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Botanical Food Supplements
Regulatory Situation in the EU

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Use of Botanicals

- E.g. Garlic

Food

Ingredient

Food Supplement

Medicinal product

Comm. E approval: support to elevated levels of blood lipids and age-dependent vascular changes

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Use of Botanicals

- E.g. Ginger

Ingredient

Food

Cosmetic

Food Supplement

Medicinal product

Comm. E approval: for dyspepsia and prevention of motion sickness

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Use of Botanicals

- E.g. Hawthorn

Ingredient

Food

Food Supplement

Medicinal product

Comm. E states: traditionally to strengthen and invigorate heart and circulatory function

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Content

- Legal framework for food supplements
  - EU law
  - National legislation
  - Mutual recognition
- Issues for botanicals
  - Nutrition and Health Claims
  - Borderline with medicinal products

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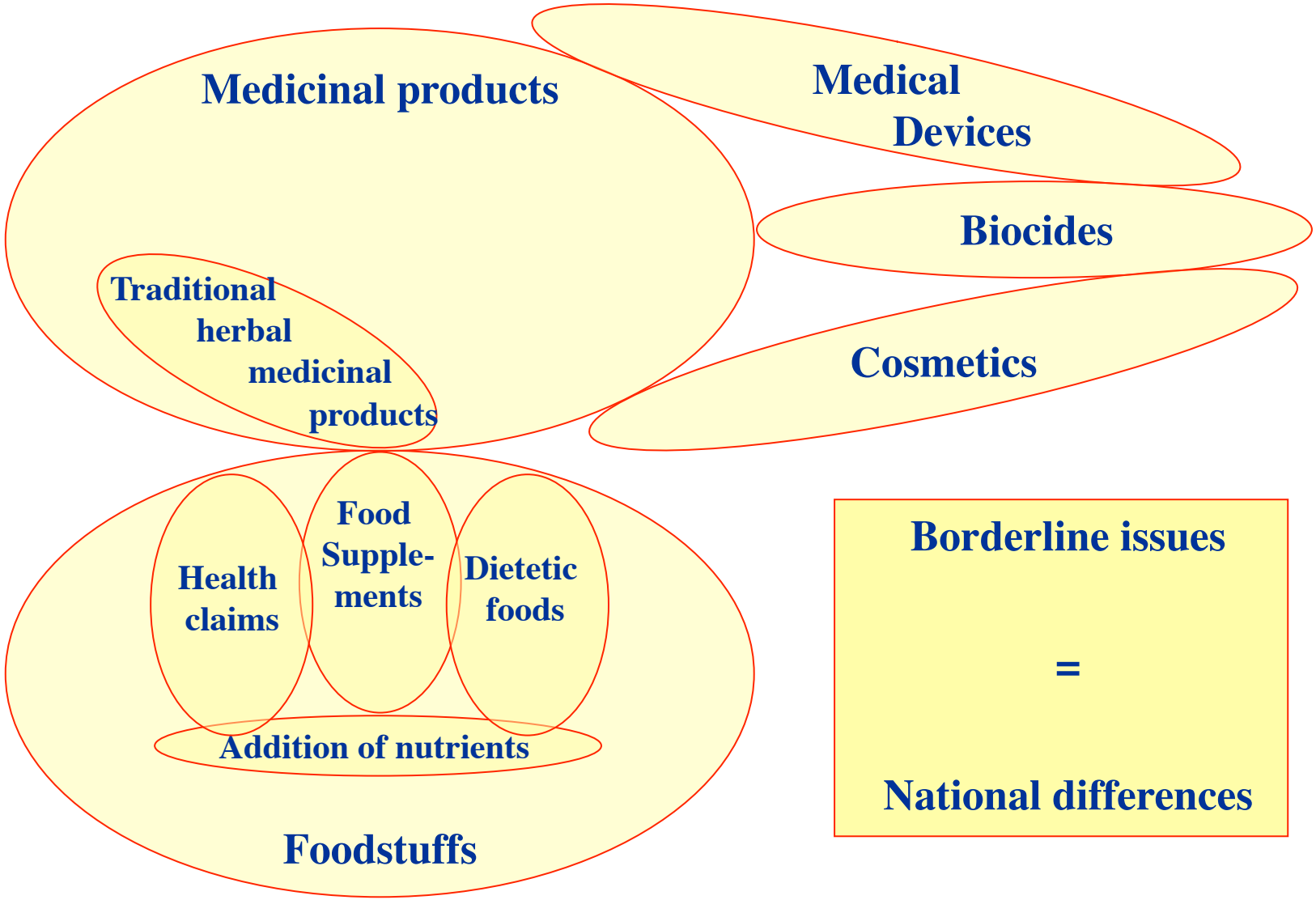
Legal Framework for Botanical Food Supplements


