Community Herbal Monographs and List Entries

New opportunities for traditional and well-established herbal products

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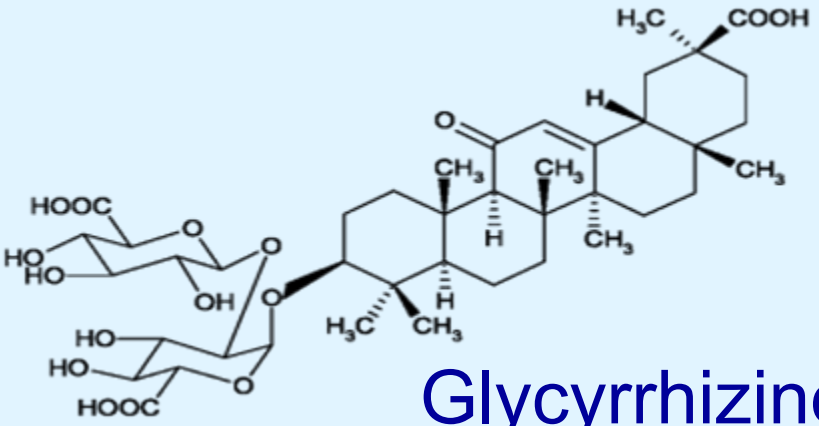


Glycyrrhizine

Herbal Medicinal Products in the EU

Access to the market

Marketing Authorization

1. **Full documentation with new tests and trials**

2. **Full bibliographic documentation (well-established use)**

3. **Mixed Applications**

Centralized or (mainly) national procedure with full access to mutual recognition or decentralized procedures

Herbal Medicinal Products in the EU

Access to the market

New option for access to the market:

Directive 2001/83 EC, Chapter 2a, Articles 16 a – 16 i

Registration

4. "Simplified dossier" for ***traditional herbal*** medicinal products

National procedure with limited access to mutual recognition or decentralized procedures

EMEA Committee on Herbal Medicinal Products

Chair / Vice-Chair: Dr. Konstantin Keller/ Dr. Heribert Pittner AU

Austria	Finland	Latvia	Romania
Estonia	France	Lithuania	Slovak Republic
Belgium	Germany	Luxembourg	Slovenia
Bulgaria	Greece	Malta	Spain
Cyprus	Hungary	Netherlands	Sweden
Czech Rep.	Ireland	Poland	United Kingdom
Denmark	Italy	Portugal	

4 co-opted Members:

Clinical Pharmacology, Pharmacology, Toxicology, Pediatrics

EEA Members:
Norway, Iceland

Observer: EDQM/Europ. Pharm.
Croatia, Turkey

Tools to facilitate access to the market

Directive 2001/83/EC

The Committee for Herbal Medicinal Products will prepare:

Article 16f

A list of traditional herbal drugs/-preparations/combinations

Article 16h

Community herbal monographs on herbal drugs or herbal drug preparations that may be used for full marketing authorisations of well-established herbal medicinal products or simplified registrations

Community herbal monographs

Article 16h

Community herbal monographs

Two types of monographs

1. monographs not depending from an application; e.g. initiatives from the Committee, Member States, scientific organisations, other stakeholders.

2. monographs following Article 16 c (4), that result from a registration procedure, i.e. referral by a Member State if the traditional use in the EU is less then 15 years.

Candidates for Community herbal monographs / list entries

Criteria for selection e.g.:

- availability of drafts and literature from previous HMPWP work
- market priority from stakeholders, e.g. from AESGP, ESCOP, GA
- availability of copies of literature, data for assessment
- ongoing discussion on risk assessment / management
- economy of work, e.g. closely related herbal substances
- availability of a rapporteur

EMEA guidance on procedures and templates is available from www.emea.europa.eu

Transparency on HMPC activities

European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 19 July 2007
Doc. Ref. EMEA/HMPC/314187/2007

COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

Meeting report, 4-5 July 2007

Detailed report after each meeting on www.emea.eu.int

Community Monographs / List
Status of assessment work

European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

London, 5 July 2007
Doc. Ref. EMEA/HMPC/278067/2006

COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

Overview of status of HMPC assessment work - July 2007

Listed in alphabetical order

R: Rapporteur assigned, D: Draft under discussion, P: Draft published,
PF: Assessment close to finalisation (pre-final), F: Final opinion adopted

Community Monographs / List
Status of assessment work

14 Final opinions adopted (Community Monographs)

Aloe (W)
Anisi fructus (T)
Anisi aetheroleum (T)
Sennae, fructus (W)
Sennae, folium (W)
Foeniculi amari fructus (T)
Foeniculi amari fructus aetheroleum (T)
Foeniculi dulcis fructus (T)
Frangulae cortex (W)
Lini semen (W) (T)
Plantaginis ovatae seminis tegumentum (W)
Plantaginis ovatae semen (W)
Psyllii, semen (W)
Valeriana officinalis L., radix (W) (T)

(W) well-established

(T) traditional

Information provided on monographs

Opinion
+ minority votes

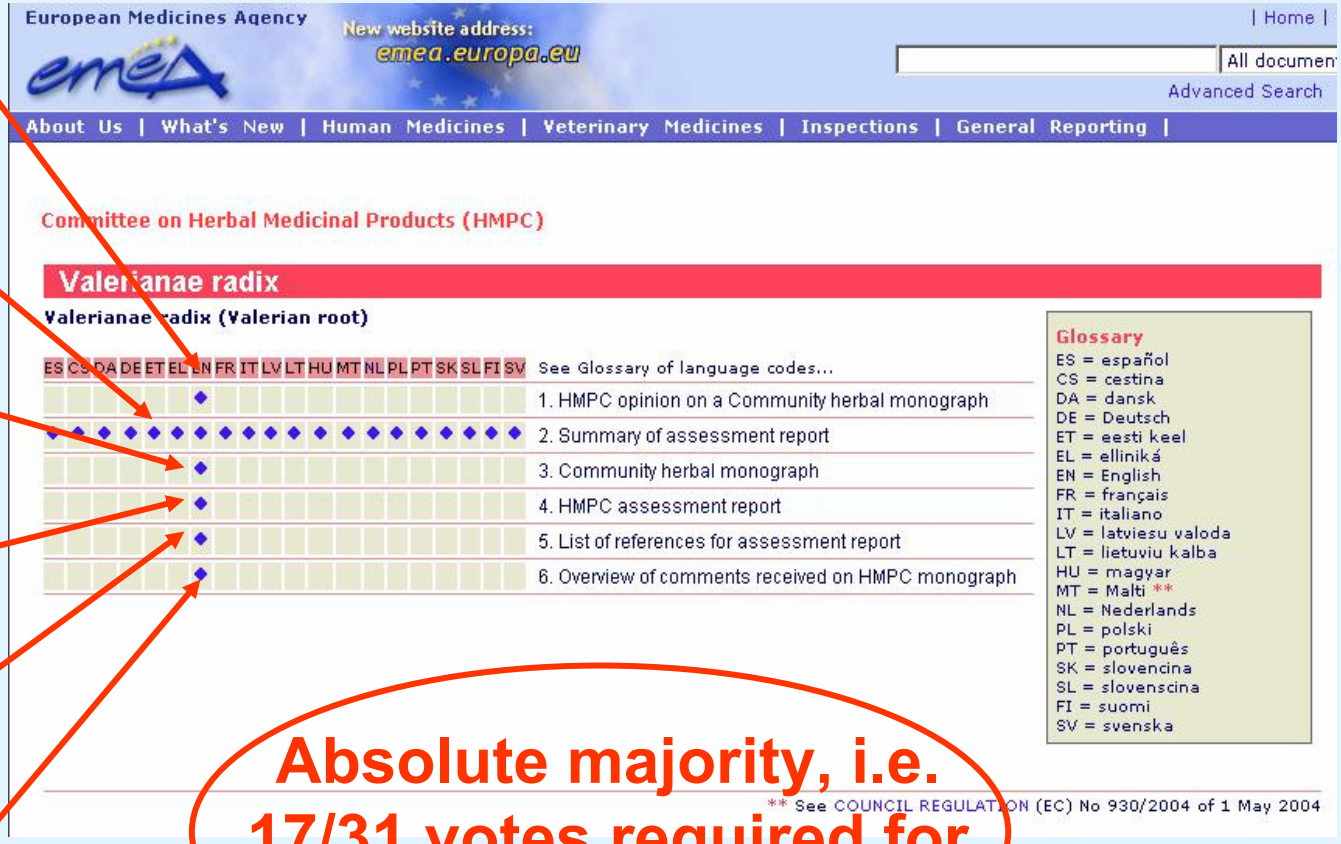
Summary AR
all languages

Monograph

Assessment Report

References

Overview of Comments



Absolute majority, i.e. 17/31 votes required for positive opinions

Community Monographs / List
Status of assessment work

14 Draft Monographs published for consultation

Betulae folium (T)
Calendulae flos (T)
Echinaceae purpureae herba (rec.) (W) (T)
Eleutherococci radix (T)
Lupuli flos (T)
Melissae folium (T)
Menthae piperitae aetheroleum (W) (T)
Menthae piperitae folium (T)
Passiflorae herba (T)
Primulae radix (T)
Primulae flos (T)
Rhamni purshianae cortex (W)
Rhei radix (W)
Thymi herba (T)

(W) well-established

(T) traditional

Community Monographs / List
Status of assessment work

10 Drafts under discussion

Avenae herba
Avenae fructus
Equiseti herba
Harpagophyti radix
Meliloti herba
Salicis cortex
Sambuci flos
Solidaginis virgaurea herba
Verbasci flos
Urticae herba

September 2007

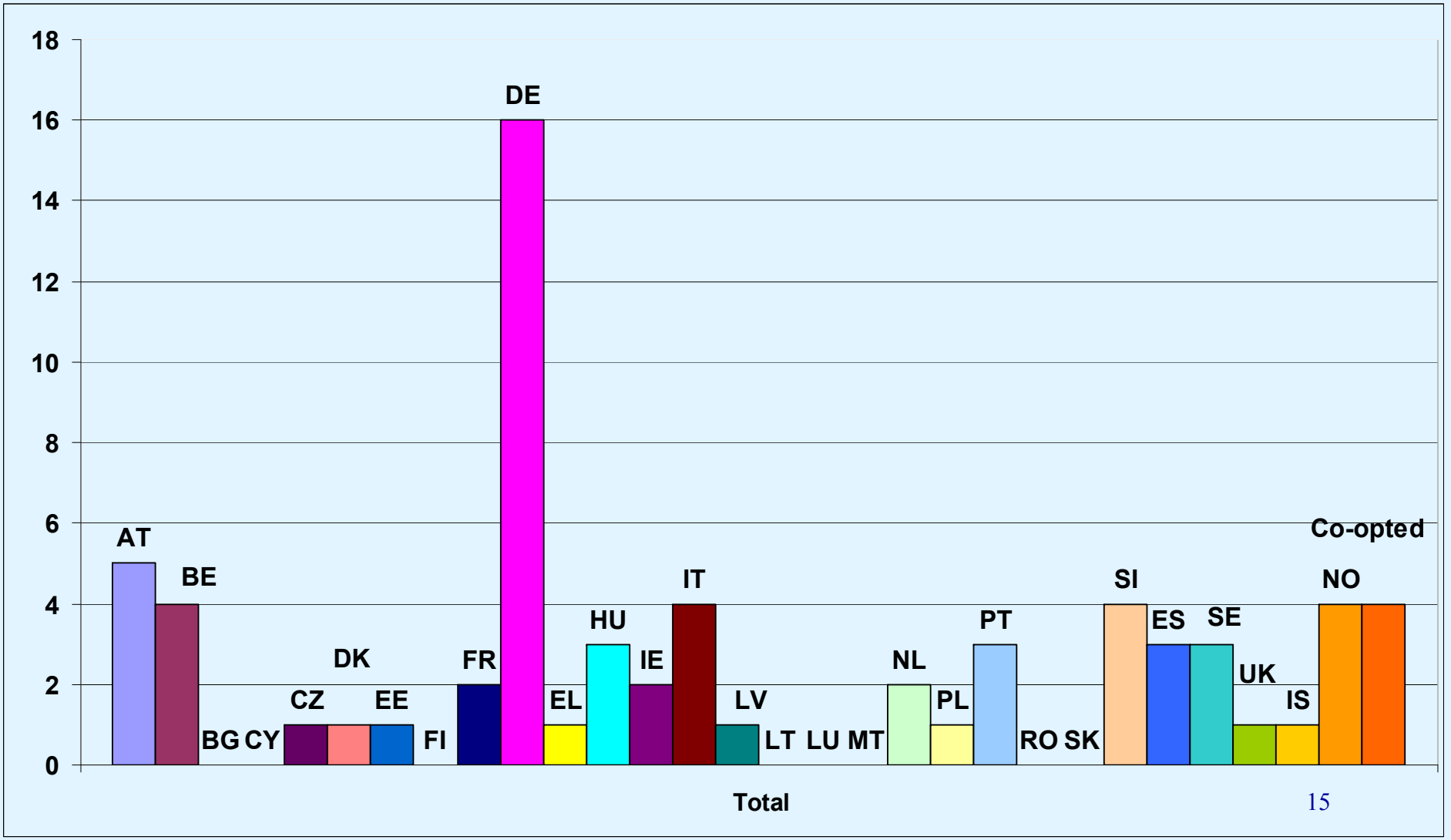
Community Monographs / List
Status of assessment work

