swissmedic

EU herbal monographs of the EMA's Committee on Herbal Medicinal Products (HMPC) and their applicability to authorisation procedures in Switzerland

Anne-Isabelle Reich, Regulatory Manager
Complementary and Herbal Medicines

The EMA and Switzerland

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

- Central regulatory authority for EU/EEA states
- Switzerland is a third-party state from the EMA's perspective
- Agreements between EMA and Switzerland, including
  - Confidentiality arrangement,
  - MRA on GMP

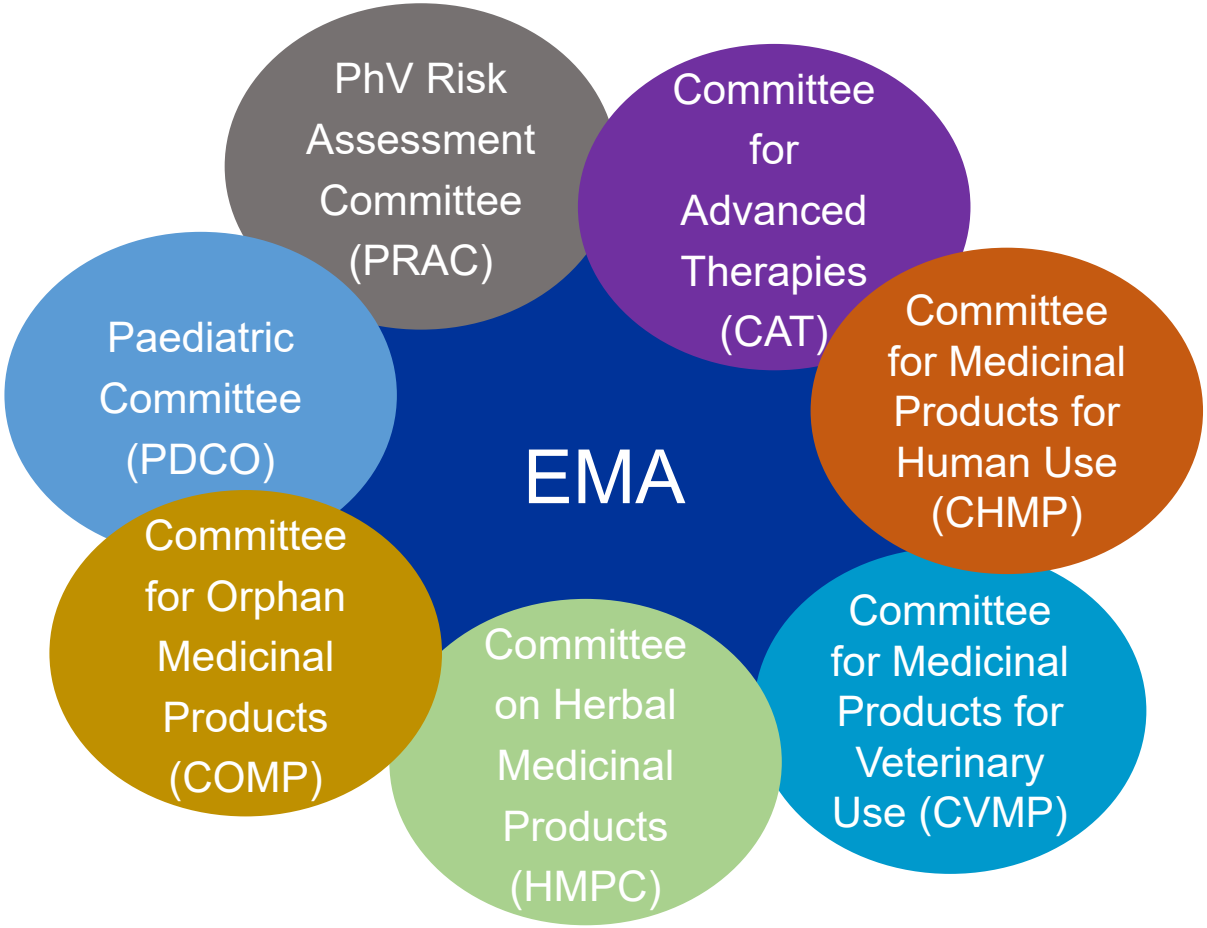
➢ *Additional bilateral agreements with individual authorities (AGES, BfArM, etc.)*

