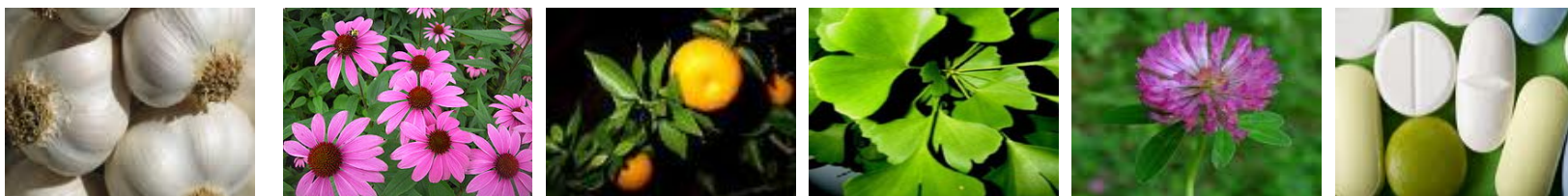


1

Harmonizing the evaluation of botanicals

The regulatory system in Belgium and the “BELFRIT” project



FPS Health, Food Chain Safety and Environment

DG Animals, Plants and Food

Section Service Food, Feed & other consumption products



2



The cutting edge ?

cutting knots



Axe or Scalpel



Joris GEELEN

Regulatory Expert Botanicals

Secretary of Advisory Commission on botanicals



3



1. Belgian legislation

- 1.1 Lists of plants
- 1.2 Notification - FoodSup
- 1.3 Advisory Commission
- 1.4 Maximum levels + Mandatory warnings

2. Harmonization: the 'BELFRIT' project

- 2.1 Concept
- 2.2 Approach
- 2.3 Future

3. Conclusions



Joris GEELEN

Regulatory Expert Botanicals

Secretary of Advisory Commission on botanicals



1. Royal decree on Plants : facts

4

- 1st publication in Belgian Official Journal 21/11/'97
- 9 decrees with adaptations '99 - '08
 - Transposition of Directive 2002/46/EC May 2003
 - Conditions of use, specific **warnings** + **maximum levels** for ~27 plants March 2005
- Amending decree notified - EU COM - TRIS April 2010
 - Justification warnings @ COM → + advice July 2011
 - Publication Belgian Official Journal 4/4/2012



1.1 Royal decree on Plants : scope

- Applies to foods and supplements that contain plants
- In annex 3 lists:

List 1:

Plants that may not be used in or as food.

→ Derogation possibility

Apply to all food

List 2:

Edible mushrooms

List 3:

Plants - predosed form. To be notified.

Only applies to Food supplements

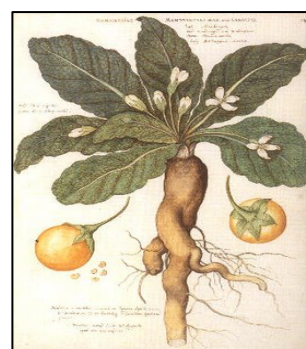
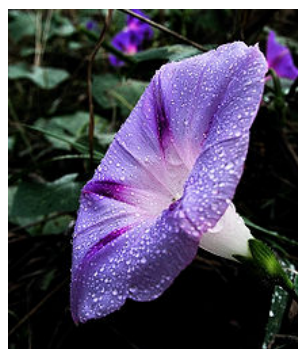
(*) Maximum levels



1.1 Royal decree on Plants : List 1

6

Aconitum spp., *Brugmansia* spp., *Ipomoea* spp.



Mandragora officinarum L. *Zigadenus* spp.



Exemptions to the prohibition
toxicological + analytical proof
free of toxic properties or substances



Borago spp.: max. 1 µg/kg toxic pyrrolizidine alkaloids

390 genera + species



1.1 Royal decree on Plants : List 2

Edible (wild and cultivated) mushrooms

Cordyceps sinensis, *Agaricus blazei*, shiitake, reishi, maitake



+ also supplement use



90 species



1.1 Royal decree on Plants : List 3

8

Aesculus hippocastanum L.



Ginkgo biloba L.



Hypericum perforatum L.



Passiflora incarnata L.



Camellia sinensis (L.) Kuntze



Valeriana repens Host



Panax ginseng C.A.Mey.



