

QUALITY OF HOMOEOPATHIC PRODUCTS IN THE NEW EUROPEAN LEGISLATIVE FRAMEWORK

Session I

General European Regulatory Background

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(9:10-10:40)



 European Commission


Enterprise and Industry

 Directorate-General

EDQM Homeopathic Symposium

Legal Framework for Homeopathic Products under the New Directive

Strasbourg, 15 February 2005
 Claire SCHARF-KRÖNER
 Pharmaceuticals Unit



 European Commission

Enterprise and Industry
Directorate-General

Introduction

- Current framework: Directive 2001/83
- Changes introduced by Directive 2004/27
 final date of transposition for Member States: 30 October 2004
- What are the main changes for homeopathic products?

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 European Commission

Enterprise and Industry
Directorate-General


Definition

(Article 1 No. 5)

Homeopathic medicinal product:

"Any medicinal product prepared from [*products,*] substances [*or compositions*] called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopeia or, in absence thereof, by the pharmacopeias currently used officially in the Member States. A homeopathic medicinal product may also contain a number of principles."


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Registration procedure (1)
(Article 13)

- Member States shall establish a simplified registration procedure according to Article 14
- Article 28 and 29(1) to (3) shall apply to registration procedure


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Registration procedure (2)
(Article 14)

- Conditions for registration (unchanged):
 - (1) administered orally or externally,
 - (2) no specific indication,
 - (3) sufficient degree of dilution
- NEW: if new scientific evidence so warrants, the Commission may amend criteria (3)
- Deletion of 14(3)

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Registration procedure/ documents
(Article 15)

- Dossier describing homeopathic use (before: nature)
- Mock-ups of packaging to be provided (no longer *additional* reference to specimen)


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Authorisation procedure/ MS rules
(Article 16)

- Authorisation and labelling: reference to Articles 8 and 10 - 11
- Member States may have specific rules on pre-clinical tests (before: toxicological and pharmaceutical tests)


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Labelling
(Article 69)

- NEW: “if the homeopathic medicinal product is composed of two or more stocks, the scientific names of the stocks on the labelling may be supplemented by an invented name”
- Warning advising the user to consult a doctor if the symptoms persist (as before) NEW: no longer limited to „during the use of the medicinal product“



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Mutual recognition procedure (MRP)
(Article 39)

- NEW for registered products: Art. 28 and Art. 29(1) - (3) apply: co-ordination group Art. 29(4) - Art. 34 do not apply: no full MRP procedure
- For products under special MS rules (Art. 16(2)): as before no MRP; Art. 28 – 34 do not apply

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Pharmacovigilance

(Article 16(3))

- Wording of Art. 16(3) unchanged
As before: pharmacovigilance does not apply to registered products

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Wholesale distribution

(Article 85)

- Provisions apply to all homeopathic medicinal products
(before: not to *registered* products)

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The European Pharmacopoeia's role for Homoeopathic Preparations

Strasbourg, 15 February 2005

**Peter Castle
Secretary to the European Pharmacopoeia
Commission**

Role of the Ph Eur

- **Provide harmonised quality standards for use by health professionals**
- **Ph Eur standards are applied in 35 Member States**
- **The current legislative framework has led to a need for official quality standards in Europe for homoeopathic preparations**

Strasbourg, 15 February 2005

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Working methods

- **Work programme: decided by the European Pharmacopoeia Commission (EPC)**
- **Proposals from: delegations, groups of experts, EDQM**
- **Elaboration of monographs allocated to a group of experts or working party**
- **Final adoption by EPC**

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Groups of experts

- **Composed of experts from Member States**
- **Proposed by the national authority, appointed by EPC**
- **Chaired by a member of the EPC**
- **3-year term of office, renewable**

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Work stages (1)

- **Addition to work programme, allocation to a group**
- **Public information on web site and via industry associations**
- **Preparation of first draft, experimental verification**

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Work stages (2)

- **Publication in Pharmeuropa**
- **3-month comment period**
- **Study of comments**
- **Adoption by EPC**
- **Publication in Ph Eur (about 5 mo after adoption)**
- **Implementation 1 year after adoption**

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Revision

- **Revision may be requested by delegations, group of experts**
- **Request must be justified with sufficient data (batch analysis results, validation data, etc)**
- **Revision follows the same stages as elaboration**

