

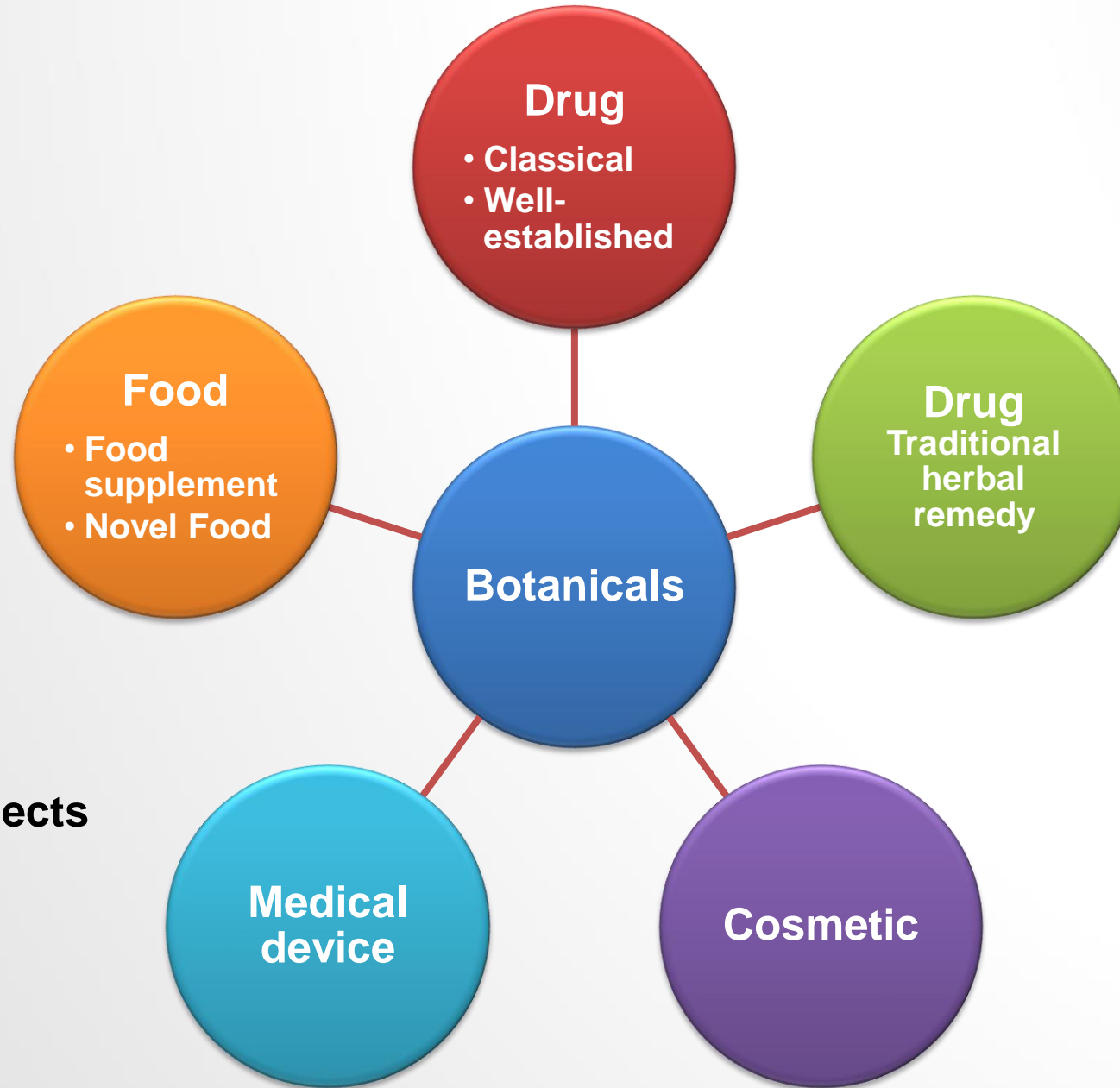
Safety, efficacy and quality of medicinal and edible plants: herbal medicines, food supplements, medical devices or food?