Zingiber officinale Roscoe



645 species

<http://plantaardigheden.nl/>
<http://www.theplantlist.org/>



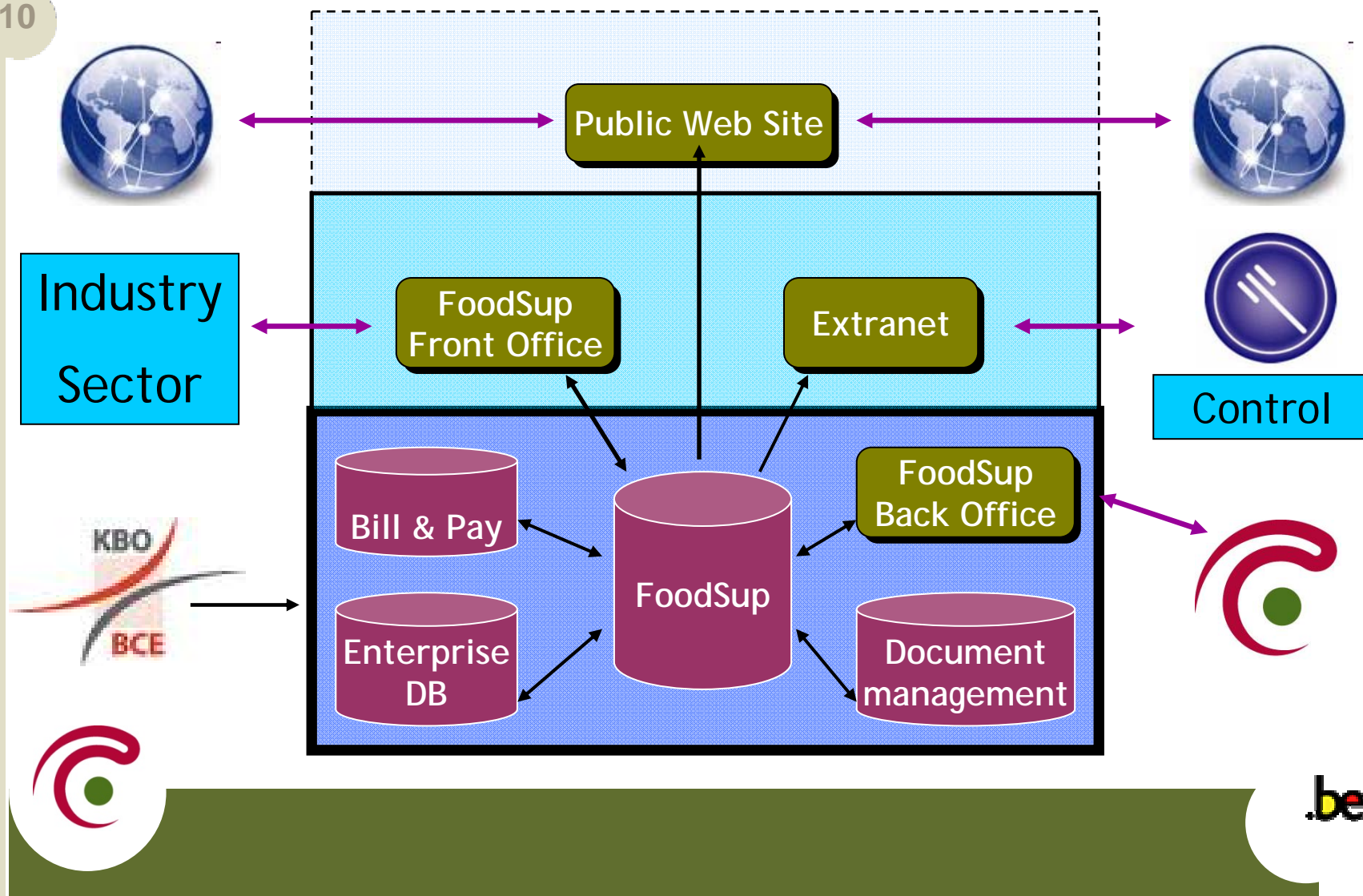
1.2 Royal decree on Plants : Notification

- Extensive notification dossier submitted at market intro
- Thorough technical and scientific evaluation of all the characteristics of the product
- Check conformity vertical & horizontal legislation
- Expert advice if necessary
- Within month letter of receipt + possibly with remarks
- Online notification system: FOODSUP



