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Botanicals on the EU market: a journey among Herbal Medicinal Products, Food Supplemements and Medical Devices

Anna Rita Bilia, Department of Chemistry

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Botanical materials (e.g. whole, fragmented or cut plants, algae, fungi, lichens) and

botanical preparations obtained from these materials by various processes (e.g. extraction, distillation, purification, concentration and fermentation)

may be used for the production of

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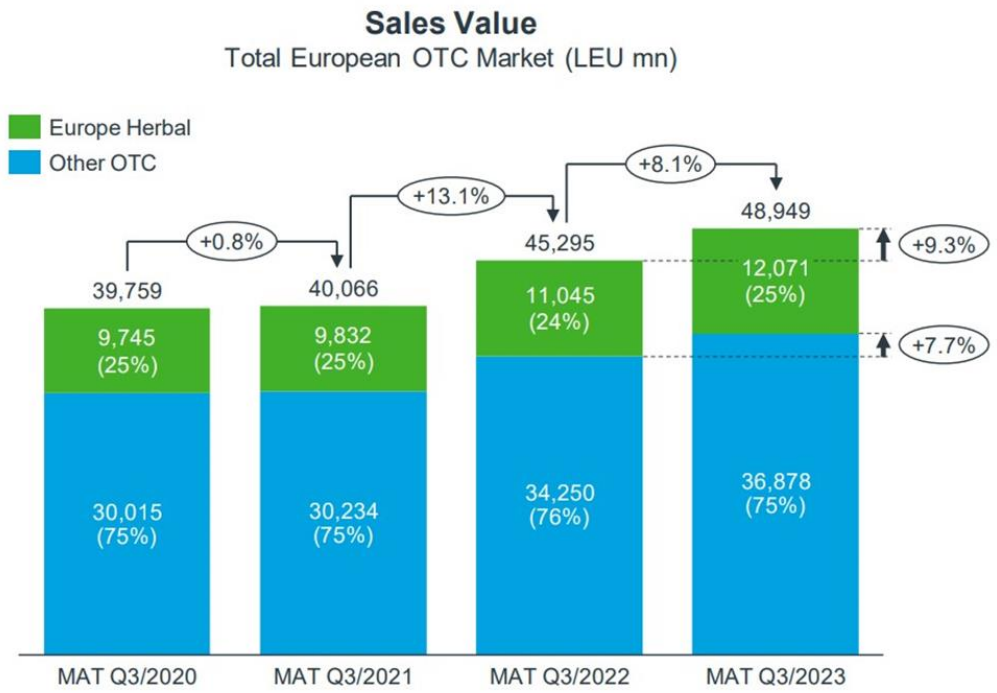
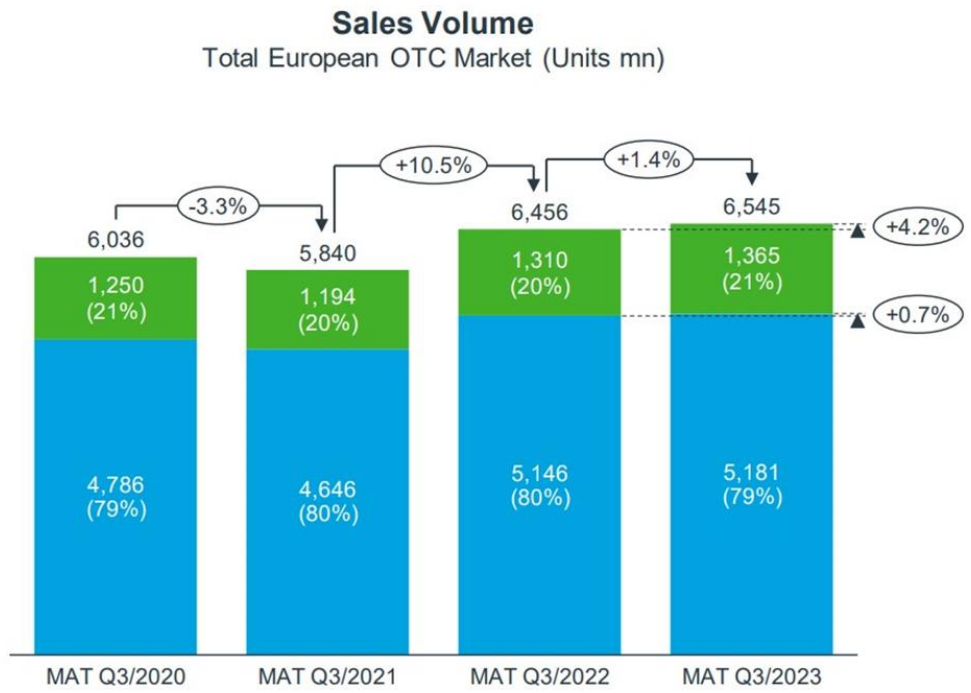
The share of herbal market in the total OTC market is stable while sales value significantly grows in 2022 and 2023

European Herbal Market Sales Value and Volume





Source: CH Customized Insights and CH Customized Insights Herbal Database, only OTC (1-19, 97), value based on LEU PUB, MAT Q3/2023

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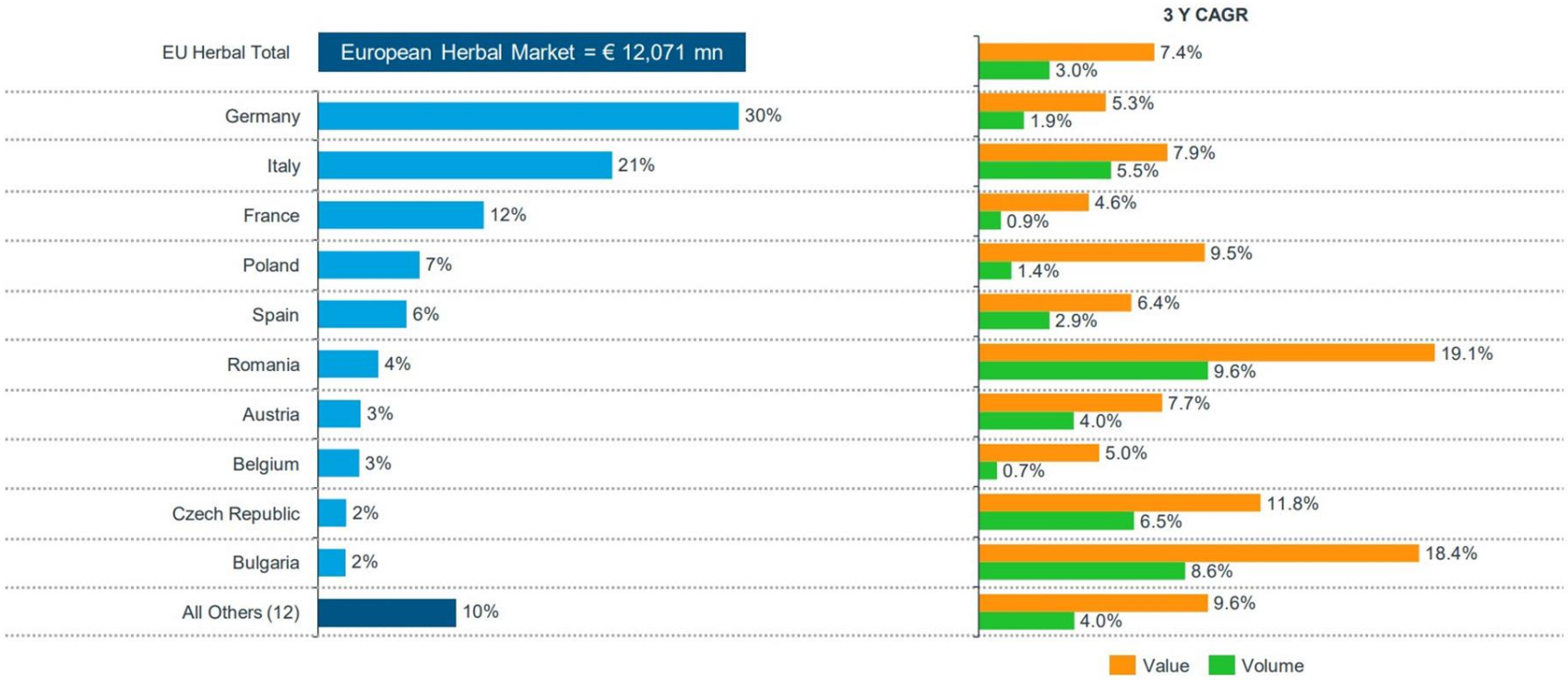
Thomas Heil. Personal communication
Vice President Consumer Health, IQVIA
thomas.heil@iqvia.com

Germany and Italy together account for half of the EU herbal market which is growing across all countries

Value Share by Country in %, Value and Volume Growth vs. PY & 3-Year CAGR



Source: CH Customized Insights Herbal Database, Value based on LEU PUB, MAT Q3/2023

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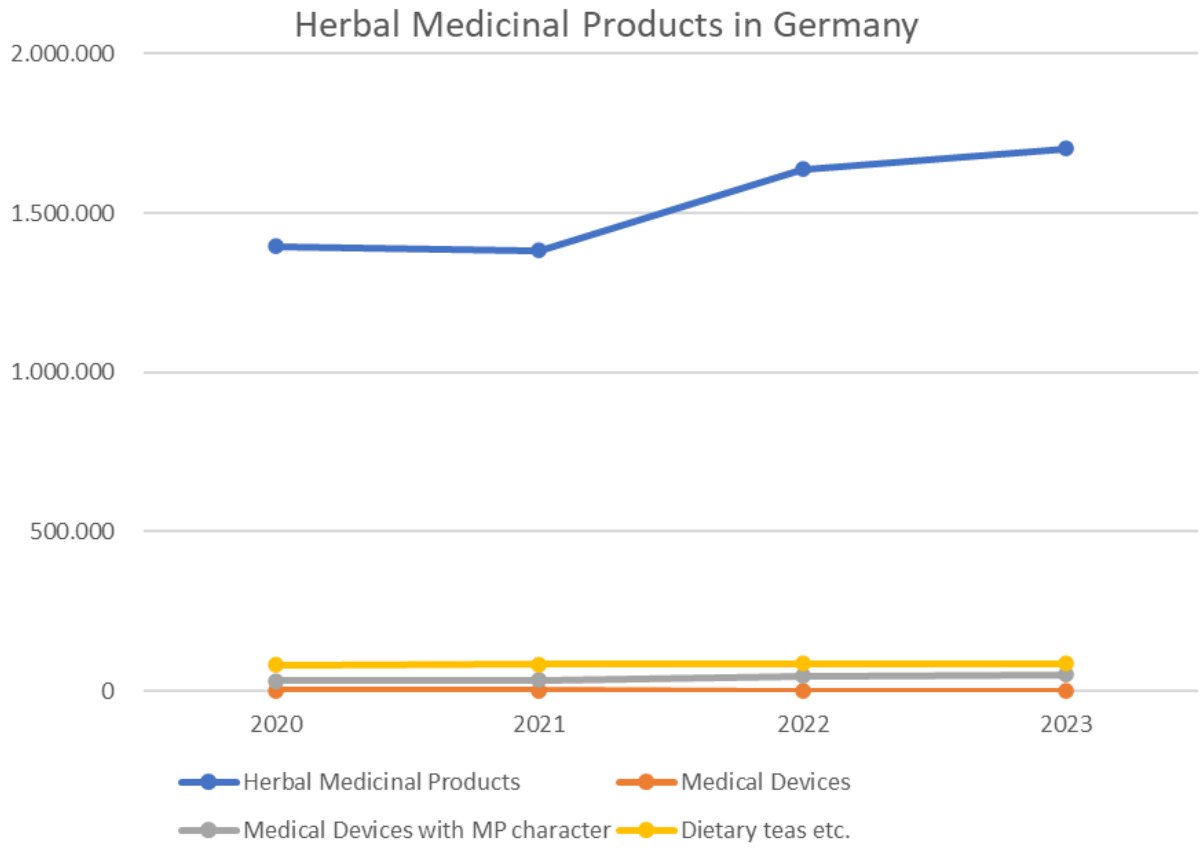
Herbal Medicinal Products - Market Figures



Eurostat (2024), ITC Trademap (2024)

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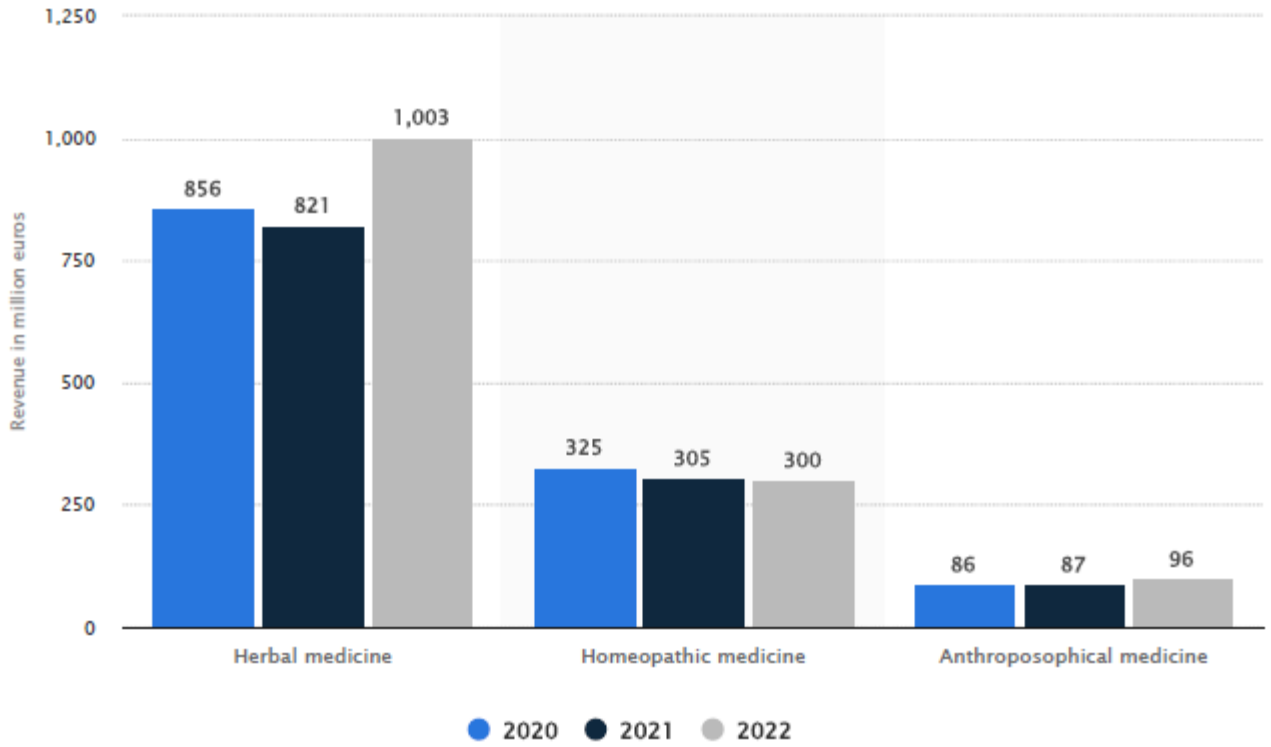
Revenues from herbal and homeopathic medicine in pharmacies in Germany from 2020 to 2022(in million euros)



https://www.statista.com/statistics/593315/herbal-homeopathic-medicine-revenues-pharmacies-germany/

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STATE OF ART OF HMPs

Phytopharmaka	zugelassen	nachzugelassen	Summe
Monopräparate	491	237	728
Kombinationspräparate	64	80	144
Summe	555	317	**872**

nach § 39a-d AMG	Registriert
Monopräparate	168
Kombinationspräparat	116
Summe	**284**

BfArM webpage (28 February 2024)

- **872 Marketing Authorizations for HMPs (mono 728, combination 144)**
- **284 Registrations for THMPs (mono 168, combination 116)**

- **56 HMPs**

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Germany: At the centre of herbal medicinal products in Europe

Italy is the leading food supplement market in Europe.

