EU regulatory update on botanical substances and preparations in animal nutrition

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66th EAAP ANNUAL MEETING - Warsaw, Poland 2015

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Classification of botanical substances and preparations in feed (Reg. (EC) No 1831/2003)

- Feed material
  - Nutritional purposes
  - Minor processing (crushed dried herbs and spices)

- Feed additive
  - Sensory additives: flavouring compounds
  - Zootechnical additive (FRESTA® F)

- Premixture of feed additives
  - Mixture of flavouring compounds
  - Mixtures of different additives (commercial products)

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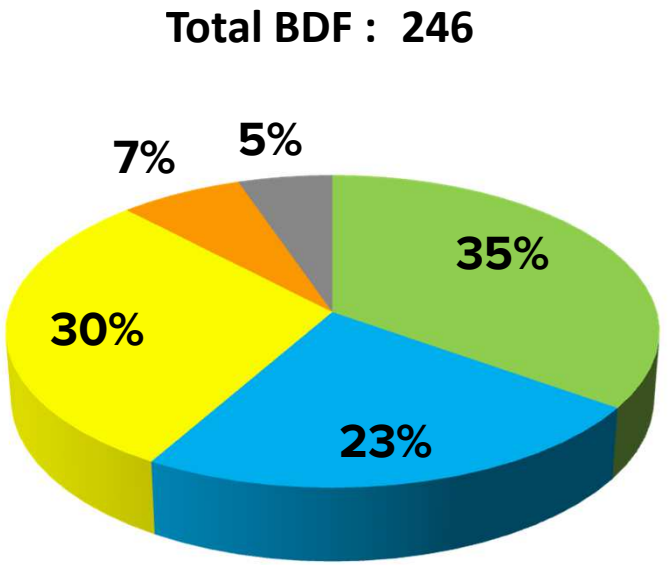
Botanically defined feed flavourings (BDF)

(by FEFANA – FFAC)

Type of Botanical

- EO → Essential oil
- EX → Extract
- Ti → Tincture
- O → Oleoresin
- R → Remains: absolute, distillate, concentrate and terpenes

Distribution of BDF



Based on the specifications of the International Organization of Standardization

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From plant to feeding though

Plant

- Farming / wild harvesting
- Basic processing of plants on farm (e.g. distillation)

Botanical

- Analytics
- Identity
- Development of specifications
- Quality control
- Standardisation
- Fractioning

Feed Flavouring

- Blending of flavouring compounds
- Coating
- Spray on carrier material

Compound Feed

- Mixing of feed materials with additives
- Processing (e.g. pelletizing)

Animal Feeding

- Feeding compound feed

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Application of botanicals as feed additive

Plant

Botanical

Feed Flavouring

Manufacturer of botanicals → **FFAC members /Applicant**

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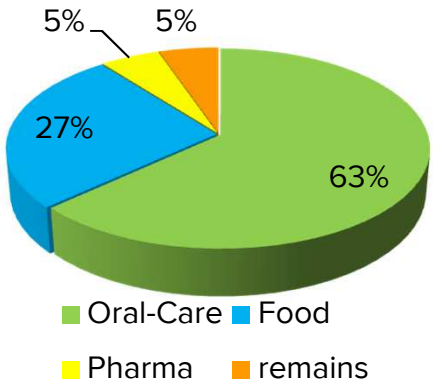
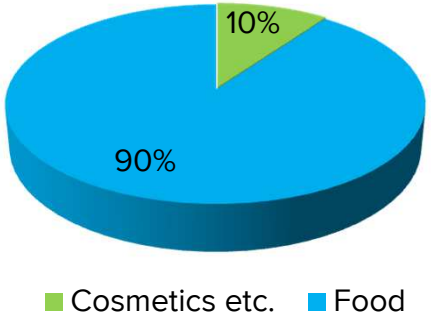
Market and trade channels

- Manufacturer of essential oils and other botanical extracts produce botanicals for different markets.
- The market distribution of essential oils and other botanical extracts differs between the botanicals.
- The predominant user of botanicals is the food industry. Less the 10% of the overall botanical production is used in the feed industry.

Mint oil: 12,500 to



Star anise oil: 4,000 to



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EFSA evaluation of botanicals

Preparatory work to streamline the evaluation process

- EFSA guidance: Safety assessment of botanical compounds and preparations
- Compendium of botanicals
- QPS concept

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Safety assessment of botanical compounds and preparations (EFSA guidance, EFSA Journal 2009; 7(9):1249)

Level A

Assessment of existing data related to the preparation

- Sufficient data available for safety assessment
- Use levels ≤ history of safe use levels
- Consideration of exposure to substances of concern (TTC, NOAEL, safety margin)

Level B

Evaluation of additional data related to the preparation

- Toxicity studies required according to OECD guidelines

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EFSA compendium of botanicals

(EFSA Journal 2012;10(5):2663)

"...The purpose of the Compendium is to assist risk assessors responsible for the evaluation of specific ingredients in food supplements, in more easily identifying the compound(s) of concern on which to focus the assessment.

