

THE EMEA'S APPROACH TO TRADITIONAL HERBAL MEDICINAL PRODUCTS

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THE MISSION AND LEGAL ROLE OF THE EMEA

- **Mission:**

- to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.

- **Legal Role:**

- coordination of existing scientific resources from Member States for the evaluation, supervision and pharmacovigilance of medicinal products.

- provision of best quality scientific advice on quality, safety and efficacy.

THE COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

- **Composition:**
 - 1 member + 1 alternate from 27 EU MS + Iceland & Norway (EEA-EFTA states)
 - Chair elected from members
 - Generally 6 meetings a year
- **Plus:**
 - Up to 5 co-opted members (European experts nominated by MS or EMEA). HMPC currently has co-opted members for clinical, experimental and non-clinical pharmacology, toxicology, paediatric and general/family medicine.
 - Observers from European Directorate for the Quality of Medicines, and from Croatia, Turkey and Macedonia (as part transition measures of the EU Enlargement Programme).

COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC): role & responsibilities

- to assist the harmonisation of procedures and provisions in Member States (MS) for herbal medicinal products (HMPs) and to further integrate HMPs in the European regulatory framework
- to provide scientific opinion on questions relating to HMPs
- preparation of a draft Community List
- establishment of Community herbal monographs

HMPC WORKING PARTIES/GROUPS

- Working Party on Community Monographs and Community List (MLWP)
- Patients & Consumers Working Party (PCWP)

Temporary Groups:

- Organisational Matters Drafting Group
- Quality Drafting Group

HMPC is also supported by:

- The Good Manufacturing Practice Inspection Services Group

HMPC Working Party on Community Monographs and Community List (MLWP)

Core task:

- assessment work on the establishment of Community herbal monographs and entries to the '*Community list of herbal substances preparations and combinations thereof for use in traditional herbal medicinal products*'.

Plus:

- Developing guidance on well-established and traditional use applications. Also safety issues (where appropriate in co-ordination with the CHMP Safety Working Party)

HMPC MONOGRAPHS: Community Herbal Monographs

- Comprise the HMPC's scientific opinion on an HMP, based on evaluation of scientific data (well-established use) and/or the historical use of the product in the EU (traditional use)
- Offer a harmonised approach to scientific assessment. Not legally binding, but must be taken into account by national competent authorities when examining a registration application.

THE COMMUNITY LIST OF HERBAL SUBSTANCES, PREPARATIONS AND COMBINATIONS THEREOF FOR USE IN TRADITIONAL HERBAL MEDICINAL PRODUCTS

- 'For each herbal substance/preparation, the list shall contain the indication, specified strength and posology, route of administration and any other information necessary for its safe use as an ingredient of a traditional herbal medicinal product'.
- The list provides a harmonised approach; it covers substances with a long history of medicinal use, which are therefore not regarded as harmful under normal conditions of use.
- The list is legally binding in so far as:
 - applicants are not required to provide evidence of safety and traditional use if the proposed product /claims comply with the information in the list
 - competent authorities may not require additional data to assess safety/traditional use of the product

CALLS FOR SUBMISSION OF SCIENTIFIC DATA FOR MONOGRAPH ASSESSMENT

- *'Procedure for calls for scientific data for use in HMPC assessment work'*
 - enables the Rapporteur to obtain a complete set of bibliographic references and scientific data for a given monograph assessment.
- Calls in 2009:
 - Leonuri cardiaca herba
 - Colae semen
 - Pelargonii radix
 - Marrubi herba
 - Melaleucaea algternifolia
 - Chamomillae romanae flos
 - Fraxini folium
 - Matricariae aetheroleum/flos
 - Foenugraeci semen

HMPC MONOGRAPHS: draft published/under discussion

- **Drafts published**

- Agni castus fructus
- Echinaceae purpureae radix
- Orthosiphonis folium
- Rosmarini aetheroleum

- **Drafts under discussion:**

- Arctii radix
- Echinaceae angustifoliae radix
- Hederae helicis folium
- Quercus cortex
- Vitis vineiferae folium

- Cimcifugae rhizoma
- Mate folium
- Ribis nigri folium
- Rosmarini folium

- Cinnamomi cortex
- Euphrasia herba
- Oenotherae biennis oleum
- Viola tricoloris herba

HMPC MONOGRAPHS: assessment close to finalisation (pre-final)

- Curcumae longae rhizoma
- Hamamelidis cortex
- Hamamelidis folium et cortex aut
- Hyperici herba
fructus
- Salviae officinalis folium
- Taraxici radix cum herba
- Urticae folium
- Gentiana radix
- Hamameledis folium
- Ramunculus destillatum
 - Juniperus pseudo-
- Taraxici folium
- Thymi aetheroleum
- Valerianae radix/Lupuli flos