- In 2023, this market was worth €3.98 billion. In 2023-2028,the market is expected to grow at an annual rate of 5.54%, reaching a value of €5.22 billion. Pharmacies are the main distribution channel, selling around 80% of food supplements
- According to Ipsos market research, Italian consumers use food supplements to feel fitter (87%) and because they feel the need to take care of their body (84%)
- According to a report by the Italian Federation of Herbal Medicine Industries, the Italian herbal product market amounted to €2.9 billion in 2022, which represents an increase of 16.2% from 2019

CBI is the Centre for the Promotion of Imports from developing countries https://www.cbi.eu/

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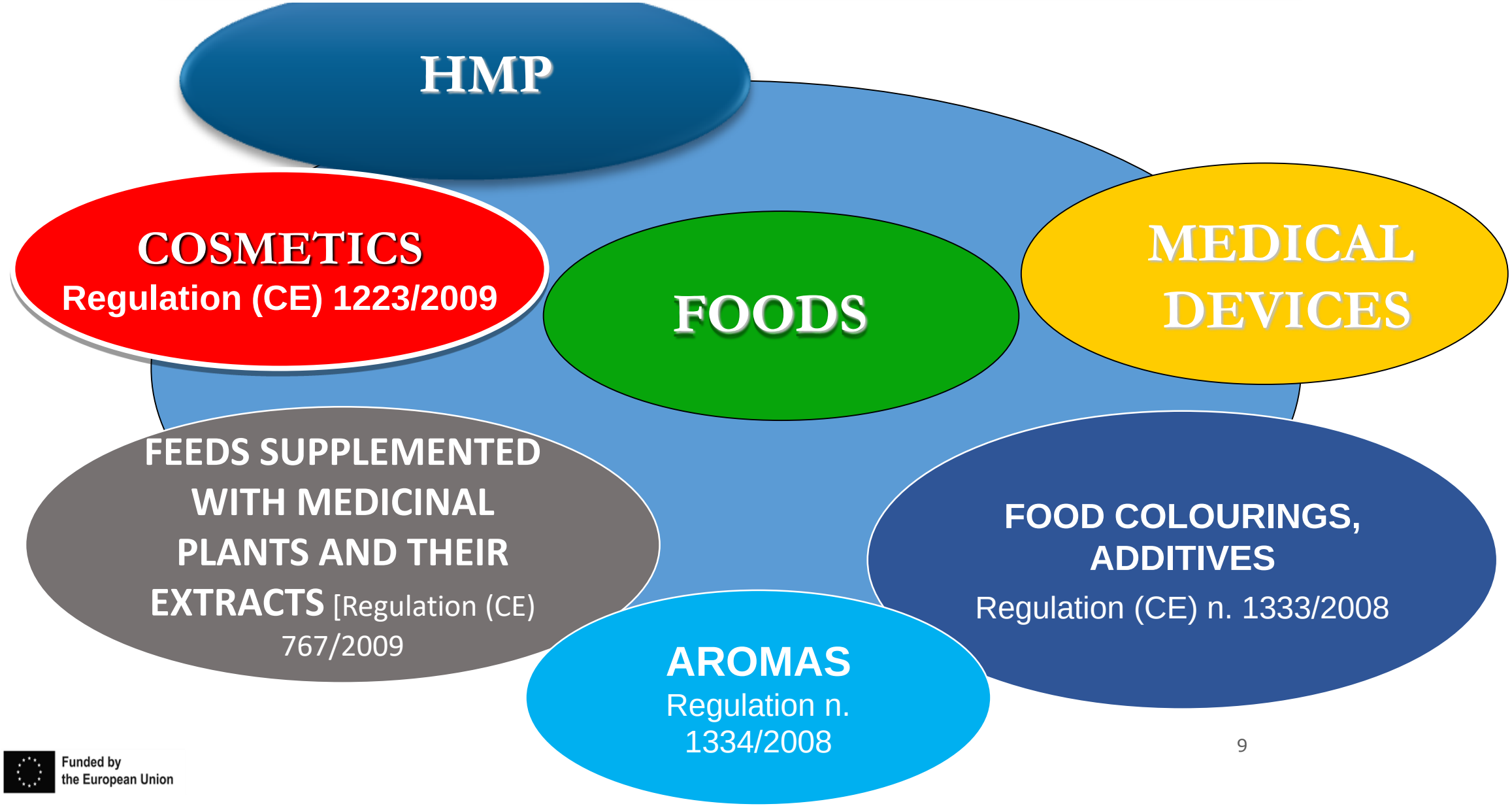
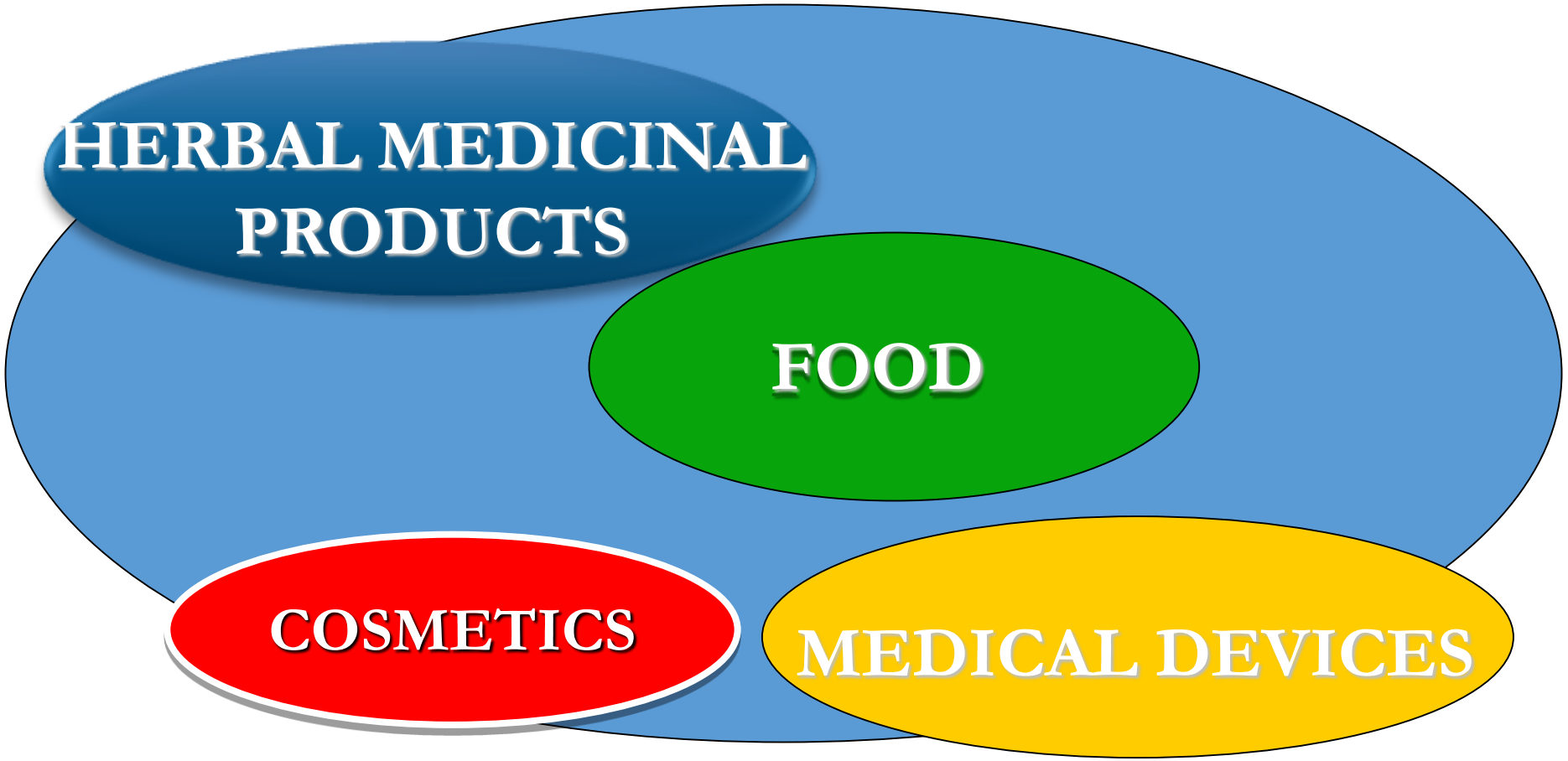
BOTANICALS


HMP
COSMETICS
Regulation (CE) 1223/2009
FOODS
MEDICAL DEVICES
FEEDS SUPPLEMENTED WITH MEDICINAL PLANTS AND THEIR EXTRACTS [Regulation (CE) 767/2009
FOOD COLOURINGS, ADDITIVES
Regulation (CE) n. 1333/2008
AROMAS
Regulation n. 1334/2008

BOTANICALS



CLASSIFICATION IS BASED ON PRESENTATION

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THMPs
WE-HMPs
FSs
HMPs
A JUNGLE
Homeopathic remedies
MDs
Functional Food
Cosmetics
Novel Food

Regulatory aspects of botanicals in the EC

As foodstuffs, cosmetics, medical devices and medicinal products are subjected to different regulatory frameworks, from a juridical point of view, it is therefore very important to first of all clarify, in each single case, whether the botanical in question is to be qualified as a foodstuff, a cosmetic product, a medical device or a medicinal product.

The legal definitions of the above products have been taken into an account at a Community level.

EXTRACT OF CENTELLA

medicinal products

dietary supplements

medical devices

cosmetic products

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WHAT IS AN HERBAL MEDICINAL PRODUCT

Herbal medicinal product: any medicinal product containing exclusively as **active ingredients one** or more herbal **substances** or one or more **herbal preparations.**..

Plant substances: All **plants** mainly whole, fragmented or cut, **plant parts,** algae, fungi, lichens in unprocessed form, usually dried, but sometimes fresh. ...

Herbal preparations: preparations obtained by subjecting herbal substances to treatments such as **extraction, distillation**, pressing, fractionation, purification, concentration or fermentation.

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Pharm. Eur.

Herbal drugs are plants or part of plants in an unprocessed state, which are used for a medicinal or pharmaceutical purpose.
A herbal drug or a preparation thereof is regarded as one active substance in its entirety whether or not the constituents with therapeutic activity are known.

Herbal drug preparations are comminuted or powdered herbal drugs, extracts, tinctures, fatty or essential oils, expressed juices, processed resins or gums, etc...prepared from herbal drugs, and preparations whose production involves a fractionation, purification or concentration process. However, chemically defined isolated constituents or their mixture are not herbal drug preparations.

EMA

Herbal Substances All mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried, form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author).

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Herbal Preparations are Herbal Drug Preparations

HERBAL DRUGS

Plantae medicinales

DEFINITION

Herbal drugs are mainly whole, fragmented, or broken plants, parts of plants, algae, fungi or lichen, in an unprocessed state, usually in dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal drugs. Herbal drugs are precisely defined by the botanical scientific name according to the binominal system (genus, species, variety and author).

Whole describes a herbal drug that has not been reduced in size and is presented, dried or undried, as harvested; for example: dog rose, bitter fennel or sweet fennel, Roman chamomile flower.

Fragmented describes a herbal drug that has been reduced in size after harvesting to permit ease of handling, drying and/or packaging; for example: cinchona bark, rhubarb, passion flower.

Broken describes a herbal drug in which the more-fragile parts of the plant have broken during drying, packaging or transportation; for example: belladonna leaf, matricaria flower, hop strobile.

Cut describes a herbal drug that has been reduced in size, other than by powdering, to the extent that the macroscopic description in the monograph of the herbal drug can no longer be applied. When a herbal drug is cut for a specific purpose that results in the cut herbal drug being homogeneous, for example when cut for herbal teas, it is a herbal drug preparation. Certain cut herbal drugs processed in this way may be the subject of an individual monograph.

A herbal drug that complies with its monograph and is subsequently cut for extraction shall comply in its cut form, except for its macroscopic description, with the monograph for that herbal drug, unless otherwise justified.

he term *herbal drug* is synonymous with the term *herbal bstance* used in European Community legislation on herbal medicinal products.

HERBAL DRUG PREPARATIONS

Plantae medicinales praeparatae

DEFINITION

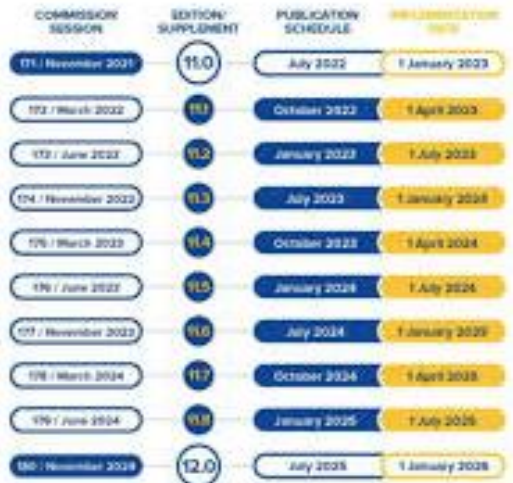
Herbal drug preparations are homogeneous products obtained by subjecting herbal drugs to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation.

Herbal drug preparations include, for example, extracts, essential oils, expressed juices, processed exudates, and herbal drugs that have been subjected to size reduction for specific applications, for example herbal drugs cut for herbal teas or powdered for encapsulation.

Herbal teas comply with the monograph *Herbal teas (1435)*.

NOTE: the term *comminuted* used in European Community legislation on herbal medicinal products describes a herbal drug that has been either cut or powdered.

The term *herbal drug preparation* is synonymous with the term *herbal preparation* used in European Community legislation on herbal medicinal products.



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Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use

Article 1

Directive 2001/83/EC is hereby amended as follows:

1) Article 1 shall be amended as follows:

(a) point 1 shall be deleted;

(b) point 2 shall be replaced by the following:

"2. **Medicinal product: (a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or**

(b) 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, or to making a medical diagnosis."

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DIRECTIVE 2004/27/CE replacing DIRECTIVE 2001/83/CE (and previous 65/65/CE)

Herbal Medicinal Products (HMP)

HMPs are medicinal products and consequently fall within the scope of the Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, formerly 65/65/ECC , as amended by Directive 2004/27/EC foresees that their marketing requires an ad hoc authorization to be granted on the basis of results of tests and experimentations concerning quality, safety and efficacy.

The definition of medicinal products by the Directive 2004/27/EC is BY 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, or to making a medical diagnosis" **or BY PRESENTATION** "Any substance or combination of substances presented as having properties for treating or preventing disease in human beings".

VALIDITY in THERAPEUTIC INTERVENTION

TREATABLE PATHOLOGY

QUALITY
PURITY

CORRECT HERBAL DRUG

CORRECT SYNTHETIC DRUG

EFFICIENT

EFFICIENT DOSAGE
APPROPRIATE PHARMACEUTICAL FORM

SAFETY

ABSENCE OF SIDE EFFECTS

PHARMACOVIGILANCE

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HERBAL MEDICINAL PRODUCTS

HMPs

Are medicinal products containing as active substances exclusively

HERBAL DRUGS
or
HERBAL DRUG PREPARATIONS

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Report from the Ad Hoc Working Group on Herbal Medicinal Products 1997/98

Willow bark

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Willow bark extract

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2

Willow bark extract formulation

3

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Aspirin

4

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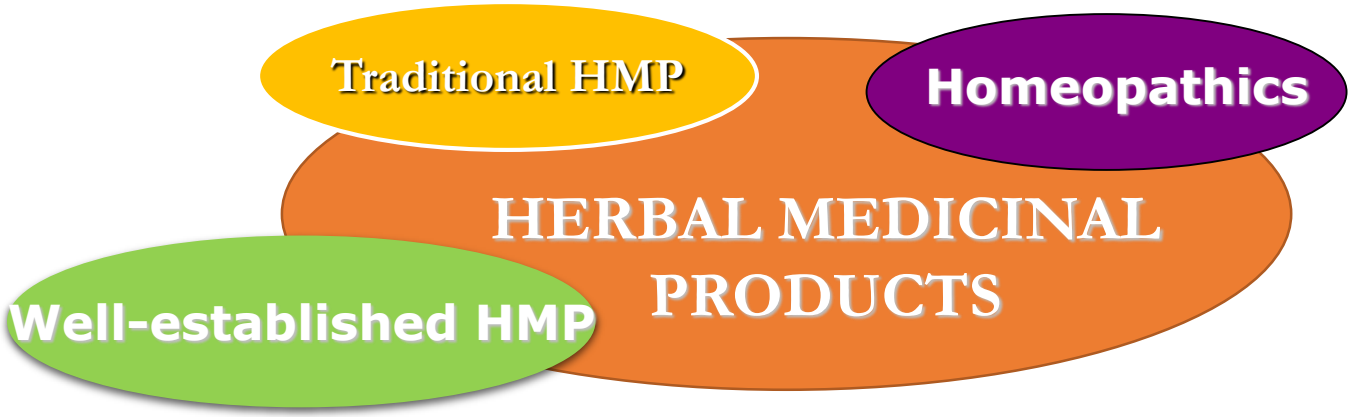
Aspirina

Bayer

6

HMPs are defined as “any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations”.

Herbal Medicinal Products registered by full or simplified registration procedures are automatically linked to pharmacy-only status.



