

QUALITY OF HOMOEOPATHIC PRODUCTS IN THE NEW EUROPEAN LEGISLATIVE FRAMEWORK

Session II

**Experiences and viewpoint of national
regulatory authorities and perspectives**

Moderator: Ms Isabelle Mercier

(11:10-12:30)



Quality of Homeopathic Medicinal Products Experiences of BfArM

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Directive 2001/83/EC as amended by Directive 2004/27/EC

Definitions

Article 1

5. Homeopathic medicinal product:

Any medicinal product prepared from ~~(products, substances or compositions)~~ substances called homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias currently used officially in the Member States. A homeopathic medicinal product may contain a number of principles.

Regulatory Approach in Germany

- scientific pluralism in therapy has to be guaranteed
- consumer has to be protected from
 - risks associated with medicinal products
 - fraudulent products / claims
- participation of specific experts in the licensing procedures
- different committees for the particular therapeutic systems (quality, safety and efficacy)

Expert Committees

I. German Homoeopathic Pharmacopoeia Committee

12 Expert Members+ Alternates

Sub-Group: Analytical Procedures

Sub-Group: Manufacturing Methods

Expert Committees

II. According to the German Medicines Act (AMG) expert committees support the work of Marketing Authorisation and Registration , providing clinical expertise in the respective therapeutic field

Commission D	Homeopathy
Commission C	Anthroposophy
Commission E	Phytotherapy

Expert Committees

Members and Alternates of the committees are experts with special theoretical knowledge and practical experience with homeopathic and anthroposophic medicinal product.

They are working in the field of :

Pharmacology/Toxicology, Clinical Pharmacology, Medical Statistics, Medical Practice, Pharmacy, Public Health Service, Research and University

Regulatory Approach in Germany

- A Individual application**
 - 1. Marketing authorisation
 - 2. Registration
- B No individual application**
 - 1. Standard Registration
 - 2. „1000 Packages a year - rule“ for products not produced in a „industrial scale“

Regulatory Approach in Germany

A 1. Homeopathic and anthroposophic medicinal products with indication claims

Council Directive 2001/83/EC as amended,
Article 16 (2)

Article 21 German Medicines Act

Regulatory Approach in Germany

A. 2 Homeopathic and anthroposophic medicinal products without indication claims

Council Directive 2001/83/EC as amended , Article 14

Article 38 German Medicines Act

Regulatory Approach in Germany

B 1. Homeopathic and anthroposophic medicinal products without indication claims

and

described by a monograph of the HAB and by a
monograph published in the
„Decree on Standardized Registrations“

No individual application required

Regulatory Approach in Germany

B 2. Homeopathic and anthroposophic medicinal products without indication claims

CD 2001/83 Art. 2

„...intended to be placed on the market in Member States and either
prepared industrially or manufactured by a method involving an
industrial process“

§ 38 (1) 2 AMG

**prepared according to a homeopathic
manufacturing method described in the pharmacopoeia**

No individual application required

A brief history of the tradition and quality of homeopathic products in Germany

1825	Carl Caspari „Homöopathisches Dispensatorium für Aerzte und Apotheker“
1845	C. Gruner „Homöopathische Pharmakopoe“
1861	H. Hager „Pharmacopoea homoeopathica nova“
1872	W. Schwabe sen. „Pharmacopoea homoeopathica polyglottica“ (german, french, english, italian, spanish, portugese and russian edition)
1924/1934	W. Schwabe jun. „Homöopathisches Arzneibuch“ 2. Edition officially used since 1934
1950	Working Group for Revision of „ Homeopathic Pharmacopoeia“

A brief history of the tradition and quality of homeopathic products in Germany

- 1978 HAB 1 German Homeopathic Pharmacopoeia
- 1985 HAB 1 Complete edition
- 1991 HAB 5th supplement to the 1. Edition
- 2000 HAB 2000 Reference to the European Pharmacopoeia
- 2001 -
- 2004 HAB 2001- 2004 referring to the provisions of the European Pharmacopoeia



HAB
Requirements related to the quality and to the manufacture

- General notices and Definitions
- General Methods
- Reagents
- Methods for the Production of Homeopathic Medicinal Products
- General regulations of manufacturing
- Vehicles and Excipients