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Meise botanic garden



DIFFERENT WAYS TO ENTER THE MARKET

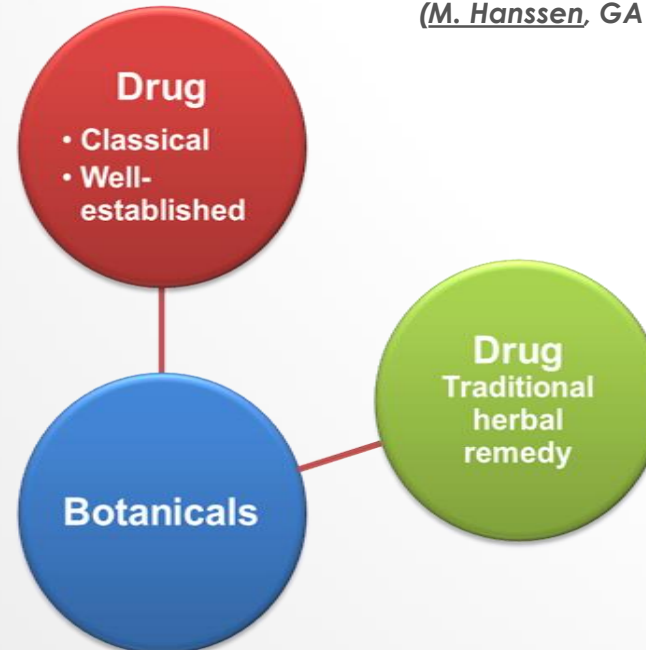


- ⇒ **Very different requirements**
- ⇒ **Very different regulatory aspects**

MARKETING AS A DRUG - REGISTRATION (1)

- Defined medical purpose
- Dosage with clear medicinal effect
- Medicinal claim(s)
 - ✓ Clinically proven : complete registration
 - ✓ Well-established
 - ✓ Traditionally used

(M. Hanssen, GA meeting, Kiel, 2003)



- Directive 2004/27/EC (*medicinal products*)
- Directive 2004/24/EC (*traditional herbal medicinal products*)

MARKETING AS A DRUG - REGISTRATION (2)

- Can be mandatory (*e.g. herbs with high activity or known risks, "new" herbs*)
- Can also be a choice of the pharmaceutical company

Complete registration → requires documenting :

- I. Quality (chemico-pharmaceutical dossier)**
- II. Pharmacology and innocuity (pharmaco-toxicological studies)**
- III. Efficacy (clinical studies)**

→ Characteristics :

- ⇒ **Extremely lengthy procedure (several years to yield appropriate data)**
- ⇒ **Extremely costly**
- ⇒ **Standard format labelling and leaflet**
- ⇒ **Limited to approved indications (proved by clinical studies)**
- ⇒ **Marketed in pharmacies only**
- ⇒ **Pharmacovigilance system implemented**

http://ec.europa.eu/health/documents/eudralex/index_en.htm

MARKETING AS A DRUG - REGISTRATION (3)

Registration under a simplified procedure

- a) Well-established use : *registered as a drug for minimum 10 years in at least one EU country* → "safety and efficacy demonstrated"
 - requires documenting :
 - I. Quality (chemico-pharmaceutical dossier)
 - II. Innocuity (bibliography + pharmacovigilance)
 - III. Efficacy (clinical studies in bibliography) → approved indications

- b) Traditional use : *marketed (not necessarily as a drug) for medical use for minimum 30 years, of which 15 years in at least one EU country* → "sufficient safety data and plausible efficacy"
 - requires documenting :
 - I. Quality (chemico-pharmaceutical dossier)
 - II. Innocuity (bibliography)
 - ⇒ Limited to symptomatic indications

