases when EMA has no information while more may be available at NCA level.

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

### 5.6.1. Planned hearings with interested parties in 2016

**Action**: for discussion

**Outcome:**
AESGP hearing at MLWP scheduled in April in analogy to the May meeting in previous years. Members (not MLWP members) willing to stay for the hearing to arrange their travels accordingly (plenary 4 April 2016, 14:00 – 19:00 and 5 April, 08:30 – 12:30, AESGP hearing 13:30-15:30)

Members invited to send proposals for other hearing options in 2016 (with specific groups or on specific topics) to the HMPC topic lead (S. Bager).

## 5.7. HMPC work plan

### 5.7.1. Projects on the HMPC work plan 2016

- Monograph and List entry systematic revision

**Action:** for discussion
Document: Presentation

**Outcome:**
HMPC members noted discrepancy between theoretical considerations regarding revisions as laid down in 2011 versus current unclarified methodology and practice - including subsequent future work load *per annum*. The secretariat encouraged adapting either current practice or the procedural guidance into a realistic basis as originally planned in the HMPC work programme 2011-2015.

The content of the HMPC reflection paper EMA/HMPC/326440/2007 was presented for the 3 types of revisions; only one of them backed by a procedure (systematic review/revision). The 2012 commitment to adjust at the end of the pilot phase, report on the experience gained and fine-tune the long-term strategy for systematic review/revision was highlighted. The 3 revision types were analysed for clarity and current practice regarding reason, trigger, responsibilities, timelines, scope and transparency. Figures showed '5 year reviews' due vs. finalised with a backlog of 51 by end of 2015. Even without backlog the current procedure requires 30-35 finalised revisions annually, while the MLWP/HMPC has a steady annual output of 15-20 finalised assessments (new and revisions) applying standard procedure also to revisions.

The MLWP Chair referred to the measures to tackle the backlog via initiative to involve HMPC members so far not active as Rapporteurs and intermediate prioritisation measures. Also the 2016 topic lead could not see the problem stating that there is possibly no need to revise existing guidance welcoming the flexibility provided in the reflection paper. Others supported the re-consideration of timelines because of the challenge to finalise 30-35 revisions annually alongside some new assessments, which seems to be an overload with respect to current resources. The HMPC Chair saw from the experiences so far and the feedback from the Eur. Com. (see 5.4.3) need for clarification of procedures with activities as outlined again in 2016 work plans being useful for Rapporteurs' work load, discussion efficiency and transparency for monograph users.

## 5.8. Planning and reporting

None

## 5.9. Legislation and regulatory affairs

None

# 6. Any other business

## 6.1. Topics for discussion

### 6.1.1. Overview of recommendations for the uses of herbal medicinal products in the paediatric population

Rapporteur: S. Girotto
**Action:** for adoption
Document: Paediatric uses of herbal medicines

**Outcome:**
Adopted

The document published on the EMA website for 2 years has been updated with the HMPC monograph outcome by Dec 2015 and slightly re-formatted to improve usability.

### 6.1.2. Planned restructuration/rewriting of herbal regulatory pages on EMA website

**Action:** for information

**Outcome:**
HMPC noted planned restructuration of EMA website and current pilot phase with herbal pages. For eventually useful double-checks by NCA users volunteered: A. Lee, E. S. Leinonen, E. Svedlund.

### 6.1.3. Occurrence and analysis of pyrrolizidine alkaloids – issues on national markets

Report: L. Anderson, HMPC Chair
**Action:** for information

**Outcome:**
HMPC members noted update from UK and Germany regarding findings on PA content (with exposure beyond the limits given in the PS EMA/HMPC/893108/2011) in products with herbal substances not naturally containing PAs.

Possible reasons and follow-up were discussed and the need for a sound analytical Ph. Eur. methodology emphasised.

The findings source from both the food and the medicines sector and seem to be linked to contamination with weeds. The effectiveness and effects of possible measures for this quality issue was discussed. Both, UK and DE will update colleagues at NCAs and EMA on further developments including an informal translation of German measures (BfArM and Ministry of Health) once available.

