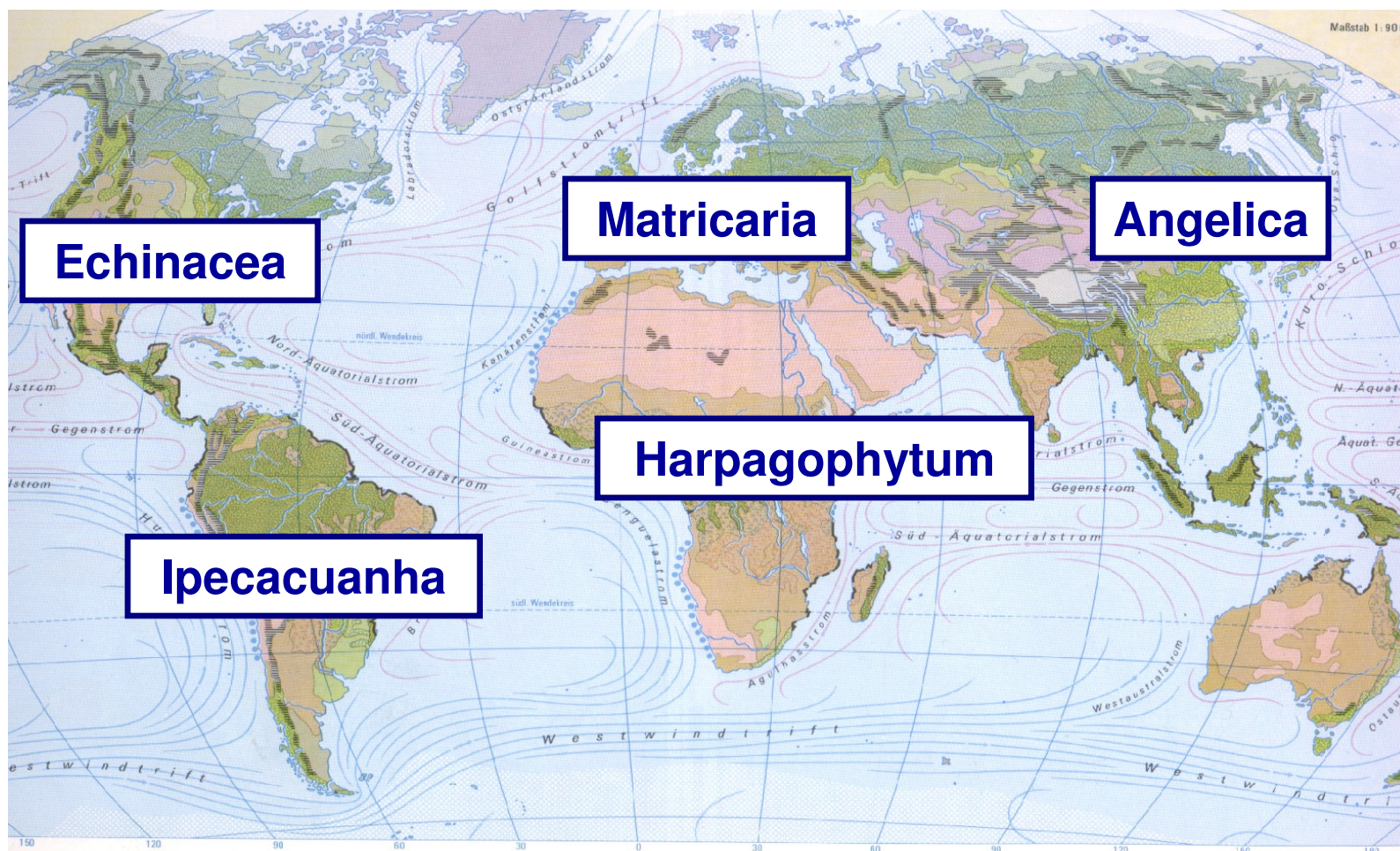




Possibilities of Licensing or Registration of Medicinal Products from Indian Traditional Medicines in Europe