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Ph Eur texts

- **Specific monographs**
- **General monographs**
- **General monographs on dosage forms**
- **General chapters**

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General monographs

- **Apply to all products within the scope of the definition (exception: general monograph *Substances for Pharmaceutical Use*)**
- **Set general rules for a class of products**

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General chapters

- **Mainly methods of analysis BUT**
- **5.2.8 Minimising the risk of transmission of agents of animal spongiform encephalopathies**
- **General chapters become mandatory when referred to in a monograph**
- **Existing general chapters apply for homoeopathic preparations when referenced in a monograph**

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Production section

- **Features in many Ph Eur monographs, particularly on biological products**
- **Deals with important aspects of the manufacturing process**
- **Often gives requirements that cannot be verified by examination of the finished product**
- **Verification by inspection or testing of in-process samples**

Strasbourg, 05 February 2005

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Homoeopathy in the Ph Eur

- **Following changes in the legislative framework, EPC recognised the need to deal with homoeopathic preparations**
- **EPC is developing the general policy to be applied**
- **The present symposium should contribute to policy development**
- **Materia medica for HP is vast so that prioritisation is essential**

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Priorities

- **General monographs identified as a clear priority to set basic requirements**
- **Harmonisation of existing national monographs**
- **Present situation: successful development of general monographs and a number of specific monographs (raw material + mother tincture)**

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General principles

- **The general rules of the Ph Eur are applicable in the field of homoeopathy**
- **Existing monographs apply also to homoeopathic use (*but* for herbals, existing monographs are usually for dried drugs)**
- **Ph Eur titles are to be used in labelling**

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General homoeopathic monographs

- **Homoeopathic preparations**
- **Mother tinctures for homoeopathic preparations**
- **Herbal drugs for homoeopathic preparations**

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Experiences of the European Pharmacopoeia Working Party

Professor Derek Calam

Scope

- **The European Pharmacopoeia Working Party**
- **Achievements**
- **Problems**
- **Sticking points**

Homoeopathy Working Party

- **Homoeopathic Directive 92/73/EEC**
 - Reference to European Pharmacopoeia
- **Working Party fully established 1997**
- **Membership restricted to national authorities**
- **To prepare monographs for European use (based on national German and French monographs)**

**Directive 2001/83/EC
Code for medicinal products**

- **Preamble 17**
 - It is necessary to adopt specific provisions for
homoeopathic medicinal products
- **Preamble 24**
 - The rules relating to the manufacture, control
and inspection of homoeopathic medicinal
products must be harmonised to permit the
circulation throughout the Community of
medicinal products which are safe and of good
quality
- **Module 3 general principles: application of
Ph Eur general and specific monographs**

**Homoeopathic section of the
European Pharmacopoeia**

Introduction

All general texts and monographs of the European
Pharmacopoeia that are relevant to homoeopathy are
applicable.

The “Homoeopathy” chapter of the European
Pharmacopoeia contains general monographs and
individual monographs describing starting materials
and preparations used virtually exclusively for
homoeopathic medicines. Reference to these
monographs for other purposes may be authorised by
licensing authorities

**Achievements:
general monographs**

- **Homoeopathic preparations**
- **Mother tinctures for homoeopathic
preparations**
- **Herbal drugs for homoeopathic
preparations**

**Apply to all relevant homoeopathic
preparations not only those in Ph Eur**

**Achievements:
inorganic monographs**

- Arsenious trioxide
- Barium chloride dihydrate²
- Cadmium sulphate 2.7 hydrate³
- Calcium iodide tetrahydrate²
- Copper
- Copper acetate monohydrate²
- Iron

² Supplement 5.2 ³ Supplement 5.3

**Achievements:
herbal and other monographs**

- Common stinging nettle
- Garlic
- Hedera helix²
- Hyoscyamus²
- Hypericum
- Oriental cashew³
- Saffron
- Honey bee

² Supplement 5.2 ³ Supplement 5.3

Problems found

- Different homoeopathic traditions
 - Parts of plant used
 - Manufacturing procedures
 - Plant/solvent ratio
- Origin of plants
- Condition of plant material
- Falsification: use of dried not fresh plant
- Assay