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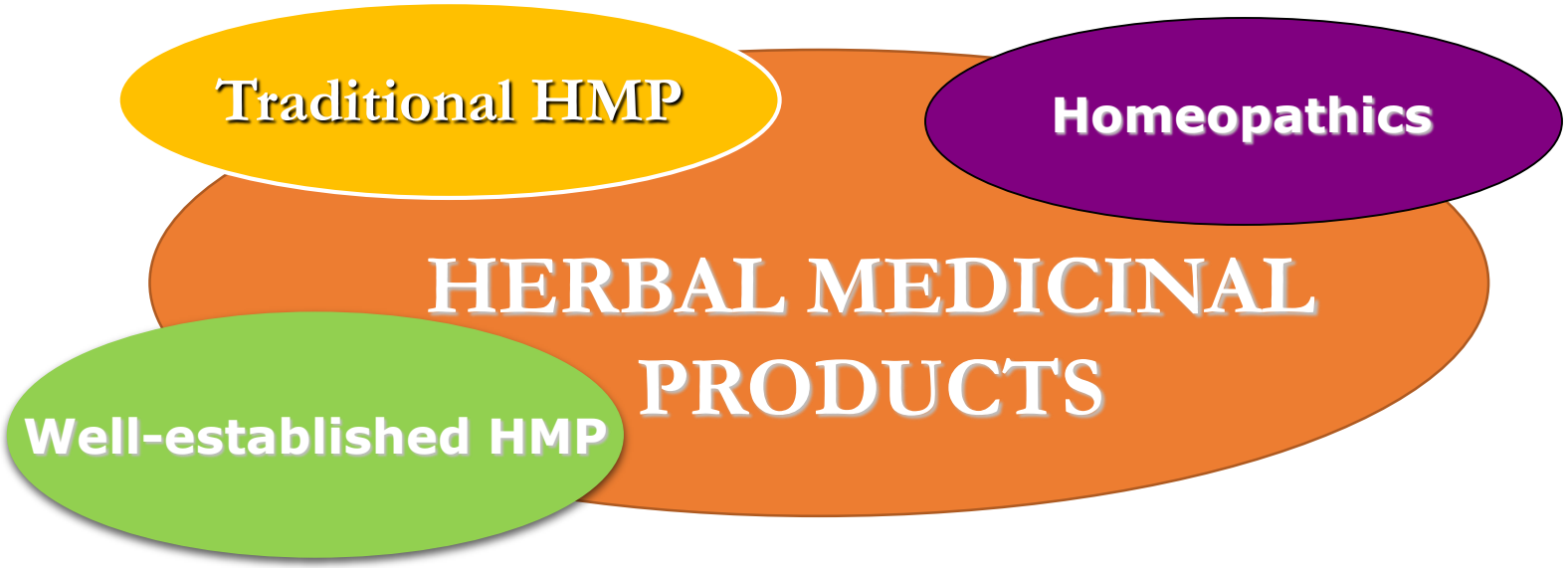
Herbal Medicinal Products registered by full or simplified registration procedures are automatically linked to pharmacy-only status.



1-over-the-counter drugs (OTC) available without special restrictions

2-prescription only medicine (POM), which must be prescribed by a licensed medical practitioner.

3- medicines which can only be sold in registered pharmacies, by or under the supervision of a pharmacist.

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HERBAL MEDICINAL PRODUCTS

- HERBAL MEDICINAL PRODUCTS
- WELL ESTABLISHED HERBAL MEDICINAL PRODUCTS
- TRADITIONAL HERBAL MEDICINAL PRODUCTS

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Classification (level of evidence)

Type of evidence

A
Ia
Ib

Evidence obtained from:
(Ia) meta-analysis of randomized controlled trials
or
(Ib) at least one randomized controlled trial

B
IIa
IIb
III

Evidence obtained from:
(IIa) at least one well-designed controlled study without randomization,
(IIb) at least one other type of well-designed quasi-experimental study,
(III) well-designed non-experimental descriptive studies, correlation studies and case control studies

C
IV

Evidence obtained from:
-expert committee reports or opinions
and/or
-clinical experience of respected authorities

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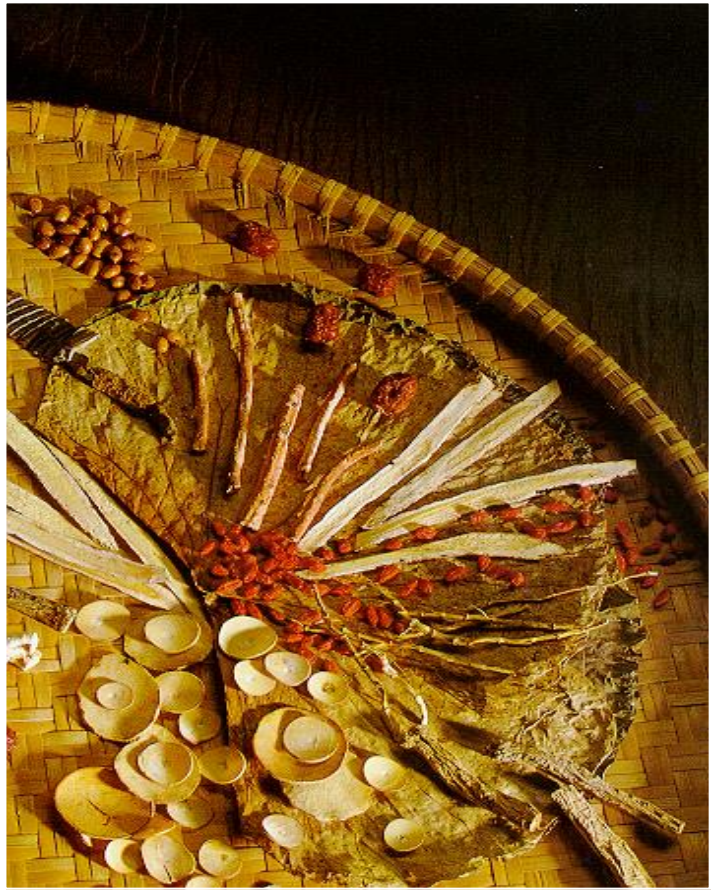
„*Traditional*“ herbal medicinal products according to EU Directive 2004/24/EC

Criteria:

- Limited indications (“OTC !!”)
- Specified strength and posology
- Oral, external or inhalation preparations
- Period of traditional use has elapsed at least 30 years (out of which at least 15 in the European Union)
- Sufficient data on traditional use and plausible efficacy



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Herbal Medicinal Products registered by full or simplified registration procedures are automatically linked to pharmacy-only status.

1-over-the-counter drugs (OTC) available without special restrictions
2-prescription only medicine (POM)

HERBAL MEDICINAL PRODUCTS

Well-established HMP

WE (marketing authorisation): demonstrated with sufficient safety and efficacy data

Traditional HMP

THMP (simplified registration): accepted on the basis of sufficient safety data and plausible efficacy

HMP: authorised after evaluation of a marketing authorisation application consisting of safety and efficacy data from the company's own development ('stand alone') or a combination of own studies and bibliographic data ('mixed application').

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Well-Established Use

Products with a well-established use may have an established efficacy and an acceptable level of safety,
demonstrated by available scientific data.
This is the case for many botanicals and botanical preparations, and this information might make extensive safety studies redundant (EMEA Ad hoc Working Group on Herbal Medicinal Products, 1999a).
Scientific monographs (e.g. ESCOP, WHO) offer a valuable and updated overview on published scientific literature, which may be used in support of the demonstration of the safety and efficacy of a botanical product in a bibliographical application.

Traditional Use

There are many botanical products with a long history of use, for which limited published, scientific data are available. This history of use is often based on decades of experience, sometimes in a limited geographical region (e.g. a region in China, India).

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Well-Established Use

Well-Established Use

WEU

Article 10(1)(a)(ii) Directive *2001/83/EC* previously known as Article 4.8 a)ii) of Directive 65/65/EEC and commonly referred to as "bibliographic references/ applications" which states that:

ARTICLE 10

1. In derogation of Article 8(3)(i), and without prejudice to the law relating to the protection of industrial and commercial property:

a) The applicant shall not be required to provide the results of toxicological and pharmacological tests or the results of clinical trials if he can demonstrate:

ii) or that the constituent or constituents of the medicinal product have a well established medicinal use, with recognised efficacy and an acceptable level of safety, by means of a detailed scientific bibliography; "

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Herbal medicinal products

Traditional Use

Directive **2004/24/EC**

Simplified **registration**:
chemical-pharmaceutical data, literature review demonstrating the safety of the medicinal product as well as traditional use of at least 30 years, 15 of which in the EC

Well Established use

Directive **2001/83/EC**

AIC 'bibliographic'
(use well known for at least 10 years in the EC): chemical-pharmaceutical data, literature data in lieu of safety tests and clinical trials

AIC 'complete':
chemical-pharmaceutical data, safety tests and clinical trials.

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What is a Traditional Herbal Medicine

- ✓ designed for use without medical intervention
- ✓ administration only at a specific dosage and dosage schedule
- ✓ oral, external or inhalation use only
- ✓ traditional employment for a period of at least 30 years of which 15 in the EU
- ✓ quality data: complete
- ✓ security data: bibliographical with additions
- ✓ efficacy data: bibliographic based on long-standing experience and use

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Traditional herbal medicines are subject to MA

Information on the herbal substance and herbal preparation must be submitted according to Module 3.2.S of the Common Technical Document (CTD)

If the herbal substance or herbal preparation has a European Pharmacopoeia monograph, *the European Certificate of Suitability of monographs of the European Pharmacopoeia* (*CEP*) issued by the European Directorate for the Quality of Medicines (EDQM) can be presented as an alternative to a complete Module 3.2.S.

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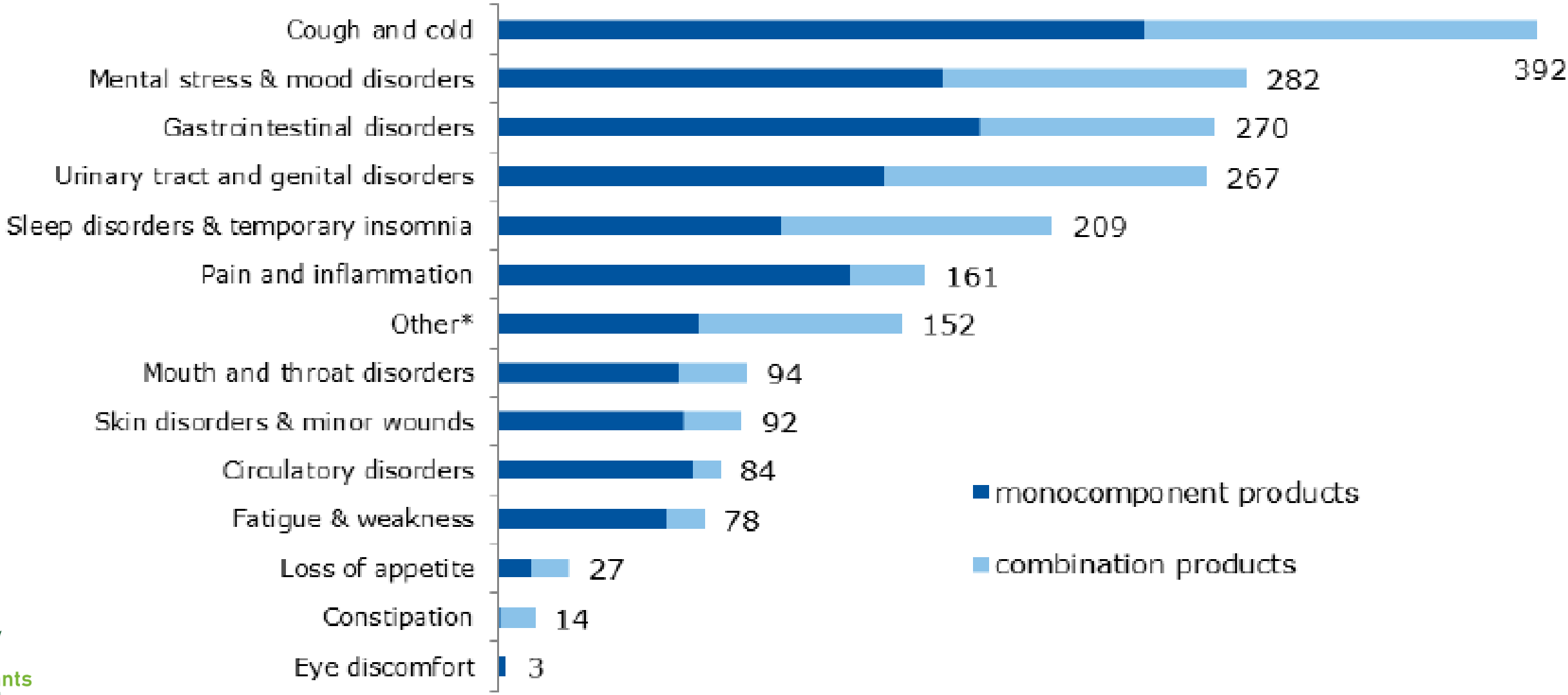
Therapeutic areas

Number of indications granted for THMPs grouped by therapeutic area



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Uptake of the traditional use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States

Source: 18 April 2017
EMA/HMPC/322570/2011 Rev. 7
Inspections, Human Medicines, Pharmacovigilance and Committees Division

Herbal Medicines Committee (HMPC)
of the European Medicines Agency (EMA)

community monographs

The EMA working group issues monographs that form the **bibliographical basis** for authorisations of medicinal products for well established and traditional use

EMA guarantees the SAFETY and EFFECTIVENESS of well established and traditional herbal medicines

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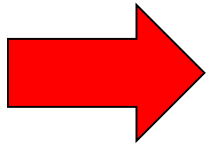
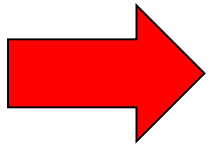
Monographs used for providing evidence in EU legislation

HMPC Monographs and list entries
EMA, Amsterdam





EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Evidence of Efficacy

Evidence of Safety

for well established and traditional use

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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

http://www.ema.europa.eu

Establishment of Monographs on Efficacy and Safety of HMPs

Committee on Herbal Medicinal Products (HMPC)

at the European Medicines Agency (EMA)

- Prepares a draft list of herbal substances, preparations and combinations (a "European positive list")
- Establishes Community monographs for traditional herbal medicinal products.
- 184 Community herbal monographs

from Achillea to Zingiber

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Status type
R: Rapporteur assigned
C: ongoing call for scientific data
D: Draft under discussion
P: Draft published
PF: Assessment close to finalisation (pre-final)
F: Final opinion adopted

EU herbal monographs

"comprises the scientific opinion of the Committee on Herbal Medicinal Products (HMPC) on safety and efficacy data concerning a herbal substance and its preparations intended for medicinal use".

The HMPC evaluates scientifically all available information including non-clinical and clinical data but also documented long-standing use and experience in the Community.
Community monographs are divided into two columns: well-established use (marketing authorisation) and traditional use (simplified registration).

- well-established use: demonstrated with sufficient safety and efficacy data,
- traditional use: accepted on the basis of sufficient safety data and plausible efficacy.

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EU herbal monographs are divided into two columns:

- well-established use (marketing authorization): demonstrated with sufficient safety and efficacy data;
- traditional use (simplified registration): accepted on the basis of sufficient safety data and plausible efficacy.

Each herbal preparation is assessed individually as information available may vary from one preparation to another. As a result, some preparations will appear in the well-established use section of the monograph and others will be in the traditional use section, as in the case of St. John's wort. Some preparations might not be included if data are insufficient.

It is inclued Latin name of the genus, Latin name of herbal substance, Botanical name of plant, English common name of herbal substance and the Status type, i.e

R: Rapporteur assigned
C: ongoing call for scientific data
D: Draft under discussion
P: Draft published
PF: Assessment close to finalization (pre-final)
F: Final opinion adopted

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp&mid=WC0b01ac058001fa1d

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COMMUNITY HERBAL MONOGRAPH ON *HYPERICUM PERFORATUM* L., HERBA (WELL-ESTABLISHED MEDICINAL USE)

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION[1, 2]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended *Hypericum perforatum* L., herba (St. John's Wort) i) Herbal substance Not applicable ii) Herbal preparations[3] A) Dry extract (DER 3-7:1), extraction solvent methanol (80% v/v) B) Dry extract (DER 3-6:1), extraction solvent ethanol (80% v/v) C) Dry extract (DER 2.5-8:1), extraction solvent ethanol (50-68% v/v)[4]	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended See document EMEA/HMPC/745582/2009

3. PHARMACEUTICAL FORM

Well-established use	Traditional use
Herbal preparation in solid dosage forms for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.	

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COMMUNITY HERBAL MONOGRAPH ON *HYPERICUM PERFORATUM* L., HERBA (TRADITIONAL USE)

1. NAME OF THE MEDICINAL PRODUCT

To be specified for the individual finished product.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION[1, 2]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended See document EMEA/HMPC/101304/2008	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended *Hypericum perforatum* L., herba (St. John's Wort) i) Herbal substance Not applicable ii) Herbal preparations[3] A) Dry extract (DER 4-7:1), extraction solvent ethanol 38% (m/m) B) Liquid extract (DER 1:4-20), extraction solvent vegetable oil[4] C) Liquid extract (DER 1: 13), extraction solvent maize oil or other suitable vegetable oil D) Tincture (Ratio of herbal substance to extraction solvent 1:10), extraction solvent ethanol 45-50% (v/v) E) Tincture (Ratio of herbal substance to extraction solvent 1:5), extraction solvent ethanol 50% (v/v) F) Liquid extract (DER 1:2), extraction solvent ethanol 50% (v/v) G) Liquid extract (DER 1:5-7), extraction solvent ethanol 50% (v/v) H) Expressed juice from the fresh herb (DER 1.1-2.5:1)[5] I) Comminuted herbal substance J) Powdered herbal substance

3. PHARMACEUTICAL FORM

Well-established use	Traditional use
	Comminuted herbal substance as herbal tea for oral use. Herbal preparations A, J in solid dosage forms for oral use. Herbal preparations C, D, E, F, G, H in liquid dosage forms for oral use. Herbal preparations B, D, E, I in liquid or semi-solid dosage forms for cutaneous use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

4.1. Therapeutic indications

Well-established use	Traditional use
Indication 1 Herbal preparations A, B: Herbal medicinal product for the treatment of mild to moderate depressive episodes (according to ICD-10).	
Indication 2 Herbal preparation C: Herbal medicinal product for the short term treatment of symptoms in mild depressive disorders.	

