

Workshop on Regulatory Affairs of Herbal Products

# Viewpoints of the Pharmaceutical Industry in Europe

7<sup>th</sup> Joint Meeting of AFERP, ASP, GA, PSE & SIF  
3<sup>rd</sup> – 8<sup>th</sup> August, Athens

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# Topics

1. Industry
2. Situation
3. Challenges
4. Perspectives
3. Summary and Conclusion

## „Herbal Industry“

- “Big Pharma” consumer care divisions
- Big generic companies, 5 to 10 HMP (WEU)
- Larger R&D driven HMP producers
- Traditional SMEs
- Food Supplement manufacturers
  - a. herbal
  - b. mixed portfolio
    - international vitamin driven business
    - direct marketers

## Situation

1. National markets stagnate
2. (nearly) no HMP reimbursement
3. Ever increasing regulatory requirements
  - Qualitative level (genotox, readability,, ...)
  - Administrative efforts (change control, pharmacovigilance ...)
4. Increasing safety and consumer protection requirements
5. poor IP protection for intermediate level innovation

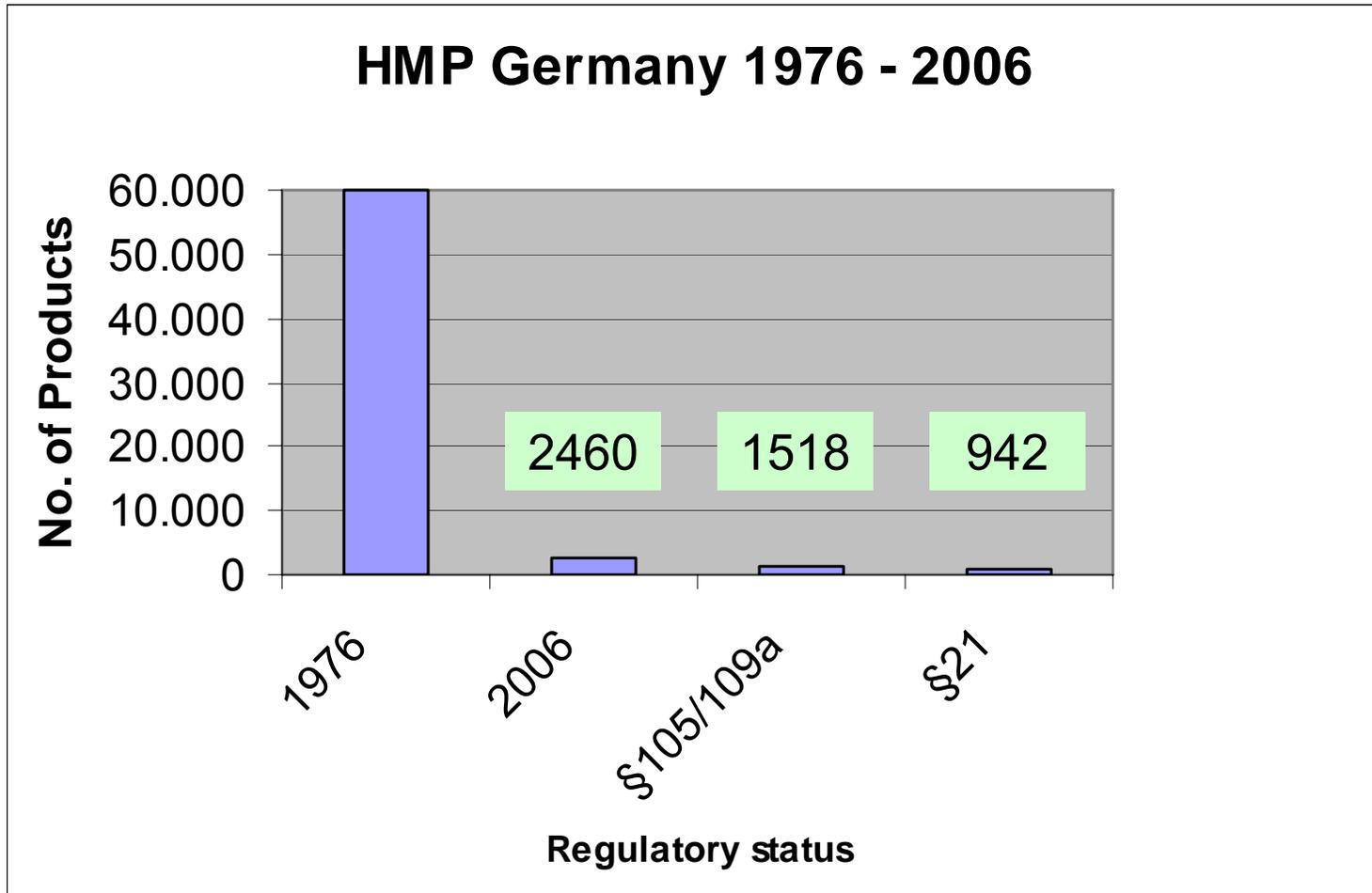
## Situation

companies head for export markets

HMP portfolios get antiquated

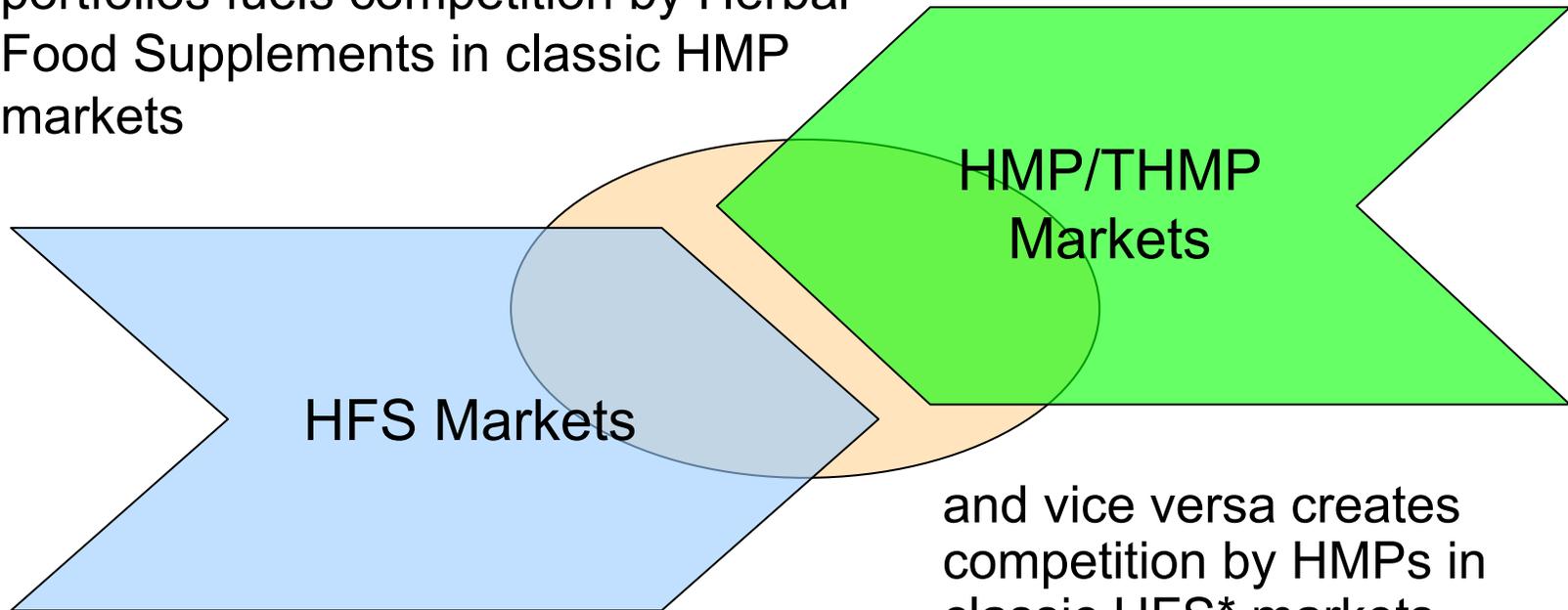
Innovation stagnates

# HMP – popular but vanishing species?



## Challenges

Need for internationalisation of herbal portfolios fuels competition by Herbal Food Supplements in classic HMP markets



and vice versa creates competition by HMPs in classic HFS\* markets

# Challenges

## 1. Harmonisation of legal framework for HMP

- legal basis for WEU and THMP implemented in all member states (2001/83 (EC) as amended)
- HMPC Guidance on major quality and safety issues
- HMPC monographs and list positions
- European Pharmacopoeia