1.2 Digital notification system: FoodSup

10



FoodSup

Language

FR NL EN

3 languages

PROD_ENVIRONMENT

Welcome joris geelen Change password Change mail

Reference list management

Enterprises management

Create notification for new product

Bill And Pay

Invoices

Product search

Advanced search

Refresh

KPI report

Filter on technical expert

All

Filter on foodsup expert

All

Bill & Pay - automated

Products waiting for decision

Number	Division	Product name	Product State	Langu...	Date submitted	Technical Expert	Food Expert	Submitted via FO	Actions
NUT_AS 1629/41	VALENTIA BIOLOGICS S.L.	Natokinase NSK-SD	1st notification waiting for decision	fr	10/09/2013	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Detail History
1629/42	VALENTIA BIOLOGICS S.L.	Malt acid	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
1629/43	VALENTIA BIOLOGICS S.L.	L-glutamine	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
NUT 2400/2	DAILYCER FRANCE	Pétales de Riz et de Blé complet aux fruits ...	Attributed	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
NUT 2400/4	DAILYCER FRANCE	Pétales de riz et de blé complet riches en vi...	Attributed	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
NUT 2400/5	DAILYCER FRANCE	Pétales de riz et de blé complet riches en vi...	Attributed	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
NUT 2400/8	DAILYCER FRANCE	Pétales de riz et de blé complet riches en vi...	Attributed	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/2	RASY PHARMA	Calcium complexe	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/3	RASY PHARMA	Calmagzinc tablé	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/4	RASY PHARMA	Day-vit active t	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/5	RASY PHARMA	Gericaps active	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/6	RASY PHARMA	Hair-vit capsules	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/7	RASY PHARMA	Kidz probio chewable tablets	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/8	RASY PHARMA	Magcitra 1900 mg tablets	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History
2482/9	RASY PHARMA	Omega 3 750mg capsules	1st notification waiting for decision	fr	10/09/2013		Dominique de Clock	<input type="checkbox"/>	Detail History

Fast search & filter in dossiers

Products rejected

Number	Division	Product name	Product State	Langu...	Date submitted	Technical Expert	Food Expert	Submitted via FO	Actions
No product found									

Products waiting to be signed

Number	Division	Product name	Product State	Date submitted	Approval	Langu...	Technical Expert	Food Expert	Submitted via FO	Actions
NUT_PL_AS 968/1	PHYTHEA	Phytalgic	Extended temporary attribution	04/07/2013	06/11/2013	fr	Steve Christiaens	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/34	NATURALEADER IMPORT EX...	Cocolider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
AS 1452/35	NATURALEADER IMPORT EX...	Condrolider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
NUT_PL 1452/36	NATURALEADER IMPORT EX...	Cranlider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
NUT 1452/37	NATURALEADER IMPORT EX...	Cromoleader	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/38	NATURALEADER IMPORT EX...	Ginsenglider americano	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/39	NATURALEADER IMPORT EX...	Ginsenglider coreano	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/40	NATURALEADER IMPORT EX...	Granadalider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/41	NATURALEADER IMPORT EX...	Harpagolider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/42	NATURALEADER IMPORT EX...	Hiperilider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
NUT_PL_AS 1452/43	NATURALEADER IMPORT EX...	Memorlider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
NUT_AS 1452/44	NATURALEADER IMPORT EX...	Probioticslider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
PL 1452/45	NATURALEADER IMPORT EX...	Reishlider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
AS 1452/46	NATURALEADER IMPORT EX...	S.O.D.lider	1st notification waiting for de...	29/07/2013	31/10/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History
NUT_PL_AS 1452/47	NATURALEADER IMPORT EX...	Saballider	1st notification waiting for de...	29/07/2013	04/11/2013	fr	Carine Desmarlières	Dominique de Clock	<input type="checkbox"/>	Edit History

Clear overview of workflow

Products ready to send

Number	Division	Product name	Signed on	Langu...	Technical Expert	Food Expert	Product State	Submitted via FO	Actions
AS 2387/1	REGIMATCH B.V.	Algooven	07/11/2013	nl	Steve Christiaens	Katrien De Pauw	Not attributed	<input type="checkbox"/>	Edit Send

Consult the user guide on the website of the FPS Public Health for more information.

Gereed

✓ Vertrouwde websites | Beveiligde modus: uitgeschakeld

100%

FoodSup

Language

FR NL EN

PROD_ENVIRONMENT

Welcome joris geelen Change password Change mail

Product

Product Name Division Nr / version Product State

Selected notification

Notification Product Ingredients Nutrients **Plant** Other Substances Nutritional Analysis Toxicity, stability and analysis Annexes

All plants Substances under the tab 'Ingredients'