PD Dr. Werner Knöss
BfArM

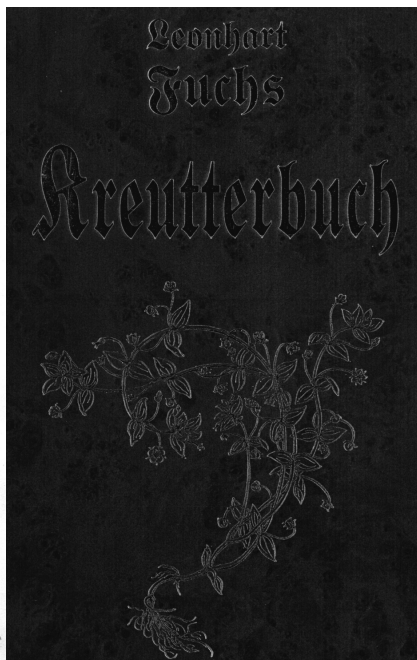
Traditional Use of Plants



Von Chamillen. Cap. VIII.

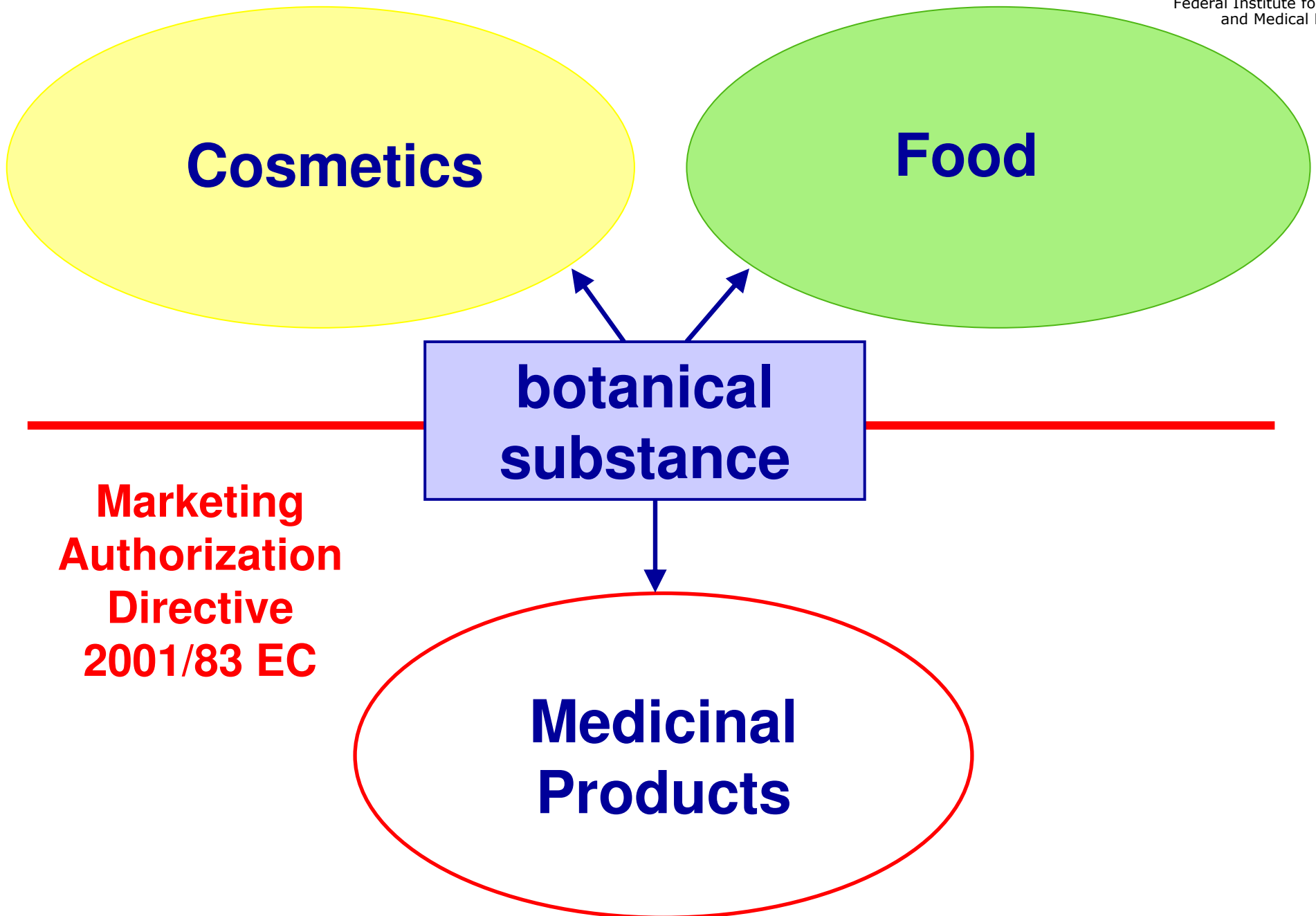
Namen.
A 7 Kraut so wie Teuffchen Chamillen beyßen / ist an Griechi-
 scher vnd Lateinischer Sprach genent Chamemelum / verhalten
 das sie ein lieblichen geschmack hat / wie ein doppel. Welchs
 zwar von der weissen Chamillen fürnemlich zu unterscheiden ist.
Geschlecht.
 Der Chamillen wie Dioscorides Hirtlich anseyget / sendt dreyerley geschlecht.
 Das erst ist weiß blumen / vnd wurt der vrsachen halben von den Griechhen
 Leucanthemum geboffen. Die Teuffchen goldgelb blumen / darumb die Griechhen
 solchs Kraut Chrysanthemum nennen. Auß Teuffchen wurt es geboffen Gold-
 blum / Struchblum / oder gute Chamill. Das drit geschlecht hat purpur-
 farb blumen / wurt vom Dioscoride genent Eranthemon / derhalben das es in
 warmen landen im Leigen am meysten bluet. Die Teuffchen beyßens Kitters-
 sporn / darumb das seine blum einem Kittersporn nit ungleich ist. Die Apotecar
 nennen drey Kraut Consolis am regeltem dreyelben das es vnter den beyset.
Schalt.
 Dieser Kreutter Alt sind selten über ein spannen hoch / ihre stengel haben vil flü-
 gel die Alt aber sendt dritt / auff welchen gewinnen sie runde blumen / welche ins-
 vordem goldgelb sendt / anffen aber rufft ombere mit weißem ober gelben / ober
 purpurfarben bluetlin / in der 2. andren blueter größe gester. Die blueter an den
 stenglen der zweyer geschlecht sind dem Dyllen nit vnähnlich. Das ander ge-
 schlecht aber hat blueter dem Kainfar oder Garbtrau gleich.