## 6.2. Documents for information

### 6.2.1. HMPC

Table of Decisions from HMPC meeting held on 23-24 November 2015

Overview of expertise of members HMPC and subgroups

Common names of herbal substances in all languages

Meeting report from HMPC meeting held on 23-24 November 2015

Overview of status of HMPC assessment work – priority list

Inventory of herbal substances for assessment work – alphabetical order

Abbreviations in HMPC agendas/minutes

### 6.2.2. MLWP

- Overview of status of MLWP assessment work
- Draft agenda of MLWP meeting to be held on 3-4 February 2016

### 6.2.3. ARSP

- English summaries for publication
  Documents: Willow herb; Centaury; Ivy leaf; Eleutherococcus root

### 6.2.4. Matching patients friendly therapeutic areas for browse search on herbal medicines for human use with TU indications to ATC therapeutic groups (level 2)

Rapporteur: B. Huber, W. Knöss
Documents: Draft document EMA/568320/2009 Rev. 1; Outcome written procedure

**Post-meeting note (Chair):** A quorum could not be fully reached by a written procedure because participation was too low. Nevertheless, a majority accepted the document, even delegates, who had expressed some concerns before. Accordingly, changes suggested in the document will be used at working level.

### 6.2.5. Other

- Comments on draft revised monograph on Thymi herba/Primulae radix. Document: Letter, 11 Jan 2016
- Article 57: Information by Pharmacovigilance Department; Documents: Article 57 Publication Dashboard Report to EMA Committees, Jan 2016; Pharmacovigilance Programme update, Dec 2015

# List of participants

Including any restrictions with respect to involvement of members / alternates / experts following evaluation of declared interests for the 1-2 February 2016 meeting.

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Werner Knöss | Chair | Germany | No interests declared | |
| Reinhard Länger | Member | Austria | No interests declared | |
| Elena Mustakerova | Member | Bulgaria | No interests declared | |
| Ivan Kosalec | Member | Croatia | No restrictions applicable to this meeting | |
| Darko Trumbetic | Alternate | Croatia | No interests declared | |
| Maria Stavrou | Member | Cyprus | No interests declared | |
| Markéta Příhodová | Alternate | Czech Republic | No restrictions applicable to this meeting | |
| Steffen Bager | Member | Denmark | No restrictions applicable to this meeting | |
| Eeva Sofia Leinonen | Member | Finland | No interests declared | |
| An Le | Member | France | No interests declared | |
| Jacqueline Wiesner | Member | Germany | No interests declared | |
| Ioanna Chinou | Member | Greece | No interests declared | |
| Zoi(Zoe) Karampourmpouni | Alternate | Greece | No interests declared | |
| Zsuzsanna Biróné Dr Sándor | Member | Hungary | No interests declared | |
| Una Mockler | Member | Ireland | No restrictions applicable to this meeting | |
| Annamarie O'Sullivan | Alternate | Ireland | No interests declared | |
| Marisa Delbò | Member (Vice-Chair) | Italy | No interests declared | |
| Anna Maria Serrilli | Alternate | Italy | No interests declared | |
| Dace Kalke | Member | Latvia | No interests declared | |
| Baiba Jansone | Alternate | Latvia | No interests declared | |
| Everaldo Attard | Member | Malta | No interests declared | |
| Emiel Van Galen | Member | Netherlands | No interests declared | |
| Burt H Kroes | Alternate | Netherlands | No interests declared | |

| Name | Role | Member State or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Steinar Madsen | Member | Norway | No interests declared | |
| Gro Anita Fossum | Alternate | Norway | No interests declared | |
| Wojciech Dymowski | Member | Poland | No interests declared | |
| Ana Paula Martins | Member | Portugal | No interests declared | |
| Samo Kreft | Alternate | Slovenia | No restrictions applicable to this meeting | |
| Adela Núñez Velázquez | Member | Spain | No interests declared | |
| Cristina Martinez Garcia | Alternate | Spain | No interests declared | |
| Per Claeson | Member | Sweden | No interests declared | |
| Linda Anderson | Member | United Kingdom | No interests declared | |
| Sue Harris | Alternate | United Kingdom | No interests declared | |
| Gioacchino Calapai | Co-opted member | Italy | No interests declared | |
| Silvia Girotto | Co-opted member | Italy | No interests declared | |
| Gert Laekeman | Co-opted member | Belgium | No interests declared | |
| Olavi Pelkonen | Co-opted member | Finland | No interests declared | |
| Maria Helena Pinto Ferreira | Co-opted member | Portugal | No interests declared | |
| Olga Maria Palomino | Expert | Spain | No interests declared | |
| Martina Holenková | Expert | Czech Republic | No interests declared | |
| Melanie Bald | Observer – via TC | EDQM | No interests declared | |
| Tina-Soon Engraff | EC Representative | European Commission | Full involvement | |