Detailed info on ingredients

Type & quantity of preparation

Latin name	French name	Dutch name	Used plant part	Used preparation	Qu. dry p recommended portion			
Vaccinium Corymbosum	Myrtille	Blauwe bes	ribes	10:1 droogextract				View - Edit
Vitis vinifera L.	Vigne cultivée, Vigne vinifère	Druif, Wijnstok, Wijngaardstok	fructus	10:1 droogextract	108	milligram		View - Edit
Rubus fruticosus L.	Ronce commune, Ronce des buissons, ...	Gewone braam	ribes	10:1 droogextract	106	milligram		View - Edit
Citrus sinensis (L.) Osbeck	Sinaasappel		fructus	10:1 droogextract				View - Edit

Scientific name

Plant part used

Latin name	Used plant part	Active Substance per recommended portion	Unit	Action
Vaccinium Corymbosum	ribes	8.59	milligram	View - Edit - Delete
Vitis vinifera L.	fructus	17.38	milligram	View - Edit - Delete
Rubus fruticosus L.	ribes	24.9	milligram	View - Edit - Delete
Citrus sinensis (L.) Osbeck	fructus	0.15	milligram	View - Edit - Delete

Active Ingredients

AI / daily dose

Possibility to add comments

Comments

Create new notification

History

Cancel

Withdrawn by administration

Withdraw from market

Consult the user guide on the website of the FPS Public Health for more information.