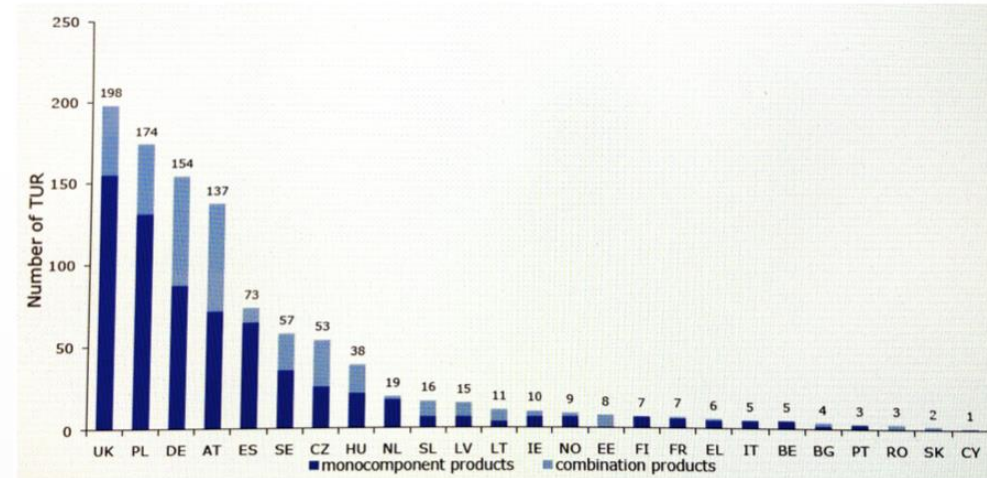
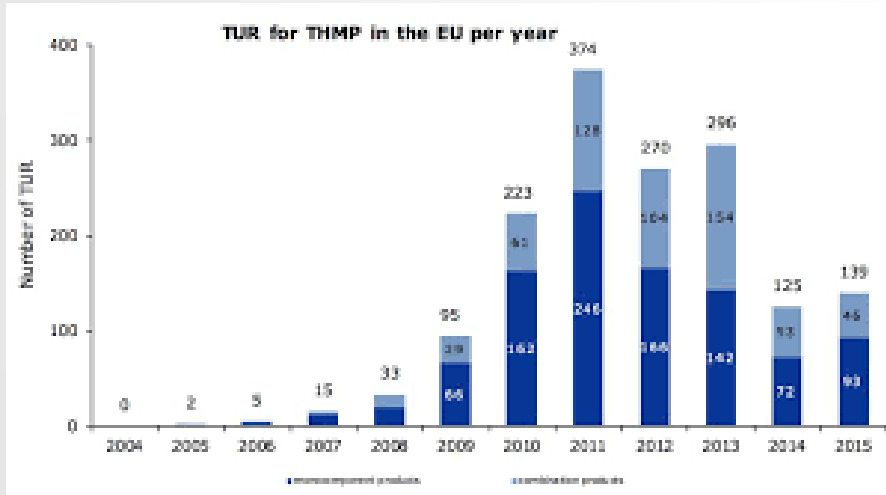
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000208.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800240cf

MARKETING AS A DRUG - REGISTRATION (4)

Characteristics of Registration under a simplified procedure

- ⇒ **Still lengthy procedure**
- ⇒ **Costly**
- ⇒ **Standard format labelling and leaflet**
- ⇒ **Limited to approved indications (well-established use)**
- ⇒ **Limited to approved symptoms (traditional use)**
- ⇒ **Marketed in pharmacies only**
- ⇒ **Pharmacovigilance system implemented**
- ⇒ **"Traditional use": Indications relating to specific concepts of traditional medicines may be acceptable. A “translation” of complex traditional terms in terms of modern medicine should be avoided.**