4.1. Therapeutic indications

Well-established use	Traditional use
	Indication 1 Herbal substance, herbal preparations A, C, D, E, F, G, H, I, J: Traditional herbal medicinal product for the relief of temporary mental exhaustion. Indication 2 Herbal preparations B, D, E, I: Traditional herbal medicinal product for the symptomatic treatment of minor inflammations of the skin (such as sunburn) and as an aid in healing of minor wounds. Indication 3 Herbal preparation I: Traditional herbal medicinal product for the symptomatic relief of mild gastrointestinal discomfort. The product is a traditional herbal medicinal product for use in specified indications exclusively based upon long-standing use.

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Community herbal monograph on *Ginkgo biloba* L., folium

1. Name of the medicinal product

To be specified for the individual finished product.

2. Qualitative and quantitative composition[1]

Well-established use	Traditional use
With regard to the marketing authorisation application of Article 10(a) of Directive 2001/83/EC as amended	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC as amended
Ginkgo biloba L., folium (Ginkgo leaf)	*Ginkgo biloba* L., folium (Ginkgo leaf)
i) Herbal substance	i) Herbal substance
Not applicable.	Not applicable.
ii) Herbal preparations	ii) Herbal preparations
Dry extract (DER 35-67:1), extraction solvent: acetone 60% m/m	Powdered herbal substance

3. Pharmaceutical form

Well-established use	Traditional use
Herbal preparations in solid or liquid dosage forms for oral use.	Herbal preparations in solid dosage forms for oral use.
The pharmaceutical form should be described by the European Pharmacopoeia full standard term.	The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

4.1. Therapeutic indications

Well-established use	Traditional use
Herbal medicinal product for the improvement of (age-associated) cognitive impairment and of quality of life in mild dementia.	Traditional herbal medicinal product for the relief of heaviness of legs and the sensation of cold hands and feet associated with minor circulatory disorders, after serious conditions have been excluded by a medical doctor.

4.2. Posology and method of administration

Well-established use	Traditional use
Posology *Adults, elderly* Single dose: 120-240 mg Daily dose: 240 mg There is no relevant indication for children and adolescents. **Duration of use** Treatment should last for at least 8 weeks. If there is no symptomatic improvement after 3 months, or if pathological symptoms should intensify, the doctor should check whether continuation of treatment is still justified. **Method of administration** Oral use.	**Posology** *Adults, elderly* Single dose: 250-360 mg Daily dose: 750 mg The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use'). **Duration of use** If the symptoms persist for more than 2 weeks, a doctor or a qualified health care practitioner should be consulted. **Method of administration** Oral use.

5.1. Pharmacodynamic properties

Well-established use	Traditional use
Pharmacotherapeutic group: Other anti-dementia drugs ATC code: N06DX02 The exact mechanism is not known. Human pharmacological data show increased EEG vigilance in geriatric subjects, reduction in blood viscosity and improved cerebral perfusion in specific areas in healthy men (60-70 years) and reduction in platelet aggregation. Additionally, vasodilating effects on forearm blood vessels causing increased regional blood flow are shown.	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

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List of Herbal substances with final EU herbal monographs (formerly known as Community herbal monograph, in alphabetical order):

Absinthii herba	Fraxini folium	Lavandulae flos	Rosae flos
Agni casti fructus (TU and WEU)	Fucus vesiculosus thallus	Lecithinum ex soya	Rosmarini aetheroleum
Agrimoniae herba	Fumariae herba	Leonuri cardiacae herba	Rosmarini folium
Agropyri repentis rhizoma	Gentianae radix	Lichen islandicus	Rubi idaei folium
Aloes folii succus siccatus	Ginkgo folium (TU and WEU)	Lini semen (TU and WEU)	Rusci rhizoma
Althaeae radix	Ginseng radix	Lupuli flos	Sabalis serrulatae fructus
Anisi aetheroleum	Hamamelidis cortex	Malvae folium	Salicis cortex (TU and WEU)
Anisi fructus	Hamamelidis folium	Malvae sylvestris flos	Salviae officinalis folium
Arctii radix	Hamamelidis folium et cortex aut ramunculus destillatum	Mate folium	Sambuci flos
Arnicae flos	Harpagophyti radix	Marrubii herba	Sennae folium

Avenae fructus	Hederae helicis folium	Matricariae aetheroleum	Sennae fructus
Avenae herba	Helichrysi flos	Matricariae flos	Sideritis herba
Betulae folium	Herniariae herba	Melaleucae aetheroleum	Silybi mariani fructus
Boldi folium	Hippocastani cortex	Meliloti herba	Sisymbrii officinalis herba
Bursae pastoris herba	Hippocastani semen (TU and WEU)	Melissae folium	Soiae oleum raffinatum
Calendulae flos	Hyperici herba (TU and WEU)	Menthae piperitae aetheroleum (TU and WEU)	Solidaginis virgaureae herba
Camelliae sinensis non fermentatum folium	Juglandis folium	Menthae piperitae folium	Species amarae
Capsici fructus	Juniperi aetheroleum	Menyanthidis trifoliatae folium	Species digestivae
Caryophylii floris aetheroleum	Juniperi galbulus	Millefolii flos	Species diureticae
Carvi aetheroleum	Lavandulae aetheroleum	Millefolii herba	Species sedativae
Carvi fructus	Lavandulae flos	Myrtilli fructus recens	Symphyti radix
Centaurii herba	Lecithinum ex soya	Myrtilli fructus siccus	Tanaceti parthenii herba
Chamomillae romanae flos	Leonuri cardiacae herba	Myrrha	Taraxaci folium
Cichorii intybi radix	Lichen islandicus	Oenotherae oleum	Taraxaci officinalis radix
Cimicifugae rhizoma	Lini semen (TU and WEU)	Oleae folium	Taraxaci radix cum herba
Cinnamomi corticis aetheroleum	Lupuli flos	Ononidis radix	Thymi aetheroleum
Cinnamomi cortex	Malvae folium	Origani dictamni herba	Thymi herba
Colae semen	Malvae sylvestris flos	Origani majoranae herba	Tiliae flos
Crataegi folium cum flore	Fraxini folium	Orthosiphonis folium	Tormentillae rhizoma
Curcumae longae rhizoma	Fucus vesiculosus thallus	Passiflorae herba	Trigonellae foenugraeci semen
Curcumae xanthorrhizae rhizoma	Fumariae herba	Pelargonii radix	Urticae folium
Cynarae folium	Gentianae radix	Phaseoli fructus (sine semine)	Urticae herba

Echinaceae angustifoliae radix	Ginkgo folium (TU and WEU)	Pilosellae herba cum radice	Uvae ursi folium
Echinaceae pallidae radix	Ginseng radix	Plantaginis lanceolatae folium	Vaccinii macrocarpi fructus
Echinaceae purpureae herba (TU and WEU)	Hamamelidis cortex	Plantaginis ovatae semen	Valerianae radix (TU and WEU)
Echinaceae purpureae radix	Hamamelidis folium	Plantaginis ovatae seminis tegumentum	Valerianae radix and Lupuli flos (TU and WEU)
Eleutherococci radix	Hamamelidis folium et cortex aut ramunculus destillatum	Polygoni avicularis herba	Verbasci flos
Epilobii herba	Harpagophyti radix	Polypodii rhizoma	Verbenae citriodorae folium
Eschscholziae herba	Hederae helicis folium	Primulae flos	Violae herba cum flore
Equiseti herba	Helichrysi flos	Primulae radix	Vitis viniferae folium (TU and WEU)
Eucalypti aetheroleum	Herniariae herba	Pruni africanae cortex	Zingiberis rhizoma (TU and WEU)
Filipendulae ulmariae flos	Hippocastani cortex	Psyllii semen	
Filipendulae ulmariae herba	Hippocastani semen (TU and WEU)	Quercus cortex	
Foeniculi amari fructus	Hyperici herba (TU and WEU)	Rhamni purshianae cortex	
Foeniculi amari fructus aetheroleum	Juglandis folium	Rhei radix	
Foeniculi dulcis fructus	Juniperi aetheroleum	Rhodiolae roseae rhizoma et radix	
Frangulae cortex	Juniperi galbulus	Ribis nigri folium	
Fragariae folium	Lavandulae aetheroleum	Ricini oleum	

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Union monographs

https://www.ema.europa.eu/en/human-regulatory-overview/herbal-medicinal-products/european-union-monographs-and-list-entries

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Herbal Medicines Committee (HMPC)
of the European Medicines Agency (EMA)

community monographs

The EMA working group issues monographs that form the **bibliographical basis** for authorisations of medicinal products for well established and traditional use

EMA guarantees the SAFETY and EFFECTIVENESS of well established and traditional herbal medicines

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ESCOP

European Scientific Cooperative on Phytotherapy

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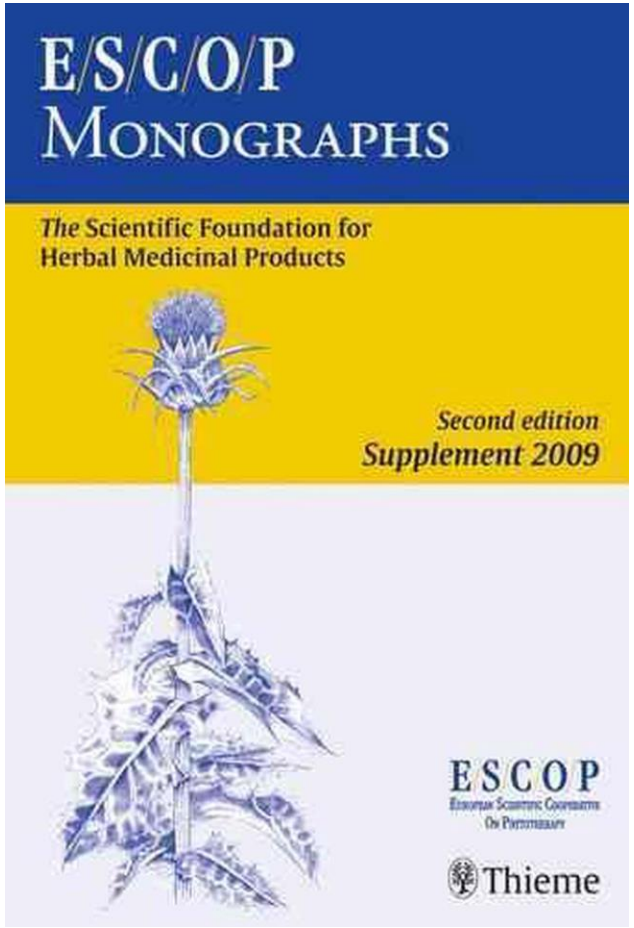

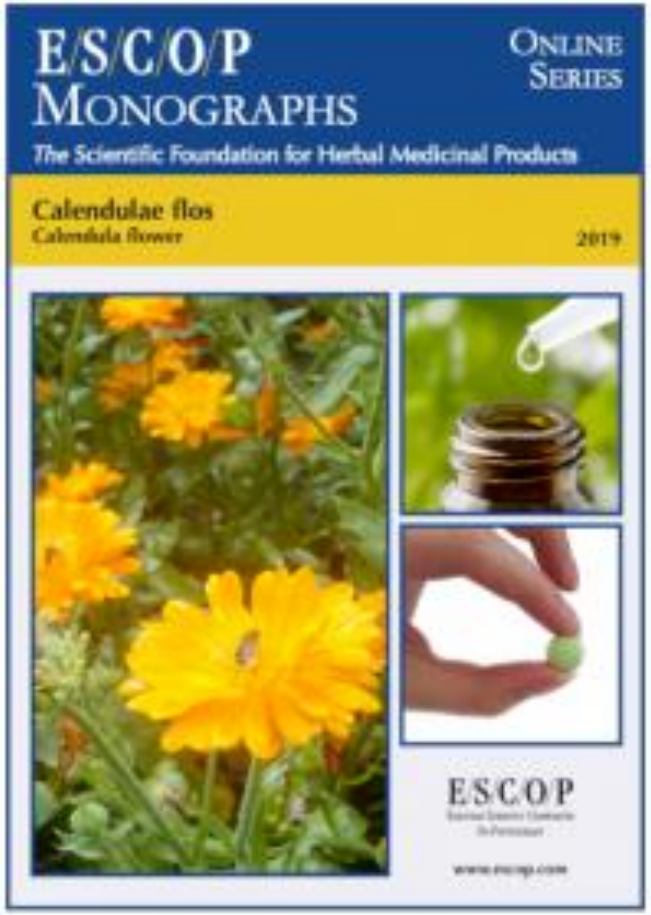

The Scientific Foundation for Herbal Medicinal Products
"Phytotherapy is the science-based medicinal use of plants and preparations derived from them, in the treatment, alleviation and / or prevention of disease or injury, according to recognised standards of quality, safety and efficacy."

https://escop.com/

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Standard Framework for an
ESCOP Herbal Monograph

Revision adopted 8 May 2020

(x)th version/ (month) (year)

Latin name for plant part [Arial 13p - bold; capitals] (1)

Common name [Arial 13p - bold, normal print] (2)

Header (right corner top of page): name of monograph, page number [Arial 10p]

Text [Arial 11p - normal]

1. **NAME OF THE MEDICINAL PRODUCT**

Not applicable.

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

Herbal substance

2.1. Definition

"(2) consists of.....(*latin species name* and author). (If necessary minimum content of a constituent). The material complies with the ... (official pharmacopoeia(s), [ref.]."
"Fresh material may also be used provided that when dried it complies with the (official pharmacopoeia(s)) [ref.]", only when this use is justified.

If available: "A draft monograph for the European Pharmacopoeia has been published [ref. Pharmeuropa]." The reference as well as the national pharmacopoeias will be replaced by Ph.Eur. when the monograph becomes official.

The ESCOP definition should be given in prose style which might in some cases differ from the EP style.
For English plant names, no capital first letter will be used (except in the title of the monograph).

2.2. Constituents

The main characteristic constituents are listed in this paragraph with references.

3. **PHARMACEUTICAL FORM**

Not applicable.

4. **CLINICAL PARTICULARS**

4.1. **Therapeutic indications**

If necessary, separate into "**Internal use**" and "**External use**". A global description should be avoided. The indication(s) should relate as precisely as possible to the results of clinical trials and / or the documentation cited under "pharmacodynamic properties" (5.1). (Symptomatic) treatment and / or prevention shall be indicated. References [ref.] must be given for each single indication.

In case published scientific evidence does not support "well-established medicinal use" indications, the following wording should be used: "In these indications, the efficacy is plausible on the basis of human experience and long-standing use."

4.2. **Posology and method of administration**

4.2.1. ***Dosage***

If necessary, separate the dosage into "oral use" and "topical use".
This section shall consist of specific dosage recommendations for
- Adults
- children (according to body weight and / or age, better would be **specific reference**)
- elderly (only mentioned in case of deviations from the adult dose)

The dosage for each type of extract/ tincture etc. should be given. Each dosage recommendation should be supported by references, if available.

4.2.2. ***Method of administration***

"For oral administration", "for cutaneous application" etc. Use EDQM standard terms for routes of administration (e.g. “topical preparations or use”).

4.2.3. ***Duration of use***

"No restriction" unless reported otherwise. A wording "If symptoms persist or worsen, medical advice should be sought" could be used case by case if applicable.

4.3. **Contraindications**

Situations where patients should never or generally not be treated. References if available. When there are no contraindications, write "None known.".

4.4. **Special warnings and precautions for use**

They are intended to warn of the possibility of adverse drug reactions occuring under normal conditions or in particular situations such as renal, hepatic or cardiac failure, elderly, young etc. except the conditions dealt with in 4.5, 4.6 and 4.7. They also describe the conditions under which the product may be recommended for use in sub-groups of patients at risk, provided that the special conditions of use are fulfilled.

Contra-indications should not be repeated here. However, restrictions of use in the paediatric population should be mentioned here.

References shall be given. In case of no special warnings and precautions, write "None required.".

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4.5. **Interaction with other medicinal products and other forms of interaction**

These are observed or potential interactions between medicinal products for the same or other indications as well as between medicinal products and daily activities e.g. meals. If necessary, recommendations or precautions should be given. References should be included.

It is important that only those interactions are included which are relevant for the patient. All other information shall be mentioned in Chapter 5.1 or 5.4, respectively. If there are no interactions, write "None reported.".

4.6. (Fertility,) Pregnancy and lactation

Fertility:
If solid data on fertility is available, this will be included under 4.6 with an amended heading “Fertility, pregnancy and lactation”.

Pregnancy and lactation:
Proposed categories:

Note: The wording may be modified according to individual cases, the recommendation given should reflect categories below, however.

1 A: The product can be used during pregnancy.
1 B: The product can be used during lactation.

2 A: In accordance with general medical practice, the product should not be used during pregnancy without medical advice.
2 B: In accordance with general medical practice, the product should not be used during lactation without medical advice.

3 A: The product should not be used during pregnancy.
3 B: The product should not be used during lactation.

4.7. **Effects on ability to drive and use machines**

If the product is likely to produce an effect, this has to be mentioned with references. When no effects are known, write "None known.".

4.8. **Undesirable effects**

These are significant adverse reactions that have been observed, with references. If possible, the frequency of the effects should be given. When no reports on adverse reactions are existing, write "None reported." Adverse events, without at least a suspected causal relationship to the investigated drug, should not be listed.

4.9. **Overdose**

Reactions resulting from overdose including management of overdose shall be mentioned, including references. If nothing has been reported, write "No case of overdose reported.".
on overdose is not applicable for the dosage form or the mode of application, t applicable.".