...without any judgment on whether they are suitable or not suitable for food applications in Europe; it has no legal or regulatory force pertaining to the legal classification of products or substances."

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EFSA compendium of botanicals

(EFSA Journal 2012;10(5):2663)

The Compendium comprises around 900 botanical entries, identifying for each of them the scientific name, the most common synonyms, the plant part containing compound(s) of concern, the chemical(s) of concern, specific remarks and references of relevance for a safety assessment.

- **Annex A**: Botanicals for which not enough information on possible substances of concern or adverse effects could be found, or for which the information present could not be verified

- **Annex B**: Botanicals for which data are available but the Scientific Committee could not identify substances of concern, or other reasons for the inclusion in the compendium

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QPS approach for botanicals (EFSA Journal 2014;12(3):3593)

Generic assessment system allowing for priority setting among botanicals to be evaluated

- The EFSA guidance for the safety assessment of botanicals foresees that botanicals for which an adequate body of knowledge exists could benefit from a “presumption of safety” without any need for further testing
- The applicability for botanical species of a Qualified Presumption of Safety (QPS) approach, similar to that developed for the assessment of selected microorganisms referred to EFSA and added to the food chain was considered
- The use of botanicals and botanical preparations in animal feed is excluded from consideration at this stage

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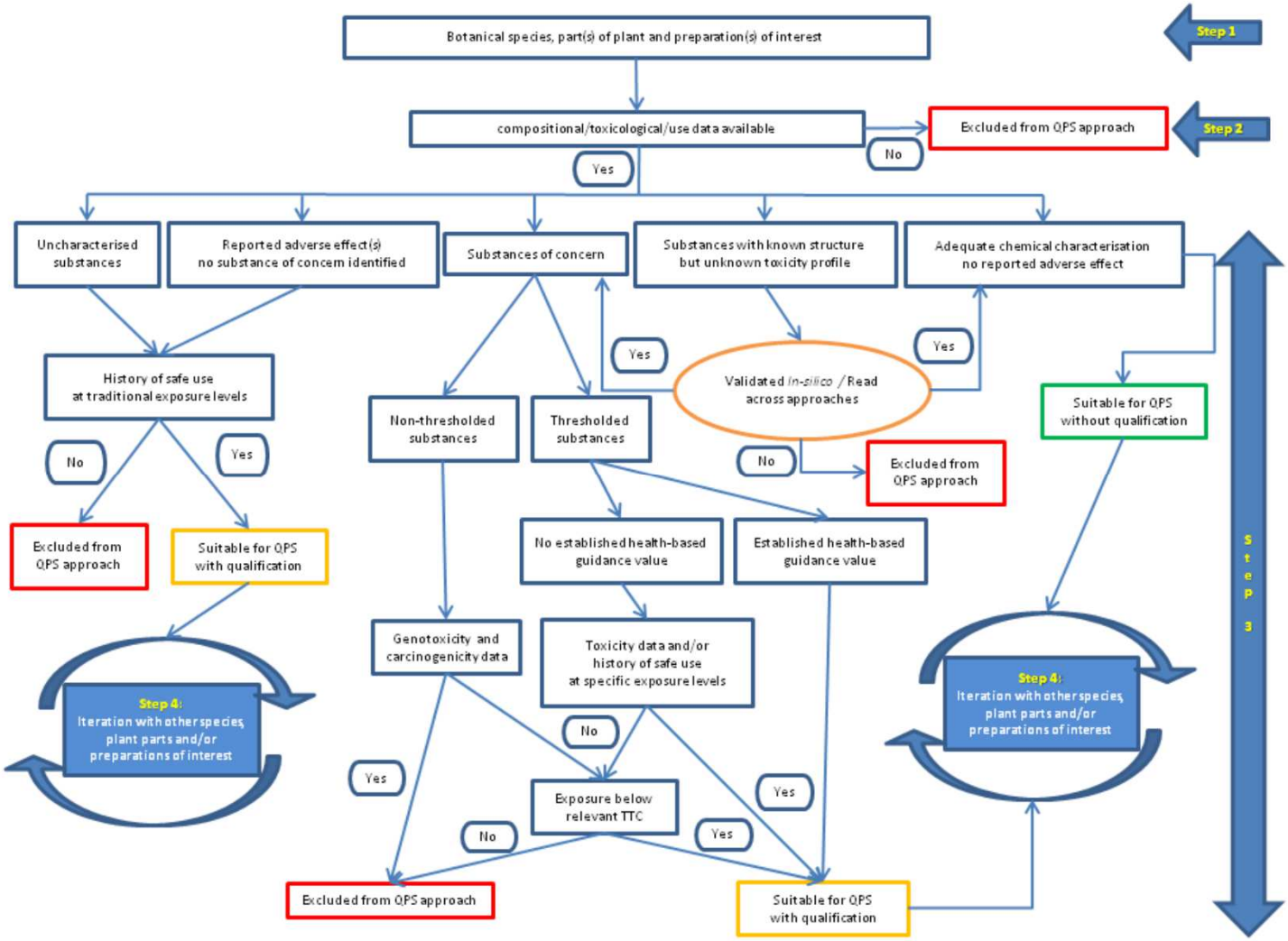
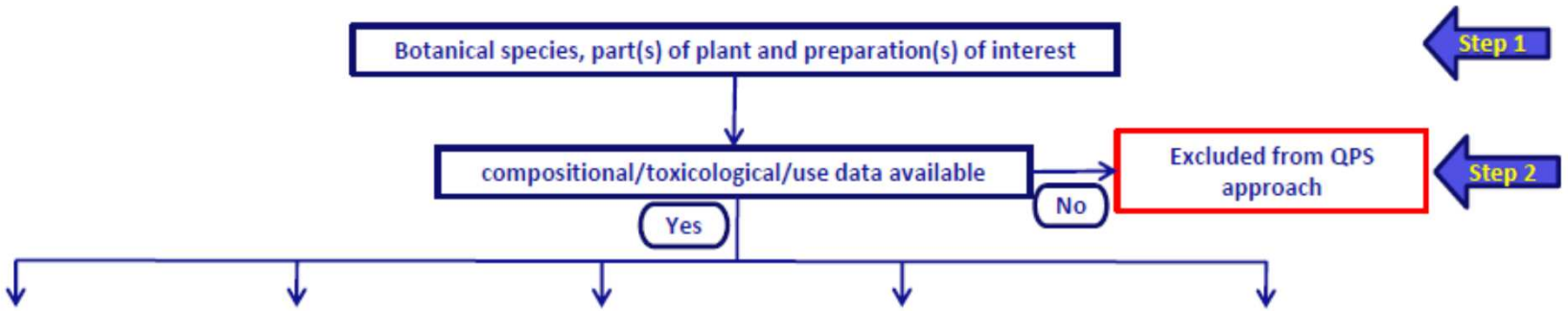
Methodology for QPS assessment (EFSA Journal 2014;12(3):3593)



