Regulation of Herbal and Traditional Medicines in Germany
BfArM in Dialogue - TradReg 2017

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BfArM; Bonn; Germany
**Medicinal Product Supervision Administration**

**Federal Level**
- Bundesamt für Verbraucherschutz und Lebensmitteleisicherheit
- Bundesinstitut für Arzneimittel und Medizinprodukte
- Paul-Ehrlich-Institut

- marketing authorisations
- dossier-related inspections
- pharmacovigilance inspections
- pharmacovigilance management
- management of product defects (Rapid Alert System)
- OMCL (PEI, vaccines)

**Laender Level**
- OMCLs
- Inspectorates

- GMP/GCP inspections
- GMP/GDP certificates
- manufacturers/importers authorisations
- export certificates
- drug testing

**ZLG**
European Union

- political union of 28 Member States
- about 500 Mio inhabitants
- 24 official languages
Key Institutions

**European Commission**
Regulatory Framework, Law Directives, Regulations

**European Parliament**

**National authorities**
Assessment
Marketing Authorisation
DCP, MRP, national

**European Pharmacopeia**
Quality standards
General
Herbal Drugs/Preparations

**EMA**
Coordination
Guidance
Centralised Procedure
Pharmacopoeia – Network and Cooperation

Pharmacopoeia (§ 55 Drug Law) → DAB

Pharmacopoeia (§ 55 Drug Law) → HAB

Transfer / Implementation

DAB → HAB

* European Pharmacopoeia (Ph. Eur.)
Herbal and Traditional Medicines in Germany

**Particular Environment**

- phytotherapy, homeopathy, anthroposophy
- long history of usage
- science, research, education
- regulation in the pharmaceutical legal framework
- acceptance among citizens
- 25% of European market
- small- and medium-sized German enterprises
Specific Expertise in Division 4

- responsibility for about 10,000 finished medicinal products
- about 35% combination products
- herbal medicinal products, traditional herbal medicinal products, homeopathic medicinal products, anthroposophic medicinal products, vitamins, minerals, water, traditional medicines
- assessment, life cycle – options and limitation
- scientific advice
- advice to the Federal Ministry of Health
Traditional Medicines in Germany - Basic Figures

2000 herbal medicinal products (23% combinations)

1700 licensed herbal medicinal products (15% combinations)

300 registered traditional herbal medicinal products
(40% combinations)

1350 licensed homeopathic medicinal products (86%)

1050 licensed anthroposophic medicinal products (62%)

3900 registered homeopathic and anthroposophic (48%) medicinal products
Specific Division for Traditional Medicines at BfArM

**Licensing 4**
Prof. Dr. W. Knöss

**Unit 41**
Project Management

**Unit 42**
Herbal and traditional medicinal products

**Unit 43**
Homeopathic and anthroposophic medicinal products

**Unit 44**
Cannabis Agency

Pie chart showing the distribution of different professions:
- Physicians: 31%
- Pharmacists: 29%
- Food chemists: 29%
- Biologists: 6%
- Chemists: 3%
- Biopharmacologists: 3%
Establishment of the Cannabis Agency

Single Convention on Narcotic Drugs, 1961 (United Nations):
... shall establish a governmental agency to control cultivation and supply of Medical Cannabis ...

"Gesetz zur Änderung betäubungsmittelrechtlicher und anderer Vorschriften" (10th March 2017)
"Der Anbau von Cannabis zu medizinischen Zwecken unterliegt der Kontrolle des BfArM. Dieses übernimmt die Aufgaben einer staatlichen Stelle ..."
Strategy on regulation of Medical Cannabis - key elements and objectives

- Patients with severe illness
- Improved access
- Prescription by doctors
- Pharmaceutical quality (DAB)
- Reimbursement

Future perspective: More marketing authorisations
European and Global Activities of Division Licensing 4

• **Active contribution to the European network**
  - substantial resources, substantial contributions
  - harmonisation in the EU (EMA; HMA; EDQM)
    numerous rapporteurships; RMS
    Chairperson Committee on Herbal Medicinal Products (HMPC, EMA) until 2016
  - coordination national authorities – EMA – EDQM

• **Global contacts and communication**
  - e.g. IRCH-meetings (WHO)
    GIZ project
    Bilateral contacts, conferences, training, education
Old standards

New standards

**Harmonised standard**
„United in diversity“

**HMPC work plan**
2016 – adopted by the Committee on 24 November 2015

**Table of Content**
1. Evaluation activities for herbal medicinal products as defined in Reg. (EC) No 726/2004 and Dir. 2001/83/EC ................................................................. 2
Pharmaceutical Legislation in the EU

- Directive 2001/83/EC („Basic“ regulation on medicinal products) amended by
  - Directive 2003/63/EC (Annex I; CTD criteria)
  - Directive 2004/24/EC (THMP)

Basic approach: Assessment of

- Quality
- Safety
- Efficacy
Pharmaceutical Legislation in the EU

Definitions:

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”)
Access to the Market – Options and Concepts

• Marketing authorisation
  - Full application (e.g. new medicinal products) [Article 8 of Directive 2001/83/EU]
  - Well-established use [Article 10a of Directive 2001/83/EU]

• Registration
  - Traditional use [Article 16a of Directive 2001/83/EU]
Recent new Herbal Medicinal Products in the EU based on a Full Application

Centralised procedure

Decentralised procedure

EPAR summary for the public

Episalvan

Birch bark extract

This is a summary of the European public assessment report (EPAR) for Episalvan. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Episalvan.