UPTAKE OF THE TRADITIONAL USE REGISTRATION SCHEME IN EU



Herbal substances	
Total (85)	260
Pelargonii radix	29
Hyperici herba	18
Harpagophyti radix	18
Valerianae radix	13
Passiflorae herba	9
Visci albi herba	9
Echinaceae purpureae radix	8
Salviae folium	8
Rhodiolae roseae rhizoma	7
Cimicifugae rhizoma	6
Echinaceae purpureae herba	6
Hippocastani semen	5
Melissae folium	5
Thymi herba	5
Arnicae flos	4
Crataegi folium cum flore	4
Equiseti herba	4
Sabalıs serrulatae fructus	4
Tanacetı parthenii herba	4

Therapeutic area	Total	Mono-component products	Combination products
Total²⁾	460	321	139
Mental stress & mood disorders	80	56	24
Cough and cold	78	58	20
Urinary tract and gynaecology disorders	58	35	23
Gastrointestinal disorders	50	39	11
Sleep disorders & temporary insomnia	44	26	18
Other (miscellaneous)	35	16	19
Pain and inflammation	33	32	1
Fatigue & weakness	26	12	14
Skin disorders & minor wounds	24	19	5
Venous circulatory disorders	14	12	2
Mouth and throat disorders	13	13	0
Loss of appetite	3	1	2
Constipation	1	1	0
Eye discomfort	1	1	0

HERBAL PRODUCTS AND COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM)

CAMbrella project

A pan-European research network for Complementary and Alternative Medicine

- FP7-HEALTH-2009, GA No. 241951; project duration: 01/01/2010 – 31/12/2012
- Deliverable 9 – Report No.2: Herbal and homeopathic medicinal products

Belgium has a general CAM law which means that the practice of health care professionals is regulated by health care professional act - the Royal Decree 78 from 10 November 1967, recently amended and confirmed.

According to this act only **physicians, dentists and midwives** are entitled to make a diagnosis and prescribe a treatment .

There is no specific regulation in Belgium on herbal medicine or phytotherapy.

Only those professionals can prescribe a CAM treatment, CAM treatment may be dispensed legally by physiotherapists on medical prescription.

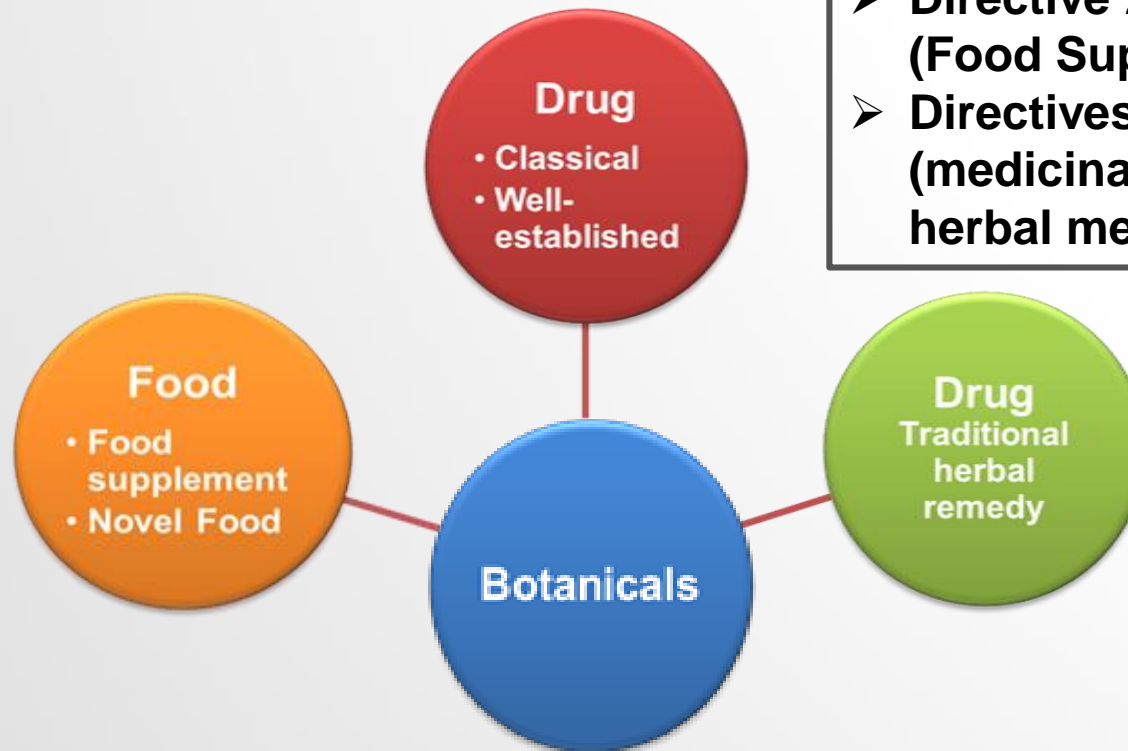
The Act of 29 April 1999 added practitioners of non-conventional medicine – **acupuncture, chiropractic, homeopathy, osteopathy** to health professionals. But this Law is not yet fully in force.