# Challenges

## 1. Harmonisation of legal framework for HFS

- EU General Food Law (EC 178/2002)
- Food Supplements Directive (EC 2004/46)
- Nutrition + Health Claims Regulation (EC 1924/2006)
- Draft Guidance on Safety Assessment of botanical preparations (EFSA 2008)

# Challenges

## Food Supplements – Close to harmonisation?

Country	Notification	Positive List	Negative List
Austria	No	X	X
Belgium	Yes	X	X
Bulgaria	Yes	No	X
Croatia	Yes	X	No
Cyprus	Yes	No	No
Czech Republic	Yes	No	X
Denmark	Yes	X	X
Estonia	Yes	X	X
Finland	Yes	No	X
France	Yes	Conditional list	

## Challenges

### Food Supplements – Close to harmonisation?

<b>Country</b>	<b>Notification</b>	<b>Positive List</b>	<b>Negative List</b>
Germany	Yes	No	No
Greece	Yes	No	No
Hungary	Yes	X	No
Iceland	Yes	X	X
Ireland	Yes	No	X
Italy	Yes	X	X
Latvia	Yes	X	X
Lithuania	Yes	No	No
Luxembourg	Yes	No	No
Malta	Yes	No	No

# Challenges

## Food Supplements – Close to harmonisation?

Country	Notification	Positive List	Negative List
Netherlands	No	No	X
Norway	Currently no	X	X
Poland	Yes	X	X
Portugal	Yes	No	No
Romania	Yes	X	X
Slovakia	Yes	No	No
Slovenia	Yes	X	X
Spain	Yes	No	X
Sweden	No	No	X
Switzerland	No/Yes	X	X
UK	No	X	X

## Challenges - Food supplement use of herbs

Plant	D*	BE*	UK*	FR*	AT*	CZ*	PL**
Crataegus spp.	P						P
Foeniculum vulgare	A	E	A				A
Ginkgo biloba	P	E	A	E		E	?
Harpagophytum proc.	P	E	P	E	P		P
Hypericum perforatum	P	E	A		P	E	P
Matricaria recutita	A	E	A	E			A
Mentha piperita	A	A	A/P	E			A
Salvia officinalis	P	A					E
Serenoa repens	P	E	A				?
Valeriana officinalis	P		A	E		E	P