D. Leonhart Fuchs seine altera im x. l. i. Jar.



From tradition ...

... to a harmonized European market



Medicinal products

Chemically defined	Dose-dependent effect
Herbal	Dose-dependent effect
Traditional	Plausible effect
Homoeopathic	Homeopathic principle
Anthroposophic	Anthroposophic principle
TCM	Mixed approach
Ayurvedic	Mixed approach

Content

- Development and status of licensing and registration of traditional medicines in Germany
- Legal framework
- Reflections on options for licensing and registration of medicinal products from Indian Traditional Medicines

History of Traditional Medicines

- **1976** German Parliament emphasises therapeutic pluralism in health care
- **1976** German medicines act (Arzneimittelgesetz AMG)
 - notification of 148.000 existing medicinal products
 - marketing authorisation of new medicinal products
- **1994** 5th amendment of AMG
 - transition acc. §105, §109a
 - applicants had to proof safety and efficacy
- **2004** Directive 2004/24 EC "Traditional herbal medicinal products"
- **2005** Registration of Traditional herbal medicinal products, implementation by 14. AMG-novellation

National Regulation of „herbals“ in the German Medicines Act (AMG)

§ 25 Abs. 7 AMG

... Medicinal products of a particular therapeutic system (Phytotherapy, Homeopathy, Anthroposophy), ...

§ 109a AMG

Traditional medicinal products
only “old products”, no “pharmacy only”
products
„Traditionally used“

National Regulation of „herbals“ in the German Medicines Act (AMG) – Expert Panels

Art. 25 (7) German Medicines Act

- Anthroposophic medicinal products - Commission C
- Homeopathic medicinal products - Commission D
- Herbal medicinal products - **Commission E**

Art. 109 a (3) German Medicines Act

- **Commission on Traditional Medicinal Products** (review procedure)

