Harmonized Assessment of (Traditional) Herbal Medicinal Products in the EU – Achievements and Future Challenges

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Chairperson, Committee on Herbal Medicinal Products, EMA
Disclaimer

• With reference to the publication policy of the European Medicines Agency (EMA) I do not speak on behalf of the Committee on Herbal Medicinal Products (HMPC) or the EMA.

• The views expressed here may not be understood or quoted as being made on behalf of the HMPC/EMA or reflecting the position of the HMPC/EMA.
Complementary and Alternative Medicines in Germany

- Science
- Research and education
- Tradition
- Options and limitations

Phytotherapy
Homeopathy
Anthroposophy
European Regulation – United in Diversity

Political union of 28 Member States

about 500 Mio inhabitants

24 official languages
The European Network

European Commission
European Parliament
Regulatory framework

Member States,
Agencies
Marketing authorisation
DCP, MRP, national

European Pharmacopeia
Quality standards
General
Herbal drugs/preparations

European Medicines
Agency
Coordination, Guidance
Centralised procedure
EU – Precautionary Principle
Medicinal Products for Public Health

Assessment of

Quality
Efficacy
Safety

Before Access to the market

Marketing authorisation or registration

Consideration of particular characteristics of self-medication and over-the-counter products (OTC)
European Regulation on Medicinal Products

Implementation into national laws

- **CD 2001/83** ("Basic" regulation on medicinal products) amended by

- **CD 2003/63** (Annex I, CTD criteria)
- **CD 2004/24** (*Traditional herbal medicinal products*)

herbal medicinal products, Directive 2001/83/EC on medicinal products for human use and an acceptable level of safety, an adequate quality of these medicinal products must be ensured. Therefore, it is necessary to ensure good manufacturing practice in the production of these products and to introduce a system to prevent fraud, theft, forgery and counterfeiting. It is essential that the implementation of this Directive does not hinder trade in traditional herbal medicinal products (products with a long history of use) in Member States or hamper the production and marketing of these products. Therefore, the necessary guarantees for the quality of these products should not always provide such guarantees.

Having regard to the proposal from the Commission (1),

Having regard to the opinion of the Economic and Social Committee (2),

Acting in accordance with the procedure referred to in Article 251 of the Treaty,
Definitions – Directive 2001/83 EU

Medicinal product
Herbal medicinal product
Traditional herbal medicinal product
   (longstanding tradition, plausibility)

Herbal substance (Eur. Ph. “Herbal drug”)
Herbal preparation (Eur. Ph. “Herbal drug preparation”)

Evaluation of (Traditional) Herbal Medicinal Products

Medicinal plant

Herbal substance

GACP

GMP

Defined by manufacturing process and specifications

Herbal preparation

Finished product
Access to the Market Options for Herbal Medicinal Products

1. New - Marketing authorisation
   full or hybrid application

2. Well-established - Marketing authorisation
   based on bibliographic data

3. Traditional - Registration
   simplified with respect to the proof of efficacy

Procedures: National Procedure,
Mutual Recognition Procedure,
Decentralised Procedure, Centralised Procedure
<table>
<thead>
<tr>
<th>Marketing Authorisation</th>
<th>Registration</th>
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<tbody>
<tr>
<td>Pharmacovigilance</td>
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<tr>
<td>Consumer information; labeling; advertising</td>
<td>applies to registered and to authorised HMP</td>
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<tr>
<td><strong>Efficacy</strong></td>
<td><strong>Registration</strong></td>
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<td>new trials</td>
<td>new tests</td>
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<tr>
<td>bibliographic</td>
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<td>traditional use</td>
<td>expert report</td>
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<td></td>
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<td>new tests</td>
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<td><strong>Safety</strong></td>
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<tr>
<td><strong>Quality Control</strong></td>
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<tr>
<td>Good Manufacturing Practices</td>
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<tr>
<td>Good Agricultural and Collection Practices</td>
<td>identical for marketing authorisations and registrations</td>
</tr>
<tr>
<td>new</td>
<td>well-established</td>
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From Commission E to Community Monographs