\*acc. to AESGP 2007

\*\* draft polish list 2008



allowed



allowed with  
conditions



prohibited



allowed  
and prohibited

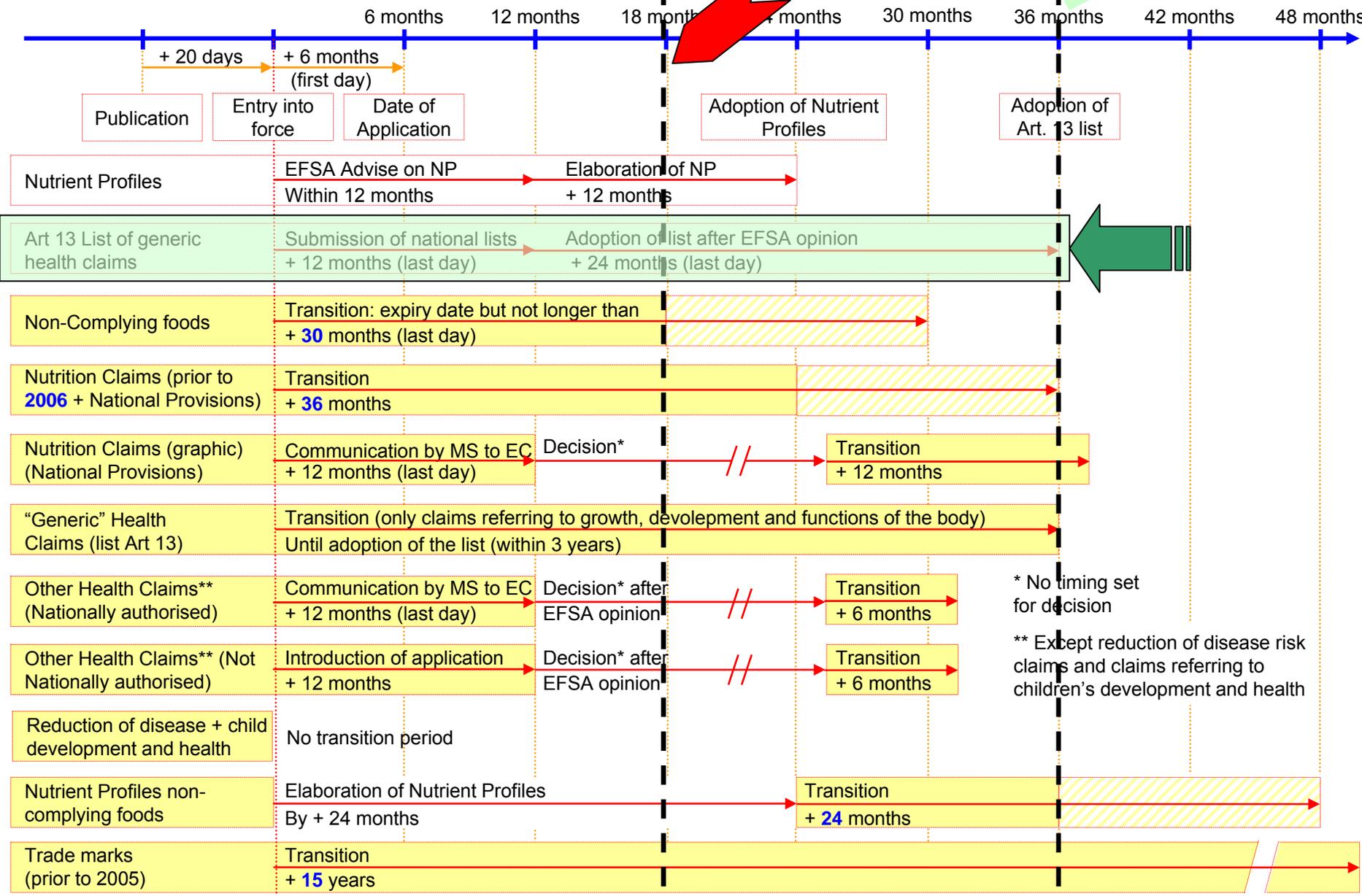
## Challenges

### Regulation on nutrition and health claims made on food 1924/2006 (EC)

- Article 13 claims (list to be established by 31 Jan 2010)
  - nutritional
  - functional inc. psychological function
  - weight control
- Article 14 claims
  - risk reduction claims
  - claims addressing children

# Health Claims Regulation – Time schedule

31 Jan. 2010



\* No timing set for decision

\*\* Except reduction of disease risk claims and claims referring to children’s development and health

## Challenges - Claims

Harpagophytum	
WEU Ger	<b>symptomatic treatment of painful osteoarthritic conditions relief of low back pain</b>
THMP UK	Traditional herbal medicinal product used for the <b>relief of backache, rheumatic or muscular pain, and general aches and pains in the muscles and joints.</b>
§109 Ger	Traditionally used for the <b>relief of rheumatic complaints.</b> This indication is based on traditional use only.
Art 13 proposal	<b>Helps strengthen the body's locomotor system</b> <b>/helps maintain joint health, flexible joints and tendons, good mobility</b>