MARKETING AS FOOD

- Considered a food by carefully interpreting the data on
 - ✓ physiological versus pharmacological effect
 - ✓ health versus disease conditions
 - ✓ a dose/concentration basis



- Directive 2002/46/EC (Food Supplements)
- Directives 2004/27/EC and 2004/24/EC (medicinal products and traditional herbal medicinal products)



MARKETING AS FOOD



BOTANICAL FOOD SUPPLEMENTS IN BELGIUM

- General provisions for botanical food supplements are harmonised by Directive 2002/46 which provides the definition of food supplements. "food supplements" means foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities).
- Compositional criteria in relation to botanicals have not yet been harmonised at EU level, therefore national rules are still applicable.
- Food supplements containing in their composition plants have to comply with the requirements of Royal Decree from 29 August 1997 on the manufacture and trade of foods composed of or containing plants or plant preparations.
- The Decree contains 3 lists:
 - List 1: a list of plants which are not allowed for use in or as foodstuffs. This means that any part, preparation or fruit of those plants must not be consumed as such and must not be used for preparing foodstuffs.
 - List 2: edible mushrooms
 - List 3: list of plants which are allowed in food supplements. For some of those plants, maximum amounts are laid down per daily portion, for which a list of recommended analysis methods has been drawn up
- Botanical food supplements in Belgium are subject to a notification procedure before being placed on the market. The Agence Fédérale des Médicaments et des Produits de Santé (AFMPS) is responsible competent authority.
- List of the ingredients are checked carefully. Health claims are strictly regulated and most claims are not allowed.
- After approval a notification number is issued.

FOOD SUPPLEMENTS AT EU LEVEL

In October 2015 the Commission has published a Roadmap on the evaluation of

- a) Regulation (EC) No 1924/2006 on nutrition and health claims made on food with regard to nutrient profiles and health claims made on plants and their preparations
- b) The general regulatory framework for their use in foods

Since its adoption in 2006, the implementation of the Regulation remains incomplete since nutrient profiles, that had to be set by January 2009, have not been established and due to the fact that health claims on plants and their preparations used in foods are not yet fully regulated.

In addition, the situation with regard to the health claims on plants and their preparations has led to a broader reflection regarding the use of plants and their preparations used in foods.

Results of public and stakeholders consultation were published on website

http://ec.europa.eu/dgs/health_food-safety/dgs_consultations/feedback/index_en.htm

On 27 May 2016 the external study was launched.

The evaluation exercise will allow to identify the needs and possible solutions for further harmonisation of the use of plants and their preparations in food and evaluation process of nutrient profiles.

- At the same time...

