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SCIENTIFIC OPINION

Safety and efficacy of a feed additive consisting of an essential oil derived from the flowering tops of *Thymbra capitata* (L.) Cav. (Spanish type origanum oil) for use in all animal species (FEFANA asbl)

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The declarations of interest of all scientific experts active in EFSA's work are available at https://ess.efsa.europa.eu/doi/doiweb/doisearch

Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of an essential oil from the flowering tops of *Thymbra capitata* (L.) Cav. (Spanish type origanum oil) when used as a sensory additive in feed and in water for drinking for all animal species. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that the additive under assessment is considered safe up to the maximum use level in complete feed of 15 mg/kg for poultry species, 30 mg/kg for pigs and horses, 20 mg/kg for ruminants, 25 mg/kg for rabbits, dogs, cats and ornamental fish, and 125 mg/kg for salmonids. These conclusions were extrapolated to other physiologically related species. For any other species, the additive is safe at 15 mg/kg complete feed. The FEEDAP Panel considered that the use level in water for drinking is safe provided that the total daily intake of the additive does not exceed the daily amount that is considered safe when consumed via feed. The use of the additive in animal feed under the proposed conditions of use is safe for the consumer and the environment. Regarding user safety, the essential oil under assessment should be considered as an irritant to skin and eyes and as a dermal and respiratory sensitiser. Since *T. capitata* and its preparations were recognised to flavour food and its function in feed would be essentially the same as that in food, no further demonstration of efficacy was considered necessary.

KEYWORDS

carvacrol, efficacy, flavouring compounds, safety, sensory additives, Spanish type origanum oil, *Thymbra capitata* (L.) Cav., thymol menthone

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1 | INTRODUCTION

1.1 | Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7. In addition, Article 10(2) of that Regulation specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, within a maximum of seven years after the entry into force of this Regulation.

The European Commission received a request from Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)[2] for authorisation/re-evaluation of 41 additives (king of bitter extract, thyme leaved gratiola tincture, svils claw extract, delvils claw tincture, lavender oil, lavender tincture, spike lavender oil, melissa oil, balm leaves extract, mentha arvensis/corn mint oil, pennyroyal oil, spearmint oil, peppermint oil, peppermint tincture, basil oil, basil tincture, olive extract, marjoram oil, oregano oil, oregano tincture, patchouli oil, rosemary oil, rosemary oleoresin, rosemary extract, rosemary tincture, Spanish sage oil, sage oil, sage tincture, clary sage oil, savoury summer oil, savoury summer tincture, Pau darco tincture, thymus, origanum oil, thyme oil, thyme oleoresin, thyme extract, thyme tincture, lilac chastetree extract, lilac chastetree tincture, Spanish marjoram oil and wild thyme tincture) belonging to botanically defined group (BDG) 01 – Lamiales, when used as a feed additive for all animal species (category: sensory additives; functional group: flavouring compounds). During the assessment, the applicant withdrew the applications for nine additives.[3] These additives were deleted from the register of feed additives.[4] In addition, during the course of the assessment, the application was split and the present opinion covers only one out of the remaining 32 additives under application: thymus origanum oil[5] from the flowering tops of *Thymbra capitata* (L.) Cav.[6] for use in all animal species.

The remaining 31 additives belonging to botanically defined group (BDG) 01 – Lamiales, under application are assessed in separate opinions.

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority deleted (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive) and under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 1 June 2011.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the feed additive consisting of Spanish type origanum oil from *Thymbra capitata* (L.) Cav., when used under the proposed conditions of use (see Section 3.3.3).

1.2 | Additional information

Spanish type origanum oil from *T. capitata* (L.) Cav. is currently authorised under the name 'Thymus origanum oil' as a feed additive according to the entry in the European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003 (2b natural products – botanically defined). It has not been assessed as a feed additive in the EU.