## Challenges - Claims

Hypericum	
WEU Ger	mild to moderate <b>transitional depressive disturbances (depressive episodes)</b>
THMP UK	A traditional herbal medicinal product used to relieve <b>the symptoms of slightly low mood and mild anxiety</b> , based on traditional use only.
§109a Ger	For <b>relief of mild nervous tension</b>
Art 13 proposal	Contributes to <b>emotional balance, optimal relaxation</b> , helps to <b>maintain a healthy sleep, a positive mood</b>

## Challenges

### Art. 13 List of generic claims (proposals for evaluation)

Aesculus hippocastanum	Hypericum perforatum
Allium sativum	Matricaria chamomilla
Aloe arborescens	Melissa officinalis
Cassia acutifolia, angustifolia	Mentha X piperita
Cimicifuga racemosa	Panax ginseng
Crataegus spec.	Passiflora incarnata
Curcuma longa, xanthorrhiza	Salix spec.
Cynara scolymus	Serenoa repens
Echinacea spec.	Silybum marianum
Ginkgo biloba	Valeriana officinalis
Glycyrrhiza glabra	Viscum album
Harpagophytum procumbens	Zingiber officinale

## Challenges – Variables for delimitation

### ➤ Type of Preparation

- general (e.g., water, < 20% ethanol)
- data based

### ➤ Dosage

- general delimitation (Belgian model)
- data based delimitation

### ➤ Claim

- „tradition based“
- data based

# Challenges - Claims



EUROPEAN COMMISSION  
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Brussels, 3 June 2008

**WORKING DOCUMENT ON  
THE NEXT STEPS FOR THE FINALISATION OF THE LIST OF  
HEALTH CLAIMS TO BE SUBMITTED TO EFSA FOR EVALUATION  
CF. ARTICLE 13(2) OF REGULATION (EC) NO 1924/2006**

## Challenges - Claims

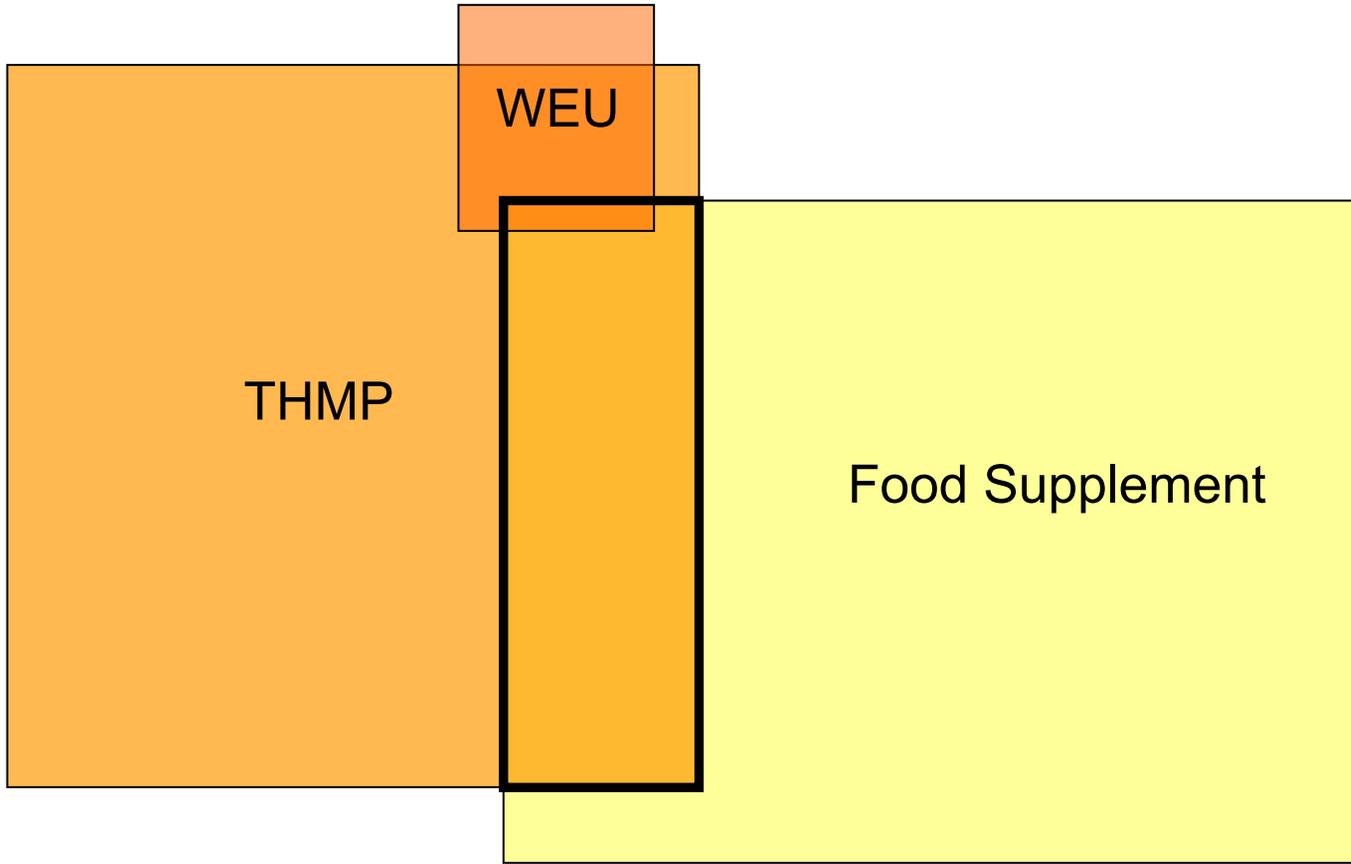
### Application of the criteria when compiling the EU list of claims for evaluation by EFSA