EU: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden
EEA: EU + Norway, Iceland, Liechtenstein

Source: European Economic Area / Wikipedia 13 Aug. 2024

swissmedic

EMA – scientific committees



+ Working parties

+ Scientific advisory groups

What is the HMPC / Committee on Herbal Medicinal Products?

- Tasks:
  - Preparing **EU herbal monographs**
  - Preparing **opinions** on subjects related to herbal medicinal products
  - Drawing up **scientific guidelines and regulatory guidance**
- 1 member per EU/EEA state + 5 co-opted scientific experts
- Swissmedic has been representing Switzerland as an **observer** since January 2024 (was already an observer in the Working Party on Monographs and Lists MLWP until its dissolution)
- 3-day plenary meetings every 2 months
  - Advance **public** agenda / minutes and meeting reports in due course

https://www.ema.europa.eu/en/committees/committee-herbal-medicinal-products-hmpc

EU herbal monographs

- HMPC's opinion on the
  - innocuousness and
  - efficacy of a herbal substance and the preparations derived from it
- Evaluation of all available information
  - Non-clinical data
  - Clinical data
  - Documented longstanding use and experience in (and outside) the EU
- List at: https://www.ema.europa.eu/en/search?f%5B0%5D=ema_search_categories%3A85

Approval of EU herbal monographs

- By **majority decision**
- Individual member states' **divergent positions** are published in the opinion
- **Examples** of divergent positions:
  - Insufficient data to demonstrate medical use
  - Safety aspects
  - Use in children
  - ➢ See e.g. *Fragariae folium, Pelargonii radix, Vaccinii macrocarpi fructus*, etc.

Publication of EU herbal monographs

- **Monograph**
- HMPC's **opinion**
  - May include **divergent positions**
- Associated **assessment report**
- List of **literature references**
- **Stakeholder comments** during the consultation process

Published documents for EU herbal monographs

Final European Union herbal monograph on Ginkgo biloba L., folium
Adopted
Reference Number: EMA/HMPC/321097/2012

English (EN) (185.92 KB - PDF)
First published: 08/04/2015 **Last updated:** 08/04/2015 View

Opinion of the HMPC on a European Union herbal monograph on Ginkgo biloba L., folium
Adopted
Reference Number: EMA/HMPC/61601/2015

English (EN) (102.61 KB - PDF)
First published: 08/04/2015 **Last updated:** 08/04/2015

Final assessment report on Ginkgo biloba L., folium
Adopted
Reference Number: EMA/HMPC/321095/2012

English (EN) (1.38 MB - PDF)
First published: 08/04/2015 **Last updated:** 08/04/2015

Final list of references supporting the assessment of Ginkgo biloba L., folium
Adopted
Reference Number: EMA/HMPC/321096/2012

English (EN) (213.98 KB - PDF)
First published: 08/04/2015 **Last updated:** 08/04/2015 View

Final overview of comments received on European Union herbal monograph on Ginkgo biloba L., folium
Adopted
Reference Number: EMA/HMPC/586885/2014

English (EN) (678.16 KB - PDF)
First published: 08/04/2015 **Last updated:** 08/04/2015 View

swissmedic

Structure of EU herbal monographs

- Primary plant and plant part(s)
- Information on herbal substance or preparation(s)
- Pharmaceutical form(s)
- Clinical particulars, incl.:
  - Indication(s)
  - Method(s) of administration
  - Contraindications, precautions, interactions, undesirable effects, overdose
  - Information on pregnancy/lactation and ability to drive
- Pharmacology, toxicology

Subdivision of EU herbal monographs

Monographs are divided into 2 sections:

- Well-established use

Demonstrated with sufficient safety and efficacy **data**

- Traditional use

Accepted on the basis of sufficient safety data and plausible efficacy **based solely on longstanding use**

All chapters/information in the monograph are divided into these 2 sections.