HAB
Requirements related to the quality and to the manufacture

- Specific manufacturing procedures (methods)
Method Nr. 1 to 51
- Methods describing the preparation of :
Mother tinctures
Dilutions, Triturations, Solutions, Mixtures
LM Potencies
Anthroposophic Medicines,
Spagyric preparations
Dosage forms

HAB Requirements related to the quality and to the manufacture

- 578 Monographs on substances of
- chemical origin
 - herbal origin (fresh plants)
 - herbal origin (dried plants)
 - zoological origin
 - minerals

Manufacturing and test procedures for preparation (mother tincture or the „lowest“ dilutions) are an integral part of each HAB monograph

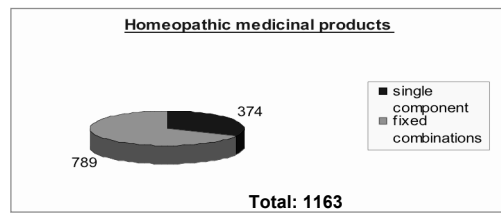
Marketing Authorisation and Registration of Homeopathic Medicinal Products

Quality control on the basis of the requirements of the European and National Pharmacopoeia

The Pharmacopoeia serves to ensure that the homeopathic medicinal products on the market are of the appropriate, constant and monitorable quality standard that corresponds to the long tradition and experience in the use of these products.

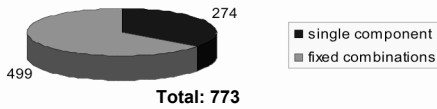
Traditional rules for production are the basis and the starting point of the assessment

Homeopathic and Anthroposophic medicinal products with completed marketing authorisation procedure on the German market



Homeopathic and Anthroposophic medicinal products with completed marketing authorisation procedure on the German market

Anthroposophic medicinal products



Registrations of Homeopathic and Anthroposophic medicinal products on the German market

Registrations



Outlook

Challenges:

Heads of Agencies (HMA) Working Group

- further guidance for uniform interpretation

Development of technical requirements for the quality of Homeopathic products must maintain the specific therapeutic experiences and tradition - A newly created mixture of the different homeopathic traditions must be avoided.

Homeopathic tradition cannot be „reinvented“ - then it would lose its basis and acceptance.

Outlook

Consequences:

Mutual understanding and recognition of the specific traditions


Clear labelling of homeopathic medicinal products, thus transparency for the patient, medical practitioners, authorities and manufacturers

(e.g. labelling of the manufacturing method and the pharmacopeia monograph)

Further agreement and commitment on requirements respecting their tradition for the different homeopathic products


**HOMEOPATHIC
MEDICINAL PRODUCTS IN
FRANCE**

Agence Française
de sécurité sanitaire
des produits de santé

afssaps 


EDQM – STRASBOURG
15 February 2005

Dr. Antoine SAWAYA

**DEFINITION OF HOMEOPATHIC
MEDICINAL PRODUCTS**
(Article L. 5121-1-11° of the F.P.H Code) *afssaps* 


- **Homeopathic medicinal products :**
Any medicinal product prepared from products, substances or compositions called stocks, in accordance with a homeopathic manufacturing process described by the European Pharmacopoeia, the French Pharmacopoeia or, in absence thereof, by one of the pharmacopoeias currently used officially in other European Member States.
- **Scope of activities of Afssaps.**
- **Assessment, control and inspection.**

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**LEGISLATION OF HOMEOPATHIC
MEDICINAL PRODUCTS** *afssaps* 


- **Decisions in accordance with**
 - Directive 2001/83/CE
 - Law 94-43
 - Decree 98-52

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PROCEDURES 

- **Marketing authorization**
 - abridged dossier
- **Registration**
Specific Requirements :
 - oral or external administration,
 - no specific therapeutic indication,
 - sufficient degree of dilution.


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GENERAL REQUIREMENTS 

- **The Guarantee of the safety,**
- **The pharmaceutical quality,**
- **The homeopathic nature.**

M.A. Procedure : justification of homeopathic traditional use.


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HOMEOPATHIC MEDICINAL PRODUCTS 

HMP, meet the same quality and safety requirements as other medicinal products.