Medicinal products
Medical Devices
Biocides
Traditional herbal medicinal products
Cosmetics
Health claims
Food Supple-ments
Dietetic foods
Addition of nutrients
Foodstuffs
Borderline issues
=
National differences

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Food Supplements Historic perspective

- Until 2002
  - Food supplements were regulated under national law
  - Wide diversity of different rules and approaches

- 2002
  - Food Supplement Directive 46/2002/EC
  - Regulated under Food Law
  - Broad definition of a food supplement to include non-vitamin and mineral ingredients (e.g botanicals)
  - Detailed rules only for vitamin and mineral supplements
  - Subject to a post-marketing notification procedure

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Botanical Food Supplements

- National legislation remains applicable
  - Negative lists / Positive lists / Restrictions or modalities for use / Maximum levels / Specific labelling / ...
- However
  - Mutual Recognition applies (Art 34/36 of EU Treaty)
    - A Member State is obliged to accept on its territory any product lawfully marketed in another Member State
    - Unless it can show that there is a danger for health
    - Regulation 764/2008 (applicable from 13 May 2009)
  - Provisions of Food Law apply
    - General Food Law Regulation
    - Novel Foods Regulation
    - All applicable rules on hygiene, additives, contaminants, etc

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Requirements for food supplements

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/852/2004

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

Dir 89/1007/EEC

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

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Botanical food supplements in the EU

Botanicals & botanical extracts	AUSTRIA	BELGIUM	BULGARIA	CYPRUS	CZECH REPUBLIC	DENMARK	ESTONIA	FINLAND	FRANCE	GERMANY	GREECE	HUNGARY	IRELAND	ITALY	LATVIA	LITHUANIA	LUXEMBOURG	MALTA	NETHERLANDS	POLAND	PORTUGAL	ROMANIA	SLOVAKIA	SLOVENIA	SPAIN	SWEDEN	UNITED KINGDOM
Aloe (*Aloe vera* (L.))	E	✓	E	E	C	L	✓	C	A	C	✖	C	✓	✓	✓	E	✓	✓	✓	✓	✓	✓	C	L/C	✓	✓	C
Ginkgo (*Ginkgo biloba*)	E	L	E	E	L	✓	✖	C	A	✖	✖	L	✖	C	L	E	✓	✓	✓	✓	✓	✓	L	✖	✖	✖	C
Ginseng (*Panax ginseng*)	E	✓	E	E	L	L	✓	C	A	✖	L	L	C	✓	L	E	✓	✓	✓	✓	✓	✓	✓	L	✓	✓	C
Garlic (*Allium sativum* (L.))	✓	✓	E	E	C	✓	✓	✓	A	C	✓	L	C	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	L	✖	✖	C
Green tea extract (*Camellia sinensis*)	E	L/C	E	E	C	E	✓	✓	A	C/A	✓	L	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✖	✓	C
Garcinia extract (*Garcinia cambogia*)	E	✓	E	E	L	✖	C	✓	A	✖	✖	L	✖	✓	✓	E	✓	✓	✓	✓	✓	✓	✓	C	✖	E	✖
Guarana extract (*Paullinia cupana*)	C	✓	E	E	C	L	✓	✓	A	C/A	✖	L	C	✓	L	E	✓	✓	✓	✓	✓	✓	✓	✓	✖	✓	✓

Symbols	
✓	Permitted for use in food supplements either under national law or internal guidelines.
L	Permitted for use in food supplements - maximum **level** established.
C	Permitted for use in food supplements under specific **conditions** (eg type of extract, ingredients combination in the final product, etc)
E	Permission may be given on a case by case basis following **evaluation**, considering issues such as ingredient function.
A	Not currently pemitted. May be permitted following a pre-marketing **authorisation**.
✖	Not permitted for use in food supplements, or regarded as medicinal.