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[7] in support of the authorisation request for the use of Spanish type origanum oil from *T. capitata* as a feed additive. The dossier was received on 30/8/2024 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2024-00541.[8]

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2]On 13/3/2013, EFSA was informed by the applicant that the applicant company changed to FEFANA asbl, Avenue Louise 130 A, Box 1, 1050 Brussels, Belgium.
[3]Thyme leaves gratiola tincture, spike lavender oil, melissa oil, pennyroyal oil, basil oil and savoury summer oil (27 February 2019); Spanish majoram oil (28 September 2023); lilac chastetree extract and savoury summer tincture (8 July 2024).
[4]Register of feed additives, Annex II, withdrawn by OJ L162, 10.5.2021, p. 5.
[5]In the current assessment referred to as Spanish origanum oil. The oil is also commonly described as Oregano oil Spanish type.
[6]Accepted name: *Thymbra capitata* (L.) Cav., synonyms: *Coridothymus capitatus* Rchb.f.; *Thymus capitatus* Hoffmanns. & Link.
[7]Dossier reference: FAD-2010-0137.
[8]The original application EFSA-Q-2010-0137 was split on 30/8/2022 and a new EFSA-Q-2024-00541 was generated.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports and experts' knowledge, to deliver the present output.

Many of the components of the essential oil under assessment have been already evaluated by the FEEDAP Panel as chemically defined flavourings (CDGs). The applicant submitted a written agreement to reuse the data submitted for the assessment of chemically defined flavourings (dossiers, publications and unpublished reports) for the risk assessment of additives belonging to BDG 01, including the current one under assessment.[9]

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the phytochemical markers in the additive. The evaluation report is related to the methods of analysis for each feed additive included in the group BDG 01 – Lamiales. During the assessment, upon request of EFSA, the EURL issued a partial report,[10] which included the additive under assessment. In particular, the EURL recommended a method based on gas chromatography with flame ionisation detection (GC–FID) for the quantification of the phytochemical markers *thymol* and *carvacrol* in *thymus origanum oil*.[11]

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Spanish type origanum oil from *T. capitata* is in line with the principles laid down in Regulation (EC) No 429/2008[12] and the relevant guidance documents: Guidance on safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements (EFSA Scientific Committee, 2009), Compendium of botanicals that have been reported to contain toxic, addictive, psychotropic or other substances of concern (EFSA, 2012), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018), Guidance on the assessment of the safety of feed additives for the users (EFSA FEEDAP Panel, 2023), Guidance document on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals (EFSA Scientific Committee, 2019a), Statement on the genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019b), Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment (EFSA Scientific Committee, 2019c).

3 | ASSESSMENT

The additive under assessment, Spanish type origanum oil, is an essential oil obtained from the flowering tops of *T. capitata* (L.) Cav. and is intended for use as a sensory additive (functional group: flavouring compounds) in feed and in water for drinking for all animal species.

3.1 | Origin and extraction

T. capitata (L.) Cav. (synonyms *Coridothymus capitatus* (L.) Rchb.f., *Origanum capitatum* (L.) Kuntze, *Thymus capitatus* (L.) Hoffmanns. & Link) is a small woody perennial shrub belonging to the family Lamiaceae. It is native to and widely distributed throughout the subtropical regions of the Mediterranean. It has many common names including conehead thyme and Spanish oregano. The aerial parts have long been used in perfumery and to flavour wines and cheese, and as aqueous extracts for medical purposes. *T. capitata* essential oil is rarely referred to as such by the flavour industry. It is more commonly described as Oregano oil Spanish type because its composition and, in particular, its high carvacrol content resembles that of the oil from *Origanum vulgare* L.

Most commercial descriptions of the essential oil recognise the currently accepted name *T. capitata* for the botanical source. However, in 2008 the International Organization for Standardization (ISO) description of the oil of Origanum, Spanish type changed the source name from *T. capitata* to *Coridothymus capitatus*, describing *T. capitata* as a synonym. This change was confirmed and retained in 2022 with the result that some commercial descriptions follow the ISO nomenclature (ISO 14717:2008).

The additive is extracted from the flowering tops of *T. capitata* by steam distillation. The volatile constituents are condensed and then separated from the aqueous phase by decantation.