Licensing 5

PD Dr. W. Knöss

**Complementary and Alternative
Medicines and Traditional
Medicines**

**Unit 51
Procedural Management**

M. Maßler

**Unit 52
Herbal and Traditional Medicinal Products**

K. Reh

**Unit 53
Homoeopathic and Anthroposophic Medicinal
Products**

C. Werner

Particular Therapeutic Systems completed procedures - approvals

herbal medicinal products	licensed	post-marketing approval*	total
single component	883	1053	1936
fixed combination	74	431	505
total	957	1484	2441
homeopathic medicinal products	licensed	post-marketing approval*	Total
single component	99	221	320
fixed combination	90	1009	1099
total	189	1230	1419
anthroposophic medicinal products	licensed	post-marketing approval*	Total
single component	99	210	309
fixed combination	3	578	581
total	102	788	890

4750
licensed
medicinal products

4056
registered
homeopathic
medicinal products

and

1037
licensed TMP

5
Registered THMP

Pharmacy in Germany



The BfArM is a Federal Institute within the portfolio of the Federal Ministry of Health

Content

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Regulatory Framework

Directive 2001/83

Ph.Eur./DAB/HAB

AMG

CTD

Regulations

HMPC

Directive 2004/24

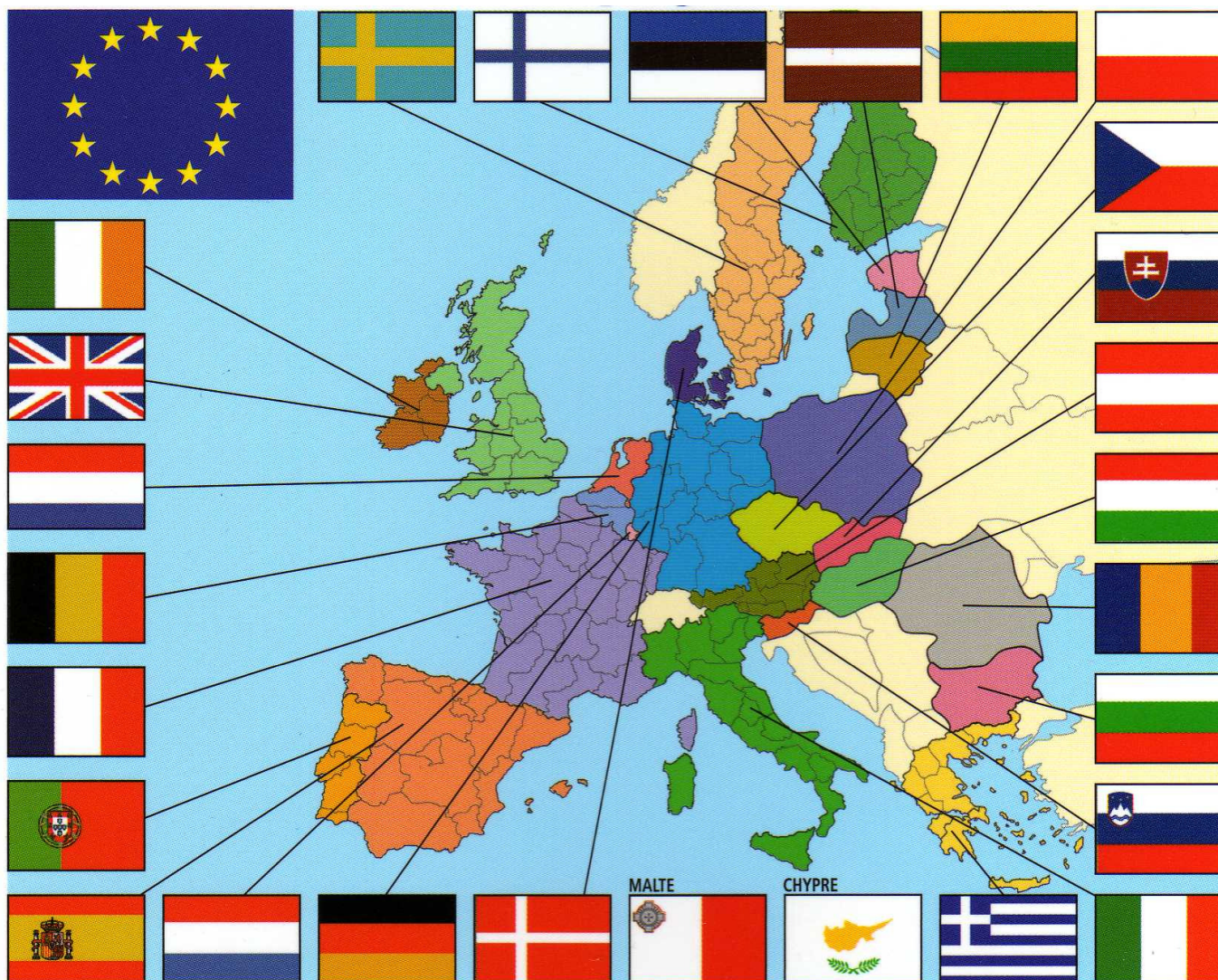
Guidelines

Expert Panels

Directive 2002/46



European Regulation



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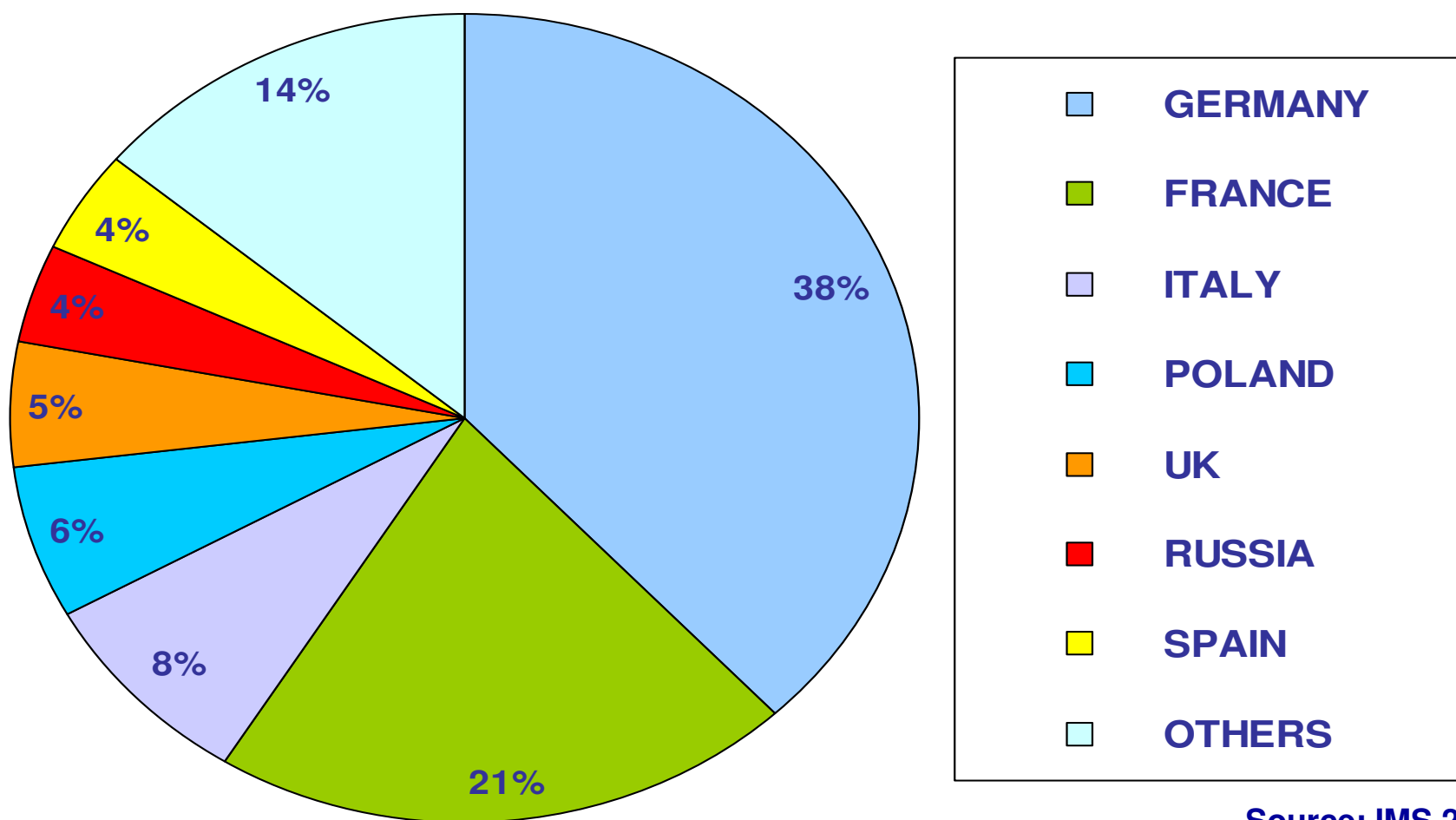
European Community Directives