Gereed

Vertrouwde websites | Beveiligde modus: uitgeschakeld

100%

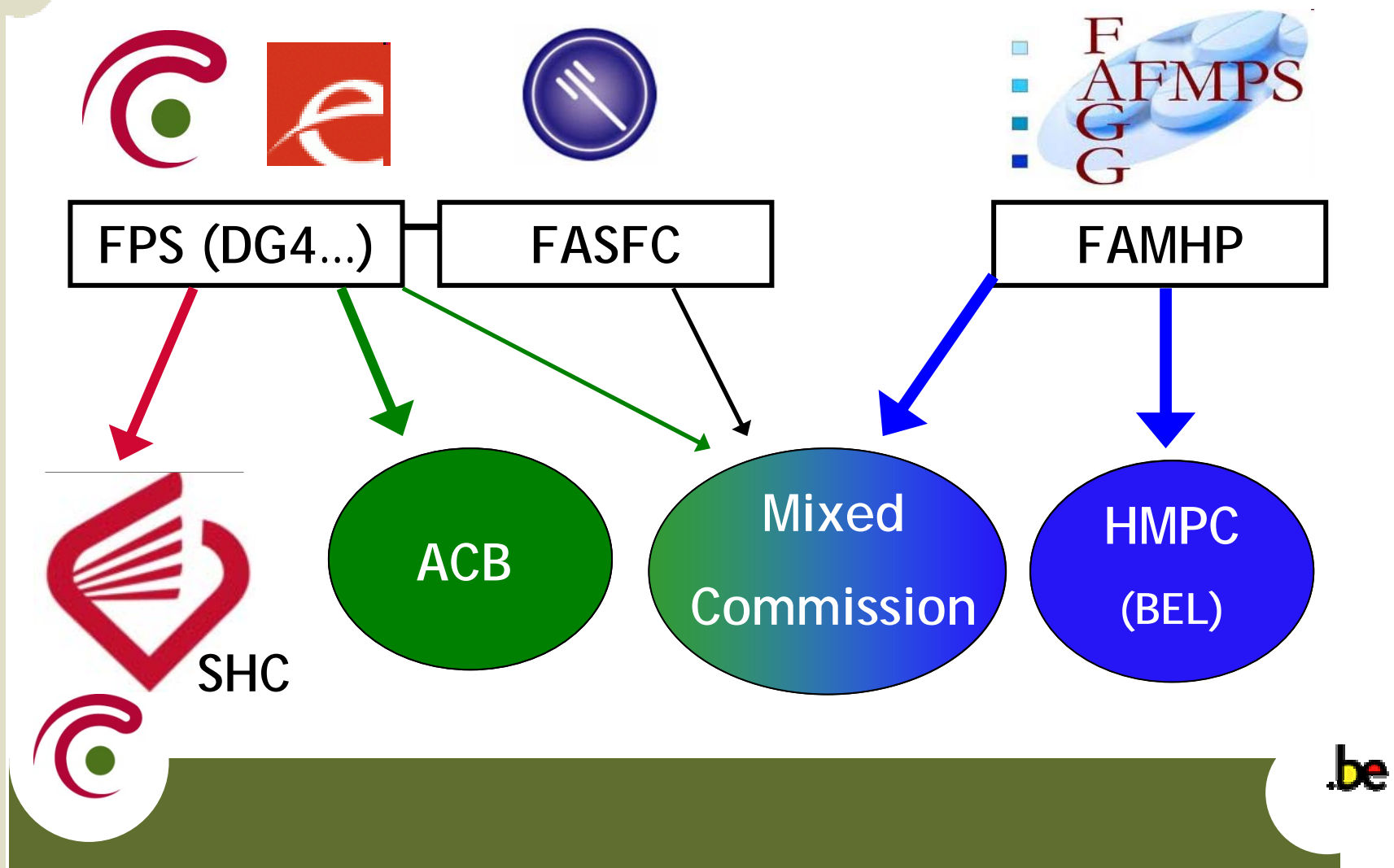
1.2 Notification - content dossier

- Labeling
- Nature of the product
(presentation, packaging, recommended daily portion)
- List of ingredients :
(plant name, part used, galenic form, amount, function)
- Nutritional analysis
- Qualitative and Quantitative data of
Nutrients, Plants (% active substances), Other subst.
- Data on Non-toxicity, Stability
- Commitment to carry out frequent analyses
- Production method, % solvent, Drug-Extract-Ratio, ...



1.3 Advisory Commissions

14



1.3. Advisory Commission for botanicals

15

= Em. Prof. Dr. A. Vlietinck + 14 experts



Scientific safety evaluation of plant preparations

- Evaluate plants not listed - conditions not fulfilled
- Advice on exemptions for plants on list 1
- Determine maximum levels / warnings
- Evaluate products with encapsulated essential oils
- Follow-up literature, side effects, incidents
- Progressive revision of the lists

