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DIRECTIVE AMENDING FOR TRADITIONAL HERBAL
MEDICINAL PRODUCTS
DIRECTIVE 2001/83/EC

RAPPORTEUR: *Giuseppe Nisticò*
MAIN CO-RAPPORTEUR: *Dagmar Roth-Behrendt*

HISTORICAL BACKGROUND

- Use of traditional herbal medicines is lost in the mists of time
 - Stone Age: use of *Papaver somniferum*
 - 3000 years b.C.: wide use in India, China, Egypt & Middle East
 - 1550 b.C.: 160 different medicinal plants *Ebers papyrus*
 - VI-V century b.C.: Experimental therapeutic use of plants
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APPROVAL OF DIRECTIVE ON TRADITIONAL HERBAL MEDICINES

1. Confers *dignity* to a series of compounds traditionally used by millions of people
 2. Put some stakes in terms of *quality & safety* standards
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SATISFACTION FOR THE DIRECTIVE APPROVAL

- 10 years of discussion
- My thanks: Commission. E. Liikanen
Paul Weissenberg
Philippe Brunet
Clara Martinez



European Parliament
Hon. Dagmar Roth Berendt
& other shadow rapporteurs



Italian Presidency
Min. Girolamo Sirchia
Vittorio Silano

EMEA
Thomas Lönngren

MAIN OBJECTIVE OF DIRECTIVE ON TRADITIONAL HERBAL MEDICINES

ENSURE MAXIMUM LEVEL OF PATIENTS' PROTECTION

- 1) High Quality Standards (GMP)
 - 2) Sufficient long-term use & experience
 - 3) Clear labelling & leaflets
 - 4) Active Pharmacovigilance
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IMPACT OF DIRECTIVE ON SOCIETY

I. Increase business mainly for SME

- harmonization = *increase distribution*
- more investments to *ensure quality* and to respond to market needs
- more jobs for research, quality, distribution

II. Traditional herbal medicines products

Include many categories of medicines: Antivaricose, Cough remedies, Circulation, Muscular pain, Bladder & Kidney, Laxatives, Calming/Sleeping, Cold remedies, Digestive, Liver remedies

III. Germany & France Dominate European *Herbal Market*

Germany (45%) Italy (6%)

IV. European herbal sales

Significant slice of sales

Herbals = 25% vs. non herbal OTC (75%)

AFTER PHARMACOGENOMICS THERE IS STILL SPACE FOR HERBAL MEDICINES?

- 1. Synergistic pharmacological activity between active principles**
 - 2. Reduction of toxicological effects**
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MODERN TECHNOLOGIES IN DRUG-THERAPY

- PHARMACOGENOMICS
 - TRANSGENIC PLANTS
 - COMBINATORIAL CHEMISTRY (DRUG DESIGN)
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IS EVERYTHING NATURAL NECESSARILY GOOD?

“NATURAL HAZARDS”

“TONIC OR TOXIC?”

FDA 2900 Cases of toxic effects
Herbal medicines

104 Cases of death

70 Cases of death from *Ephedra sinica*

WIDE USE IN USA

123 millions (50% popul.) use herbal/vitam./food suppl.

Obesity/Prevention cancer

> Sex Activity > Immune functions

Anorexic effects

Body building

CNS: > Mood/Sleep/Memory

Prevent Pain

PRUDENT USE

1.HIGH QUALITY STANDARDS

Degradation of active ingredients

2.HIGH TOXICOLOGICAL PROFILE (Acute, chronic)

3.POLLUTION (Chemical, physical, biological)

Herbicides

Pesticides

Dioxin

Heavy Metals

Other toxic herbs

4.HERBAL/HERBAL AND HERBAL/DRUG INTERACTION

- **Absorption, Protein binding, Metabolism, Elimination**
 - **Receptors**
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PRUDENT USE: WHY?

ONLY FEW EXAMPLES

Rawolfia

Depression-Suicide
Gastric bleeding

Aristolochia

Carcinogenetic

St. John's Wort

Neurological lesions
(demyelinating)

Ephedra

FDA: 70 cases of death

Agitation, palpitations
Tachy-arrhythmias

Khat (*Catha Edulis*)

Chronic liver dysfunction

**SCOPE OF
PRESENT DIRECTIVE
WELL DEFINED**

IT DOES NOT AFFECT:

- 1. Use of herbals as food supplements or food fortification**
 - 2. Use of herbals as cosmetics**
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COMPOSITION OF TRADITIONAL HERBAL MEDICINES

- Possible addition of **vitamins and minerals**, provided their action is ancillary to herbal active ingredients
 - By July 2007: Commission presents a *report* to include additional categories (aminoacids, fatty acids)
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MAIN POINTS OF THE DIRECTIVE

1. Simplified registration procedure for traditional herbal medicines
 2. Specific committee at the Emea level for herbal medicinal products (HMPC)
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SIMPLIFIED REGISTRATION PROCEDURES

1. Physic-chemical, biological and microbiological tests (GMP)
 2. No required the full dossiers as for drugs
 3. Required only bibliographical **review** or expert report on the traditional use and safety data
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PERIOD OF USE FOR TRADITIONAL HERBAL MEDICINES

- At least a *period of 30 years* of which at least 15 years in EU
 - However, committee for Herbal Medicinal Products can authorise marketing of products with *less than 15 years* of use in EU (*Community Herbal Monographs*)
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EUROPEAN PARLIAMENT INSISTED ON THE POSSIBILITY OF:

MUTUAL RECOGNITION BY MEMBER STATES



COMMON POSITION



MUTUAL RECOGNITION for all herbal products covered by a

Community monograph (or list of herbals)

INFORMATION ON TRADITIONAL HERBAL MEDICINAL PRODUCTS

- 1. Clear, understandable by general public, rigorously scientific**
 - 2. Avoid claims not supported by scientific evidence**
 - 3. Indications of side and toxic effects and possible dangerous drug interactions**
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LABELLING & LEAFLETS

*E.P. proposed more reasonable wording to
avoid frightening of patients*

*“Indication exclusively based upon long-standing
use & experience”*

NEW COMMITTEE FOR HERBAL MEDICINAL PRODUCTS (HMPC)

- **HIGH QUALITY EXPERTS**
 - **SAME TASKS & RESPONSIBILITIES AS CHMP**
 - **PREPARE DRAFT LIST OF HERBAL MEDICINAL PRODUCTS**
 - **ESTABLISH COMMUNITY MONOGRAPHS**
 - **FINAL DECISION IN ARBITRATION PROCESSES**
 - **COORDINATION WITH CHMP BY EXECUTIVE DIRECTOR OF EMEA**
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“SWEET” APPLICATION OF THE DIRECTIVE

TRANSITION PERIOD OF 7 YEARS

Allow manufacturers to make appropriate adjustments in order to comply with Directive requirements



CONCLUSIONS

- EXPRESS SATISFATION OF EUROPEAN PARLIAMENT
 - CONFERS DIGNITY & PUT IN ORDER A CONFUSED CONTROVERSIAL FIELD
 - TO EXPRESS A WISH AS SCIENTIST THAT THERE WILL BE AN INCREASE IN SCIENTIFIC RESEARCH IN THIS FIELD
 - FINALLY TO EXPRESS IN MY NEW POSITION AS MEMBER OF CHMP:
 1. *A wish for a full implementation by Member States & industries*
 2. *A wish for a good coordination of CHMP and HMPC through executive director*
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Ciao Dagmar !

