THEME: THE IMPORTANCE OF A RISK-BENEFIT ANALYSIS FOR THE MARKETING AUTHORIZATION AND / OR REGISTRATION OF (TRADITIONAL) HERBAL MEDICINAL PRODUCTS (HMPs)

CHAIRS : A.J. VLIETINCK AND S. ALBAN
## WORKSHOP OF THE PERMANENT COMMITTEE ON REGULATORY AFFAIRS OF HERBAL MEDICINAL PRODUCTS (2009 – 2010) (2)

### PROGRAMME

<table>
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<tr>
<th>Time</th>
<th>Speaker</th>
<th>Institution</th>
<th>Topic</th>
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<td>14:00</td>
<td>A.J. Vlietinck, University of Antwerp (UA)</td>
<td>Belgium</td>
<td>Introduction</td>
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<td>14:05</td>
<td>G. Laekeman, Catholic University of Leuven</td>
<td>Belgium</td>
<td>Taking the Risk of the Benefit: The Unbalanced Situation of Herbal Medicinal Products</td>
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<td>14:35</td>
<td>J. Wiesner, Federal Institute for Drugs and Medical Devices</td>
<td>Germany</td>
<td>National Practice: Experiences with the Safety Assessment for (Traditional) Herbal Medicinal Products</td>
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<td>15:05</td>
<td>B. Steinhoff, European Scientific Cooperative of Phytotherapy</td>
<td>Germany</td>
<td>European Practice: Experiences with a Risk-Benefit Analysis of HMPs for the Elaboration of ESCOP-Monographs</td>
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<td>15:35</td>
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<td>Coffee Break</td>
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<td>16:00</td>
<td>G. Meng, Dr. Wilmar Schwabe GmbH &amp; Co, KG</td>
<td>Germany</td>
<td>European Practice: Well-Established Use of Herbal Medicinal Products and Clinical Research</td>
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<td>16:30</td>
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<td>Panel Discussion and Conclusion</td>
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<td></td>
<td>- Is a Benefit-Risk Analysis Indispensable for the Marketing Authorisation or Registration of Herbal Medicinal Products?</td>
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EUROPEAN UNION LEGISLATION

MILESTONES WITH PARTICULAR RELEVANCE FOR HERBAL MEDICINAL PRODUCTS

• COMMISSION DIRECTIVE 1999/83/EC OF 8 SEPTEMBER 1999
  CLARIFICATION ON PROVISIONS FOR WELL-ESTABLISHED USE

• COMMISSION DIRECTIVE 2003/63/EC OF 25 JUNE 2003
  ANNEX 1 TO CD 2001/83: SPECIFIC PROVISIONS FOR HERBAL MEDICINAL PRODUCTS, INTEGRATION OF CD 1999/83/EC ON WEU

• DIRECTIVE 2004/24/EC OF 31 MARCH 2004:
  SIMPLIFIED REGISTRATION FOR TRADITIONAL HERBAL MEDICINAL PRODUCTS

• REGULATION 726/2004/EC OF 31 MARCH 2004:
  ESTABLISHMENT OF A SCIENTIFIC COMMITTEE ON HMPs AT THE EMEA
THE EU PYRAMID OF PERMITS FOR HERBAL PRODUCTS

PRODUCTS

- HERBAL MEDICINAL PRODUCTS (HMPs)
  - FULL MARKETING AUTHORIZATION
  - WELL ESTABLISHED USE HMPs (WEU)
  - TRADITIONAL HMP (THMPs)

- HERBAL FOOD SUPPLEMENTS

- HERBAL NOVEL FOODS

- HERBAL COSMETIC INGREDIENTS

LEGISLATION

- MEDICINAL PRODUCTS

- FOOD SUPPLEMENTS
  CD 2002/46 EC AND CD 2006/C80E

- NOVEL FOODS
  REGULATION 258/97

- COSMETICS
  CD 76/768
OVERVIEW OF LEGAL FRAMEWORK FOR HMPs IN THE EU

**Legal basis**
- Art. 8.3(i) CD 2001/83/EC “Complete application”
- Art. 10.1(a)(ii) CD 2001/83/EC "Bibliographical application"
- Annex 1: Specific provisions for HMPs

**Medicinal use**
- < 10 years
- ≥ 10 years
  - + demonstration of “well established use” (WEU)

**Conditions**
- Serious and minor diseases
- Possible intervention of medical practitioner
- No restrictions regarding strength, posology, route of administration

**Labelling**
- HMPs for treatment, prevention...

**LEVEL OF EVIDENCE**

- **New product**
  - A
- **Major claim**
  - B
- **Minor claim**
  - C
- **Limited route of administration, strength & posology**
  - T
- **THMP for use in specific indication(s) exclusively based upon long standing use.**
  - X

**Fraudulent or misleading claims**
### OVERVIEW OF LEGAL FRAMEWORK FOR HMPs IN THE EU

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<td>GACP</td>
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<tr>
<td>New</td>
<td>Well-Established (WE)</td>
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<td>Marketing Authorisation (MR)</td>
<td>Traditional (T)</td>
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<td>Registration (R)</td>
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EVALUATION OF THE POSITIVE BENEFIT ARGUMENTS AGAINST THE NEGATIVE RISK ARGUMENTS WHEN ASSESSING A MEDICINAL PRODUCT

AFTER BECKMANN, 1999
HIERARCHY OF SOURCES

- NO DATA
- ANIMAL EXPERIMENTS, REPORTED EXPERIENCES FROM "AUTHORITIES" (THEORY)
- INDIVIDUAL CASES WEIGHTED ACCORDING TO CAUSALITY
- CASE SERIES, DATA BASES
- CONTROLLED OBSERVATIONAL STUDIES
- NON-RANDOMIZED CONTROLLED INTERVENTION STUDIES
- RANDOMIZED CONTROLLED INTERVENTION STUDIES

- TRADITIONAL TOLERATION
- POSITIVE MONOGRAPH
- AUTHORIZATION

AFTER BECKMANN, 1999