- CD 2001/83 (“basic” regulation)
- CD 2003/63 of 25 June 2003 (Annex I, criteria)
- CD 2004/24 (Traditional herbal medicinal products)
- CD 2004/27 of 31 March 2004 (**HMPC**)
- **Further Guidance Documents (www.emea.eu)**



European herbals market

Value share % in latest year



Source: IMS 2005

Definition Medicinal Product

- (a) Any substance or combination of substances **presented** as having properties for **treating** or **preventing disease** in human beings; or
- (b) Any substance or combination of substances which may be used in or admitted to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medicinal diagnosis.

Definition

Herbal Medicinal Products

Any medicinal product **exclusively** containing
as active ingredients

one or more **herbal substances** or

one or more **herbal preparations**, or

one or more such herbal substances in
combination with one or more such herbal
preparations.

Challenges

30.4.2004

EN

Official Journal of the

L 136/85

DIRECTIVE 2004/24/EC OF THE EUROPEAN

THE COUNCIL

of 31 Mar

amending, as regards traditional herbal medic
Community code relating to med

2001/83/EC on the
use

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE
EUROPEAN UNION



Having
Comm



European

Having

(1).

Having
Social

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Acting in accordance with the procedure laid down in Article
251 of the Treaty (3).

level of safety and are not eligible for
ation. To maintain these products
Member States have enacted differing
provisions. The differences that
between the provisions laid down in
the Member States may hinder trade in traditional
medicinal products within the Community and lead to
discrimination against
manufacturers
an important
necessary
not always

(4)

Having
medicinal
desirable
procedure
However



Challenges

30.4.2004

EN

Official Journal of the European Union

L 136/85

DIRECTIVE 2004/24/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 31 March 2004

amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty establishing the European Community, and in particular Article 177,

Having regard to the proposal from the Commission,

Having regard to the opinion of the Economic and Social Committee (2),

Acting in accordance with Article 251 of the Treaty (3),

and an acceptable level of safety and are not eligible for



To maintain these products in the Member States have enacted differing provisions. The differences that exist between the provisions laid down in the Member States hinder trade in traditional medicinal products in the Community and lead to a distortion of competition between medicinal products. They may also have a negative impact on public health since the quality, safety and efficacy are not always assured.

Particular characteristics of these medicinal products, especially their long tradition, it is necessary to provide a special, simplified registration procedure for traditional medicinal products. This procedure should be used

Definition Traditional Herbal Medicinal Products

A herbal medicinal product that fulfils the
conditions laid down in **Article 16a(1)**.

Vitamins and minerals may be added if their
action is ancillary to the herbal
constituent(s) (Article 16a(2))

Traditional Herbal Medicinal Products

Inclusion Criteria (Article 16a)

- **indication(s) appropriate** to traditional herbal medicinal products,
- use **without the supervision** of a medical practitioner for diagnosis, prescription or monitoring of treatment,
- specified **strength / posology**,
- only **oral use, external use and inhalation**.
- **sufficient data** on traditional use of the product (...safety)
- **pharmacological effects / efficacy plausible** on the basis of long-standing use and experience

Traditional Herbal Medicinal Products

Registration of traditional herbal medicinal products
applicable to **traditional** herbal medicinal products

Article 16c 1 (c)

- > 30 years of medicinal use within the EU or
- > 15 years in and > 15 years outside the EU

Deviations may be decided by the
Herbal Medicinal Products Committee (HMPC, EMEA)
if requested by a Member State

Medicinal Products

Guidance from the European legislative framework is differentiating

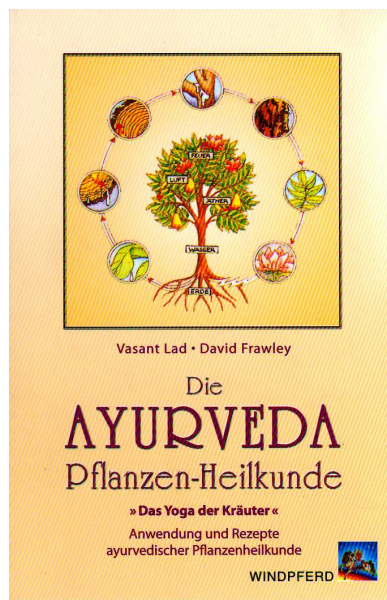
Known substances

New substances

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Reality in Germany



„Globalisation“ of therapeutic pluralism

- WHO (Homeopathy in India, USA, ...)
- 7th framework European Union (Coordination)
- Contact HMPC and Delegation from India
- HMPC-monograph on Fennel
- Monographs in the Pharmacopeia Europea