[9]Technical dossier/Supplementary information August 2024/Letter dated 27/08/2024.

[10]Additives included in the partial report: Spanish sage oil, peppermint oil, thymus origanum oil, patchouli oil, clary sage oil, lavender oil and sage oil.

[11]The full report is available on the EU Science Hub https://joint-research-centre.ec.europa.eu/eurl-fa-eurl-feed-additives/eurl-fa-authorisation/eurl-fa-evaluation-reports_en.

[12]Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

3.2 | Uses other than feed flavouring

There is no specific EU authorisation for any preparations of *T. capitata* when used to provide flavour in food. However, according to Regulation (EC) No 1334/2008[13] flavouring preparations produced from food, may be used without an evaluation and approval as long as 'they do not, on the basis of the scientific evidence available, pose a safety risk to the health of the consumer and their use does not mislead the consumer'.

3.3 | Characterisation

3.3.1 | Characterisation of Spanish type origanum oil

The essential oil is obtained from the flowering tops of *T. capitata* sourced from Spain and is a clear, yellow to brown, mobile liquid with a characteristic odour. Spanish type origanum oil is identified with the single Chemical Abstracts Service (CAS) number 8007-11-2, the European Inventory of Existing Commercial Chemical Substances (EINECS) number 290-371-1, the Flavor Extract Manufacturers Association (FEMA) number 2828 and the Council of Europe (CoE) number 454. In five batches of the additive, the refractive index (20°C) was within the range of proposed specification (1.504–1.508).[14]

For Spanish type origanum oil, the specifications used by the applicant are based on the standard developed by ISO 14717:2008 for oil of Origanum, Spanish type.[15] Five components contribute to the specifications as shown in Table 1, with carvacrol and thymol selected as the phytochemical markers. Analysis of five batches of the additive showed compliance with the specifications when analysed by GC-FID and expressed as percentage of gas chromatographic peak area (% GC area).

TABLE 1 Constituents of Spanish type origanum oil, as defined by specifications: batch to batch variation based on the analysis of five batches by gas chromatography with flame ionisation detector (GC–FID). The content of each constituent is expressed as the area per cent of the corresponding chromatographic peak (% GC area), assuming the sum of chromatographic areas of all detected peaks as 100%.

Constituent EU register name	CAS No	FLAVIS No	% GC area		
			Specification[a]	Mean	Range
Carvacrol	499-75-2	04.031	60–75	69.9	69.1–70.3
Thymol	89-83-8	04.006	0–5	1.4	1.1–1.6
p-Cymene (1-isopropyl-4-methylbenzene)	99-87-6	01.002	5.5–9	7.7	6.8–8.4
γ-Terpinene	99-85-4	01.020	3.5–10	5.3	4.1–6.7
β-Caryophyllene	87-44-5	01.007	2–5	3.2	3.0–3.5

Abbreviations: CAS No, Chemical Abstracts Service number; EU, European Union; FLAVIS No, EU Flavour Information System numbers.

[a]Specification defined based on GC–FID analysis.

The applicant provided a full analysis of the same five batches obtained by gas chromatography–mass spectrometry (GC–MS).[16] In total, up to 65 peaks were detected in the chromatograms, 62 of which were identified and accounted for on average 99.2% (98.9%–99.8%) of the % GC area. The five compounds indicated in the product specifications accounted for 89.5% on average (range 88.4%–90.5%) of the % GC area when measured by GC–MS (Table 2). Besides these five compounds, 25 compounds were detected at individual levels of > 0.1% and are also listed in Table 2. These 30 compounds together account on average for 98.6% (range 98.2%–99.5%) of the % GC area. The remaining 32 compounds (ranging between 0.1% and 0.004%) and accounting for 0.6% on average of the GC area are listed in the footnote.[17] Based on these data, Spanish type origanum oil is considered a fully defined mixture (EFSA Scientific Committee, 2019a).

[13]Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Regulation (EC) No 1601/91 of the Council, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC. OJ L 354, 31.12.2008, p. 34.