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Botanical food supplements in the EU

Botanicals & botanical extracts	AUSTRIA	BELGIUM	BULGARIA	CYPRUS	CZECH REPUBLIC	DENMARK	ESTONIA	FINLAND	FRANCE	GERMANY	GREECE	HUNGARY	IRELAND	ITALY	LATVIA	LITHUANIA	LUXEMBOURG	MALTA	NETHERLANDS	POLAND	PORTUGAL	ROMANIA	SLOVAKIA	SLOVENIA	SPAIN	SWEDEN	UNITED KINGDOM
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Ginkgo (*Ginkgo biloba*)	E	L	E	E	L	✓	✖	C	A	✖	✖	L	✖	C	L	E	✓	✓	✓	✓	✓	✓	L	✖	✖	✖	C
Ginseng (*Panax ginseng*)	E	✓	E	E	L	L	✓	C	A	✖	L	L	C	✓	L	E	✓	✓	✓	✓	✓	✓	✓	L	✓	✓	C
Garlic (*Allium sativum* (L.))	✓	✓	E	E	C	✓	✓	✓	A	C	✓	L	C	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	L	✖	✖	C
Green tea extract (*Camellia sinensis*)	E	L/C	E	E	C	E	✓	✓	A	C/A	✓	L	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✖	✓	C
Garcinia extract (*Garcinia cambogia*)	E	✓	E	E	L	✖	C	✓	A	✖	✖	L	✖	✓	✓	E	✓	✓	✓	✓	✓	✓	✓	C	✖	E	✖
Guarana extract (*Paullinia cupana*)	C	✓	E	E	C	L	✓	✓	A	C/A	✖	L	C	✓	L	E	✓	✓	✓	✓	✓	✓	✓	✓	✖	✓	✓

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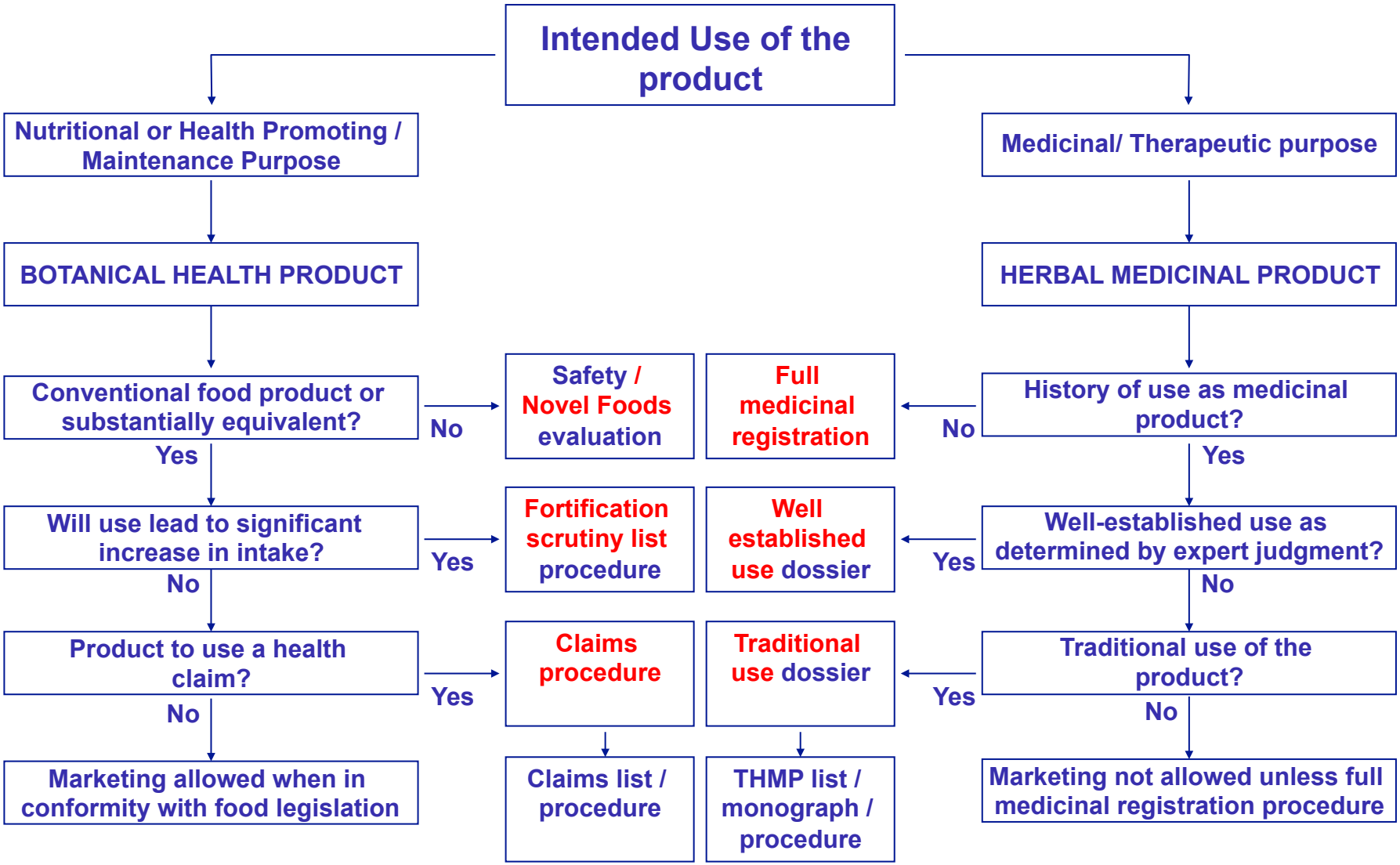
Intended Use of the product
Nutritional or Health Promoting / Maintenance Purpose
Medicinal/ Therapeutic purpose
BOTANICAL HEALTH PRODUCT
HERBAL MEDICINAL PRODUCT
Conventional food product or substantially equivalent?
No
Safety / Novel Foods evaluation
Full medicinal registration
No
History of use as medicinal product?
Yes
Yes
Will use lead to significant increase in intake?
Yes
Fortification scrutiny list procedure
Well established use dossier
Yes
Well-established use as determined by expert judgment?
No
No
Product to use a health claim?
Yes
Claims procedure
Traditional use dossier
Yes
Traditional use of the product?
No
No
Marketing allowed when in conformity with food legislation
Claims list / procedure
THMP list / monograph / procedure
Marketing not allowed unless full medicinal registration procedure