Rapporteurs assigned for 27 herbal substances

Absinthii herba
Althaeae radix
Boldi folium
Carvi fructus
Centaurii herba
Cimicifugae rhizoma
Crataegi folium c. flore
Crataegi fructus
Curcumae longae rhiz.
Cynarae folium
Echinaceae ang. radix
Echinaceae pall. radix
Echinaceae purp. radix
Hamamelidis cortex
Hamamelidis folium
Hamamelidis fol.et cort., dist
Hippocastani semen
Hyperici herba
Lichen islandicus
Polygalae radix
Polypodii radix
Ribis nigri folium
Salviae folium
Urticae folium
Urticae radix
Uvae ursi folium
Zingiberis rhizoma

September 2007

Distribution of rapporteurship for monographs / list entries



Plantago ovata, sem. tegumentum
final monograph 26 October 2006

Well-established use

a) treatment of habitual constipation;

b) conditions in which easy defaecation with soft stool is desirable, e.g. in cases of painful defaecation after rectal or anal surgery, anal fissures and haemorrhoids;

c) in patients to whom an increased daily fibre intake may be advisable e.g. as an adjuvant in constipation predominant irritable bowel syndrome, as an adjuvant to diet in hypercholesterolemia

Traditional use

none

Menthae piperitae aetheroleum

draft monograph 8 May 2007

Well-established use

Oral use

1. symptomatic relief of minor spasms of the gastrointestinal tract, flatulence and abdominal pain, especially in patients with irritable bowel syndrome.

Cutaneous use

2. symptomatic relief of mild tension type headache.

Traditional use

Cutaneous and transdermal use

1. relief of symptoms in coughs and colds
2. symptomatic relief of localised muscle pain
3. symptomatic relief of localised pruritic conditions in intact skin

Inhalation

4. relief of symptoms in coughs and colds

Oromucosal use

5. relief of symptoms in coughs and colds

Echinaceae purp. herba

draft monograph 27 March 2007

Well-established use

oral use

Treatment of early symptoms of common cold

Traditional use

Cutaneous use

Treatment of small superficial wounds

Foeniculi fructus

final monograph 6 August 2007

Well-established use

none

Traditional use

a) symptomatic treatment of mild, spasmodic gastro-intestinal complaints including bloating and flatulence.

b) symptomatic treatment of minor spasm associated with menstrual periods.

c) as an expectorant in cough associated with cold.