Solutions

- **Origin of plants**
 - Non-quantitative identification to ensure marker compounds present
- **Parts of plant used**
 - Priority to national monographs where same part of plant described
- **Method of manufacture**
 - Not specified. Only type of solvent and first extract characterised

Solutions

- **Mother tincture**
 - Limits to include known composition and content ranges
- **Condition of plant material**
 - General monograph
- **Falsification**
 - Set upper limits to exclude dried material with high content of constituent
- **Assay**
 - Only for toxic constituent or for stability/quality

Hedera helix for homoeopathic preparations

Fresh, young, fully developed but not yet lignified branch, harvested immediately before or at the beginning of flowering

- **Macroscopic identification**

Tests

- **Foreign matter (2.8.2)** If required by the competent authority
- **Loss on drying (2.2.32)** If required by the competent authority

Hedera helix for homoeopathic preparations

Mother tincture

- Compliance with general monograph
- Prepared using ethanol of suitable concentration
- Content: min 0.15% m/m hederacoside C
- Identification TLC
- Relative density range
- Ethanol 60 to 70 %
- Dry residue minimum 2.0%
- Assay HPLC using reference

Sticking points

- Freshness of plants
 - Visual inspection
 - Loss on drying
- Foreign matter
 - Visual inspection to minimise
 - Measurement: default limit max. 2%
- Balance between Good X Practice and specification

Sticking points

- Storage of fresh plant material deep frozen or in solvent
- Mother tinctures
 - Density
 - Ethanol content
- Time of maceration
- Methanol content of mother tincture
- Mercury-containing materials
 - Environmental impact

Sticking points

- **Dilution of stocks**
 - **Undiluted: allowed or not?**
- **Pillules**
 - **Definitions - undiluted stocks**
 - **Tests - uniformity of mass**
 - **impregnation**
 - **disintegration**
- **Nomenclature - safety issues**

Key issues to be addressed

- **Need for harmonised regulatory approach imposed by Directive**
- **Control to be based on need to establish good quality and on sound science**
- **Respect for homoeopathic traditions**

HOMOEOPATHIC PREPARATIONS NOMENCLATURE

ISABELLE MERCIER
EDQM

EU Legal framework

- 2001/83/EC, Article 15
« scientific name or other name given in a pharmacopoeia of the homeopathic stock or stocks ... »
- 2003/63/EC, Annex 1, Module 3
« a) Terminology: the Latin name of the homeopathic stock ... must be in accordance with the Latin title of the Eur. Ph. or, in absence thereof, by an official pharmacopoeia of a MS. Where relevant, the traditional name(s) used in each MS shall be provided. »

First attempts



- Saffron
Crocī stigma
- Arsenious trioxide
Arsenii trioxidum
- Potassium sulphate
Kalii sulfas

First attempts (2)



Opposition from one delegation to include synonyms in Ph. Eur. because against aims of Ph. Eur. i.e. standardisation, harmonisation, ease of free circulation
Need for a common name
BUT ... long tradition

Existing monographs in Ph. Eur.



1997/1998
Raw materials used in homoeopathy having already a monograph in the Ph. Eur.

+ Latin titles from HAB and Ph. Fr.

Titles used in Homoeopathy



- Include them in list of raw materials and call the list:
Titles used in Homoeopathy
- Publish the list in Pharmeuropa for information

Titles used in homoeopathy (2)



- Member States indicate
- other Latin titles used nationally
 - titles that are not acceptable on safety grounds:
chloratum
bromatum
iodatum

Titles used in homoeopathy (3)



- Pharmeuropa 13.3
- Pharmeuropa 16.4
- Together with HMP WG ...

Mother tinctures for hom. prep.

LABELLING

The label states:

- that the product is a mother tincture for homoeopathic preparations (designated as "TM" or "Ø"),
- the name of the raw material using the Latin title of the European Pharmacopoeia monograph where one exists,
- the method of preparation,
- the ethanol content or other solvent content, in per cent V/V, in the mother tincture,
- the ratio of raw material to mother tincture,
- where applicable, the storage conditions.

One title but ...



- which title when:
- HAB and Ph. Fr. describe different parts of the plant?
 - HAB and Ph. Fr. describe different collection period?

...



WHAT DO YOU NEED?