HMPC WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP): overview of status of assessment as at September 2009 – Final Opinions Adopted

- Absinthii herba
- Anisi fructus
- Boldi folium
- Echinaciae pallida radix
- Equiseti herba
- Foeniculi dulcis fructus
- Hippocastini semen
- Meliloti herba
- Menthae piperitae folium
- Plantaganis ovatae semini tegumentum
- Primulae flos
- Rhamni purshianae cortex
- Salicis cortex
- Sennae fructus
- Urticae herba
- Aloe Althaeae radix
- Avenae herba
- Calendulae flos
- Echinaciae purpureae radix
- Foeniculi amari fructus
- Frangulae cortex
- Lini semen
- Melissa folium
- Passiflora herba
- Primulae radiix
- Rhei radix
- Sambuci flos
- Solidaginis virgaurae herba
- Valeriana radix
- Anisi aetheroleum
- Betulae folium
- Centaurii herba
- Eleutherococci radix
- Foeniculi amari fructus aether.
- Harpogophyti radix
- Lupuli flos
- Menthae piperitae aetheroleum
- Plantaganis ovatae semen
- Polypodii radix
- Psyllii semen
- Rusci aculeato rhizoma
- Sennae folium
- Thymi herba
- Verbasci flos

HPMC MONOGRAPHS: Future work - Rapporteur assigned

- Achillae millefolii flos	2010	- Agrimonae herba	2011
- Agropyri repentis bulbus	2011	- Arctii folium	2010
- Arnicae flos	2010	- Capsella bursa-pastoris herba	2010
- Cardui mariae fructus	2011	- Carvi aetheroleu	2011
- Carvi fructus	2011	- Caryophyllii flos	2011
- Chelidonii herba	2011	- Cichorii intybi radix/folium planta tota	2011
- Crataegi folium cum flore	2011	- Crataegi fructus	2011
- Curcurbitae semen	2010	- Curcumae xanthorrhizae rhizoma	2011
- Cynarae folium	2010	- Eucalypti aetheroleum	2011
- Eucalypti folium	2011	- Filipenduale ulmareiae flos	2011
- Foenugraeci semen	2011	- Ginkgo folium	2011
- Ginseng radix	2011	- Junglandis folium	2011
- Juniperi aetheroleum	2010	- Lavandulae aetheroleum	2011
- Levistici radix	2011	- Lichen islandicus	2011
- Liquiritiae radix	2011	- Millefolii herba	2011

HPMC MONOGRAPHS: Future work - Rapporteur assigned

- Myrrha (Commiphora molmol)	2011	- Myrtilli folium	2011
- Myrtilli fructus siccus	2011	- Oleae folium	2010
- Plantaginis lanceolatae folium	2010	- Pruni spinosa flos	2011
- Pruni spinosa summitates	2011	- Rhodiolae roseae rhizoma	2011
- Serenoae repentis fructus	2011	- Solani dulcamarae stipites	2011
- Symphyti radix	2010	- Taneciti parthenii herba	2010
- Thymi herba/Primulae radix	2010	- Tormentillae rhizoma	2011
- Uvae uris folium	2010	- Visci albi herba	2011
- Zingiberis rhizoma	2011		

HMPC MONOGRAPHS: public statements

- A method of highlighting areas of specific concern or specific monographs:

- *Centella asiatica*:

Community monograph could not be drafted because data concerning specific products do not refer to a herbal preparation. Further data sought

- *Urtica dioica* L, *Urtica urens* L :

Not all the requirements for the acceptance of well-established and traditional use were considered to be fulfilled. Further data sought.

- *Salviae officinalis*:

Concerns about the toxicity of the oil – genotoxicity issues. Further data sought.

HMPC MONOGRAPHS: Community herbal monographs and divergent opinions

- The aim, not always achieved, is to reach consensus on each monograph
- Currently, national competent authorities may have different positions on some Community herbal monographs/may ask for further data on safety/traditional use.
- Some national competent authorities may take differing views on indications for use

GUIDANCE DOCUMENTS: some examples

- **General**
 - *Overview of questions and answers relating to EU pharmaceutical legislation and regulatory aspects applicable to herbal medicinal products*
- **Community List and Monographs**
 - *Procedure for calls for scientific data for use in HMPC assessment work*
- **Quality**
 - *Draft reflection paper on stability testing of herbal medicinal products preparations*
- **Safety**
 - *Draft Guideline on selection of test materials for genotoxicity testing for herbal medicinal products/preparations*
- **Efficacy**
 - *Guideline on the Clinical Assessment of fixed Combinations of Herbal substances/Preparations*
- **Organisational matters**
 - *Guideline on the use of the CTD format in registration applications*
- **Pharmacovigilance**
 - *Public Statement on herbal medicinal products containing Cimicifugae racemosae rhizoma*

HMPC WORKING PARTY ON COMMUNITY MONOGRAPHS AND COMMUNITY LIST (MLWP): work programme 2009

- **Guidelines**
 - Guideline on the preparation of herbal teas
- **Public Statements/Reflection Papers**
 - Reflection paper on ethanol content in herbal medicinal products and traditional herbal products used in children
- **Organisational matters**
 - Discussion/implementation of initiatives for process improvement with a view to achieving a greater number of Community herbal monographs/Community list entries
 - Tracking system for assessment work (development of a database on herbal substances/preparations covered by Community herbal monographs/Community list entry)

THMP MONOGRAPHS: a question?