EFSA shall advise whether the health claims fulfil the requirement stipulated in Article 13(1) that they are "based on **generally accepted scientific evidence**". However, as explained in recital 29 to the Regulation the wording of health claims shall also be taken into account by EFSA in formulating its opinion. Consequently, EFSA shall consider whether the wording of the claim reflects the scientific evidence.

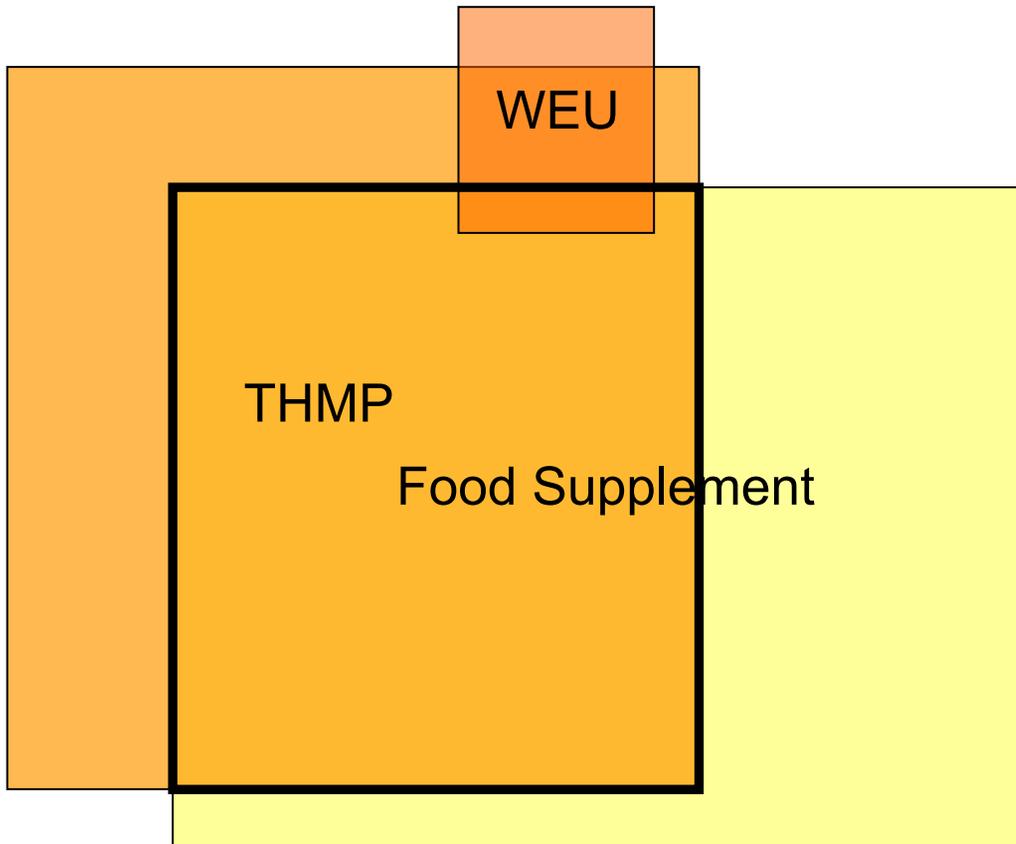
- EFSA's assessment will include assessment of the type of preparation