[14]Technical dossier/Supplementary information July 2023/Annex_II_SIn_reply_ Thymus_origanum_oil_COA_chrom.

[15]Technical dossier/Supplementary information July 2023/Annex_III_SIn_reply_Thymus_origanum_oil_ISO_14717_2008.

[16]Technical dossier/Supplementary information July 2023/Annex_II_SIn_reply_ Thymus_origanum_oil_COA_chrom.

[17]Additional constituents ($n = 30$) between < 0.1 and ≥ 0.004%: carvacryl acetate, *(E)*-α-bisabolene, palustradiene, δ-3-carene, octan-3-one, 4-terpinenyl acetate, *l*-carvone, linalyl acetate, dihydrocarvone, aromadendrene, abietatriene, (+)-δ-cadinene, eugenol, β-thujone, *trans*-3,7-dimethyl-1,3,6-octatriene, 2-(4-methylphenyl)propan-2-ol, octan-3-ol, viridiflorol, *trans*-3,7-dimethylocta-2,6-dienal, lavandulyl acetate, neral, *trans-p*-2-menthen-1-ol, viridiflorene, γ-cadinene, carvenone, *(Z)*-nerol, geranyl acetate, spathulenol, linalool oxide, methyl citronellate, *cis*-3,7-dimethyl-1,3,6-octatriene and γ-muurolene.

TABLE 2 Constituents of Spanish type origanum oil accounting for > 0.2% of the composition: batch to batch variation based on the analysis of five batches by gas chromatography–mass spectrometry (GC–MS). The content of each constituent is expressed as the area per cent of the corresponding chromatographic peak (% GC area), assuming the sum of chromatographic areas of all detected peaks as 100%.

Constituent			% GC area	
EU register name	**CAS No**	**FLAVIS No**	**Mean**	**Range**
Carvacrol	499-75-2	04.031	72.14	71.22–73.10
Thymol	89-83-8	04.006	1.72	1.24–2.06
p-Cymene (1-isopropyl-4-methylbenzene)	99-87-6	01.002	7.72	6.81–8.28
γ-Terpinene	99-85-4	01.020	4.56	3.58–5.72
β-Caryophyllene	87-44-5	01.007	3.32	2.96–3.69
Linalool	78-70-6	02.013	1.21	1.02–1.34
α-Terpinene	99-86-5	01.019	1.21	0.84–1.45
Myrcene	123-35-3	01.008	0.98	0.12–1.25
α-Pinene (pin-2(3)-ene)	80-56-8	01.004	0.86	0.84–0.88
4- Terpinenol	562-74-3	02.072	0.78	0.71–0.82
α-Thujene	2867-05-2	–	0.77	0.67–0.88
d,l-Borneol	507-70-0	02.016	0.42	0.33–0.46
β-Caryophyllene epoxide	1139-30-6	16.043	0.36	0.20–0.57
Oct-1-en-3-ol	3391-86-4	02.023	0.24	0.10–0.34
d-Limonene[a]	5989-27-5	01.045	0.24	0.14–0.39
1,8-Cineole	470-82-6	03.001	0.23	0.16–0.28
α-Phellandrene	99-83-2	01.006	0.22	0.17–0.26
β-Pinene (pin-2(10)-ene)	127-91-3	01.003	0.21	0.20–0-23
β-Phellandrene	555-10-2	01.055	0.21	0.20–0.23
Thymohydroquinone	2217-60-9		0.19	0.19–0.20
Terpineol	8000-41-7	02.230	0.16	0.15–0.18
β-Bisabolene	495-61-4	01.028	0.16	0.14–0.17
Terpinolene	586-62-9	01.005	0.15	0.14–0.16
Sabinene hydrate	546-79-2	02.085	0.15	0.13–0.17
Camphor[b]	76-22-2	–	0.14	0.04–0.22
α-Thujone[c]	546-80-5	–	0.13	0.07–0.19
Camphene	79-92-5	01.009	0.13	0.09–0.15
3,7,10-Humulatriene	6753-98-6	01.043	0.12	0.09–0.15
2-Methyl-5-(propan-2-ylidene)cyclohexane-1,4-diol	–	–	0.11	0.10–0.12
1-Isopropyl-2-methoxy-4-methylbenzene	1076-56-8	04.043	0.11	0.05–0.25
Total			98.60	98.16–99.54[d]

Abbreviations: CAS No, Chemical Abstracts Service number; EU, European Union; FLAVIS No, EU Flavour Information System number.

