Homeopathy Workshop at the European Medicines Agency

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Aude Sapere (Dare to know)

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Evaluation of homeopathic and herbal medicinal products

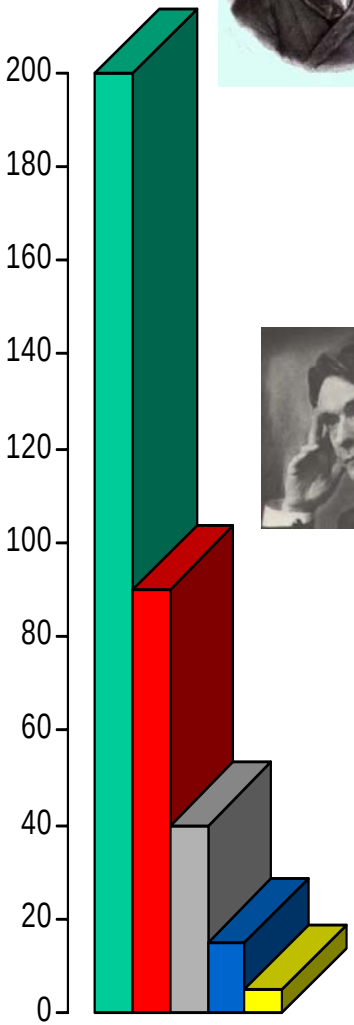
A View on the regulatory framework

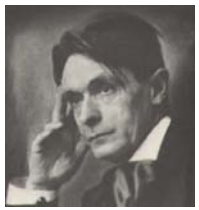
- Registration and Authorisation
  - Review of 10 years experience in one Member State
  - A simplified procedure for homeopathic medicinal products
  - Ways to marketing authorisation
  - restraints and complaints
  - SWOT

- Mutual recognition
  - Why MRP should work for this group of medicines
  - Mutual recognition versus national procedures
  - How to solve disagreements?
  - Exploration of the future

- Anthroposofic medicinal products
  - Homeopathic medicinal products intended for antroposofic use
  - What is Antroposophic Medicine?