Harmonised European assessment
European Medicines Agency

CHMP
Committee on Medicinal Products for Human Use

COMP
Committee on Orphan Medicinal Products

PDCO
Paediatric Committee

HMPC
Committee on Herbal Medicinal Products

CAT
Committee on Advanced Therapies

CVMP
Committee on Medicinal Products for Veterinary Use

PRAC
Pharmacovigilance Risk Assessment Committee

COMPOSITION:
1 member per Member State
1 member each from Norway and Iceland (EEA-EFTA states)
optional co-opted Members

Each member nominated by a Member State also has an alternate

HMPC
Chair
Werner Knöss
Vice-Chair
Marisa Delbo
European Medicines Agency - EMA

- Central European Authority with specified tasks
- Committees and Working Parties
- Herbal Medicinal Products Committee – HMPC
- Monographs and List Working Party - MLWP
- Coordination of National Competent Authorities
- Guidance Documents (www.ema.europa.eu)
HMPC - Harmonisation

Community Monographs on safety and efficacy
Guidance documents
## Two Concepts

<table>
<thead>
<tr>
<th>Well-established use</th>
<th>Traditional use</th>
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<tbody>
<tr>
<td>&lt;The product is a traditional herbal medicinal product for use in specified indication(s) exclusively based upon long-standing use.&gt;</td>
<td></td>
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</tbody>
</table>
Structure of HMPC – Monographs

- Qualitative and quantitative composition
- Pharmaceutical from
- Clinical particulars
  - Therapeutic indications
  - Posology, method of administration
  - Contraindications
  - Special warnings and precautions for use
  - Interactions
  - Pregnancy and lactation, fertility
  - Effects on ability to drive and use machines
  - Undesirable effects
  - Overdose
- Pharmacological properties
- Pharmaceutical particulars
Traditional Herbal Medicinal Products

Registration of traditional herbal medicinal products applicable to *traditional* herbal medicinal products

Article 16c 1 (c)

> 30 years of medicinal use within the EU or

> 15 years in and > 15 years outside the EU

Deviations may be decided by the Herbal Medicinal Products Committee (HMPC, EMA) if requested by a Member State
Traditional Herbal Medicinal Products

- **Indication(s) appropriate** – minor diseases,
- **Without the supervision** of a medical practitioner for diagnosis, prescription or monitoring of treatment,
- Only **oral, external and inhalation**,
- **Sufficient data** on traditional use,
- **Pharmacological effects / efficacy plausible** on the basis of long-standing use and experience.

- **30 years of tradition**, basically EU, deviations by HMPC
Concepts – Well-established Use

The applicant shall not be required to provide the results of toxicological and pharmacological tests or the results of clinical trials if he can demonstrate that the constituent or constituents of the medicinal product have a well established medicinal use with recognised efficacy and an acceptable level of safety, by means of a detailed scientific bibliography;

Article 10a of Directive 2001/83/EC
Concepts – Well-established Use

Considerations:

- Time of use
- >10 years in the European Union
- Quantitative aspects of use of the substance
- Degree of scientific interest in the use of the substance
- Coherence of scientific data, scientific assessments and published scientific literature
- Monographs: at least one controlled clinical trial of good quality
HMPC – documents

- **HMPC-Monographs** on efficacy and safety – recommendation to Member States
- **List Entries** – published by EC, binding to Member States
- **Public Statements** – specific information (e.g. no release of a monograph, safety of specific constituents)
- **Revisions** – every 5 years, sustainability of the system
- **Guidelines** – recommendations to national competent authorities and applicants, consensus on harmonized assessment
- **Reflection Paper, Questions & Answers** – regulatory perspectives on selected topics
HMPC - Harmonisation