[a]Stereochemistry not given, however considering that the naturally occurring limonene is typically *d*-limonene, it is assumed that this form also occurs in Spanish type origanum oil.

[b]Present in the additive as a mixture of enantiomers (*d,l*-camphor), the ratio between *d*- and *l*-stereoisomers not given.

[c]Substance (α- and β-thujone) which shall not be added as such to food (Annex III), maximum level in food is set by Regulation (EC) No 1334/2008, including alcoholic beverages, except those produced from Artemisia species (10 mg/kg), alcoholic beverages produced from Artemisia species (35 mg/kg) and non-alcoholic beverages (0.5 mg/kg).

[d]The values given for the Total are the lowest and the highest values of the sum of the components in the individual batches analysed.

The essential oil contains low concentrations of α-thujone (≤ 0.19%) and β-thujone (≤ 0.03%) which are included in the list of substances which shall not be added as such to food according to Annex III of Regulation (EC) No 1334/2008, and for which maximum levels in food are set by Regulation (EC) No 1334/2008.[18] α-Thujone and β-thujone have previously been evaluated as components of feed additives (EFSA FEEDAP Panel, 2021). The applicant performed a literature search for the chemical composition of *T. capitata* and its preparations to identify the presence of any other recognised substances of concern.[19] Apart

[18]Regulation (EC) No 1334/2008 of the European Parliament and of the Council of 16 December 2008 on flavourings and certain food ingredients with flavouring properties for use in and on foods and amending Council Regulation (EEC) No 1601/91, Regulations (EC) No 2232/96 and (EC) No 110/2008 and Directive 2000/13/EC. OJ L 354, 31.12.2008, p. 34.

[19]Technical dossier/Supplementary information July 2023/Literature search_Thymus_origanum_oil.

from thujones reported in two publications (Jayari et al., 2022; Maniki et al., 2023), no other substances of concern were identified. The EFSA compendium did also not report the occurrence of substances of concern (EFSA, 2012).[20]

3.3.1.1 | *Impurities*

The applicant referred to the 'periodic testing' of some representative flavourings premixtures for mercury, cadmium, lead, arsenic, fluoride, dioxins and polychlorinated biphenyls (PCBs), organo-chlorine pesticides, organo-phosphorous pesticides, aflatoxins (B1, B2, G1, G2) and ochratoxin A. However, no data were provided on the presence of these impurities.

3.3.2 | Shelf-life

The typical shelf-life of Spanish type origanum oil is stated to be at least 12 months, when stored in tightly closed containers under standard conditions (in a cool, dry place protected from light).[21] However, no data supporting this statement were provided.

3.3.3 | Conditions of use

Spanish origanum oil is intended to be added to feed and water for drinking for all animal species without a withdrawal period. The maximum proposed use levels in complete feed for all animal species and categories are listed in Table 3. No use level has been proposed by the applicant for the use in water for drinking.

TABLE 3 Maximum proposed use levels of Spanish type origanum oil in complete feed.

Animal category	Maximum use level (mg/kg complete feed)
Chickens for fattening	15
Laying hens	15
Turkeys for fattening	15
Piglets	30
Pigs for fattening	30
Sows	30
Veal calves (milk replacer)	20
Cattle for fattening	20
Dairy cows	20
Sheep/goats	20
Horses	30
Rabbits	25
Salmon	125
Dogs	25
Cats	25
Ornamental fish	25
Other(s)	15

3.4 | Safety

The assessment of the safety of Spanish type origanum oil is based on the maximum use levels in complete feed proposed by the applicant (Table 3).