Coming of Age

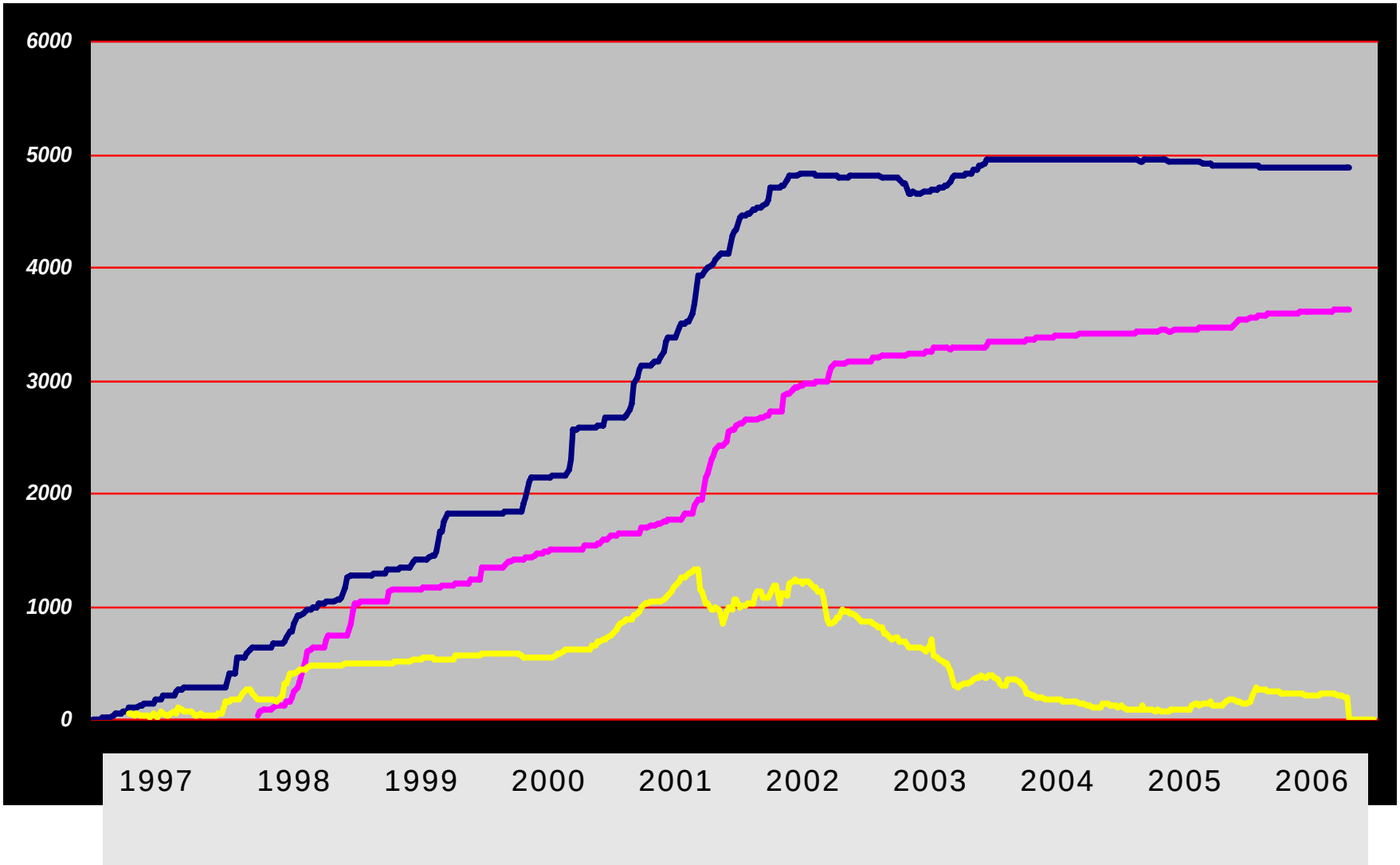




- Homeopathy 200 years
- Antroposophic medicine 90 years
- EU Legislation 40 years
- for homeopathics: 15 years
- steps to harmonisation 5 years

Dutch MEB Registrations by October 2006

		art. 14	art. 16.2	Of which as antroposophic medicines
Applications since 1997		**3680**	**1208**	87 / 174
Of which registered / MA		**3125**	**510**	72 / 6
Applications refused		148		0
Different applicants:		**13**	**31**	**3**
Different homeopathic substances (stocks) registered		***625***		


6000
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2006

A simplified procedure

(17) It is necessary to adopt specific provisions for immunological medicinal products, homeopathic medicinal products,……..

(21) Having regard to the particular characteristics of these homeopathic medicinal products, such as the very low level of active principles they contain and the difficulty of applying to them the conventional statistical methods relating to clinical trials, it is desirable to provide a special, simplified registration procedure for those homeopathic medicinal products which are placed on the market without therapeutic indications in a pharmaceutical form and dosage which do not present a risk for the patient.

(23) It is desirable in the first instance to provide users of these homeopathic medicinal products with a very clear indication of their homeopathic character and with sufficient guarantees of their quality and safety.

(24) The rules relating to the manufacture, control and inspection of homeopathic medicinal products must be harmonized to permit the circulation throughout the Community of medicinal products which are safe and of good quality.

(25) The usual rules governing the authorisation to market medicinal products should be applied to homeopathic medicinal products placed on the market with therapeutic indications or in a form which may present risks which must be balanced against the desired therapeutic effect. In particular, those Member States which have a homeopathic tradition should be able to apply particular rules for the evaluation of the results of tests and trials intended to establish the safety and efficacy of these medicinal products provided that they notify them to the Commission.