*(FSA Interested Parties' letter: Commission Working Group on Nutrition and Health claims, 21 April 2008)*

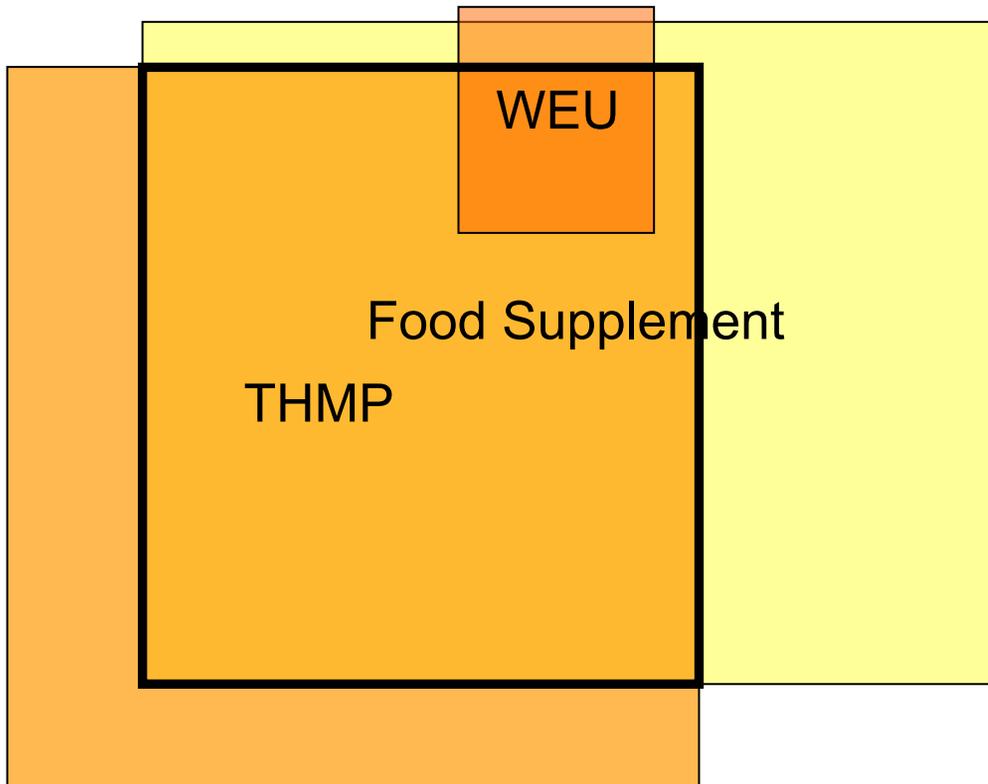
# Scenario 1



## Scenario 2



## Scenario 3



# One herb, three faces

## Ispaghula Husk



### Medicinal Product

HMPC Monograph, WEU

> Diarrhea, Constipation,  
M. Crohn\*, IBS

\*1 of 3 HMP reimbursed in Ger



### Food Supplement

Combined with Inulin  
„Intestinal Health“



### Medical Device

„Cholesterol control“

## Perspectives

- discussion about delimitation of Herbal Medicinal Products vs Food Supplements has a backward orientation
- markets of the future will require innovative products
- what are the options for both segments?