Thymi herba

draft monograph 8 May 2007

Well-established use

none

Traditional use

as an expectorant in cough associated with cold.

Passiflorae herba
draft monograph 8 march 2007

5.3. PRECLINICAL SAFETY DATA

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

Information on missing pre-clinical data; pre-clinical safety not fully assessed

The impact of EU herbal monographs

Article 16 h (3)
Community herbal monographs

3.

….

When Community herbal ***monographs within the meaning of this paragraph*** have been established, they ***shall be taken into account*** by the ***Member States*** when examining an application. ….

When new Community herbal monographs are established, the ***registration holder*** shall consider whether it is necessary to modify the registration dossier accordingly. The ***registration holder*** shall notify any such modification to the competent authority of the Member State concerned.

Herbal Medicinal Products in the EU

Marketing Authorization (bibliographic)

2001/83/EC as amended by CD 2004/27/EC
Article 10a

…

By way of derogation from Article 8(3)(i), … the applicant shall not be required to provide the results of pre-clinical tests or clinical trials if he can demonstrate that the active substances of the medicinal product have been in well-established medicinal use within the Community for at least ten years, with recognized efficacy and an acceptable level of safety in terms of the conditions set out in the Annex.

In that event, the test and trial results shall be replaced by appropriate scientific literature.

European Commission, March 2006:
Guideline on the definition of a potential serious risk to public health

- "risk": probability that an event will occur
- "serious": hazard that could result in death, could be life-threatening, result in patient hospitalization, ... persistent or significant disability or incapacity, or could be a congenital anomaly/birth defect or prolonged signs in exposed humans.

Any major objection must be scientifically justified taking into account the nature and degree of any hazards, the magnitude of the risks involved, the benefits ... and the practicability of any measures to mitigate the risk.

Guideline on the definition of a potential serious risk to public health

Annex (NTA Volume 2C)

Examples that would normally not be considered as "Potential serious risks to public health":

...

- The absence of studies in non-target populations e.g. children
- differences in national practices
- WEU: absence of data from new pre-clinical tests or clinical studies if posology is based on "systematic and documented use" and the safety is based on pharmacovigilance data
- THMP: the lack of documentation on pre-clinical tests and clinical trials

...

List entries published

6 Drafts published for comments:

- Anisi fructus
- Calendulae flos
- Echinaceae purp. herba (topical use)
- Eleutherococci radix