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Conclusion

- Botanical food supplements are subject to the extensive requirements of food law ensuring their safe and effective use
- Safety is covered by
  - General Food Law requirements
  - Novel foods legislation
  - Hygiene rules
  - Residues and contaminants legislation
- Specific rules for the use of botanicals and other ingredients are not harmonised but subject to national law
  - Negative and positive lists
  - Conditions of use

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Further Harmonisation ?

- EC Report 2008
  - Further harmonisation is not feasible
    - Too many national differences
    - Scientific and methodological difficulties to be overcome
  - Further harmonisation is not necessary
    - Full food law framework is applicable
      - Legislation covers many aspects
    - Application of new legislation
      - Reg 1924/2006 Nutrition and Health Claims
      - Reg 1925/2006 Addition of Nutrients
      - Reg 258/1997 Novel foods
    - Mutual Recognition

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Nutrition and Health Claims

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Regulation 1924/2006

- Pre-marketing approval for all Health Claims
  - General function claims
    - Establishment of a generic list
  - Function claims based on new scientific evidence or with a request for the protection of proprietary data
    - Application for approval (Article 18 procedure)
  - Reduction of disease risk claims and Claims relating to children's development and health
    - Application for approval (Article 14 procedure)
- Scientific assessment of Health Claims
  - By the European Food Safety Authority (EFSA)

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Outcome so far

- Article 13
  - Many claims for essential nutrients (Vitamins / Minerals / Fatty acids)
  - Few claims for other substances (Probiotics, Botanicals, Lutein, Glucosamine)
  - No positive opinions for botanicals
- Article 13.5
  - Only two positive opinions
- Article 14
  - Few positive opinions (e.g. Phytosterols, Chewing gum and Calcium, DHA)

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Reasons

- Chaotic management of the Article 13 process
  - Over 44.000 submissions
- Lack of guidance
- Poor quality of many submissions
- Many claims rejected because of formalistic reasons
  - Strong focus on the details of the application
- EFSA requires Human intervention trials
  - Demonstrating measurable effects on validated end-points or biomarkers within a healthy population
  - The value of traditional use is not recognised