5. **PHARMACOLOGICAL PROPERTIES**

Pharmacological properties should be described only as far as this information is relevant for therapeutic purposes or interesting for future research on new therapeutic indications. The statements should be brief and precise.

5.1. **Pharmacodynamic properties**

The therapeutic group and the mechanism of action, if known, as well as the pharmacodynamic effects relevant for use should be described. Pharmacological effects of the plant or its extract/tincture/infusion etc. and of isolated constituents must be clearly separated. It must be differentiated which effects have been seen in animals and which in humans. This information should include as far as possible dose (including drug:extract ratio and extraction solvent as far as applicable and available) and way of application as well as number of patients or volunteers in case of clinical studies. References have to be included for each pharmacodynamic property described in this chapter [ref.].

Data on combination products: except for safety data, in principle no data on combinations shall be used.

The following sub-headings should be used if applicable In vitro experiments

- In vivo experiments
- Pharmacological studies in humansClinical studies

The following order is applied: the higher level is: in vitro, in vivo, etc., the lower level is the pharmacological effect. The following levels of print types are used:

- bold upright (e.g. **pharmacodynamic properties**)
- bold italics (***In vitro, In vivo, Pharmacological studies in humans, Clinical studies***)
- italics (*effects*) - this heading will not be followed by a line space

Optionally, tables presenting a systematic review of the clinical studies can be used. They should be structured as follows:

author, year [reference]	study design	diagnoses, no. of patients (test/control)	medication verum/ control, treatment period	results a) efficacy b) tolerability/ safety

In case no clinical studies are available, the following statement is used: "No published clinical data currently available." A further statement under "indications" is required.

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5.2. Pharmacokinetic properties

Relevant information should be given on absorption, distribution and elimination with a clear separation into properties of herbal preparations and isolated substances, including references.

The following groups of sub-headings can be used if applicable:

- ***Pharmacokinetics in animals***
- ***Pharmacokinetics in humans***

- *Absorption*
- *Distribution*
- *Metabolism*
- *Elimination*

If there is no information, write "No data available.".

5.3. Preclinical safety data

Information should be given on any findings in the preclinical testing which could be of relevance for the safe use of the product, that means as far as possible data on toxicological properties of the herbal substance or herbal preparation thereof and/or of the constituents, including references [ref.].

The following sub-headings should be used if applicable:

Acute toxicity
Repeated dose and chronic toxicity studies
Mutagenicity and carcinogenicity
Reproductive toxicity

If no information is available, write "No data available.". If existing data are not regarded as relevant for human use in the described dosage and application form, write “Available data not relevant”.

5.4. Clinical safety data

If clinical studies are presented and summarized in the monograph, a clinical safety data section is always required.

- End of monograph text -

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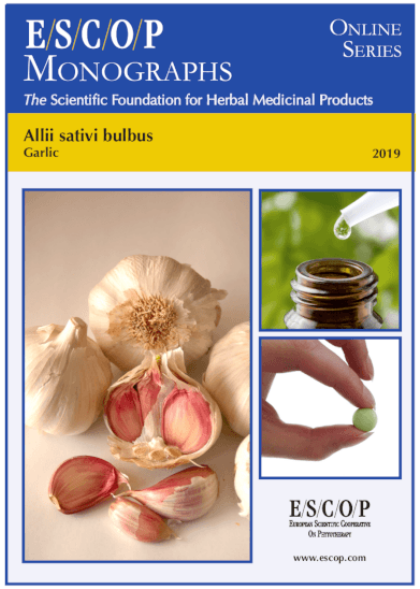
ESCOP MONOGRAPHS

-Characteristic constituents, the essential oil; α-and β-thujone, carnosol, carnosic acid, oleanolic acid, phenolic diterpenes.
-Dyspeptic complaints such as heartburn and bloating; hyperhidrosis; hot flushes; hyperglycaemia and hyperlipidaemia;
inflammations of the mouth or throat including stomatitis, gingivitis and pharyngitis.

-Characteristic constituents apigenin, apigenin-7-glucoside, flavone derivatives, (-)-α-bisabolol, herniarin and matricin (which is converted to chamazulene on distillation of the oil).
-Gastrointestinal complaints such as minor spasms, epigastric distension, flatulence and belching. For external use they are minor inflammation and irritations of skin and mucosa, including the oral cavity and the gums (mouth washes), the respiratory tract (inhalations) and the anal and genital area (baths, ointments).



-Characteristic constituents alliin, the main sulphur-containing amino acid, its conversion to allicin, S-methyl-L-cysteine sulphoxide and S-allyl-cysteine are included.
-Prophylaxis of atherosclerosis; treatment of elevated blood lipid levels if insufficiently controlled by diet; supportive treatment of hypertension; reducing severity of upper respiratory tract infections and catarrhal conditions.

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Monographs used for providing evidence in EU legislation

HMPC Monographs and list entries
EMA, London

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Evidence of Efficacy

Evidence of Safety

for well established and traditional use

Pharmacopoeia Monographs
(Validated methods)
EDQM, Strasbourg

Evidence of Quality

edqm
European Directorate for the Quality of Medicines & HealthCare

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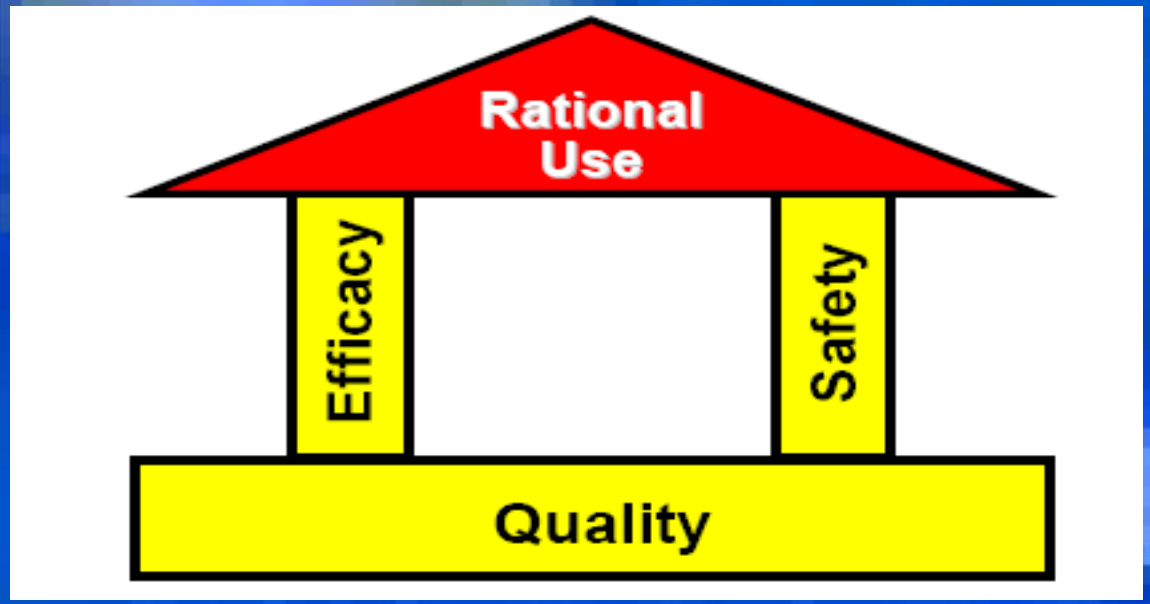
European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

Pharmaceutical quality is the basis for reproducible efficacy and safety



HDs, HDPs and HMPs: Quality control is mandatory

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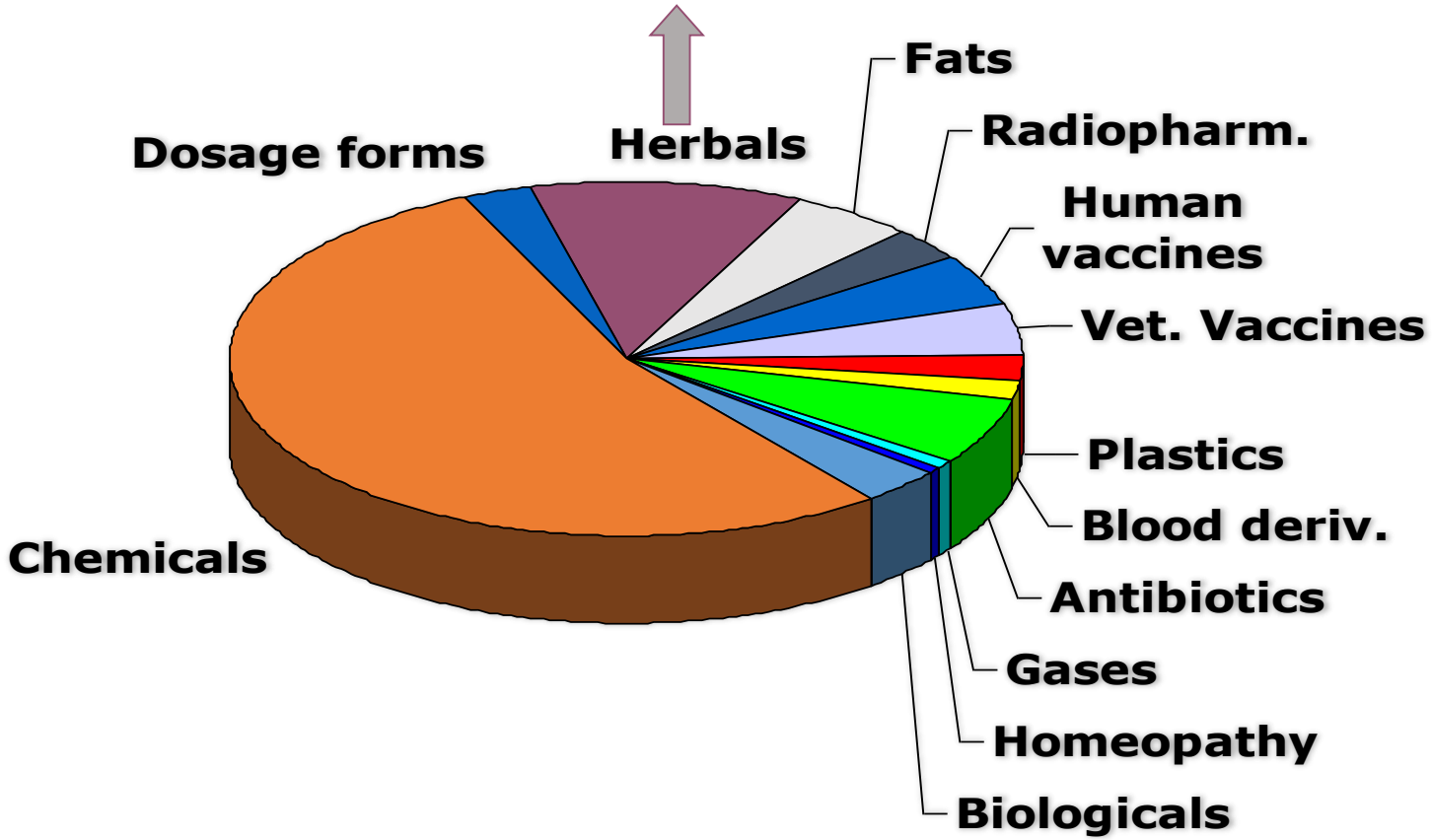
Contents of the European Pharmacopoeia: more than 2500 monographs

Herbal drugs including TCM, Herbal Drug Preparations, Essential Oils



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Quality of HMPs

The quality of HMPs has to comply the Directive 2001/83/EC as amended by Directive 2003/63/EC.
The quality has to comply the *Note for guidance on quality of herbal medicinal products (CPMP/QWP/2819/00)* which should be read in conjunction with Annex 7 “Manufacture of Herbal Medicinal Products”, GMP for medicinal products, Volume 4, Rules governing Medicinal Products in EU; GMP recommendations should be respected.

Quality of HMPs can only be assured if starting material (HDs/HDPs) are defined in a rigorous and detailed manner.

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07/2015:1294

BELLADONNA LEAF DRY EXTRACT, STANDARDISED

Belladonnae folii extractum siccum normatum

DEFINITION

Standardised dry extract obtained from *Belladonna leaf (0221)*.

Content: 0.95 per cent to 1.05 per cent of total alkaloids, expressed as hyoscyamine ($C_{17}H_{23}NO_3$; M_r 289.4) (dried extract).

PRODUCTION

The extract is produced from the herbal drug by a suitable procedure using ethanol (70 per cent *V/V*).

TESTS

Atropine. Thin-layer chromatography (*2.2.27*).

Test solution. To 0.20 g of the extract to be examined add 10.0 mL of *0.05 M sulfuric acid*, shake for 2 min and filter. Add 1.0 mL of *concentrated ammonia R* and shake with 2 quantities, each of 10 mL, of *peroxide-free ether R*. If necessary, separate by centrifugation. Dry the combined ether layers over about 2 g of *anhydrous sodium sulfate R*, filter and evaporate to dryness on a water-bath. Dissolve the residue in 0.5 mL of *methanol R*.

Reference solution. Dissolve 50 mg of *hyoscyamine sulfate R* in 9 mL of *methanol R*. Dissolve 15 mg of *hyoscine hydrobromide R* in 10 mL of *methanol R*. Mix 1.8 mL of the hyoscine hydrobromide solution and 8 mL of the hyoscyamine sulfate solution.

Plate: *TLC silica gel plate R*.

ASSAY

At each extraction stage it is necessary to check that the alkaloids have been completely extracted. If the extraction is into the organic phase this is done by evaporating to dryness a few millilitres of the last organic layer, dissolving the residue in *0.25 M sulfuric acid* and verifying the absence of alkaloids using *potassium tetraiodomercurate solution R*. If the extraction is into the acid aqueous phase, this is done by taking a few millilitres of the last acid aqueous phase and verifying the absence of alkaloids using *potassium tetraiodomercurate solution R*.

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European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

01/2013:1874

ST. JOHN'S WORT DRY EXTRACT, QUANTIFIED

Hyperici herbae extractum siccum quantificatum

DEFINITION

Quantified dry extract obtained from *St. John's wort (1438)*.

Content:

- *total hypericins, expressed as hypericin* ($C_{30}H_{16}O_8$; M_r 504.5): 0.10 per cent to 0.30 per cent (anhydrous extract);
- *flavonoids, expressed as rutin* ($C_{27}H_{30}O_{16}$; M_r 610.5): minimum 6.0 per cent (anhydrous extract);
- *hyperforin* ($C_{35}H_{52}O_4$; M_r 536.8): maximum 6.0 per cent (anhydrous extract) and not more than the content stated on the label.

Top of the plate	
	A yellowish-orange fluorescent zone
	2 red fluorescent zones (hypericin and pseudohypericin)
	3 yellowish-orange fluorescent zones
Hyperoside: a yellowish-orange fluorescent zone	A yellowish-orange fluorescent zone (hyperoside)
	Yellow and blue possibly superimposed fluorescent zones
Rutin: a yellowish-orange fluorescent zone	A yellowish-orange fluorescent zone (rutin)
Reference solution	**Test solution**

ASSAY

Total hypericins. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 70.0 mg of the extract to be examined in 25.0 mL of *methanol R*. Sonicate and centrifuge the solution. Expose the solution to a xenon lamp at about 765 W/m² for 8 min.

Reference solution. Dissolve a quantity of *St. John's wort dry extract HRS* corresponding to 0.15 mg of hypericin in 25.0 mL of *methanol R*. Sonicate and centrifuge. Expose the solution to a xenon lamp at about 765 W/m² for 8 min.

Hyperforin and flavonoids. Liquid chromatography (*2.2.29*). *Carry out the assay protected from light.*

Solvent mixture: *water R, methanol R* (20:80 *V/V*).

Test solution. Dissolve 75.0 mg of the extract to be examined in 20.0 mL of the solvent mixture. Sonicate and centrifuge.

Reference solution (a). Dissolve 20.0 mg of *rutoside trihydrate CRS* in 200.0 mL of the solvent mixture.

Reference solution (b). Dissolve 75.0 mg of *St. John's wort dry extract HRS* in 20.0 mL of the solvent mixture. Sonicate and centrifuge.

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04/2008:1827

GINKGO DRY EXTRACT, REFINED AND QUANTIFIED

Ginkgonis extractum siccum raffinatum et quantificatum

DEFINITION

Refined and quantified dry extract produced from *Ginkgo leaf (1828)*.

Content:

- *flavonoids, expressed as flavone glycosides* (M_r 756.7): 22.0 per cent to 27.0 per cent (dried extract);
- *bilobalide*: 2.6 per cent to 3.2 per cent (dried extract);
- *ginkgolides A, B and C*: 2.8 per cent to 3.4 per cent (dried extract);
- *ginkgolic acids*: maximum 5 ppm (dried extract).

Top of the plate	
	A blue fluorescent zone
	Several faint coloured zones
	A brown fluorescent zone
	A green fluorescent zone
	An intense light blue fluorescent zone sometimes overlapped by a greenish-brown fluorescent zone
Chlorogenic acid: a light blue fluorescent zone	
	One or two green fluorescent zones
Rutin: a yellowish-brown fluorescent zone	One or two yellowish-brown fluorescent zones
	Several green and yellowish-brown fluorescent zones
Reference solution	**Test solution**

ASSAY

Flavonoids. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.200 g of the extract to be examined in 20 mL of *methanol R*. Add 15.0 mL of *dilute hydrochloric acid R* and 5 mL of *water R* and dilute to 50.0 mL with *methanol R*. Transfer 10.0 mL of this solution into a 10 mL brown-glass vial. Close the vial with a tight rubber membrane stopper and secure with an aluminium crimped cap. Heat on a water-bath for 25 min. Allow to cool to 20 °C.