No studies to support the safety for target animals, consumers and users were performed with the additive under assessment. The applicant carried out an extensive database search (no time limits) to identify data related to the chemical composition and the safety of preparations obtained from *T. capitata*.[22] Four cumulative databases (LIVIVO, NCBI, OVID and ToxInfo), 13 single databases and 12 publishers' search facilities including Elsevier, Ingenta, Springer and Wiley were used. The keywords used covered different aspects of safety and the inclusion and exclusion criteria were provided by the applicant.

[20]Online version: https://www.efsa.europa.eu/en/data-report/compendium-botanicals.

[21]Technical dossier/Section II.

[22]Technical dossier/Supplementary information July 2023/ Literature search_Thymus_origanum_oil.

Many of the individual components of the essential oil have been already assessed as chemically defined flavourings for use in feed and food by the FEEDAP Panel, the EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food (AFC), the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) and/or by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). The flavouring compounds currently authorised for food[23] and/or feed[24] use, together with the EU Flavour Information System (FLAVIS) number, the chemical group as defined in Commission Regulation (EC) No 1565/2000,[25] and the corresponding EFSA opinion are listed in Table 4.

TABLE 4 Flavouring compounds already assessed by EFSA and/or by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) as chemically defined flavourings, grouped according to the chemical group (CG) as defined in Commission Regulation (EC) No 1565/2000, with indication of the EU Flavour Information System (FLAVIS) number and the corresponding EFSA/JECFA opinion.

CG	Chemical group	Product (EU register name)	FLAVIS No	EFSA/JECFA opinion,* year
01	Straight-chain primary aliphatic alcohols/aldehydes/acids, acetals and esters with esters containing saturated alcohols and acetals containing saturated aldehydes	Methyl citronellate[a]	09.517	WHO (2000) (JECFA)
03	a, ß-Unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters	(Z)-Nerol	02.058	2016a
		Neral	05.170	
		trans-3,7-Dimethylocta-2,6-dienal (geranial)	05.188	
		Geranyl acetate	09.011	
04	Non-conjugated and accumulated unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals and esters	Lavandulyl acetate	09.612	2011a, CEF
05	Saturated and unsaturated aliphatic secondary alcohols, ketones and esters with esters containing secondary alcohols	Oct-1-en-3-ol	02.023	2020
		Octan-3-ol	02.098	2015a
		Octan-3-one	07.062	
06	Aliphatic, alicyclic and aromatic saturated and unsaturated tertiary alcohols and esters with esters containing tertiary alcohols ethers	Linalool	02.013	2012a
		2-(4-Methylphenyl) propan-2-ol	02.042	
		α-Terpineol	02.014	
		4-Terpinenol	02.072	
		Terpineol	02.230	
		Linalyl acetate	09.013	
		Sabinene hydrate	02.085	WHO (2000)
08	Secondary alicyclic saturated and unsaturated alcohols, ketones, ketals and esters with ketals containing alicyclic alcohols or ketones and esters containing secondary alicyclic alcohols	*d,l*-Borneol	02.016	2016b
		l-Carvone	07.147	
		d-Camphor[b]	07.215	
		Dihydrocarvone[a,c]	07.128	WHO (2000)
13	Furanones and tetrahydrofurfuryl derivatives	Linalool oxide[d]	13.140	2012b
16	Aliphatic and alicyclic ethers	1,8-Cineole	03.001	2012c, 2021
18	Allylhydroxybenzenes	Eugenol	04.003	2011
25	Phenol derivatives containing ring-alkyl, ring-alkoxy and side-chains with an oxygenated functional group	Thymol	04.006	2012d
		Carvacrol	04.031	
26	Aromatic ethers including anisole derivatives	1-Isopropyl-2-methoxy-4-methylbenzene	04.043	2012e

[23]Commission Implementing Regulation (EU) No 872/2012 of 1 October 2012 adopting the list of flavouring substances provided for by Regulation (EC) No 2232/96 of the European Parliament and of the Council, introducing it in Annex I to Regulation (EC) No 1334/2008 of the European Parliament and of the Council and repealing Commission Regulation (EC) No 1565/2000 and Commission Decision 1999/217/EC. OJ L 267, 2.10.2012, p. 1.