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Traditional Use

- Traditional Herbal Medicinal Products (Dir 2004/24)
  - No proof of efficacy needed
    - if on the market for 30 years (15 in EU)
    - " Having regard to [...] especially their long tradition, it is desirable to provide a special, simplified registration procedure [to] be used only where no marketing authorisation can be obtained pursuant to Directive 2001/83/EC, in particular because of a lack of sufficient scientific literature demonstrating a well-established medicinal use with recognised efficacy and an acceptable level of safety. "
    - " The long tradition [...] makes it possible to reduce the need for clinical trials, in so far as the efficacy of the medicinal product is plausible on the basis of long-standing use and experience. "
- Nutrition and Health Claims rules (Reg 1924/2006)
  - No consideration of Traditional use
  - Botanicals taken out of the claims process (September 2010)

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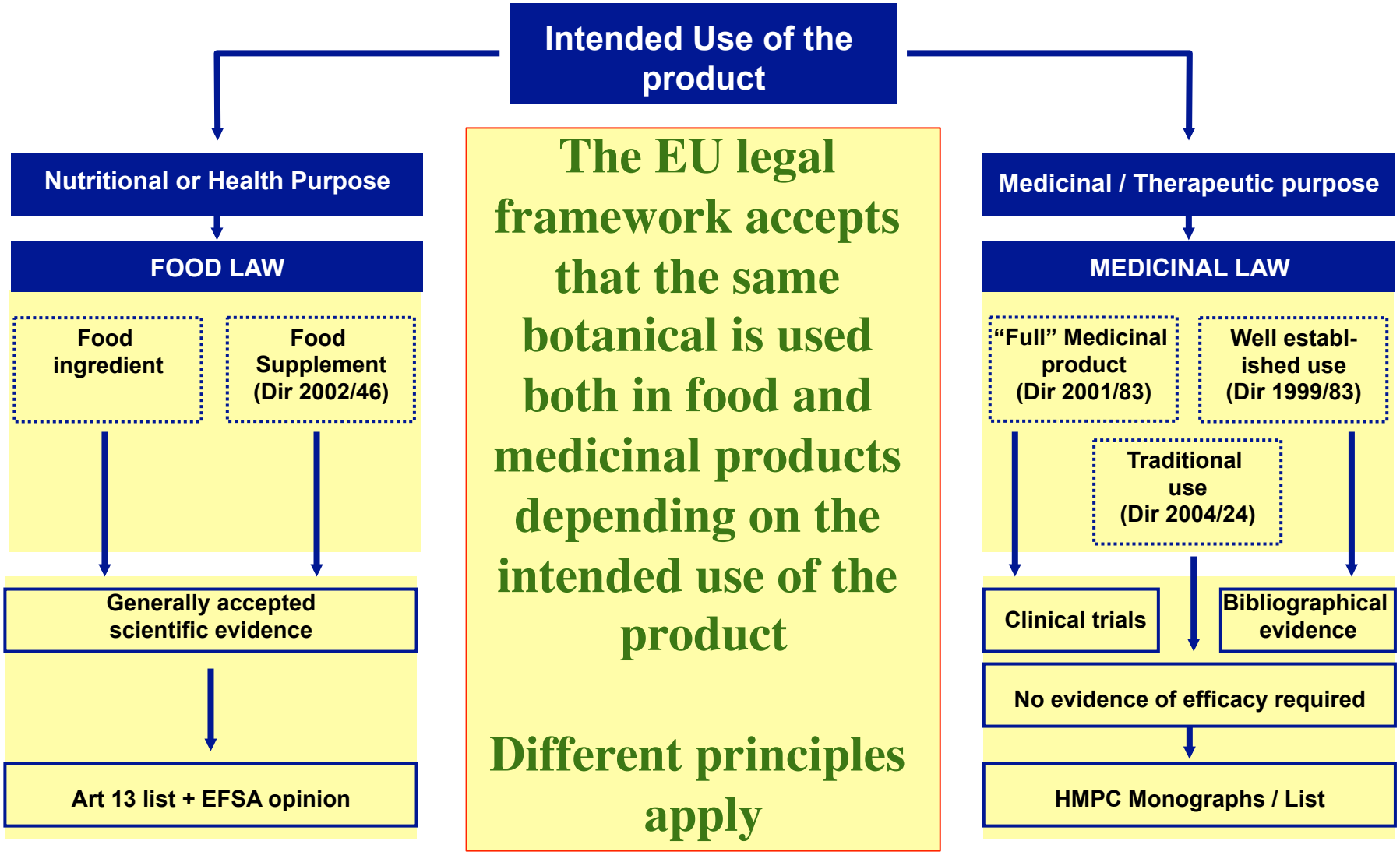
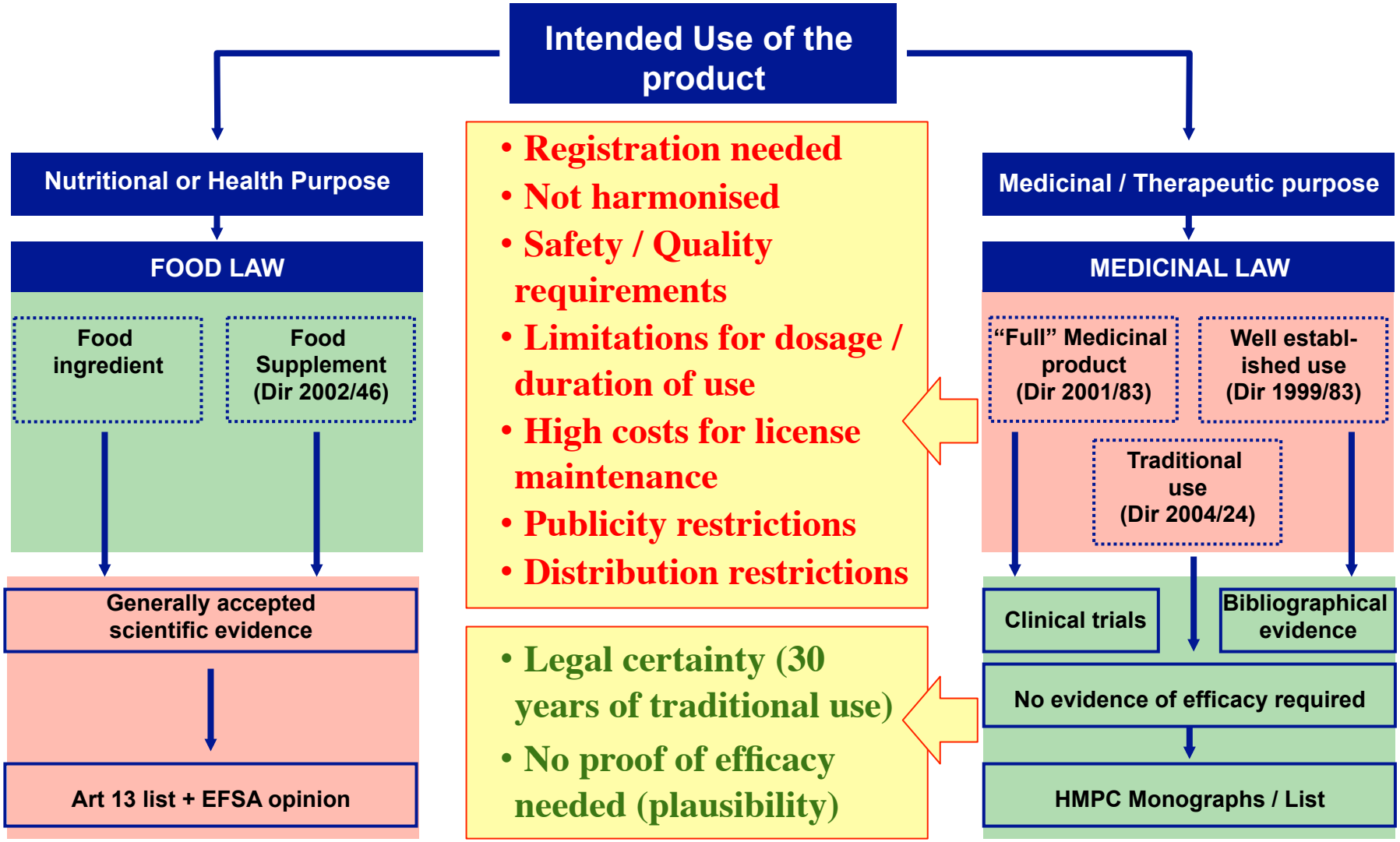
Borderline with medicinal products


Intended Use of the product
Nutritional or Health Purpose
FOOD LAW
Food ingredient
Food Supplement (Dir 2002/46)
Generally accepted scientific evidence
Art 13 list + EFSA opinion
The EU legal framework accepts that the same botanical is used both in food and medicinal products depending on the intended use of the product
Different principles apply
Medicinal / Therapeutic purpose
MEDICINAL LAW
"Full" Medicinal product (Dir 2001/83)
Well establ-ished use (Dir 1999/83)
Traditional use (Dir 2004/24)
Clinical trials
Bibliographical evidence
No evidence of efficacy required
HMPC Monographs / List


