Herbal Preparations as Medicinal Products

PD Dr. Orlando Petrini,
Chairman, AESGP Committee on Herbal Medicinal Products
Pharmaton SA /Boehringer Ingelheim
Lugano, Switzerland

Regulatory Affairs on HMPs, Kiel, 3.09.03
Herbal Medicinal Products vs Chemical Products

<table>
<thead>
<tr>
<th>Herbal Medicinal Products (HMP)</th>
<th>Chemical Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>• extracts, powders, …</td>
<td>• well-defined composition</td>
</tr>
<tr>
<td>• long-standing tradition of use</td>
<td>• no traditional use</td>
</tr>
<tr>
<td>• used to treat “soft” problems</td>
<td>• used to prevent and cure (serious) diseases</td>
</tr>
<tr>
<td>• safe record of use</td>
<td>• often relevant safety problems</td>
</tr>
<tr>
<td>• PK/(PD) often impossible to be carried out</td>
<td>• PK/PD more or less easy to be carried out</td>
</tr>
<tr>
<td>• ….</td>
<td>• ….</td>
</tr>
</tbody>
</table>

**But:** Pharmacology, Toxicology, Safety Clinical Data and Double-blind, Controlled Clinical Trials possible for both categories!
Features of herbal medicinal products

- safety pharmacology not always available or up-to-date
- large body of experience often available
- data from clinical trials rarely available
Constituents of herbal medicinal products

- Known clinical activity (active principles)
- Known pharmacological activity (active markers)
- Relevant for quality control (analytical markers)
- Accompanying constituents (inert substances)
- Potential negative impact (allergens, toxins)
- Matrix substances
Some definitions (WHO / EU)

- **Herbal drugs**
  Plants or part of plants in an unprocessed state

- **Herbal drug preparations**
  Comminuted or powdered herbal drugs, extracts (including purified extracts), tinctures, fatty or essential oils, resins or gums, etc. ...

- **Herbal medicinal products**
  A medicinal product containing as active substance exclusively herbal drugs or herbal drug preparation
Present regulatory status of herbal medicinal products in the EU

- Food
- Dietary Supplement
- OTC (Non-prescription medicine)
- Prescription medicine
## Levels of Evidence


<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Meta-analysis of randomized controlled trials</td>
</tr>
<tr>
<td>Ib</td>
<td>at least one randomised controlled trial</td>
</tr>
<tr>
<td>Ila</td>
<td>at least one well-designed contr. study without randomisation</td>
</tr>
<tr>
<td>IIb</td>
<td>at least one other type of well-designed quasi-experimental study</td>
</tr>
<tr>
<td>III</td>
<td>well-designed non experimental descriptive studies, such as comparative studies, correlation studies, case-control studies</td>
</tr>
<tr>
<td>IV</td>
<td>expert committee reports or opinions and/or clinical experiences of respected authorities</td>
</tr>
</tbody>
</table>
Grading of Recommendations (Keller, 1999)

- **A** - expert committee reports, opinions and/or clinical experience of respected authorities; minimum: documented long term use and supportive experimental data.

- **B** - no or negative expert committee reports, opinions / clinical experience of respected authorities; documented long or short term use without supportive experimental data; new uses without clinical data.

- **C** - quantity of information.

- **X** - quality of information.
Herbal Medicinal Products

• Well-established herbal medicinal products:
  » proven clinical efficacy
  » at least 10 years of use in the EU

• Traditional use
  » only traditional use documented
  » insufficient or no clinical support for indication
  » at least 30 (15+15) years of documented use
... and future requirements

- Well-established herbal medicinal products:
  » quality documentation
  » use of monographs
  » complementation through additional non-clinical and clinical data
  » Mutual Recognition Procedure (MRP)

- Traditional use
  » quality documentation
  » use of monographs
  » national registration
Implementation of different levels of scientific evidence

Major claims: High level of evidence (Level Ia, Ib; Grade A)
  - For treatment, cure or management of any serious disease or disorder
  - For prevention of any serious disease or disorder

Medium claims: Medium level of evidence (Level IIa, IIb, III; Grade B)
  - Reduction of risk of a disease/disorder
  - Reduction in frequency of a discrete event
  - Aids/assist in the management of a symptom/disease/disorder
  - Relief of symptoms

Minor claims: General Level of evidence (Level IV; Grade C)
  - Relief or management of symptoms of a minor, self-limiting disease/disorder that does not require medical intervention
  - Description of a pharmacological action related to management of symptoms of a minor, self-limiting disease

(Draft Concept, HMPWG, 21st May 2003)
AESGP wishes for the future of herbal medicinal products

• An independent EMEA Committee for herbal medicinal products
• A clear legislation and definition for well-established vs. traditional herbal medicinal products
• Adequate protection of intellectual property
  - data exclusivity for significant data
• ESCOP and WHO monographs should form the base of the EMEA monographs