Reference solution. Dissolve 10.0 mg of *quercetin dihydrate CRS* in 20 mL of *methanol R*. Add 15.0 mL of *dilute hydrochloric acid R* and 5 mL of *water R* and dilute to 50.0 mL with *methanol R*.

Terpene lactones. Liquid chromatography (*2.2.29*).

Test solution. Place 0.120 g of the extract to be examined in a 25 mL beaker and dissolve it in 10 mL of *phosphate buffer solution pH 5.8 R* by stirring. Transfer the solution into a chromatography column, about 0.15 m long and about 30 mm in internal diameter, containing 15 g of *kieselguhr for chromatography R*. Wash the beaker with 2 quantities, each of 5 mL, of *phosphate buffer solution pH 5.8 R* and transfer the washings to the chromatography column. Allow to stand for 15 min. Elute with 100 mL of *ethyl acetate R*. Evaporate the eluate to dryness at a pressure not exceeding 4 kPa in a water-bath at 50 °C. The residue of solvent is eliminated by an air-current. Take up the residue in 2.5 mL of the mobile phase.

Ginkgolic acids. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.500 g of the powdered extract to be examined in 8 mL of *methanol R*, sonicating if necessary, and dilute to 10.0 mL with the same solvent. Centrifuge if necessary.

Reference solution. Dissolve 10.0 mg of *ginkgolic acids CRS* in 8 mL of *methanol R*, sonicating if necessary, and dilute to 10.0 mL with the same solvent. Dilute 2.0 mL of this solution to 10.0 mL with *methanol R*.

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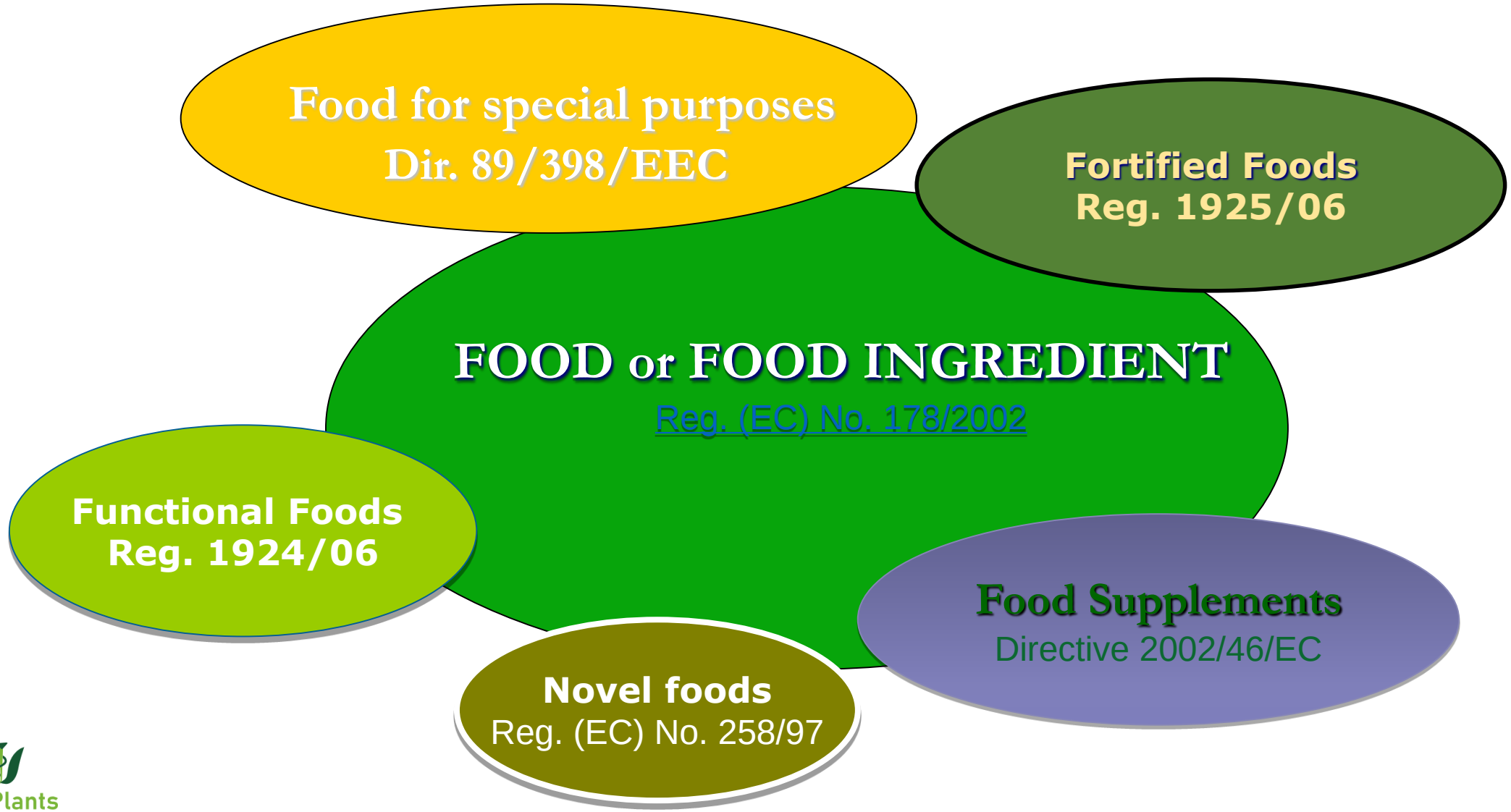
Herbal Medicinal Products

- Pharmacy (OTC or POM)
- Therapeutic indications
- Contra-indications
- Limitations of use (dose, age, pregnancy, ability to drive etc…)
- Overdose
- Interactions with food and other medicines
- Pharmacological activity

- Marketing authorisation
- Medicines Health Authority inspection



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Directive of the European Union on Food Supplements 2002/46/EC

- Food supplements are concentrated sources of nutrients or other substances **with a nutritional or physiological effect** whose purpose is to supplement the normal diet
- Marketed in dose form namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drops dispensing bottles and other similar forms of liquids and powders designated to be taken in measures small unit quantities.
- According to the Directive, "nutrients" are vitamins and minerals. For the "other substances" however, things become vague. The list includes (but is not limited to): "amino acids, essential fatty acids, fibre and various plants and herbal extracts." Specific definitions and rules were postponed to a "later stage," and national laws will be applied until then.
- **Claims must be substantiated by studies. No disease-related claims is accepted**
- **No «marketing authorization» but «notification»**
- For the European Food Safety Authority "various plants and herbal extracts" are food supplement ingredients that come from plants, algae, fungi or lichens.

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Botanical name	Family	Parts of plants of possible concern	Chemical of concern	Remarks on toxic/adverse effect(s) not known to be related to the identified chemical(s) of concern	Specific References
Abrus precatorius L.	Fabaceae (Leguminosae)	Seed	Glycoproteins (lectins): e.g. abrin		Frohne D., Pfänder H.J. and Anton R. 2009. Plantes à risques. Ed. Tec et Doc-Lavoisier, ISBN: 978-2-7430-0907-1
Acacia spp.	Fabaceae (Leguminosae)	Bark, leaf and seed	Genus in which species may contain dimethyltryptamine derivatives and cyanogenic glycosides (e.g. prunasin, sambunigrin, acacipetalin)		Seigler D.S. and Ebinger J.E. 1987. Cyanogenic Glycosides in Ant-Acacias of Mexico and Central America. Southwest. Nat. 32(4), 499-503.
Achillea abrotanoides Vis.	Asteraceae (Compositae)	Aerial part	Essential oil: bicyclic monoterpenes: beta-thujone (16.8%), pinocarvone (15,6%), camphor (14%), and monoterpene etheroxide: 1,8-cineole (11,3%)		Bicchi C. et al. 1988. On the composition of Achillea abrotanoides (Vis.) Vis. essential oil. Flavour Frag. J. 3(3), 101-104
Achillea fragrantissima Sch.Bip.	Asteraceae (Compositae)	Aerial part	Essential oil: bicyclic monoterpenes: thujones		Elgamal M.H.A. et al. 1991. Constituents of Achillea fragrantissima. Fitoterapia. 62(4), 362

National legislations may foresee:

- Positive lists of botanicals which may be used.
- Negative lists of botanicals which may not be used.
- Restrictions / modalities for their use (maximum limits; labeling requirements, i.e. No specific rules at EU level warnings)

MINISTERO DELLA SALUTE **DECRETO 9 luglio 2012** **Disciplina dell'impiego negli integratori alimentari** **di sostanze e preparati vegetali** **(G.U. 21-7-2012 serie generale n. 169)**			**LINEE GUIDA MINISTERIALI** **DI RIFERIMENTO PER GLI EFFETTI FISIOLOGICI** applicabili in attesa della definizione dei claims sui "botanicals" a livello comunitario
ALLEGATO 1 aggiornato al 16 gennaio 2013			*Gli effetti fisiologici sono volti ad ottimizzare le funzioni dell'organismo nell'ambito dell'omeostasi, secondo il modello definito al riguardo dal Consiglio d'Europa [Homeostasis, a model to distinguish between foods (including food supplements) and medicinal products – 07.02.2008].*
NOME BOTANICO	**PARTE UTILIZZATA**	**NOTE**	
ABAREMA COCHLIOCARPOS (GOMES) BARNEBY & J. W. GRIMES	oleum		**oleum:** Naturali difese dell'organismo. Azione di sostegno e ricostituente.
ABELMOSCHUS ESCULENTUS (L.) MOENCH	fructus		**fructus:** Funzionalità delle mucose dell'apparato respiratorio. Benessere della gola. Azione emolliente e lenitiva (sistema digerente; vie urinarie)

Italian Ministry of Health

ESTRATTI VEGETALI NON AMMESSI NEGLI INTEGRATORI ALIMENTARI

NOME	PARTE
ABRUS PRECATORIUS L.	seme
ACOKANTHERA OUABAIO CATH.	legno, seme
ACOKANTHERA SCHIMPERI BENTH ET HOOK	frutto, legno
ACONITUM ANTHORA L.	fiore, pianta erbacea, radice
ACONITUM CHASMANTHUM STAP.	radice
ACONITUM FEROX WALL.	radice
ACONITUM HETEROPHYLLUM WALL.	pianta erbacea, radice
ACONITUM NAPELLUS L.	foglia, pianta erbacea, radice, tubero
ACONITUM VARIEGATUM L.	radice

Possible restrictions in dosage and, age of patients, contraindications, interactions are also reported.

Cimicifuga racemosa (Note of the Health Ministry n. 600.12/I.5.i.h./4160, 1 February 2007), *Citrus aurantium* ssp. *amara* (Note of the Health Ministry n. 600.12/AG45.1/2688, 20 October 1999), *Ginkgo biloba* (Note of the Health Ministry n. 600/AG45.1/9113 21 November 2001) and *Hypericum perforatum* (Note of the Health Ministry n. 600/12/AG45.1/2688 etc…)

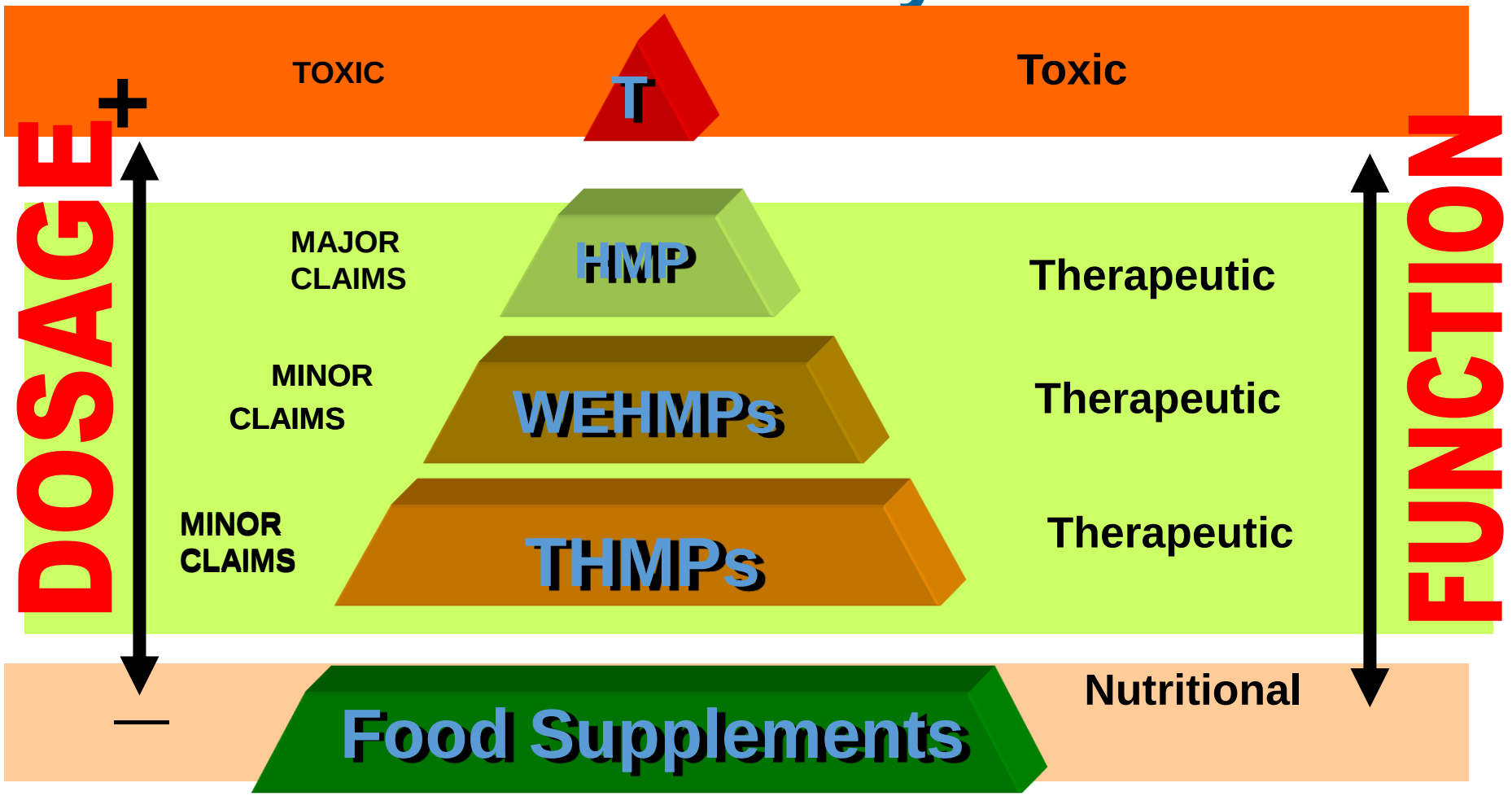
- *Cimicifuga racemosa* Nutt. (rhizome) …Contraindications are hepatic diseases and there are restrictions in the dosages.
- *Citrus aurantium* ssp. *amara* …Dosage of sinefrin is required in the label with a maximum dose of 30 mg/die, corresponding to about 800 mg of *Citrus aurantium* containing 4% sinefrin. Restrictions of use are pregnancy, breast-feeding and age less than 12.
- *Ginkgo biloba* L. has restrictions due to the concomitant use of anticoagulants or blood platet antiaggregants , pregnancy and breast-feeding.
- *Glycine max* (L.) Merr. a maximum intake of 80 mg/die isoflavones is admitted.
- *Hypericum perforatum* L. is reported to normalize the humor, to relax and mental wellness. Daily dose of hypericin is not more than 0,7 mg and the ratio hyperforins/hypericin not more than 7. Restrictions are represented by the age of consumers and the possibility of the interaction with the metabolism

BOTANICAL NAME	FAMILY	SYNONYM	PART TRADITIONALLY USED/SPECIFIC PREPARATIONS	NOTES
Abelmoschus esculentus (L.) Moench	Malvaceae		fruit	
Abelmoschus moschatus Medik.	Malvaceae		seed	
Abies alba Mill.	Pinaceae		bark, branch, needle, seed, resin	
Abies balsamea (L.) Mill.	Pinaceae		bark, needle, resin, twig; essential oil	
Abies nordmanniana subsp. *Equitrojani* (Asch. & Sint. ex Boiss.) Coode & Cullen	Pinaceae	*Abies pectinata* DC. var. *equi-trojani* Asch. & Sint. Ex Boiss	bark, branch, needle	
Abies sibirica Ledeb.	Pinaceae		bark, branch, needle, seed, resin	
Abroma augusta L.f.	Malvaceae		root bark	
Acacia catechu (L.f.) Willd.	Fabaceae		flower, wood, gum	
Acacia decurrens Willd.	Fabaceae		flower, wood, gum	
Acacia farnesiana (L.) Willd.	Fabaceae		flower, pod, wood	
Acacia nilotica (L.) Delile	Fabaceae	*Acacia arabica* (Lam.) Willd.	bark, fruit, gum	
Acacia senegal (L.) Willd.	Fabaceae		bark, gum	
Acalypha indica L.	Euphorbiaceae		leaf, root	

BELFRIT list: the harmonized list of admissible plants in food supplements (more than 1,000), as jointly defined by BELgium, FRance and ITaly.