- Monographs: 130
- List Entries: 12
- Revisions: 10
- Public Statements: 13
- Guidance: about 30

www.ema.europa.eu
Monographs – Just 3 mouse clicks
assessment report, references, public comments
Committee on Herbal Medicinal Products (HMPC)
Agenda of the 30 June–1 July 2014 meeting

30 June 2014, 14:00 – 19:00, room 3A, plenary
1 July 2014, 08:30 – 12:30, 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

Committee on Herbal Medicinal Products (HMPC)
Minutes of the 5-6 May 2014 meeting

5 May 2014, 14:00 – 19:00, room 3A, plenary
6 May 2014, 08:30 – 12:30, room 3A, plenary
AESCOP hearing 13:30-15:30, room 2A

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 show the detailed instructions to the delegates and print with consensus notes which are needed.
Monographs – Input of Data  www.ema.europa.eu

Call for scientific data for use in HMPC assessment work on Paonieae radix
Submission period: 15 February 2014 - 15 May 2014

The HMPC invites all interested parties such as pharmaceutical industry associations, health care professional groups, learned societies, consumers and patients' associations, governmental institutions as well as EU and EEA-EFTA Member States to submit any scientific data, which may be used in the assessment of Paonieae radix as part of the establishment of Community herbal monographs and/or Community list entries.

Scientific contributions should be sent to:

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<th>By post</th>
<th>By email</th>
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<tr>
<td>European Medicines Agency</td>
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<td>7 Wharfery Circus</td>
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<tr>
<td>Canary Wharf</td>
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<tr>
<td>UK London EC14 4NB</td>
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<td>Attn: HMPC secretariat</td>
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<tr>
<td>or hard copy on CD-ROM or paper prints (2 copies)</td>
<td></td>
</tr>
<tr>
<td><a href="mailto:hmpc.secretariat@ema.europa.eu">hmpc.secretariat@ema.europa.eu</a></td>
<td></td>
</tr>
</tbody>
</table>

If an interested party intends to send scientific contributions in response to several calls for scientific data, responses should be sent separately to each call.

A list of all scientific contributions and their references should be enclosed.

The name and contact details of the interested party providing the scientific contributions is required.

Unpublished data may be included, however, the consent of the data owner is a necessary requirement. The owner of the data will be given the opportunity to review the assessment report to remove any confidential data. The HMPC will consider such submissions on a case-by-case basis.

Submitting parties are bound to obey existing copyrights. Contributors should also take duly into account the rights of interested parties, as the documentation provided will be used for the development of Community list entries and Community herbal monographs. Such development is
HMPC – achievements or „shift of tasks over time“
Registration of Traditional Herbal Medicinal Products (reference: www.ema.europa.eu)
Therapeutic Areas
Reference www.ema.europa.eu

- Cough and cold: 287
- Mental stress & mood disorders: 231
- Gastrointestinal disorders: 215
- Urinary tract and gynaecology disorders: 181
- Sleep disorders & temporary insomnia: 171
- Other*: 151
- Pain and inflammation: 114
- Skin disorders & minor wounds: 80
- Mouth and throat disorders: 72
- Fatigue & weakness: 66
- Venous circulatory disorders: 48
- Loss of appetite: 23
- Constipation: 9
- Eye discomfort: 3

Legend:
- monocomponent products
- combination products
HMPC – Work Programme 2012 - 2015

High

– Regulatory guidance for non-European interested parties – 2012

Initiate pilot projects for herbal substances with a non-European traditional background. **Identify central questions or obstacles** and provide specific information in conjunction with a training for assessors.

High

Questions & Answers on the EU framework for (traditional) herbal medicinal products, including those from a ‘non-European’ tradition

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Conclusions

- Different traditions in the Member States of the EU are being harmonised by European community monographs.
- European legislation provides professional options for non-European traditional medicines.
- Global usage of traditional medicines should strive for harmonised standards based on communication of regulators and scientific community.
  - Scientific data must be provided.
  - Suitable pilot projects are useful.
Thank you for your attention!