Intended Use of the product
Nutritional or Health Purpose
FOOD LAW
Food ingredient
Food Supplement (Dir 2002/46)
Generally accepted scientific evidence
Art 13 list + EFSA opinion
• Registration needed
• Not harmonised
• Safety / Quality requirements
• Limitations for dosage / duration of use
• High costs for license maintenance
• Publicity restrictions
• Distribution restrictions
• Legal certainty (30 years of traditional use)
• No proof of efficacy needed (plausibility)
Medicinal / Therapeutic purpose
MEDICINAL LAW
"Full" Medicinal product (Dir 2001/83)
Well establ-ished use (Dir 1999/83)
Traditional use (Dir 2004/24)
Clinical trials
Bibliographical evidence
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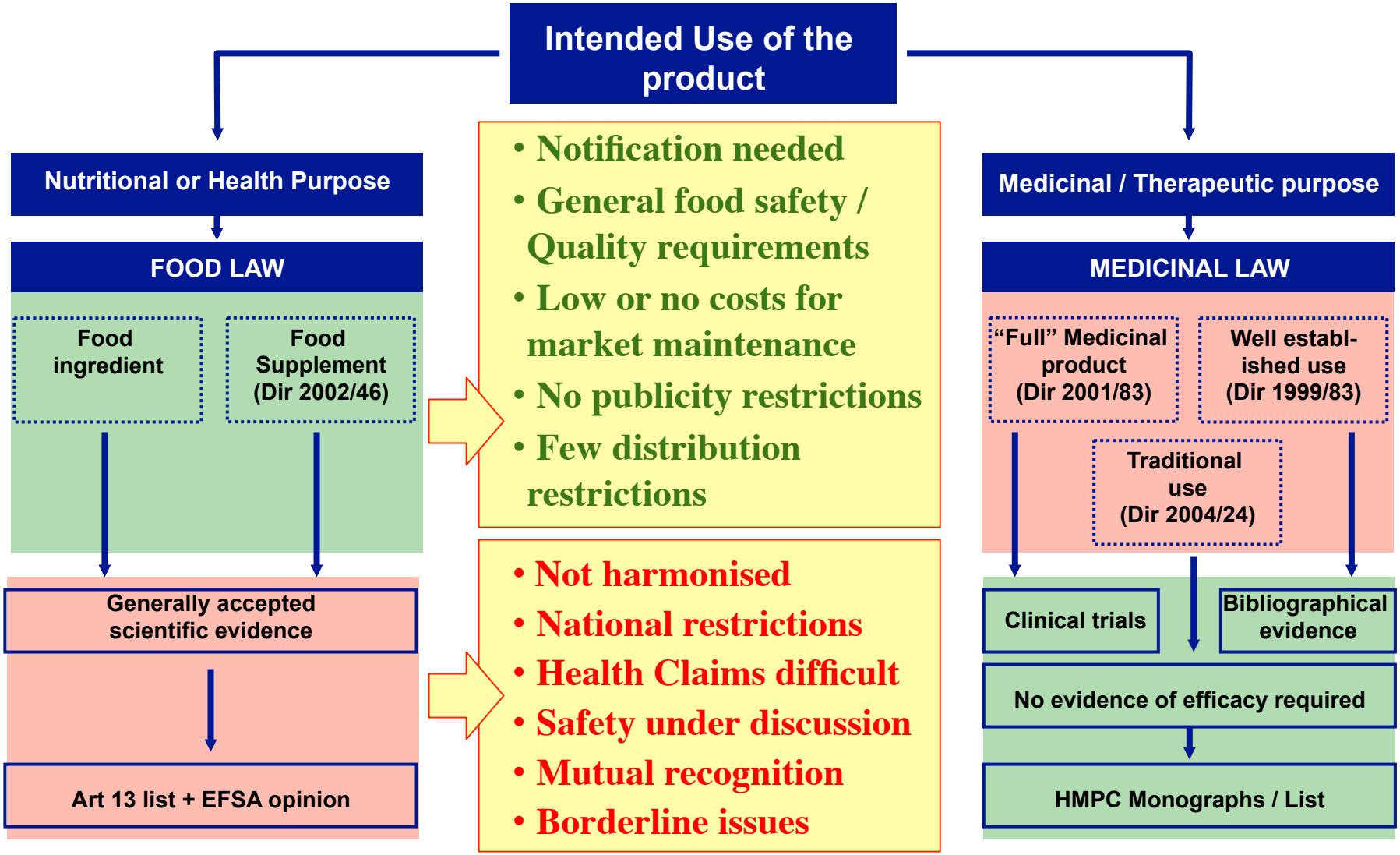
Intended Use of the product
Nutritional or Health Purpose
FOOD LAW
Food ingredient
Food Supplement (Dir 2002/46)
Generally accepted scientific evidence
Art 13 list + EFSA opinion
• Notification needed
• General food safety / Quality requirements
• Low or no costs for market maintenance
• No publicity restrictions
• Few distribution restrictions
• Not harmonised
• National restrictions
• Health Claims difficult
• Safety under discussion
• Mutual recognition
• Borderline issues
Medicinal / Therapeutic purpose
MEDICINAL LAW
"Full" Medicinal product (Dir 2001/83)
Well establ-ished use (Dir 1999/83)
Traditional use (Dir 2004/24)
Clinical trials
Bibliographical evidence
No evidence of efficacy required
HMPC Monographs / List