CHAPTER 2

Specific provisions applicable to homeopathic medicinal products

the simplified procedure for homeopathic medicinal products:

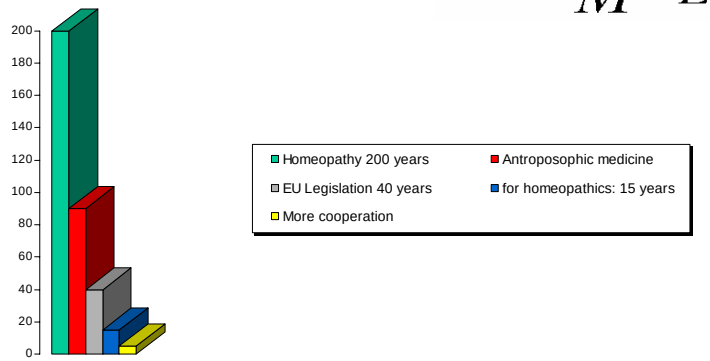
- Applicable to the majority of homeopathic medicines used in the EU
- Compliance with pharmaceutical quality standards
- Safety requirements defined in legislation, taking into account the dilution-process
- Safe use linked to limited ways of administration
- Labelling requirements defined in legislation
- No proof of efficacy, no indications allowed
- Exclusively based upon homeopathic justification of use

Simplified procedure and homeopathic reality

- **For a large amount of different homeopathic remedies**
- **The “classical” way of “unitarian” homeopathy**
- **Mainly oral use**
- **Always diluted**
- **Purely based on homeopathic thinking**
- **A massive task for both CA and companies**
- **A perfect way for real harmonisation**

- **Not applicable to products with indications, often combination products**
- **Not applicable to Ø or mothertinctures or the first dilution steps**
- **Not applicable to injectables**
- **National regulations offer fragile balances**
- **Assessment of indications = assessment of efficacy**
- **Triggers scientific controversy**

1992 – birth of the Simplified procedure
1999 – first cooperation between MS
2004 – Revision of Directive
2004 – Homeopathic Working Group HMA
2006 – Homeopathy workshop at EMEA



- **Does the simplified procedure works on a national level ?**
- **Does the regulatory framework works for all homeopathics ?**
- **Does the regulatory framework works for antroposophical medicines as well ?**
- **Is there an increase of harmonisation between MS ?**
- **Does Competent authorities have sufficient knowlegde and resources ?**
- **Does homeopathic manufacturers really want full harmonisation ?**
- **What are the opportunities and threats of MRP / DCP for homeopathic and antroposophic companies ?**
- **Have we made progress in the past 10 years ?**

Strengths	Weaknesses
Homeopathy relies on a mutually recognised broad range of remedies, used under one clear therapeutic principle No constant need for innovation Manufacturing methods are clearly defined Availability of remedies is of general interest Discrete network in EU between companies and prescribers European cooperation on different levels General accepted principles for use in patients Decades of experience for several issues	Pharmaceutical development along two main lines: German and French homeopathic pharmacopoeias Solutions for technical issues often influenced by traditional sentiments Indifference: "nothing will change after all" Quality improvement not possible without suppliers (90% based on raw material with natural variability) An enormous amount of different medicines is used, one remedy cannot be replaced by an alternative one Progress based on tradition, rather than on natural selection
Opportunities	**Threats**
One European market for homeopathic medicines already exists; harmonisation is the next step MRP ideal to avoid duplication of (regulatory) work MRP can be used for "work sharing" Homeopathic treatment in Estonia is the same as in Portugal Recognition of quality and safety will improve confidence in this way of treatment A range of antroposophic medicines can be evaluated as well under this legislation	Lack of sufficient pharmaceutical and regulatory knowlegde in this area Homeopathic community is reluctant to strive for a full harmonised EU market No "specialisation" between companies ("me too") Member States never consider this area as a priority for Public Health Availability of the whole range of homeopathic remedies can become a grey-market

(14) This Directive represents an important step towards achievement of the objective of the free movement of medicinal products. Further measures may abolish any remaining barriers to the free movement of proprietary medicinal products will be necessary in the light of experience gained, particularly in the abovementioned Committee