FOOD SUPPLEMENTS AT EU LEVEL

Belgium, France and Italy works on Belfrit project

- This project lists plants that are (a) not permitted for food, (b) edible mushrooms and (c) plants which can be used with some restriction. It has been compiled from three domestic plant lists and limited to food supplement use only.
- The single or harmonised version of the list contains 1043 plants and fungi.

There are some initiatives in the EU (e.g. Italy, UK) to revise existing databases and validate them in order to create on-line platforms which could be used to find reliable, science-based information about medicinal plants and their products for the professionals of the field and general public.

Italian researchers are working on ,popular science of Phytotherapy'. From 750 first entries 40 sites were selected for detailed analysis. It was observed the total absence of Bibliography References or References links, the presence of inadequate Authors and the lack of transparency (those results were presented in International Conference on biodiversity of medicinal and edible plants, June 2015 at University of Padova).

www.progettofficinafitoterapia.it

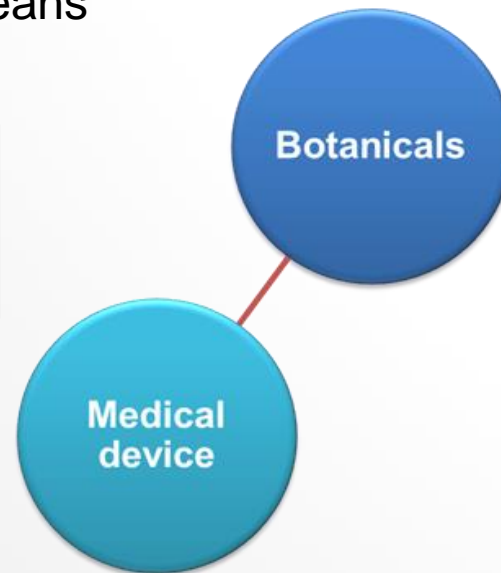
MARKETING AS A MEDICAL DEVICE

“Any instrument, apparatus, appliance, software, material or other article....
intended by the manufacturer to be used for human beings for the purpose of:

- ✓ diagnosis, prevention, monitoring, treatment or alleviation of disease,
- ✓ diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- ✓ investigation, replacement or modification of the anatomy or of a physiological process or control of conception,

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means”

Classical example:
Cement for hips prosthesis
Bearing gentamicin: not a drug



MARKETING AS A MEDICAL DEVICE

➤ Herpes stick



GSE Herpex1 Stick

Lips pommade stick with vegetal extracts useful for the prevention of herpes and treatment of correlated inflammatory symptoms.

Extract of grapefruit seed, melissa, prunella, camellia sinensis, vitamin E, glycyrrhetic acid, karite butter and beeswax

- **Ear Drops**
- **Appetite Suppressant**
- **.....**

BOTANICAL MEDICAL DEVICES IN BELGIUM

Sanofi:

- Neomycolog gel: gel d'huile d'olive ozonée (action semblable à celle de dérivé réactif de l'oxygène); détruit les structures des mycoses et bactéries par oxydation.
- Rhina Pulmo sirop fraction polysaccharidique du plantain et fraction flavonoïque du thym, miel

Melisana

- Junior angin sirop mousse d'islande et mauve
- Junior angin pastilles mousse d'islande et pantothénate de calcium