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EFFICACY DATA ?



- **M.A. Procedure :**
Dispense to perform P.T.C. Trials
 - ⇒ requirements :
 - well established use,
 - full guarantee of safety.
- **Registration Procedure :**
No therapeutic indication.

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VALIDATION
(Law 94-43 ; 18 January 94)



- **HMP authorized and marketed before 18 January 94 must apply for a Marketing authorization or Registration.**
- **These products can still be on the market until new decisions from AFSSAPS.**


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MODE OF ENFORCEMENT OF THE LAW




- **Application dossier (all relevant data).**
- **Submission in accordance with a published schedule.**
- **Date of submission :**
 - stocks listed or not in the Ph. Fr,
 - alphabetical order,
 - 2001 → 2012 : 7000 dossiers.

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MARKETING AUTHORIZATION DOSSIER 

- **P.T.C :**
 - M.A. Application dossier is adapted to the specific nature of the HMP and to the traditional use.
- **Quality :**
 - The general requirements of medicinal products should apply, except assays of the active substance in the case of high dilutions.
 - Virological safety (HMP of animal origin) : documentation in accordance with the european note for guidance.

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REGISTRATION DOSSIER 

- **Statement : various routes of administration, pharmaceutical forms and degree of dilution.**
- **Documents demonstrating the quality and homogeneity of the HMP.**


Stocks :

- obtention and control (assays)
- homeopathic nature.

Pharmaceutical form :


- manufacturing and control,
- method of dilution and potentization,
- stability data.

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HOMEOPATHIC MEDICINAL PRODUCTS AND PHARMACOPOEIAS 


- **Pharmaceutical form**
 - Monographs of Ph. Eur. are usually used except for specific pharmaceutical forms.
- **Stocks**
 - Stocks of chemical or mineral origin : stock = raw material generally, Ph. Eur. Monographs apply
 - Stocks of botanical or zoological origin : stock (mother tincture) obtained from raw material generally, Ph. Fr is the choice.

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EVALUATION OF HOMEOPATHIC MEDICINAL PRODUCTS 

- **Homeopathic working group of the M.A. Commission.**
- **Composition : pharmacists, physicians, pharmacognosists, toxicologists, biologists ...**


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PERSPECTIVES 

- **Mutual Recognition : New challenge**
- **Need for harmonisation :**
 - **expression of dilutions**
 - **Mode of preparation**

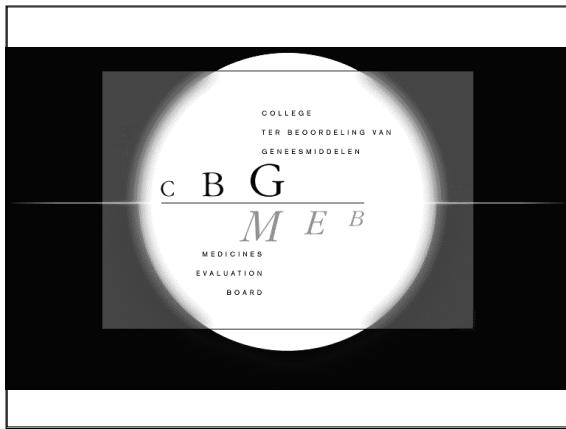
, **elaboration of monographs (general and specific)**

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CONCLUSIONS 

- **Homeopathic products are medicinal products.**
- **Evaluated and controlled by the AFSSAPS.**
- **Have guarantees of quality and safety.**
- **Standards of quality as other medicines.**

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Registration of homeopathic medicinal products 1997 – 2005 in the Netherlands:

“Acting between the best of both Worlds”

**Emiel van Galen
Netherlands**

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Simplified registration in the Netherlands 1998 - 2005

Simplified registration article 14 (2001/83/EC)

**Experiences with different Pharmacopoeias
A review on different traditions, - stocks and - applicants.
And our view on Pharmacopoeias and the future for homeopathics**