Access to the Market

- Marketing authorisation
 - full, bibliographic or mixed application
- Registration (simplified with respect to the proof of efficacy)
- Prescription (Formula magistralis)

Access to the Market

- Usage of the therapeutic approach is already possible (by prescription for individual patients)



- Economic-scale access to the market requires a professional strategy fulfilling the usual requirements on

Quality, Efficacy and Safety of medicinal products

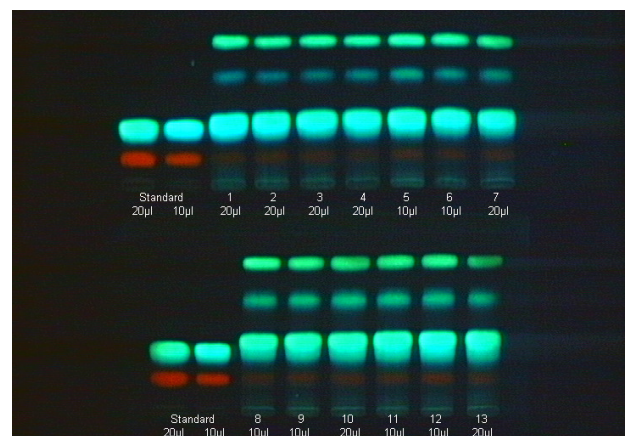
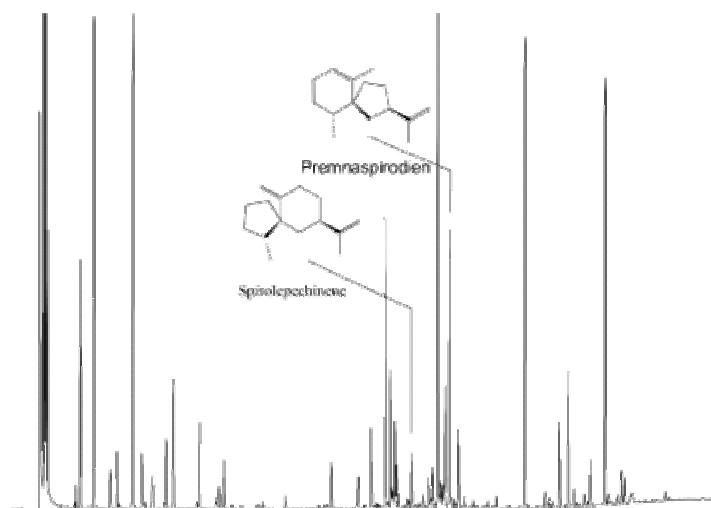
Herbal medicinal products - quality



**Herbal medicinal products
are defined by
manufacturing process
and specifications**



European Pharmacopeia



Quality

- Many new substances
 - Different processing
 - Material of animal, mineral origin
 - Combinations
-
- Development of Monographs from Asian Traditional Medicines (Ph. Eur.)



Safety

- Many new substances
- Knowledge is limited
- Adulterations
- Toxicologic concerns
- Ethnological considerations

- Longstanding tradition
- Ongoing work on scientific data



Efficacy

- Different therapeutic approach
- Transfer of indications
- Prescription/non-prescription
- Suitability of guidelines on clinical trials
- Proof of efficacy or plausibility

- Longstanding tradition
- Experience and acceptance



Legal Framework

Marketing authorisation

- Possible, but probably expensive



Registration

- Reasonable approach, but
- Supervision, animal material
- Lack of 15 years EU
- Limited data on safety



HMPC



Summary

Indian Traditional Medicines

- Therapeutic option is possible
- Professional marketing authorisation is possible
- Access to market via registration is in principal possible, professional strategy is obligatory
- 1. step: usage of available options
- 2. step: evaluation whether change of legislation is necessary, reasonable, realistic

Summary



... means efforts in

- Work
- Investment, Meetings, Reliability
- Communication, Understanding, Acceptance
- Scientific Data