Methodology for QPS assessment (EFSA Journal 2014;12(3):3593)



Step 1: Definition of the botanical due to variation in composition

- Plant species/subspecies
- Plant origin/environmental conditions
- Plant parts
- Plant processing

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Composition of Rosemary oil of different origin

	Rosemary oil	
Composition %	Spanish type	Moroccan type
a-pinene	18 - 26	9 - 14
camphene	8 - 12	2.5 - 6.0
b-pinene	2.0 - 6.0	4.0 - 9.0
b-myrcene	1.5 - 5.0	1.0 - 2.0
limonene	2.5 - 5.0	1.5 - 4.0
cineole	16 - 25	38 - 55
p-cymene	1.0 - 2.2	0.8 - 2.5
camphor	13 - 21	5.0 - 15
bornyl acetate	0.5 - 2.5	0.1 - 1.5
a-terpineol	1.0 - 3.5	1.0 - 2.6
borneol	2.0 - 4.5	1.5 - 5.0
verbenone	0.7 - 2.5	< 0.4

Definition of the botanical

- Variation in chemical composition is huge
- Availability of information on full composition is limited
- Are analytical methods available?
- Description of plant extracts in scientific trials is limited

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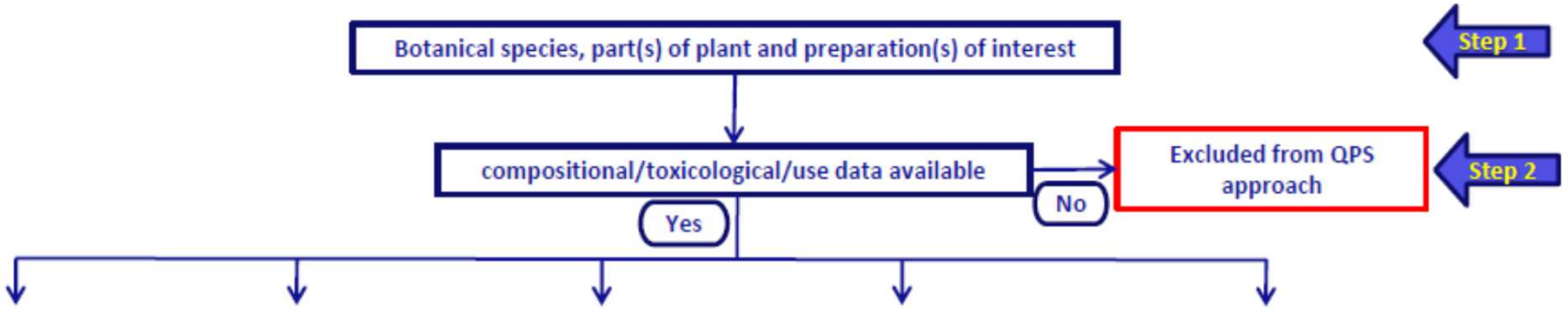
Methodology for QPS assessment (EFSA Journal 2014;12(3):3593)