Example: European Union herbal monograph on *Ginkgo biloba* L., folium

2. Qualitative and quantitative composition[1,2]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended
Ginkgo biloba L., folium (Ginkgo leaf)	*Ginkgo biloba* L., folium (Ginkgo leaf)
i) Herbal substance	i) Herbal substance
Not applicable.	Not applicable.
ii) Herbal preparations	ii) Herbal preparations
Dry extract (DER 35-67:1), extraction solvent: acetone 60% m/m[3]	Powdered herbal substance

4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product for the improvement of (age-associated) cognitive impairment and of quality of life in mild dementia.	Traditional herbal medicinal product for the relief of heaviness of legs and the sensation of cold hands and feet associated with minor circulatory disorders, after serious conditions have been excluded by a medical doctor. The product is a traditional herbal medicinal product for use in specified indication exclusively based upon long-standing use.

swissmedic

Use of EU herbal monographs in Switzerland

1. For **simplified authorisation** under Art. 14 para. 1 let. c^{bis} TPA for herbal medicinal products with well-established use and herbal medicinal products with traditional use

- Reference to **recognised monographs** possible (Art. 11 KPAV) if there is sufficient information on **efficacy** and **tolerability**:
  - EU herbal monographs plus respective assessment report
  - ESCOP, WHO, Kommission E → Assess monograph recognition on case-by-case basis

  ➢ **Equivalence** (pharmaceutical equivalence) is a prerequisite!

- Scope of preclinical and clinical documentation / specifications in Guidance document *Authorisation of herbal medicinal products*

Use of EU herbal monographs in Switzerland

- Proof of medical use **independently of a monograph** to be provided via **comparable medicinal product**
- *NB*: Many EU herbal monographs (with traditional use) are not based on authorised/registered medicinal products ("products on the market"), but solely on **documented use in the literature**

  ➢ Read and take account of assessment report and divergent positions!
- Swissmedic's perspective: Use in the literature (handbooks, reviews, etc.) is not a sufficient data basis from which to extrapolate safety or plausibility of efficacy

Use of EU herbal monographs in Switzerland

2. To **update medicinal product information** to the current state of science and technology (Art. 28 TPO)

- EU herbal monographs are reviewed every 5 years = current state of science and technology
- The transferability of safety information – such as precautions and undesirable effects – should be reviewed on a case-by-case basis for medicinal products that are already authorised.

  ➢ If required: Applications for variations (C.I.4)

Scientific guidelines = current state of science and technology

- https://www.ema.europa.eu/en/human-regulatory-overview/research-and-development/scientific-guidelines/multidisciplinary-guidelines/herbal-medicinal-products-scientific-guidelines
- **Quality**

  Guidelines (e.g. declaration, GACP, quality of HMP, specifications, etc.), Q&A on quality, Reflection papers (e.g. markers, stability testing, etc.), concept papers
- **Non-clinical**

  Guidelines (e.g. Assessment of genotoxicity, etc.)
- **Clinical**

  Guidelines (e.g. Assessment of clinical safety and efficacy in the preparation of EU herbal monographs, Clinical assessment of fixed combinations), Reflection papers (e.g. Studies in paediatric population, etc.)

Other publications = current state of science and technology

- **Public statements**

  e.g.
  - Use of herbal medicinal products containing estragole (Revision 1: 9 June 2023)
  - Use of herbal medicinal products containing pyrrolizidine alkaloids (PAs)
  - If an EU herbal monograph is not issued following evaluation (e.g. greater celandine *Chelidonium majus*) or if a current monograph is no longer supported (e.g. fennel oil, 29 May 2024), this is mainly because of safety concerns.

- **Reflection papers**

  e.g.
  - Ethanol content in (T)HMPs used in children

Take-home message

- EU herbal monographs have relevance for Switzerland
  - New application
  - Variations
- Evaluate pharmaceutical equivalence
- EMA publications = current state of science and technology