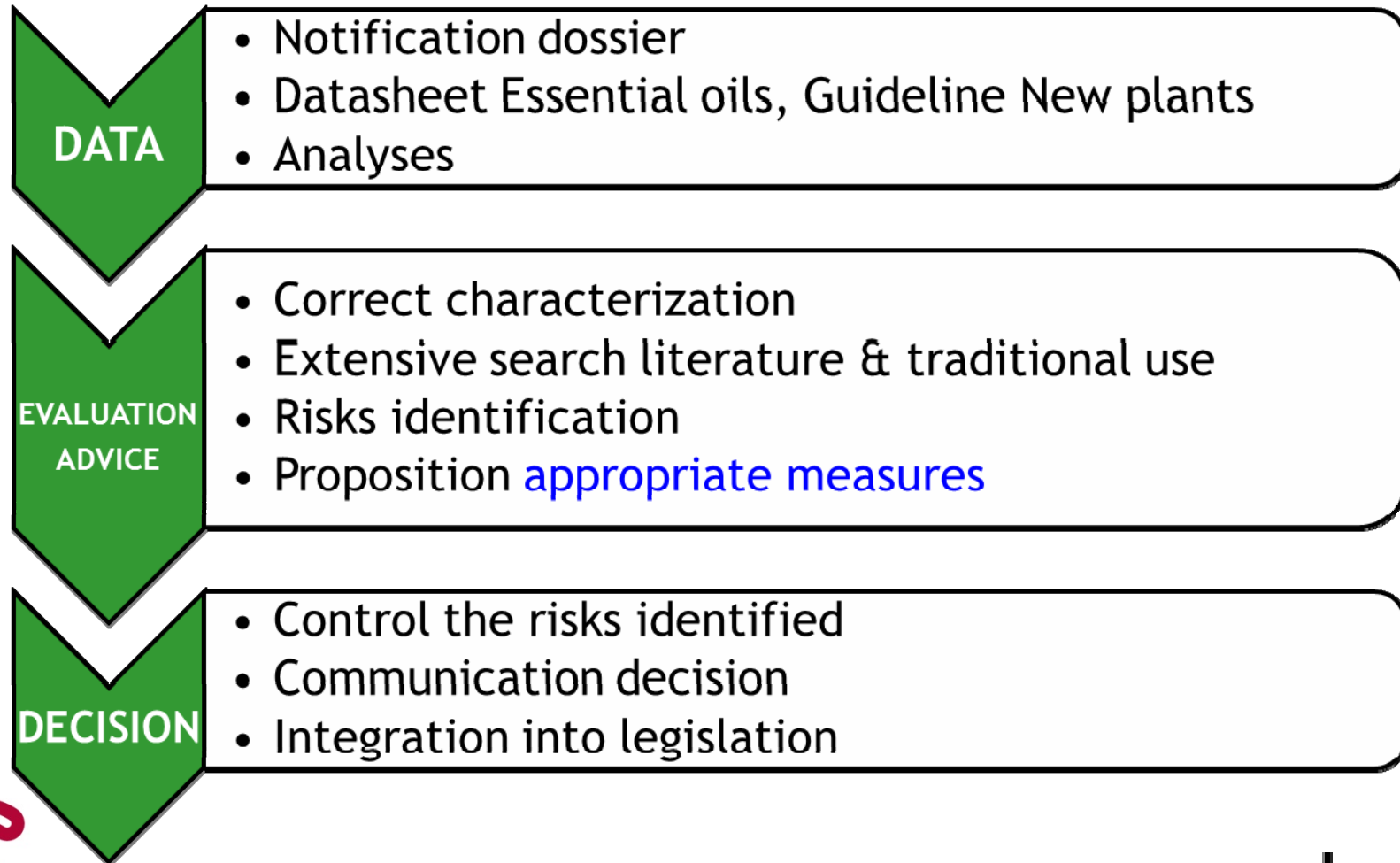


Advice is published online



1.3 Advisory Commission for botanicals

16



1.4 Maximal levels - Substances of concern

17

Dangerous substances known to be present in plant →
Assure not present in botanical preparation

1.Characterization of the botanical

Scientific name, plant part, nature of preparation, CoU

2.Collection of bibliographic data

- National or Int. regulatory bodies or advisory org.: EFSA...
- Recognized standard reference text books
- Monographs, Pharmacopoeia
- Extensive literature search in various scientific databases

3.Collection of information from traditional use



1.4 Maximal levels - Active ingredients

18

Distinction between food & medicine → ECJ cases

- Garlic case: Case-by-case approach, all characteristics
- Red rice case: Dose is key factor
- COM >< ESP: MEDs proven significant pharm. properties
- If **necessary + possible** for “ambivalent” plants (list 3 *)
- Max. level = % of Minimal Daily Therapeutic Dose (MDTD)
obtained after evaluation of clinical trials
- Taking into account all info: TU, EMA monographs...



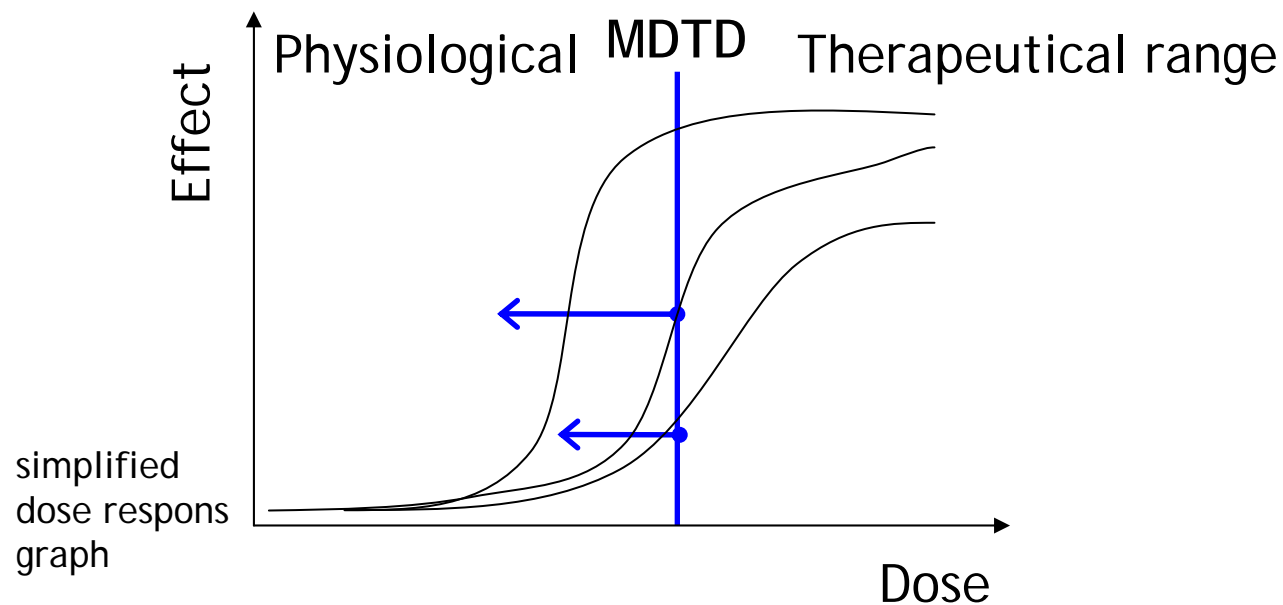
1.4 Maximal levels: MDTD

19

Maximal level = % of Minimal Daily Therapeutic Dose

Higher levels may lead to therapeutic or prophylactic properties

% depending on physiological activity of preparation



1.4 Maximum levels: %

20

- Literature studies

Maximum level = % of Minimal Daily Therapeutic Dose

- 20 % or more depending on physiological activity of preparation

→ -10 % conformity demands - analytical fluctuations

→ -10 % bio-equivalence = 80 % e.g. Echinacea, Valerian

-15 % = 75 % e.g. Hypericum, Ginkgo
Aesculus, Glycine max

→ -20 % safety profile = 70 % e.g. Senna

- No literature studies → Limiting substances with possible negative effect after long-term use