(15) In order better to protect public health and avoid any unnecessary duplication of effort during the examination of application for a marketing authorization for medicinal products, Member States should systematically prepare assessment reports in respect of each medicinal product which is authorized by them, and exchange the reports upon request. Furthermore, a Member State should be able to suspend the examination of an application for authorization to place a medicinal product on the market which is currently under active consideration in another Member State with a view to recognizing the decision reached by the latter

CHAPTER 4

Mutual recognition procedure and decentralised procedure

Article 39

Article 29(4), (5) and (6) and Articles 30 to 34 shall not apply to the homeopathic medicinal products referred to in Article 14.

Articles 28 to 34 shall not apply to the homeopathic medicinal products referred to in Article 16(2)

Mutual recognition and Decentral Procedure

- Both MRP and DCP are applicable to article 14 homeopathics
- Normal timeframes
- MRP based on identical dossier
- Dossier should comply with CTD structure
- Reference Member State must write AR
- Specific guidance documents already endorsed by MS

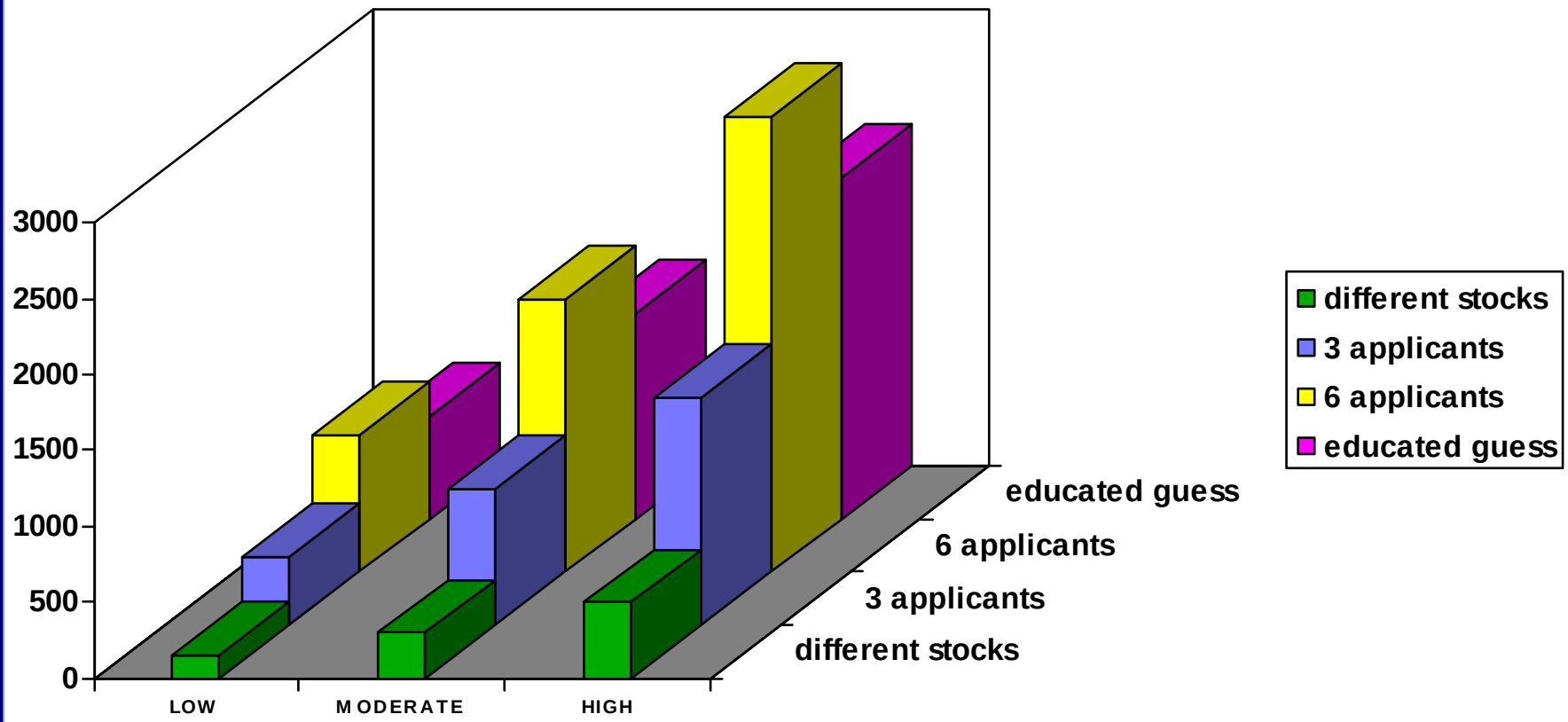
- No experience whatsoever
- No harmonisation of dossier content between MS for already registered products
- Although Ph. Eur is leading, national registrations still are based on HAB and Ph.Fr.
- No arbitration possible: what about disagreements?
- Is CMD prepared to handle numerous, comparable procedures