For practical information about using Episalvan, patients should read the package leaflet or contact their doctor or pharmacist.

What is Episalvan and what is it used for?

Episalvan is a medicine used in adults to treat partial-thickness skin wounds. These are wounds where the upper layers of the skin have been lost, for example by a burn or during surgical skin grafting.

Episalvan contains a dry extract from birch bark.

How is Episalvan used?

Episalvan is available as a gel that should be applied as a thin layer (1 mm in thickness) to the wound, which should then be covered by a wound dressing. The gel should be re-applied with every dressing change, until the wound is healed, for up to 4 weeks.

The medicine can only be obtained with a prescription.

How does Episalvan work?
Tasks

**EMA**
- HMPC Monographs
- Safety + Efficacy Guidelines

**European Pharmacopeia**
- Eur. Ph. Monographs
- Quality

**Standards**

**National authorities or EMA (centralised)**
- Product Applications
- Assessment
- Licensing
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Marketing Authorisation | Registration

Pharmacovigilance

- Consumer information; labeling; advertising

- Efficacy
  - new trials
  - bibliographic
- Safety
  - new tests
  - bibliographic

Quality Control

- Good Manufacturing Practice
- Good Agricultural and Collection Practice

new | well-established | traditional

applications to registered and to authorised HMP

may be replaced by a monograph or the list from the HMPC in registrations (WEU/TRAD)

identical for marketing authorisations and registrations
First Registration of a Traditional Herbal Medicinal Product in Europe

Legislation 2004
December 2005:
Traditional registration
Continuous access to the market
Combination (n=13)
Quality guideline conform
Plausibility
Additional data
Monographs - Contributions of BfArM (source: EMA)
Specific Division for Traditional Medicines at BfArM

Licensing 4
Prof. Dr. W. Knöss

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Complementary Medicines and Traditional Medicines

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>physicians</td>
<td>31%</td>
</tr>
<tr>
<td>pharmacists</td>
<td>29%</td>
</tr>
<tr>
<td>food chemists</td>
<td>29%</td>
</tr>
<tr>
<td>biologists</td>
<td>6%</td>
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<tr>
<td>chemists</td>
<td>3%</td>
</tr>
<tr>
<td>biopharmacologists</td>
<td>3%</td>
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</tbody>
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Homeopathy – a Traditional Therapeutic System

- **Samuel Christian Hahnemann (1755 – 1843)**
  „Essay on a New Principle for Ascertaining the Curative Powers of Drugs“ (1796)
  Germany and France

- **Medicinal Products Act (1976)**
  Scientific pluralism in medical therapy
  Regulation as Medicinal Products
Regulatory Approach in Germany

- Integration of homeopathic and anthroposophic medicines in the regulatory framework for medicines
- Evaluation of medicinal products before access to the market
- Unit with special expertise at BfArM
- Consideration of particular characteristics in assessment of quality, safety and efficacy
- Protection of patients
  - risks
  - fraudulent products / claims/ information
- Expert committees
  - Commission C  anthroposophic medicinal products
  - Commission D  homeopathic medicinal products
Section 4

Definitions of additional terms

26) A homeopathic medicinal product is any medicinal product prepared in accordance with a homeopathic manufacturing procedure described in the European Pharmacopoeia or, in the absence thereof, in the pharmacopoeias currently used officially in the EU Member States. ...
National Procedures

Registration (§ 38 f)

Without any indication claim
Mandatory labelling: „Homeopathic Medicinal product without approved therapeutic indication“
„Consult a doctor if symptoms persist during the use of the medicinal product“

Marketing authorisation (§ 21 ff )

With indication claim
Instead of results of pharmacological and toxicological tests and of clinical trials „... other scientific documents may be presented ....”. „...Furthermore, the medical experience gained by the specific schools of therapy must also be taken into consideration. ...“
Quality – reproducibility by process

Homeopathic medicinal products are characterised by the **homeopathic manufacturing procedure and specifications**.

Raw materials and dosage forms have to comply with the requirements of the GHP and Ph. Eur.
Safety

**Regulatory strategy by BfArM (Germany)**

- Common regulatory standards for safety evaluation
- No compromise
- Consideration of particulars
- Lack of data
- Regulatory responsibility
- Publication of concept

*Buchholzer et al., 2014.* Regulatory Toxicology and Pharmacology 68, 193–200

Current concepts on integrative safety assessment of active substances of botanical, mineral or chemical origin in homeopathic medicinal products within the European regulatory framework.
European Network - HMPWG

Forum for exchange of regulatory and scientific expertise

Guidance on assessment for national authorities

Guidance on registration to applicants

Non-clinical safety (safe dilution grade) (art. 14(1) of Dir. 2001/83/EC)

Advice and expertise on procedural, regulatory and scientific issues
BfArM: Dialogue and solutions

Examples

- Scientific advice (scientific, clear, target-oriented)
- BfArM in Dialogue
- Meetings with associations
  - Viscum
  - Pyrrolizidine alkaloids
  - Virus validation in homeopathy
  - Interactions
Dialogue and solutions

Strategy of BfArM (Germany)

- Clear commitment on regulation of herbal and traditional medicines
- Allocation of resources to the European network and global initiatives
- Availability of medicinal products and public health
- Consideration of particulars
- Science-based decision making within legal framework
- Regulatory responsibility for options and limitations
Thank you very much for your attention!

Contact

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