1.4 Mandatory warnings

21

- to ensure a high but proportional level of consumer protection + information
- inform specific target group
- based on case-by-case risk assessment
- available scientific data, EFSA Compendium, monographs
- potentially adverse effects identified
- the extent of scientific uncertainty evaluated
- measures take into account precautionary principle



1.4 Maximal level + Mandatory warnings: example

22

Rheum officinale Baill.

- Plant parts allowed: rhizome, root.
- Maximal level : 25 mg anthrachinones (calculated as rhein)
- Analytical results for each batch of products.
- Mandatory warning of labeling ~
 - "Do not use below 12 years"
 - "No prolonged use without professional advice"
 - "When pregnant or breastfeeding consult your doctor"



2. Harmonization: current situation

23

General Food Law Reg EC 178/2002 General food safety requirements Manufacturer responsibilities Notification duty Recall	Food Supplements Law Dir 2002/46/EC Definition Permitted forms (vitamins/minerals) Maximum levels (vitamins/ minerals) Specific labeling provisions	Food Hygiene Reg EC 853/2004 Rules for hygienic production based on the principles of HACCP Microbiological criteria
Novel Foods Regulation Reg EC 258/97 Pre-marketing approval procedure for novel ingredients	General labelling rules Dir 2000/13/EC How to label content, composition, etc Quantitative ingredient declaration (QUID) Allergen labelling	Health Claims Regulation Reg EC 1924/2006 Pre-marketing approval procedures for nutrition and health claims
Fortification legislation Reg EC 1925/2006 Risk assessment and risk management procedure in case the use of a substance would result in harmful effects	Additives legislation Reg EC 1333/2008 Pre-marketing approval procedures Allowed additives, including sweeteners and colourings Conditions of use	Contaminants Reg EC 1881/2006 Maximum levels of selected contaminants in ingredients that can be used in foods
Pesticides residues Reg EC 396/2005 Maximum residue levels	Extraction solvents Dir 2009/32/EC Permitted extraction solvents	Irradiation Dir 1999/2/EC Permitted ingredients to be irradiated

2. Harmonization

No harmonisation for botanicals at this point

•Variety of risk management measures

- Notification: Label → Extensive dossier
- Lists subst./ plants (Negative / Positive lists)
- Conditions of use (Restrictions, Max. levels)
- Labelling requirements
- Scientific advisory bodies
- Guidance / ...

•Different attitudes

- Established markets based on FS or Meds
- Botanicals considered 'medicinal by function'

NFR?

Mutual
Recognition?

Discrepancies

Uncertainty
Safety &
Quality



2. Harmonization : current situation

- Free movements of goods : Art 34/36 of EU Treaty
- Regulation 764/2008 mutual recognition

MS has to accept on its territory any product lawfully marketed in another Member State.

Unless it can show that there is a danger for health

- Proof of lawfull marketing by competent authorities?
- Not sufficient to govern borderline issues
- Degression to lower level of consumer information & protection



2.1 Harmonization : the BELFRIT project

- Initiative of BELgium, FRance and ITaly
 - Harmonize evaluation of botanicals in food supplements
 - Started 2 years ago
 - Accelerated mutual recognition on a scientific basis
- Authorities besides myself:
 - Guillaume Cousyn (DGCCRF)
 - Bruno Scarpa & Stefania Dalfrà (Ministero della Salute)
 - Experts pharmacognosy:
 - Robert Anton: University of Strasbourg, France
 - Mauro Serafini: Sapienza University, Italy
 - Luc Delmulle: IFAO Proform education, Luxembourg