BOTANICAL NAME	FAMILY	SYNONYM	PART TRADITIONALLY USED/SPECIFIC PREPARATIONS	NOTES
Bovista plumbea Pers.	Agaricaceae		fruiting body	
Cordyceps sinensis (Berk.) Sacc.	Ophiocordycipitaceae	*Paecilomyces hepiali* Q.T. Chen & R.Q. Dai	fungus	
Ganoderma lucidum (Curtis) P. Karst.	Ganodermataceae		fungus	
Grifola frondosa (Dicks.) Gray	Meripilaceae		fruiting body	
Grifola umbellata (Pers.) Pilat	Meripilaceae		fruiting body	
Lasiosphaera gigantea Batch Ex Pers.	Lasiosphaeriaceae		fruiting body	
Lentinula edodes (Berk.) Pegler	Marasmiaceae		fungus	
Monascus purpureus	Monascaceae		microfungi	
Pleurotus ostreatus (Jacq. : Fr.) P. Kumm	Pleurotaceae		fungus	
Polyporus umbellatus (Pers.) Fr.	Polyporaceae	*Grifola umbellata* (Pers.) Pilát	fungus	
Wolfiporia extensa (Peck) Ginns	Polyporaceae	*Poria cocos* F. A. Wolf	sclerotium	

Action of an Herbal Drug on the body



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Nutrition and Health Claims

On July 1, 2007, a regulation on nutrition and health claims entered into force.

Regulation 1924/2006 sets EU-wide conditions for the *use of nutrition claims* such as "low fat" or "high in vitamin C" and health claims such as "helps lower cholesterol". The regulation applies to any food or drink product produced for human consumption that is marketed on the EU market. Only foods that fit a certain nutrient profile (below certain salt, sugar and/or fat levels) will be allowed to carry claims.

Nutrition and health claims will only be allowed on food labels if they are included in one of the EU positive lists. Food products carrying claims must comply with the provisions of nutritional labeling Directive 90/496/EC and its amended version Directive 1169/2011 on information to consumers mentioned further below.

In December 2012, a list of approved functional health claims went into effect. The list includes generic claims for substances other than botanicals which will be evaluated at a later date. Disease risk reduction claims and claims referring to the health and development of children require an authorization on a case-by-case basis, following the submission of a scientific dossier to the European Food Safety Authority (EFSA).

Health claims based on new scientific data will have to be submitted to EFSA for evaluation but a simplified authorization procedure has been established.

http://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public/?event=search

EU Register on nutrition and health claims

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference	Commission regulation	Status	Entry Id
Art.13(1)	Alpha-linolenic acid (ALA)	ALA contributes to the maintenance of normal blood cholesterol levels	The claim may be used only for food which is at least a source of ALA as referred to in the claim SOURCE OF OMEGA 3 FATTY ACIDS as listed in the Annex to Regulation (EC) No 1924/2006. Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 2 g of ALA.	maintenance of normal blood cholesterol concentrations	2009;7(9):1252, 2011;9(6):2203	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	493, 568
Art.13(1)	Activated charcoal	Activated charcoal contributes to reducing excessive flatulence after eating	The claim may be used only for food which contains 1 g of activated charcoal per quantified portion. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with 1 g which should be taken at least 30 minutes before and 1 g shortly after the meal.	reduction of excessive intestinal gas accumulation	2011;9(4):2049	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1938
Art.13(1)	Barley grain fibre	Barley grain fibre contributes to an increase in faecal bulk	The claim may be used only for food which is high in that fibre as referred to in the claim HIGH FIBRE as listed in the Annex to Regulation (EC) No 1924/2006.	increase in faecal bulk	2011;9(6):2249	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	819
Art.13(1)	Beta-glucans from oats and barley	Consumption of beta-glucans from oats or barley as part of a meal contributes to the reduction of the blood glucose rise after that meal	The claim may be used only for food which contains at least 4 g of beta-glucans from oats or barley for each 30 g of available carbohydrates in a quantified portion as part of the meal. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained by consuming the beta-glucans from oats or barley as part of the meal.	reduction of post-prandial glycaemic responses	2011;9(6):2207	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	821, 824

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference	Commission regulation	Status	Entry Id
Art.13(1)	Dried plums of 'prune' cultivars (*Prunus domestica* L.)	Dried plums/prunes contribute to normal bowel function	The claim may be used only for food which provides a daily intake of 100 g of dried plums (prunes). In order to bear the claim, information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 100 g of dried plums (prunes).	Maintenance of normal bowel function	2010;8(2):1486, 2012;10(6):2712	Commission Regulation (EU) 536/2013 of 11/06/2013	Authorised	1164
Art.13(1)	Monascus purpureous (red yeast rice)	Monacolin K from red yeast rice contributes to the maintenance of normal blood cholesterol levels	The claim may be used only for food which provides a daily intake of 10 mg of monacolin K from red yeast rice. In order to bear the claim, information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 10 mg of monacolin K from fermented red yeast rice preparations.	maintenance of normal blood LDL-cholesterol concentrations	2011;9(7):2304	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1648, 1700
Art.13(1)	Oat grain fibre	Oat grain fibre contributes to an increase in faecal bulk	The claim may be used only for food which is high in that fibre as referred to in the claim HIGH FIBRE as listed in the Annex to Regulation (EC) No 1924/2006.	increase in faecal bulk	2011;9(6):2249	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	822
Art.13(1)	Olive oil polyphenols	Olive oil polyphenols contribute to the protection of blood lipids from oxidative stress	The claim may be used only for olive oil which contains at least 5 mg of hydroxytyrosol and its derivatives (e.g. oleuropein complex and tyrosol) per 20 g of olive oil. In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 20 g of olive oil.	protection of LDL particles from oxidative damage	2011;9(4):2033	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1333, 1638, 1639, 1696, 2865
Art.13(1)	Plant sterols and plant stanols	Plant sterols/stanols contribute to the maintenance of normal blood cholesterol levels	In order to bear the claim information shall be given to the consumer that the beneficial effect is obtained with a daily intake of at least 0.8 g of plant sterols/stanols.	maintenance of normal blood cholesterol concentrations	2010;8(10):1813, 2011;9(6):2203	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	549, 550, 567, 568, 713, 1234, 1235, 1466, 1634, 1984, 2909, 3140
Art.13(1)	Walnuts	Walnuts contribute to the improvement of the elasticity of blood vessels	The claim may be used only for food which provides a daily intake of 30 g of walnuts. In order to bear the claim, information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 30 g of walnuts.	Improvement of endothelium-dependent vasodilation	2011;9(4):2074	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	1155, 1157

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference	Commission regulation	Status	Entry Id
Art.13(5)	Cocoa flavanols	Cocoa flavanols help maintain the elasticity of blood vessels, which contributes to normal blood flow	Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 200 mg of cocoa flavanols. The claim can be used only for cocoa beverages (with cocoa powder) or for dark chocolate which provide at least a daily intake of 200 mg of cocoa flavanols with a degree of polymerisation 1-10		Q-2012-00002	Commission Regulation (EU) No 851/2013 of 03/09/2013	Authorised *	N/A
Art.13(5)	Cocoa flavanols	Cocoa flavanols help maintain the elasticity of blood vessels, which contributes to normal blood flow.	Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 200 mg of cocoa flavanols. The claim can be used only for capsules or tablets containing high-flavanol cocoa extract which provide at least a daily intake of 200 mg of cocoa flavanols with a degree of polymerisation 1-10.		Q-2013-00832	<style isUnderline="true" forecolor="#0000FF" href="http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015R0539&from=EN">Commission Regulation (EU) 2015/539 of 31/03/2015</style>	Authorised *	N/A
Art.13(5)	Water-Soluble Tomato Concentrate (WSTC) I and II	Water-Soluble Tomato Concentrate (WSTC) I and II helps maintain normal platelet aggregation, which contributes to healthy blood flow	Information to the consumer that the beneficial effect is obtained with a daily consumption of 3g WSTC I or 150 mg WSTC II in up to 250 ml of either fruit juices, flavoured drinks or yogurt drinks (unless heavily pasteurised) or with a daily consumption of 3 g WSTC I or 150 mg WSTC II in food supplements when taken with a glass of water or other liquid.		Q-2009-00229, Q-2010-00809	Decision 2009/980/EU of 17/12/2009, Amended by Decision 2010/770/EU of 13/12/2010	Authorised *	N/A

Claims whose status is marked with a * indicate a claim for which protection of proprietary data is granted (and for which the right of use of the claim is restricted to the benefit of the applicant). For further information please go to: http://ec.europa.eu/nuhclaims/?event=getListOfPropClaims

THERAPEUTIC INDICATIONS OF HMP

Cough and cold
Mental stress & mood disorders
Sleep disorders & temporary insomnia
Gastrointestinal disorders
Constipation
Urinary tract and genital disorders
Pain and inflammation
Mouth and throat disorders
Skin disorders & minor wounds
Circulatory disorders
Fatigue & weakness
Loss of appetite
Eye discomfort

PHYSIOLOGICAL INDICATIONS OF FS

Respiratory tract health and natural defenses
Relaxation in case of stress, normal mood
Mental health and night rest
Intestinal health, constipation
Digestion, stomach acidity
Urinary tract health
Joint function
Functionality of the mucous membranes of the respiratory system
Throat health
Trophism and skin function
Cardiac health
Cholesterol control
Tonics
Restoratives
Vision health

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FOOD SUPPLEMENTS: "healthy lifestyle and illness prevention"

The European FD market was worth €8.3 billion in 2015, the Italian botanical market is one of the most prosperous markets in the EU with just under €1 billion (May 2015 to May 2016)!

The channels for distribution vary by country, with the majority of sales occurring in pharmacies (UK) but also independent pharmacies (F, D, DK and I), grocery stores (UK), drug stores (A), health food stores (DK), supermarkets (I), internet

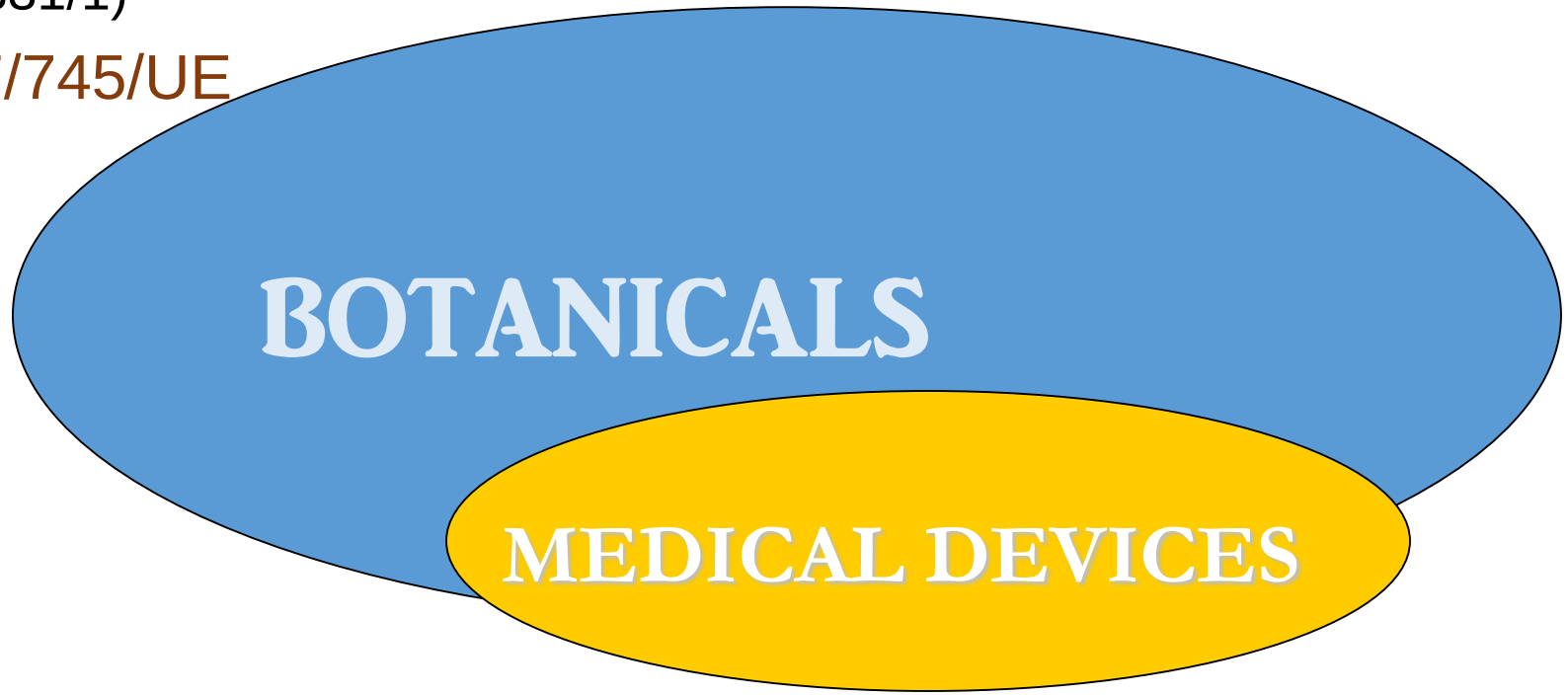
Food supplements

- Supermarket, drug store, internet etc.
- Health or nutrition claims
- Rarely contra-indications, limitations of use, interactions
- Physiological or nutritional properties to support or maintain a good health status
- Pharmaceutical appearance, in the form of tablets, powders, liquids, capsules etc..

- Notification (in 22 of 25 EU countries, not in NL)
- Food Authority: inspection of label

Medical Device Directives

- Medical Devices — Council Directive 93/42/EEC of 14 June 1993 (OJ No L 169/1 of 1993-07-12)
- Active Implantable Medical Devices —Council Directive 90/385/EEC of 20 June 1990 (OJ No L 189/17 of 1990-07-20)
- In-vitro diagnostic medical devices — Directive 98/79/EC of 27 October 1998 (1998-12-07 OJ No L 331/1)
- Regulation 2017/745/UE



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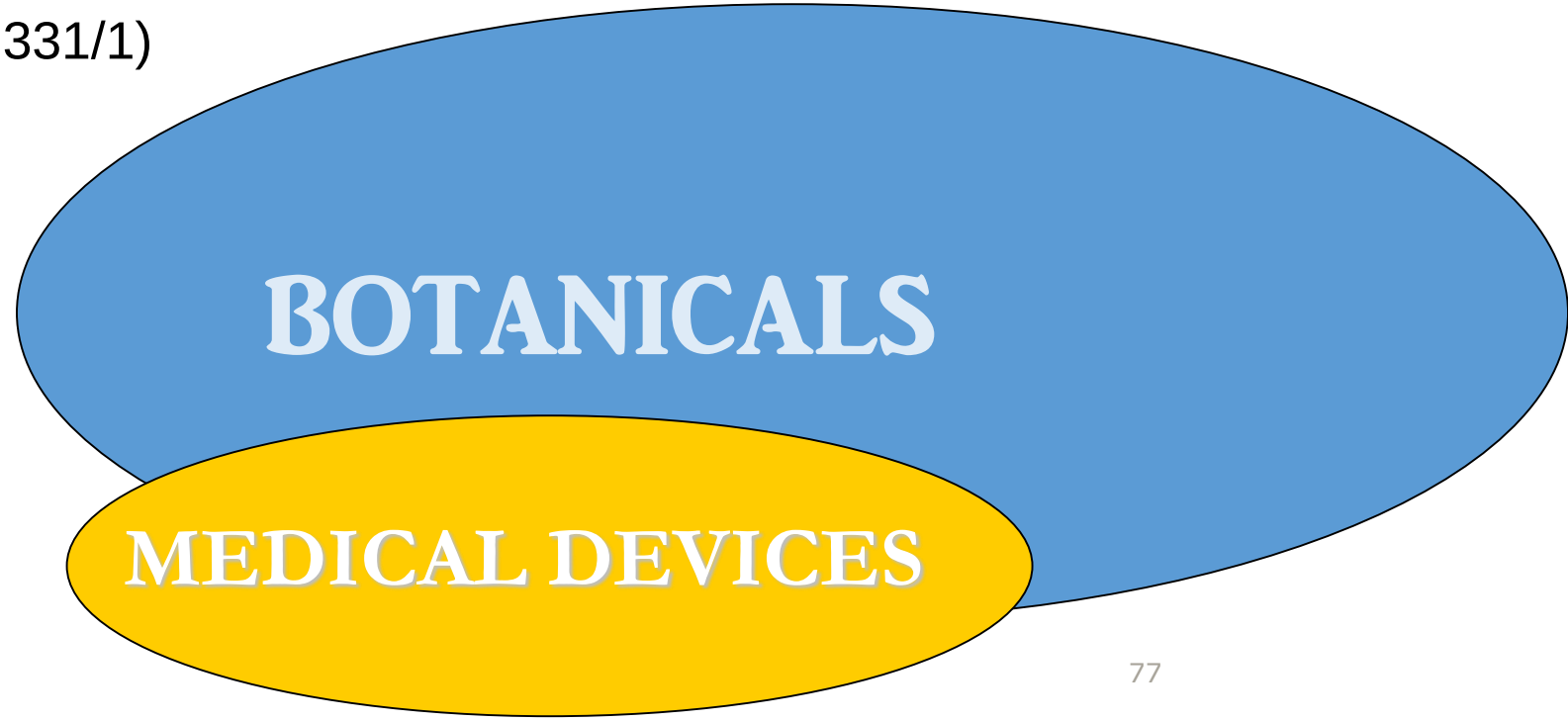
- In-vitro diagnostic medical devices — Directive 98/79/EC of 27 October 1998 (1998-12-07 OJ No L 331/1)



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`Medical device' means any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article:

a) intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:

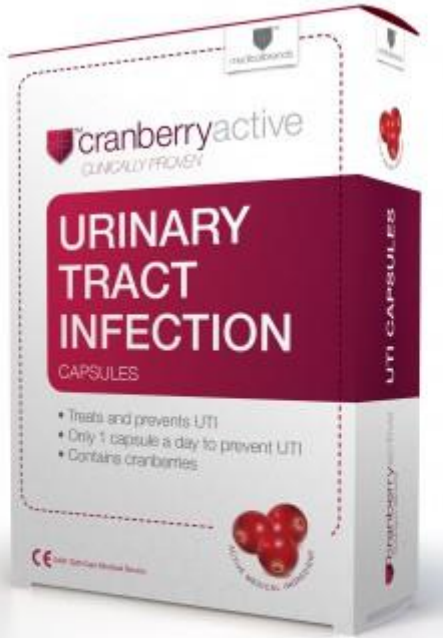
- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices,
- providing information for medical or diagnostic purposes by means of in-vitro examination of specimens derived from the human body;

and

b) which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.