Boehringer

- Bisol duo pastilles mousse d'islande et alun

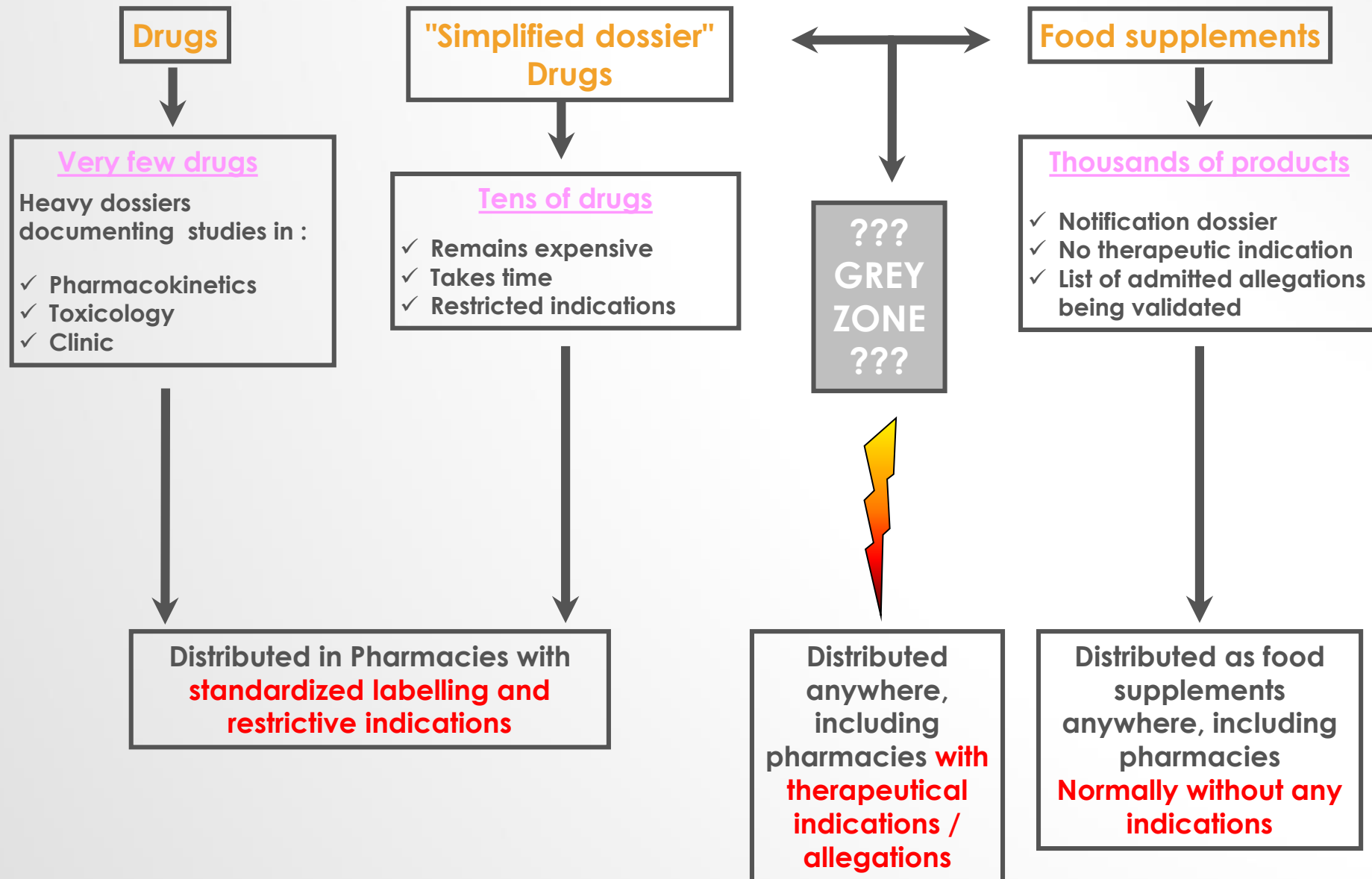
Aboca

- Grintux sirop (plantain, grindelia, helichryse somm fleuries, huiles essentielles)
- Salvigol pastilles et spray gorge (sauge, myrrhe inuline,...)
- Fitomagra Libramed (polysaccharides)
- Fitonasal (tanins polysaccharides flavonoides)
- Fitostill gttes yeux (camomille ext lyophilisé de fleurs ligulées...)