2.2 BELFRIT : 1st phase

Harmonization of the lists of authorized plants

- Combined 3 lists → BEL: 645, FR: 548, IT: 1182 = +2000 species
- Verify accepted botanical names & synonyms
 - theplantlist.org, ars.grin.gov, experts botanicals garden (Meise)
 - algaebase.org, indexfungorum.org and lichens.ie
- Mention :
 - Synonyms
 - Families (chemo-taxonomical relation)
 - Traditional used plant parts
 - Plant parts of concern
 - Chemicals (substances, markers)
 - Further info (subst., preparations, essential oils, effects...)
 - References
- Advice (to analyse certain substances, safety warnings)



2.2 Harmonization: 1st phase, literature

For each plant literature research was done :
used plant parts, chemistry, preparations, traditional knowledge
side-effects, contra-indications, case-reports...

with

- Standard reference books : Council of Europe, EFSA, AFSSA...
- Monographs: Pharmacopoeia, WHO monographs & guidelines
ESCOP, EMA
- Other references: AFNOR, ISO, ICH....
- Many bibliographic data available
- Data bases: COSING...
- Official advice
- Publications till 2013



2.2 Harmonization: 1st phase, result

Harmonized list (section A): +1000 plants

396 in 3 countries

180 in 2 countries

449 in 1 country

Some plants taken out because:

- No accepted name
- Subspecies, variety or hybrid fall under general species (if chemical profile is similar)

Section B: ~ 150 plants for which more info is needed about:

- Traditional use, ...
- Safety, substances, toxicity



3.2 Harmonization: 1st phase

- Provides a precise identification of the plants = 1st step
- Indicates some key points to control in the production and regulation of PFS
- Takes the traditional knowledge into account
- Based on expert advice
- Can be a pragmatic tool for risk managers and operators, to assure quality and safety of botanical preparations
- It's a 'living' list
- List of other MS could be evaluated
- Plants can be added or taken of depending available info



2.2 Harmonization: publications

4 accompanying articles of experts

→ European Food and Feed Law Review

1. Traditional Knowledge for the Assessment of Health Effects for Botanicals - A Framework for Data Collection" - Issue 2/2012, pp. 74-80

2. The role of Traditional Knowledge in the Safety Assessment of Botanical Food Supplements - Requirements for Manufacturers - Issue: 5/2012, pp. 241-250

3. The Substantiation of Claims for Botanical Food Supplements in Relation to Traditional Use - Issue: 5/2013, pp. 321-328

4. The BELFRIT project - Harmonizing the Use of Plants in Food Supplements in the European Union: Belgium, France and Italy - A first Step - Issue 3/2013, pp. 27-40



2.3 Harmonization : the way forward

- 2012 - 2013 : BELFRIT consultations
 - Drafting of the harmonized list by experts
 - Finalization of harmonized list
 - Meetings with EC, member states, stakeholders
- 2014 - 2015 : Integration into national legislation
 - Further consultation to harmonize conditions
(Maximal levels & mandatory warning)
 - Consultation sector
 - Update the lists
 - Improve exchange of scientific advice
 - Evaluation of other MS lists



3. Conclusions

- Belgian system = proof of concept
Notification / Lists / Advisory Commission
- Applicable framework for botanicals is not adapted
- Harmonization is possible and necessary
 - Coherent policies based on scientific advice
 - Pragmatic approach
 - Appropriate and proportionate measures
 - Taking traditional use into account
 - Assure safety and consumer information
 - Legal security for SMEs



Contact

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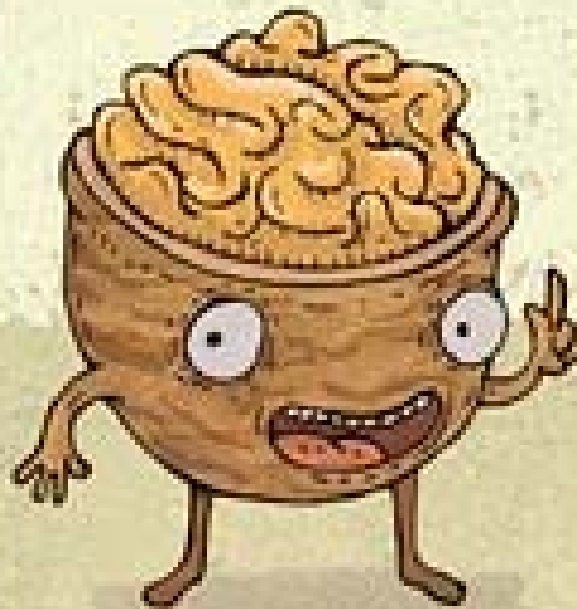
> Food safety > Foodstuffs > Food supplements



I'm a brocolli and
I look like a tree



I'm a walnut and
I look like a brain



I'm a mushroom
and I don't like
this game