A possible burden for MRP: time for an educated guess

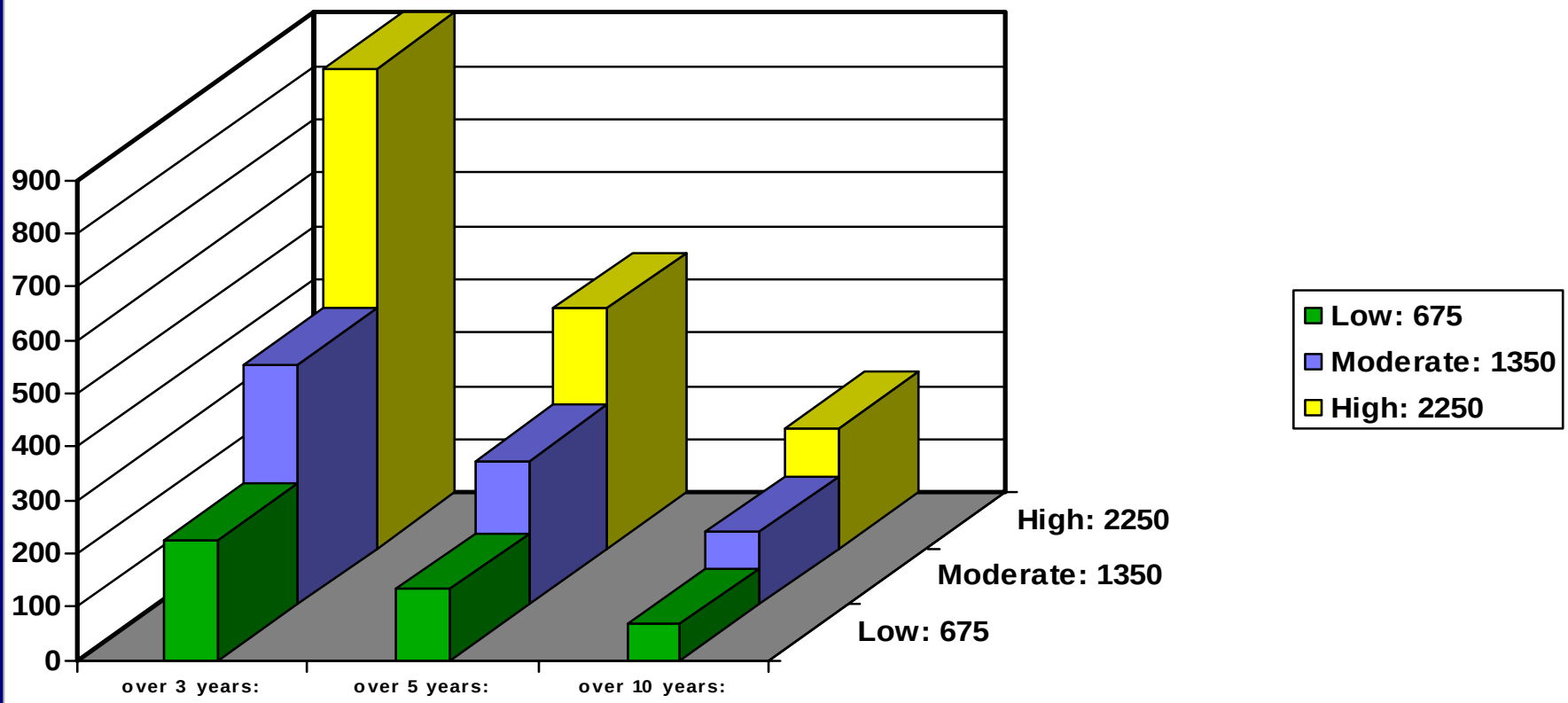
Procedures: different stocks	3 applicants	6 applicants	educated guess
low: 150	450	900	**675**
Basic: 300	900	1800	**1350**
high: 500	1500	3000	**2250**