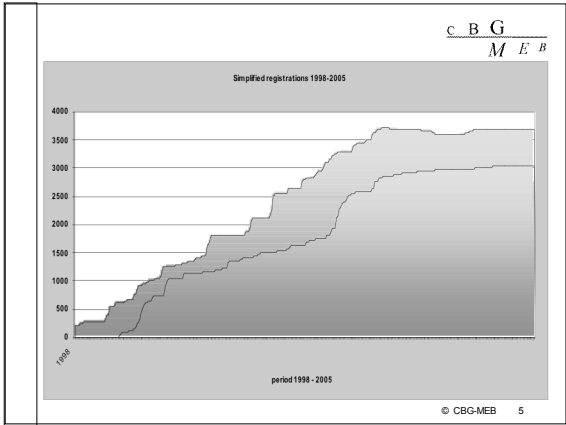
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The Dutch regulatory framework for homeopathic medicinal products:

• Simplified procedure art. 14	• Yes
• Additional national regulations art. 16.2	• Yes
• Homeopathy in former National Pharmacopoeia	• NO
• Reference to Ph. Eur accepted	• Yes
• Reference to Ph. Franc accepted	• Yes
• Reference to HAB accepted	• Yes
• Different traditions indicated on label	• NO
• Compliance with most recent version of pharmacopoeia monographs is compulsory	• Yes
• Participation in EDQM Homeopathy WP	• Yes

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**Exploration of figures:
(focus on art. 14)**

- 3689 submissions received, of which
- 3057 have been registered since 1998

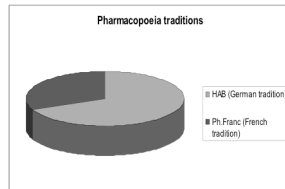
- Tablets, granules, globules, drops, oral powder
- D (DH), C (CH), K and LM potency ranges

- 855 single homeopathic products registered, representing 555 different stocks.

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Applicants and Pharmacopoeias

- Applicants from:
- Netherlands: 4
- Belgium: 1
- Germany: 3
- France: 2



What do we really want?



1. All homeopathic manufacturing methods included in the European Pharmacopoeia;
2. Harmonised monographs for raw materials,
3. preferably in conjunction with harmonised monographs for homeopathic tinctures,
4. A fully functioning Certification scheme for stocks;
5. A Homeopathy expert group under the coordination of the European Pharmacopoeia commission;
6. Harmonisation of scientific names for homeopathic remedies;

Second best



1. Combined publication of the content of the HAB and the part "preparations homeopathiques" of the French Pharmacopoeia, in one binder,
2. HAB-monograph on the right- and French monograph on the left page,
3. Loose-leaves, and translation in at least one more EU language of monographs would facilitate the common use in the Community.



Regulatory Experience with Homeopathic Products in Ireland

Dr. Gwen Glasgow

Irish Medicines Board



Simplified Registration Procedure

- Directive 92/73*: provision for a SRP for Homeopathic Medicinal Products.
 - Placed on the market without therapeutic indications;
 - in a form (oral and external) and dosage which do not present risk to the patient.

**Now superseded by 2001/83/EC & 2004/27/EC (Oct.2005)*





Requirements for HMP.

- Monograph in a Pharmacopoeia.
- Manufactured according to a Homeopathic Manufacturing Method.
- Homeopathic use: Justified by Bibliography.



Outside SRP

- Products with therapeutic indications,
- Parenterals
- Products with substances below a potency of 4x.
 - must apply for full Product Authorization.

Except where Member States have made special provisions for such HMP under Art. 16.ii. (National Ru





Situation in Ireland - 2001

The EC directives had been transposed into Irish National Legislation under:

Statutory Instrument Number 142 of 1998.

- Hence a legal mechanism existed for the registration of Homeopathic Medicinal Products.





IMB Homeopathic Project

- **GOAL**

To set up this Simplified Registration Procedure.



AIM:

To create a regulated environment which allows patients to maintain access to the Homeopathic Medicinal Product of their choice,

- provided all precautions are taken to ensure the quality and safety of these products
- and to provide users of these products with a clear indication of their homeopathic character
- and to harmonise the rules relating to the manufacture, control and inspection of HMP.