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Frameworks are Mutually Exclusive

- Food Legislation
  - General Food Law (Reg 178/2002)
    - " Food shall not include Medicinal Products "

- Medicinal Product Legislation
  - Medicinal product Directive (Dir 2001/83):
    - " Where a product comes clearly under the definition of other product categories, in particular food, food supplements, [...] this Directive should not apply "
  - Traditional Herbal Medicinal Product Directive (Dir 04/2004)
    - " This Directive allows non-medicinal herbal products, fulfilling the criteria of food legislation, to be regulated under food legislation in the Community "

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Medicinal Law

- Definition by virtue of Presentation
  - « any substance or combination of substances presented as having properties for treating or preventing disease in human beings »
  - Only refers to treating or preventing disease in human beings

- Definition by virtue of Function
  - « any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action [...] »
  - "modifying physiological functions" vs. "beneficial nutritional or physiological effect" ?

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Medicinal Law

- Medicinal product legislation (Article 2.b of Dir 2001/83)
  - « In cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a "medicinal product" and within the definition of a product covered by other Community legislation the provisions of this Directive shall apply »
  - Superiority of medicinal law, but applies only
    - To individual products: Medicinal law is products-specific licensing; "medicinal by function" is contrary to this principle
    - In cases of doubt and requires a case-by-case assessment
    - All the product's characteristics need to be considered, not only its conformity with the definition
  - And subject to review by the Courts

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ECJ Case Law

- Art 2.b. : In line with ECJ Case law
  - " [...] it is for the national authorities to determine, subject to review by the courts, for each product, having regard to all of its characteristics, in particular its composition, its pharmacological properties as they may be ascertained in the current state of scientific knowledge, the way in which it is used, the extent to which it is sold, its familiarity to the consumer and the risks which its use might entail, whether or not it constitutes a medicinal product within the meaning of the definition set out in Article 1 (2) of [the medicinal product Directive] "

- Consequence:
  - as long as rules for Food Supplements are not harmonised, it is possible that a given product is considered as a medicinal product by one Member State and as a Food Supplement by another
  - However, the ECJ has set criteria for the assessment of the status

ECJ Case Law

- Presentation criterion: Broad interpretation
  - Must cover all products, also those with no demonstrated efficacy
- Function criterion: Narrow interpretation
  - "Physiological effect" is not specific to medicinal products but is also among the criteria used for the definition of food supplement
  - In order to preserve the effectiveness of that criterion, it is not sufficient that product has properties beneficial to health in general, but it must strictly speaking have the function of treating or preventing disease
  - Medical purpose or therapeutic effect must be present
    - Cfr. article 26: medicinal licence to be refused if therapeutic efficacy is lacking or is insufficiently substantiated

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Conclusion

- The EU legal framework accepts the use of the same botanicals in both foods and medicinal products
- Both legal frameworks are mutually exclusive. However, in case of doubt, medicinal law applies
- The ECJ has established extensive case law to differentiate between food and medicinal use
  - National authorities are competent to decide
  - Assessment must be carried out on a case-by-case basis
  - It must take all the product's characteristics into account
  - A medicinal/therapeutic pharmacological property must be established

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Thank you for your attention

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