- THMP monographs are a collection of the available data, characterised by low doses of herbs/and or preparations
- Is there an assessment of whether *all* of the doses and/or preparations fulfil the criteria of a medicinal product: to treat, cure or prevent disease or adverse condition, or to correct, restore or modify physiological function?

THMP MONOGRAPH dosages: a question?

- *Valeriana officinalis*: single dose
 - 1 – 3 g dried valerian root for preparation of a tea
 - Dry extracts prepared with water corresponding to 1 to 3 g of the herbal substance
 - 0.3 – 1g dried valerian root (e.g. as a powdered herbal substance)
 - Valerian tincture corresponding to 0.3 to 1 g of the herbal substance
 - 15ml of expressed juice
 - 15mg of valerian root oil
- Do all these doses restore, correct or modify by exerting a pharmacological action?

THMP monographs: indications – another question?

- Valeriana officinalis
 - *Traditional herbal medicinal product for support of mental relaxation and to aid natural sleep*
- Hypericum: a traditional herbal for the relief of 'fatigue'
- Are such indications really appropriate for medicinal products?

HMPC Monographs - is the EMEA approach to traditional herbals achieving its objectives?

- 'No significant deviations with regard to main objectives are observed except for the output of the HMPC' (Mid-year report, 2009 from the EMEA Executive Director)
- Monograph development is slow. (Estimated that over 300 needed for the efficient working of the THMPD)
- Only one Community List monograph published in the Official Journal

HERBAL MEDICINAL PRODUCTS, THE TRADITIONAL HERBAL MEDICINAL PRODUCTS DIRECTIVE AND 'SIMPLIFIED REGISTRATION'

- **Directive 2004/24/EC amends Directive 2001/83/EC on the Community Code relating to medicinal products for human use, introducing a new way of marketing herbal medicinal products: '*Simplified Registration*'**
 - data to support 30 years tradition of use
 - bibliographic evidence of safety
 - pharmaceutical-standard quality dossier
 - appropriate indications for use: symptomatic relief of self-limiting conditions

THR REGISTRATIONS: is the EMEA approach to traditional herbals achieving its objectives?

- **To stay on the market after April 30th 2011 (the end of the transition period), all traditional herbal medicinal products currently on the market must be THR registered or otherwise market-authorised by that date.**
- **TH registration numbers are generally low:**
 - Many MS have none
 - UK: 97 applications, 46 granted, covering 40 herbs. 10 combination products. No refusals
 - Germany: 11 granted

ISSUES FOR BOTANICAL FOOD SUPPLEMENTS

- EFSA's approach to safety guidance/the review of health claims –

Problems:

- Few level 'A' botanicals
The existence of the Compendium
- The extrapolation of medicinal data to substantiate health effect
- The absence of data from trials on healthy people and the difficulty/cost in performing same
- The acceptance data on traditional use
- the need for the *totality of the available scientific data* to be reviewed and 'weighed' to determine its plausibility
- The clarification of the borderline between the medicinal and food use of botanicals

HERBAL MEDICINAL PRODUCTS/BOTANICAL FOOD SUPPLEMENTS

- Is EMEA's current approach to traditional herbal medicinal products achieving its objectives?
- What are the likely outcomes of EFSA's current approach to the safety of botanicals and the review of health claims?

Liaison between EFSA/EMA/The European Commission: the shape of things to come?

- ‘The HMPC initiated a dialogue with the European Food Safety Agency (EFSA) with support of European Commission DG Enterprise and Industry and DC SANCO on possible coordination at the borderline between herbal medicinal products and food supplements in the clinical data evaluation for the efficacy assessment of (Traditional) Herbal Medicinal Products by HMPC and the substantiation of health claims for ‘Botanicals’ by the EFSA NDA panel’. (HMPC meeting Report July 09)
- Pharmaceuticals to transfer to the Health & Safety (DGIII) area of the Commission?

THE EMEA'S APPROACH TO TRADITIONAL HERBAL MEDICINAL PRODUCTS

- To learn more about the activities of the EMEA and human medicines, see <http://www.emea.europa.eu/index/indexh1.htm>
- To learn more about the activities of the HMPC, click on 'Herbal medicines'

Thank you for your attention –

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