Strategy

- Review of Legislation EU and Irish
- Contact Organisations: National and International (18).
 - These included Doctor, Practitioner, Pharmacist & Patient groups as well as other interested parties.
- Contact Manufacturers (22), (Irish 1) and Distributors (10) with HMP on the market.
- Set up Database of HMP on the Irish market.
- Set up Simplified Registration Scheme (SRS).



Irish Legislation

- Prescription and Control of Supply Regulations, S.I. No. 256 of 1996, precluded the OTC sale of many commonly used and well established HMP already on the market: e.g. Belladonna, Arsenicum album, Gelsemium.
- No art. 16.ii. in Irish legislation.
- Definition of external use does not include nasal or throat sprays (S.I. 540 of 2003).





Irish Legislation

- Prescription and Control of Supply Regulations, S.I. No. 256 of 1996, amended to S.I. No.627 of 2002 & S.I. 540 of 2003, which includes a specific schedule (Schedule 2 part 3) exempting HMP at D6 or more from prescription control.
- Art.16.ii. Status: Currently under review.
- External use:-nasal/throat sprays: Currently under review.



Second Schedule

Part 3

(Regulation 20(4))

Substances which when contained in certain homeopathic medicinal products may be supplied without a prescription and in non-pharmacy outlets

Aconitum napellus L.
Anamirta cocculus (L.) Wight & Arn.
 Arsenic
Atropa belladonna L.
Caulophyllum thalictroides (L.) Mich.
Conium maculatum L.
Cystis scoparium L.
Digitalis purpurea L.
Ephedra vulgaris Rich.
Gelsemium nitidum L.
Ginkgo biloba L.
Hypericum perforatum L.
Mandragora autumnalis Bertol.
 Phytolacca species
 Podophyllum species
Pilocarpus jaborandi Holmes
Rauwolfia serpentina (L.) Benth. ex Kurtz
Schoenocaulon officinale (Schlect & Cham) A.Gray
 Snake Venoms
Strychnos ignatii Berg.
Strychnos nux vomica L.
 Symphytum species
Veratrum album L.
Viscum album L.



Database

- Information submitted by Manufacturers and Distributors was used to compile a database of all HMP on the Irish Market.
 - Total 8000
- Majority available through Doctors or Homeopathic Practitioners on a named patient basis only.



Homeopathic Product Survey.

	No. of Prod.	%	Registration
● Mineral	79	23	2003
● Plant	116	34	2004
● Animal	35	10	2004
● Complex	114	33	2005

OTC total: - 344



Simplified Registration Scheme (SRS)

- Guidance notes to applicants :
 - General, Stock, Dilutions.
- Registration forms were made available to :
 - ◇ Manufacturers
 - ◇ Distributors



Operation of SRS

Applications to Register Homeopathic Medicinal Products are being accepted in the following order:

- ◇ Mineral
- ◇ Plant
- ◇ Animal
- ◇ Complex



Process -Internal

- Set up Receipts and Validation
- Set up assessment procedures:
 - Quality/Safety
- Set up Approval procedures
- Issuing of Registration Certificates
- Procedures and documentation for Variations and Renewals
- Fee structures



Registration Fees -1

- Single product€618
- Single product reduced fee - 1.....€464
- Single product reduced fee - 2.....€361





Registration Fees -2

- Complex products
- 2-5 Mother tinctures.....€824
 - Reduced fee -1.....€618
 - Reduced fee -2.....€464
 - 6> Mother tinctures.....€1.030
 - Reduced fee -1.....€721
 - Reduced fee -2.....€515



SRS applications

- Applications received to date 87.
 - Single Mineral/Single Plant products.
 - Single Animal products due in by March 2005
 - Complex products – 2005 (date to be announced).



Challenges for Homeopathic Medicines.

- Mutual Recognition.
- Products with indications.
- Parenterals.
- New Homeopathic Remedies.



Mutual Recognition

- MR art 14 registered products - Coordination Group now CMD.
- Common template CTD
 - HMPWG – Guidance document for HMP.
- Monographs HM – Pharmacopoeia.
- Accepted list of approved bibliographic sources for 'homeopathic use' – HMPWG.





Goal

- Consumer access to the fullest possible range of Homeopathic Medicines:
 - guaranteed safe and of the highest quality.

Achieve this:

- Cooperation of industry in submitting all the necessary data.