## Perspectives – Medicinal Products

	Cat.	Particulars	TTM	IP	Cost ca. €	EU access
<b>Medicinal Products</b>	<b>NHE</b>	Derived by modification of existing herbal drug preparation <b>or</b> Newly developed from a plant not used as medicinal product in EU before	6 - 10 y	Patent	8 - 15 mio	CP
	<b>WEU</b>	based on HMPC monographs for ca. 10 - 20 plants/products or Proprietary products	3 y	/	100.000	MRP
	<b>THMP</b>	until 2010 ca. 50 - 60 plants/150 preparations available + individual combinations mainly national	3 y	/	100.000 - 180.000	No

## Perspectives – Medicinal Products

	Cat.	Particulars	TTM	IP	Cost ca. €	EU access
Medicinal Products	<b>WEU NI</b>	New indication based on an existing WEU product, combined, e.g. with special dosage form, galenic, dose regimen	ca 3-5y	patent	300.000 – 1 mio	DCP, MRP
	<b>THMP to WEU</b>	Higher level of indication	Ca 3 y	/	250.000 – 500.000	No
	<b>„New“ THMP</b>	THMP from outside EU	Ca. 4y	/	150.000-200.000	No

## Perspectives – Food Supplements

	Cat.	Particulars	TTM	IP	Cost ca. €	harm. access
Food	<b>HFS Art. 13</b>	Functional claim Choice from catalogue from plants/plant preparations and claims from 2010 on	3 - 9 m	no	15 000 – 50 000	?
	<b>HFS Art. 13 New</b>	Functional claim Based on literature or new studies	2 - 5	yes	100.000 – 1 mio	yes
	<b>HFS Art. 14</b>	Risk reduction claim (Art. 14)	2-5y	yes	150.000 - 10 mio	yes
	<b>NF</b>	Only exceptionally a basis for a development of food supplements	3 – 6 y	Yes	0.5 – 3 mio	Yes

## Perspectives

Traditional yesterday – well established today

- *Crataegus spec.*
- *Hypericum perforatum*
- *Lycopus europaeus*
- *Pelargonium sidoides*
- *Salix spec.*
- ...



Rezeptfrei erhältlich  
in Ihrer Apotheke

## Perspectives – new indication for traditional herb

### *Artemisia absinthium*, **Wormwood**

- Commission E (BAnz. of 5.12.1984)
  - Loss of appetite
  - Dyspepsia
  
- *RCT, 40 CD Patients, Artemisia absinthium plv 3 x 500mg/d vs. Placebo*
- *„The results strongly suggest that wormwood has a steroid sparing effect ... and an effect on the mood and quality of life of CD patients,...“*



*Steroid-sparing effect of wormwood (Artemisia absinthium) in Crohn's disease: a double-blind placebo-controlled study. Omer et al, Phytomedicine 2007 Feb;14(2-3):87-95*

## Perspectives - NHE



### MediGene AG submits marketing authorization application for **Polyphenon® E Ointment** in Europe

Martinsried/München – March 28, 2007. The biotech company MediGene AG (Frankfurt, Prime Standard: MDG) today submitted the Marketing Authorization Application (MAA) for Polyphenon® E Ointment\* for the treatment of genital warts to the regulatory authorities in Germany, Austria and Spain. The approval in these countries is supposed to be a reference for the submission of MAAs in further European countries.

## Summary and Conclusion

1. Majority of companies use both HMP and HFS
2. Both HMP and HFS are under pressure
3. Harmonisation leads to a new market order within 5-10 years
4. Major impact of Art. 13 list outcome on existing portfolios
5. Delimitation will be clearer for new products
6. Facetted though restrictive options for development of HMP portfolios
7. Very limited options for HFS portfolios

## Summary and Conclusion

- constructive discussion between industry and regulators should be continued and intensified
- work of HMPC is appreciated
- WEU products should be strengthened
- future focus of all parties must be on innovation rather than protection of acquired possession
- stronger fiscal and regulatory support for innovation

Thank you