Step 2: Evaluation of available data (compositional/toxicological/use)

- 99% characterisation
- Quantify active substances
- History of use

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QPS approach for botanicals

- Reiterative applications of the assessment scheme to related botanicals or different botanical preparations obtained from the same plant variety can allow a QPS status to be derived for specific botanical groupings.
- The particularity of botanicals makes the possibility of establishing QPS status at high taxonomic levels quite limited.
- Still, the structured safety assessment scheme provides a practical method of implementing the Level A of the 2009 EFSA Guidance
- the QPS approach, while possible, offers only limited advantages over the existing procedure and may not be cost-effective in the short term

Bernard Bottex, Scientific Committee and Emerging Risks Unit
EFSA workshop: Barcelona, 6 May 2015

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Substances of concern

FEEDAP: 109th Plenary Meeting (27-29 January 2015):

"A discussion took place regarding the presence of substances with genotoxic-carcinogenic properties, like estragole and methyl- eugenol, in feed additives. These substances are components of essential oils of botanical origin, like star anise oil and clove oil. The Panel stated that the intentional addition of such substances to the food chain via feed additives is not acceptable. This applies independently from the origin of the substances (chemical synthesis or botanical origin)."

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Botanicals containing substances of concern - examples

Plant	Additive	Substance	%
Ocimum basilicum	Basil oil	Estragole Methyl eugenol	10 – 90 0 – 2.5
Pimpinella anisum	Anise oil	Estragole	0 – 10
Illicium verum	Anise star tincture	Estragole	0 – 6
Foeniculum vulgare	Fennel tincture	Estragole	0 – 7
Artemisia dracunculus	Tarragon oil	Estragole	70 – 90
Laurus nobilis	Laurel leaves extract/oleoresin	Methyl eugenol	0 – 3
Cananga odorata	Ylang-ylang oil	Methyl eugenol	0 – 2
Pimenta racemosa	Bay oil	Methyl eugenol	1 – 3
Pimenta dioica	Allspice oil	Methyl eugenol	2 – 10

~ 30% of botanicals are affected

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Substances of concern – restriction in food

Regulation (EC) Nº 1334/2008, Annex III Part B

Substance	Restriction in food	max. level mg/kg
Methyleugenol	Dairy products	20
	Meat products	15
	Fish products	10
	Soups and sauces	60
	Ready-to-eat savouries	20
	Non-alcoholic beverages	1

No maximum use levels defined for feed

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Threshold of Toxicological Concern concept

(EFSA Journal 2012;10(7):2750)

Cramer class	Max. safe feed use (mg/kg feed)	Max. intended use of botanical (mg/kg feed)	
		5	25
I	1.0	20%	4%
II	0.3	6%	1.2%
III	0.05	1%	0.2%

Andrew Chesson, WG on Botanical Feed Flavourings
EFSA workshop: Barcelona, 6 May 2015

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Safety evaluation – key issues to be solved

- “Substances of concern” occurring in botanical flavourings enter the feed chain in lower dosages if compared to food
- Considerations of the PlantLIBRA project: toxicity of botanicals is not the arithmetical sum of the toxicity of its ingredients
- Target animal safety
  - Short life time of food producing animals
  - Metabolic pathways at low dosages
- Consumer safety
  - exposure calculation should consider metabolism by animals
  - Crucial parameter for safety evaluation should be the presence of residues in animal tissues.

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Industry activities

- Provide additional data on the identity of the botanical
  - Additional resources required
  - Support of manufactures?
  - Support from research institutes for identity?

- Clean-up the list of botanicals that will supported by FFAC
  - Amount of substances
  - Target animal species
  - Use level

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EFSA workshop - Barcelona, 6 May 2015

Key issues for the assessment of botanical flavourings

http://www.efsa.europa.eu/en/events/event/150506a

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Impact on the industry

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Outlook – to be discussed....

- How many botanical substances will be authorized as feed additives?
- Who will provide additional resources to characterize botanicals (research institutes, EU-funding....)
- How will the authorisation procedure effect future product development and research activities?
- ...

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Foto: www.pestodigenova.it