- Lini semen *
- Valerianae radix *

* procedure suspended

List entries published

2 Proposals finalised:

- Foeniculi amari fructus
- Foeniculi dulcis fructus

The impact of the EU list

Article 16 f

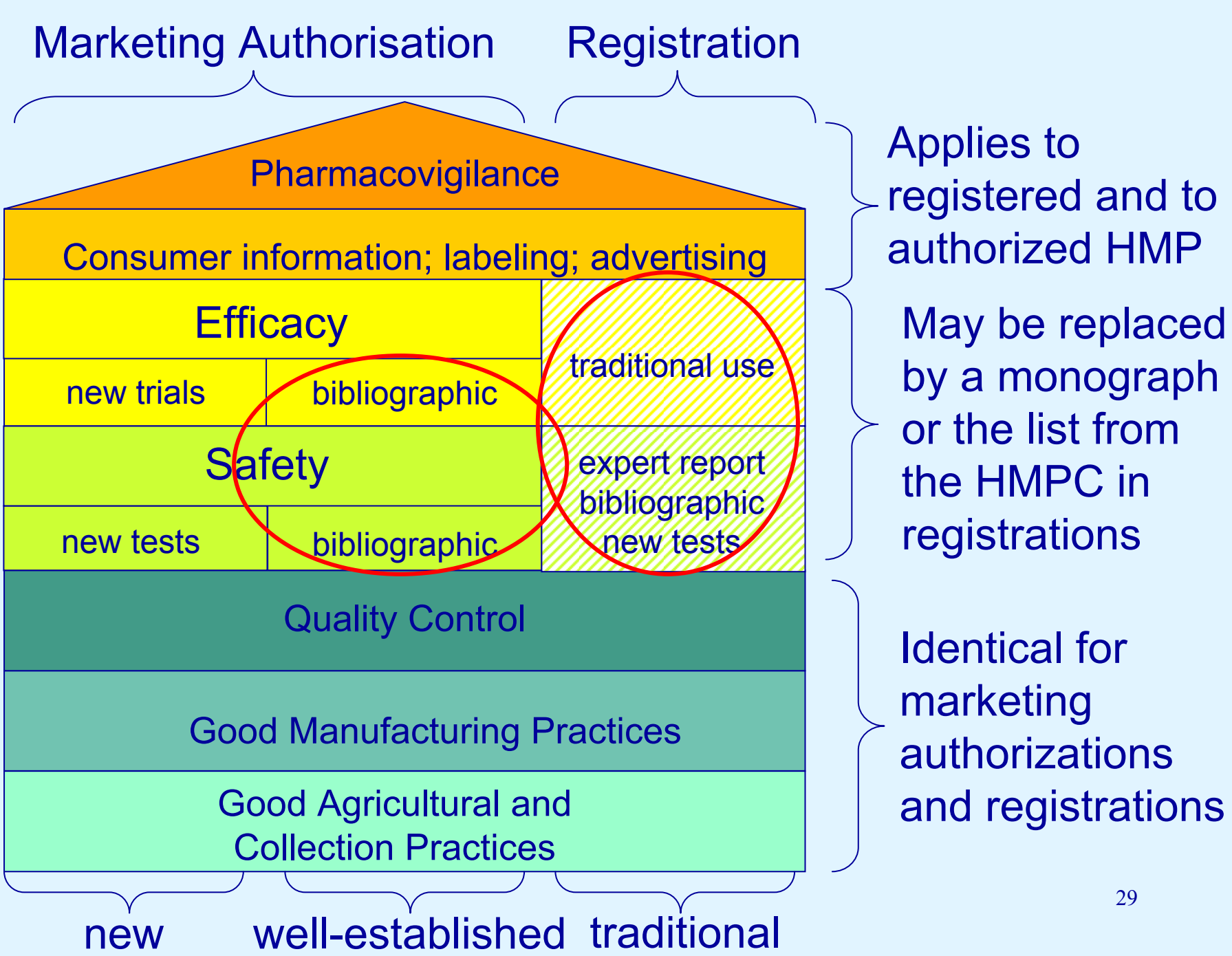
2. If an application for traditional-use registration relates to a herbal substance, preparation or a combination thereof contained in the list referred to in paragraph 1, the data specified in Article 16c(1)(b)(c) and (d) do not need to be provided. Article 16e(1)(c) and (d) shall not apply.

Applicant does not need to submit:

- information on previous authorisations/registrations
- evidence on traditional use
- bibliographic / expert evidence on safety

Competent authority cannot refuse the application:

- because the product could be harmful
- because of lack of plausibility / sufficient traditional use


Marketing Authorisation
Registration
Pharmacovigilance
Consumer information; labeling; advertising
Efficacy
new trials
bibliographic
Safety
new tests
bibliographic
traditional use
expert report
bibliographic
new tests
Quality Control
Good Manufacturing Practices
Good Agricultural and
Collection Practices
Applies to registered and to authorized HMP
May be replaced by a monograph or the list from the HMPC in registrations
Identical for marketing authorizations and registrations
new
well-established
traditional

Perspectives

- Essential guidance on quality, safety, efficacy and procedural guidance finalised
- Transparent requirements for quality, safety efficacy
- Important monographs adopted, new drafts published
- Legislation has been implemented in most of EU MS
- EMEA offers scientific services to applicants
- A number of applications submitted to national authorities already successfully processed
- Extension to other active substances is proposed by EC

Essential tools are ready, the opportunities are there!

We are ready to go!

Applications are welcome!