Assessment Reports needed	3 years	5 years	10 years
guess 675	225	135	67
guess 1350	450	270	135
guess 2250	750	450	225

An educated guess I: a calculation of simple MRP's (homeopathic products art. 14)



An educated guess II: Assessment reports required over 3 years / 5 years / 10 years



Possible items for discussion during MRP procedures

- Interpretation of specific quality aspects
- Interpretation of stability data
- Safety concerns related to toxicological components
- Safety concerns related to biological origin
- Establishing the first safe dilution
- Standards in absence of European Pharmacopoeia monographs (for homeopathic use)
- Standards in absence of HAB or Ph. Franc monographs
- Justification of homeopathic use and tradition
- Nomenclature for homeopathic stocks
- Different oral pharmaceutical forms used

What to do with disagreement ?

- "*for homeopathic medicinal products eligible for registration according to Article 14, Articles 28 and 29 (1) to (3) applies. However Article 29 (4), (5) and (6) shall not apply (see article 39). That means that the same procedure as for other medicinal products should be followed except for the possible referral to CHMP. If the discussion in CMD do not solve the disagreements the matter shall not be referred to CHMP.*"

- *From: CMD Standard Operating Procedure Disagreement in Procedures – Referral to CMD Final October 2005*

TITLE I
DEFINITIONS
Article 1

For the purposes of this Directive, the following terms shall bear the following meanings:

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5. *Homeopathic medicinal product:*
Any medicinal product prepared from 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.

Antroposophic medicinal products described in an official pharmacopoeia

(22) The anthroposophic medicinal products described in an official pharmacopoeia and prepared by a homeopathic method are to be treated, as regards registration and marketing authorization, in the same way as homeopathic medicinal products.

and prepared by a homeopathic method

are to be treated…..in the same way as homeopathic medicinal products

Antroposophic medicinal products

- **Antroposophic medicine is not identical to homeopathy**
- **Nevertheless, homeopathic medicinal products are used in antroposophic therapy**
- **From a formal point of view as: “homeopathic medicines for antroposophic use”**
- **For this group: the same definition Directive 2001/83 applies**
- **But what about : “justification of the antroposophic use of the stock(s)” ?**
- **Antroposophic bibliographical references are not the same as homeopathic materia medica**

"Dare to know"

some conclusions:

1. **The simplified procedure works for article 14 homeopathic products, but still mainly on a national scale**
2. **In principle also true for antroposophic art 14 products, but yet without impressive results**
3. **This has induced first steps towards harmonisation**
4. **Separate additional regulations for art. 16.2 products in each MS are an option, but will bring no harmonisation**
5. **Harmonisation between MS without implications for national registrations obtained earlier, is unrealistic**
6. **European Pharmacopoeia is extremely important for further development of both homeopathic- and antroposophic med.**
7. **The existing MRP/DCP system should be aware of the huge amount of possible procedures for mutual recognition**
8. **From now on, more effort and resources are necessary to harmonize whatever possible, to prevent problems during mutual recognition**