Medical Devices: different routes of administrations, oral, ocular, nasal, mucosal, external uses etc..

According to the legal definition:
"….intended by the manufacturer to be used…
-for treatment or alleviation of disease,
-for alleviation of or compensation for an injury,
- …modification, or support .. of a physiological process,
-…which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.



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- Class I – low risk:

-Non-sterile dressings, bandages, hospital gowns, light sources
-Sterile: disposable surgical instruments, urine drainage bags, eye drops
-Measuring: scales, digital thermometers
-**Substance-based medical devices including botanical ingredients**

- Class IIa – medium risk

– catheters, tubings for anaesthesia/ventilation, ultrasound devices

- Class IIb – elevated risk

– intra-ocular lenses, breast implants, endoprostheses, ventilators

- Class III – high risk

– heart valves, reabsorbable implants

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Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC

HAVE ADOPTED THIS REGULATION:

CHAPTER I

SCOPE AND DEFINITIONS

Article 1

Subject matter and scope

1. This Regulation lays down rules concerning the placing on the market, making available on the market or putting into service of medical devices for human use and accessories for such devices in the Union. This Regulation also applies to clinical investigations concerning such medical devices and accessories conducted in the Union.

2. This Regulation shall also apply, as from the date of application of common specifications adopted pursuant to Article 9, to the groups of products without an intended medical purpose that are listed in Annex XVI, taking into account the state of the art, and in particular existing harmonised standards for analogous devices with a medical purpose, based on similar technology. The common specifications for each of the groups of products listed in Annex XVI shall address, at least, application of risk management as set out in Annex I for the group of products in question and, where necessary, clinical evaluation regarding safety.

The necessary common specifications shall be adopted by 26 May 2020. They shall apply as from six months after the date of their entry into force or from 26 May 2020, whichever is the latest.

Notwithstanding Article 122, Member States' measures regarding the qualification of the products covered by Annex XVI as medical devices pursuant to Directive 93/42/EEC shall remain valid until the date of application, as referred to in the first subparagraph, of the relevant common specifications for that group of products.

This Regulation also applies to clinical investigations conducted in the Union concerning the products referred to in the first subparagraph.

3. Devices with both a medical and a non-medical intended purpose shall fulfil cumulatively the requirements applicable to devices with an intended medical purpose and those applicable to devices without an intended medical purp

Article 2

Definitions

For the purposes of this Regulation, the following definitions apply:

(1) 'medical device' means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

— diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,

— diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,

— investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,

— providing information by means of *in vitro* examination of specimens derived from the human body, including organ, blood and tissue donations,

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

The following products shall also be deemed to be medical devices:

— devices for the control or support of conception;

cifically intended for the cleaning, disinfection or sterilisation of devices as referred to in nd of those referred to in the first paragraph of this point.

MAKING AVAILABLE ON THE MARKET AND PUTTING INTO SERVICE OF DEVICES, OBLIGATIONS OF ECONOMIC OPERATORS, REPROCESSING, CE MARKING, FREE MOVEMENT

Article 5

Placing on the market and putting into service

1. A device may be placed on the market or put into service only if it complies with this Regulation when duly supplied and properly installed, maintained and used in accordance with its intended purpose.

2. A device shall meet the general safety and performance requirements set out in Annex I which apply to it, taking into account its intended purpose.

3. Demonstration of conformity with the general safety and performance requirements shall include a clinical evaluation in accordance with Article 61.

4. Devices that are manufactured and used within health institutions shall be considered as having been put into service.

5. With the exception of the relevant general safety and performance requirements set out in Annex I, the requirements of this Regulation shall not apply to devices, manufactured and used only within health institutions established in the Union, provided that all of the following conditions are met:

(a) the devices are not transferred to another legal entity,

(b) manufacture and use of the devices occur under appropriate quality management systems,

(c) the health institution justifies in its documentation that the target patient group's specific needs cannot be met, or cannot be met at the appropriate level of performance by an equivalent device available on the market,

(d) the health institution provides information upon request on the use of such devices to its competent authority, which shall include a justification of their manufacturing, modification and use;

(e) the health institution draws up a declaration which it shall make publicly available, including:

(i) the name and address of the manufacturing health institution;

(ii) the details necessary to identify the devices;

(iii) a declaration that the devices meet the general safety and performance requirements set out in Annex I to this Regulation and, where applicable, information on which requirements are not fully met with a reasoned justification therefor,

(f) the health institution draws up documentation that makes it possible to have an understanding of the manufacturing facility, the manufacturing process, the design and performance data of the devices, including the intended purpose, and that is sufficiently detailed to enable the competent authority to ascertain that the general safety and performance requirements set out in Annex I to this Regulation are met;

(g) the health institution takes all necessary measures to ensure that all devices are manufactured in accordance with the documentation referred to in point (f), and

(h) the health institution reviews experience gained from clinical use of the devices and takes all necessary corrective actions.

Member States may require that such health institutions submit to the competent authority any further relevant information about such devices which have been manufactured and used on their territory. Member States shall retain the right to restrict the manufacture and the use of any specific type of such devices and shall be permitted access to inspect the activities of the health institutions.

This paragraph shall not apply to devices that are manufactured on an industrial scale.

From May 26th, 2020, the new Medical Device Regulation 2017/745) will be in force. Since it is a regulation and not a directive, national implementation is required to be as close to the original text as possible, allowing no room for interpretation.

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Substance-based medical devices can no longer be classified as Class I but at least Class IIa or IIb according to the new regulation, Rule 21: ”devices that are composed of substances, or of combinations of substances, intended to be introduced into the human body—via an orifice or applied to the skin and absorbed, or locally dispersed in the human body—are classified as class III or class IIa and IIb, respectively”.

CE Marking indicates that your medical device complies with the applicable EU regulations and enables the commercialization of your products in the European countries

Class I Conformity Assessment

- Manufacturer *self-declares* conformity for performance a*nd* for quality system (in view of the low level of vulnerability associated with such devices)
- Aspects of sterile products and measuring devices relating to sterility and/or metrology are certified by a Notified Body.

- For class IIa, class IIb and class III devices, an appropriate level of involvement of a notified body should be compulsory and at least the Technical Documentation needs to be updated according to the new requirements.
- Reclassification may include biological and clinical evaluations, which can be either literature-based or based on product-specific clinical or pre-clinical data.
- Clinical trials according to ISO 14155, and biocompatibility testing according to ISO 10993, may need to be performed.
- The affected products will then have to be re-certified for new CE marks.

The MDR is expected to come into effect in May 2020. Certificates issued prior to final implementation of the MDR will have a maximum validity of five years. However, all CE Mark certifications issued before implementation of the new regulations will automatically expire four years after the new regulations come into force.

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More transparency for patients and increased traceability: Development of the central European database, Eudamed

- The new Eudamed will provide information on manufacturers, notified bodies, clinical investigations, certificates, medical devices and incidents involving medical devices. Moreover, the database will provide information about the products marketed in the EU.
- Authorities, patients, healthcare professionals and the public will get access to Eudamed. The general public will get access to non-confidential information on manufacturers and devices in Eudamed.
- Medical devices must have a unique device identification (UDI) to facilitate the traceability throughout the supply chain from manufacturer to patient.

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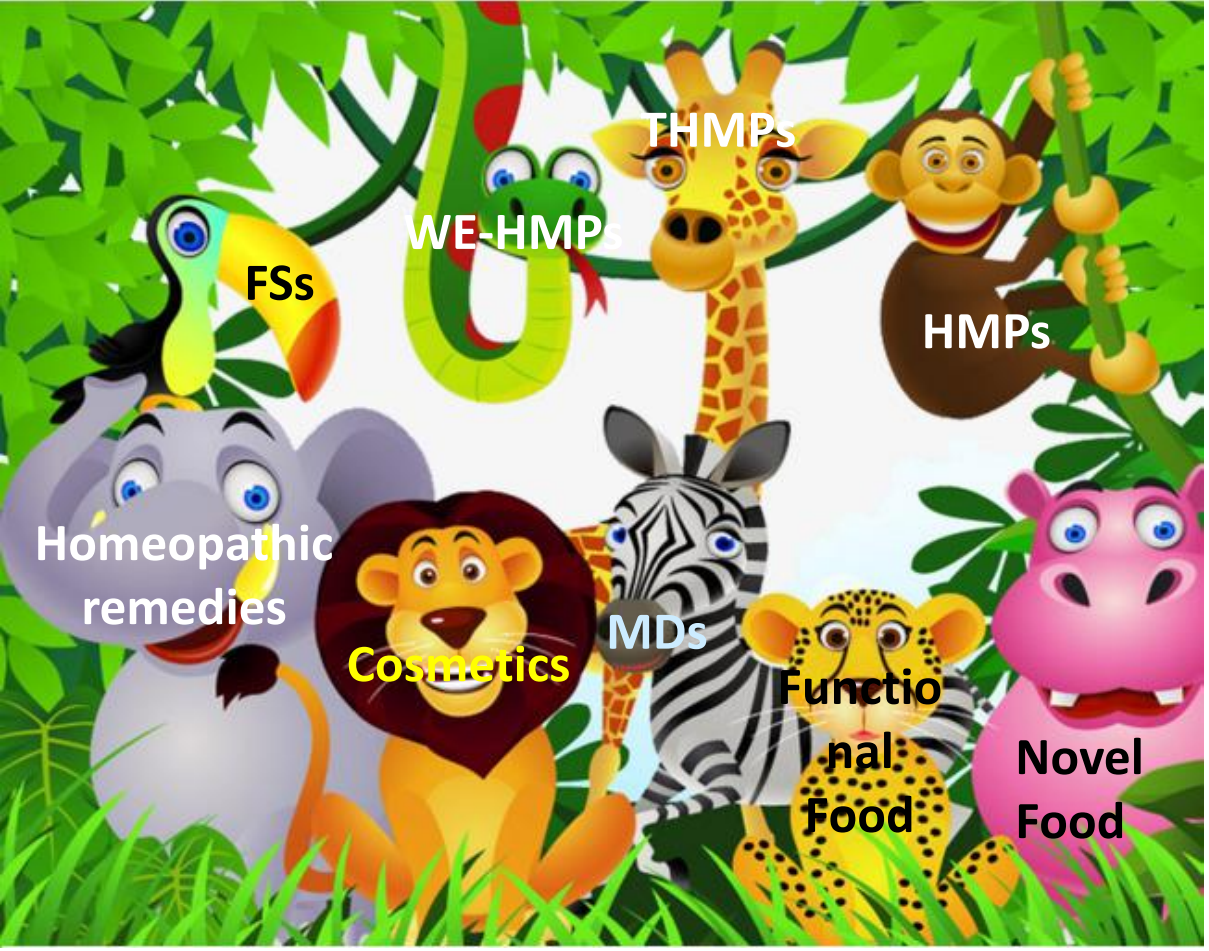
Medical Devices

- Pharmacy, drug store, etc.
- Medicinal claims
- Pharmaceutical appearance, in the form of tablets, eye drop, liquids, caspules etc..
- Appropriate level of involvement of a notified body (compulsory)
- Technical Documentation according to the class requirements
- Reclassification may include biological and clinical evaluations (literature-based or product-specific pre-clinical or clinical ISO 14155 studies)
- ISO 10993 biocompatibility testing
- Recertification for new CE marks or

- move to FS (marketability should be checked, incl. all additives and adjuvants)


Many products are hard to distinguish from a medicine or a medical device or food supplements.
Food Supplements
Pharmaceutical Products
Medical Devices
BORDERLINE PRODUCTS

	Plant										
Country	Camellia sinensis (L.) Kuntze (green tea, Theaceae)		Ginkgo biloba L. (ginkgo, Ginkgoaceae)		Panax ginseng C.A. Meyer (ginseng, Arialiaceae)		Hypericum perforatum L. (St. John's wort, Hypericaceae)		Valeriana officinalis L. (valerian, Valerianaceae)		Conditions of use: Quality or Safety Restrictions
	HMP	Others	HMP	Others	HMP	Others	HMP	Others	HMP	Others	
Austria	MP for topical use	Leaf as food	MP	Not included in list for teas/ tea-like products as food; use in FS only under limitations	MP, THMP	Roots included in list for teas/ tea-like products as food; use in FS only under limitations	MP, THMP, THMPC	Not included in list for teas/ tea-like products as food; use in FS only under limitations or for flavouring	MP, THMPC	Not included in list for teas/ tea-like products as food; use in FS only under limitations or for flavouring	Footnote 1
Belgium	THMP	FS, FSC	THMP	FS, FSC	THMP	FS, FSC	THMP	FS, FSC	THMP	FS, FSC	Footnote 2
France	THMP	FS, FSC	MP, THMP	FS, FSC	THMP	FS, FSC	MP	None	THMP	FS, FSC	Footnote 3
Germany	None	Food, for use as a tea	MP	Food, for use as a tea	MP	Food, for use as a tea	MP, THMP	Food	MP, THMP	Food	Footnote 4
Hungary	Paramedicines	Leaf, no restriction	MP, Paramedicines	Leaf, no restriction	Paramedicines	Root, no restriction	MP, THMP, Paramedicine	None	MP, THMP, Paramedicine	Roots, no restriction	Footnote 5
Ireland	None	FS, FSC	THMP	None	THMPC	FS, FSC	THMP	None	THMP, THMPC	None	Footnote 6
Italy	None	Leaf as food, extracts for FS, FSC, MD for internal and topical use, CP	MD for external use	FS, FSC, CP	None	Food, FS and FSC, CP	MP	FS/FSC	MP, THMPC when associated to Hop	FS/FSC	Footnote 7
Netherlands	MP	FS,FSC, CP	MP, THMP	FS, FSC	THMP	FS, FSC	MP, THMP, CP	FS, FSC	MP,THMP	FS, FSC	
Poland	None	FS, for use as a tea	MP	FS	MP	FS	MP-extract or tea	FS, for use as a tea, extract	MP	FS	
Portugal	MP (antiviral, ointment)	FS, FSC	MP	FS; FSC	MP	FS; FSC	None	FS; FSC	MP	FS, FSC	Footnote 8
Romania	None	FS/FSC	None	FS, FSC	None	FS, FSC	None	FS/FSC	None	FS, FSC	
Russia	MP	FSC	MP	FS, FSC	MP	FSC	MP	FSC	MP	FSC	Footnote 9
Spain	None	Leaf as food, extracts for FS, FSC, CP, MD, both for internal and topical use	MP	FS, FSC, CP/MD for external use	MP	Food, FS and FSC	None	FS, FSC	None	FS, FSC	
United Kingdom	MP	FS, FSC	None	FS, FSC	None	FS, FSC	THMPC	None	THMPC	Some very low dose FS & FSC	



THE JUNGLE OF BOTANICALS

Ginkgo biloba is sold as a food supplement in UK, I, B and NL, as a registered medicine in D, A, B and F but only as a 'prescription only' medicine in Ireland, as cosmetic and medical device in I. Both FS and Medicine in Russia and CH.

For colds and coughs in UK, for the prevention of arteriosclerosis in D (as FS). In the UK garlic products are licensed as medicines or FSs. In Italy garlic is only marketed as FS

Italy: only POM or FS with a dose of hypericin should be not more than 0,7 mg and the ratio hyperforins/hypericin not more than 7, without any restrictions. In UK as THMP, in CH as **hom./anthropos. MP** and THMP, in Russia both THMP and FS, in D, Hungary and A as THMP and MP, in B as FS and THMP, in Ireland only THMP, in F only MP. In Portugal only as FS.

A: THMP, MP or FS with limitations; B, I and F: FS or THMP; D: MP; I: FS or cosmetic, Poland and P: MD or FS; Romania, UK and Turkey: FS; Russia: FS and MP; CH: FS, MP, THMP;