VSM

- Optilan Blueberry gttes oculaires (hyaluronate, ext liq de myrtille)

SITUATION OF THE HERBAL PRODUCTS MARKET





TILMAN

One of the biggest Belgian herbal medicines and botanical food supplements producer and supplier created in 1956 (more than 50 years of experience)

Distributes their products exclusively in the pharmacies

25 % of production is exported to more than 30 countries around the world (33 mln euros in 2017)



ORTIS LABORATOIRES

Family company created in 1958

2 hectares visiting site, 8000 m² are dedicated to medicinal plants



ARKOPHARMA

- One of the biggest herbal medicines and botanical food supplements French suppliers in Belgium
- Company is created in 1980 in France, Carros, next to Nice



HERBORISTERIE DE PEPIN, BRUSSELS



HERBORISTERIE DESMECHT, BRUSSELS



HERBORISTERIE MODERNE, BRUSSELS



HEALTH MARKETS, BRUSSELS



WHAT ARE THE REQUIREMENTS TO OPEN A HERBORISTERIE?

- At the moment there is no legal status in Belgium for herbalist shops.
- It is considered to be as any other shop, the owner is considered as 'Chef d'entreprise'.
- However when selling botanical plants and food supplements it has to respect a Royal Decree from 29 August 1997 on the manufacture and trade of foods composed of or containing plants or plant preparations.
- Contrary to France where formally only pharmacists are allowed to run herbalist shops, Belgium has not such a requirement.
- In France Herbalist certificate issued by schools of pharmacy or medical jury was created in 1803 and abolished 11 September 1941. This profession almost disappeared - however discussions are coming back claiming that the herbalist profession 'will offer possibilities for new forms of medicine' (J.-L. Ficher, French Senate).

EUROPEAN FEDERATION OF HERBALISTS

The Fédération Européenne d'Herboristerie (F.E.H.) unites different associations to promote use of medicinal plants in Europe.

The F.E.H. aims to:

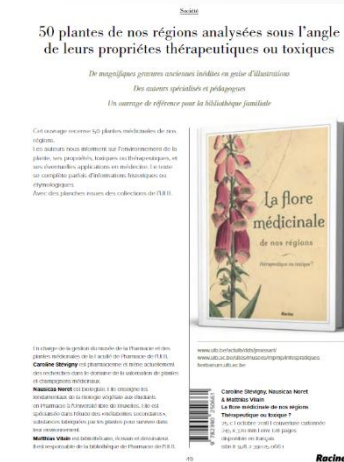
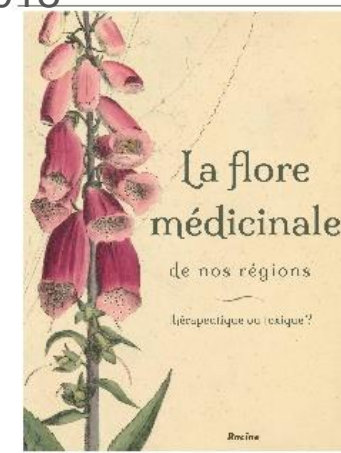
- Produce, transform and distribute medicinal plants
- Teach about herbalism and phytotherapy
- Create gardens of medicinal plants
- Collect historical sources about the use of medicinal plants
- Participate actively in the research of ethnobotany and ethnopharmacognosy
- Promote knowledge of medicinal plants to the society

NEXT STEPS

I would like to present 2 upcoming projects on health effects of medicinal plants that I will be involved in the future:

Musée des Plantes Médicinales et de la Pharmacie (ULB): activities of the museum, conferences, workshops, guided visits about history of medicinal plants, their current uses in our society and ongoing scientific research on medicinal plants at ULB.

Announcement : newly edited book available at the museum 'La flore médicinale de nos régions. Thérapeutique ou toxique ?'
Caroline Stévigny, Nausicaa Noret, Matthias Vilain, Editions Racine, 2018



NatureMinded: project on nature therapy in urban gardens and forests in cooperation with scientist Katriina Kilpi. We are working on scientific knowledge sharing and awareness raising on therapeutic landscapes for health promotion and disease prevention.



NatureMinded