[24]European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed-eu-reg-comm_register_feed_additives_1831-03.pdf.

[25]Commission Regulation (EC) No 1565/2000 of 18 July 2000 laying down the measures necessary for the adoption of an evaluation programme in application of Regulation (EC) No 2232/96 of the European Parliament and of the Council. OJ L 1 80, 19.7.2000, p. 8.

TABLE 4 (Continued)

CG	Chemical group	Product (EU register name)	FLAVIS No	EFSA/JECFA opinion,* year
31	Aliphatic and aromatic hydrocarbons and acetals containing saturated aldehydes	1-Isopropyl-4-methylbenzene (*p*-cymene)	01.002	2015b
		Terpinolene	01.005	
		α-Phellandrene	01.006	
		α-Terpinene	01.019	
		γ-Terpinene	01.020	
		d-Limonene	01.045	
		Pin-2(10)-ene (β-pinene)	01.003	2016c
		Pin-2(3)-ene (α-pinene)	01.004	
		β-Caryophyllene	01.007	
		Myrcene	01.008	
		Camphene	01.009	
		δ-3-Carene	01.029	
		3,7,10-Humulatriene[a,e]	01.043	2011b, CEF
		β-Phellandrene[a,e]	01.055	
		Limonene[a,f]	01.001	2015a, CEF
		β-Bisabolene[a]	01.028	
		cis-3,7-Dimethyl-1,3,6-octatriene	01.064	
		cis-β-Ocimene[a]		
32	Epoxides	β-Caryophyllene epoxide[a]	16.043	2014, CEF

*FEEDAP opinion unless otherwise indicated.

[a]Evaluated for use in food. According to Regulation (EC) 1565/2000, flavourings evaluated by JECFA before 2000 are not required to be re-evaluated by EFSA.

[b]JECFA and EFSA evaluated the enantiomer *d*-camphor [07.159] (name in the register: *(1R,4R)*-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one) for use in food (EFSA, 2008) and in feed (EFSA FEEDAP Panel, 2016b).

[c]JECFA evaluated dihydrocarvone [07.128] as a mixture of *cis*- and *trans*-dihydrocarvone.

[d]Linalool oxide [13.140]: A mixture of *cis*- and *trans*-linalool oxide (5-ring) was evaluated [13.140] (EFSA FEEDAP Panel, 2012b).

[e]Evaluated applying the 'Procedure' described in the Guidance on the data required for the risk assessment of flavourings to be used in or on food (EFSA CEF Panel, 2010). No longer authorised for use as flavours in food, as the additional toxicity data requested (EFSA CEF Panel, 2011b) were not submitted and the CEF Panel was unable to complete its assessment (EFSA CEF Panel, 2015a).

As shown in Table 4, a number of the components of Spanish type origanum oil, accounting for about 95% of the GC peak areas, have been previously assessed and considered safe for use as flavourings. They are currently authorised for use in food[26] without limitations and for use in feed[27] at individual use levels higher than those resulting from the intended use in feed of the essential oil under assessment, with the exception of carvacrol.[28] Subsequently, thymol, carvacrol and *l*-carvone were assessed in tolerance studies with a mixture of flavourings referred to as 'Herbal' in chickens for fattening, piglets, cattle for fattening and salmons. The tolerance studies showed that thymol and carvacrol are safe up to 125 mg/kg complete feed for all animal species and *l*-carvone up to 10 mg/kg complete feed (EFSA FEEDAP Panel, 2023b).

Two compounds, listed in Table 4, namely 3,7,10-humulatriene [01.043] and β-phellandrene [01.055], have been evaluated in Flavouring Group Evaluations (reference to FGE.25Rev2) by applying the procedure described in the Guidance on the data required for the risk assessment of flavourings to be used in or on foods (EFSA CEF Panel, 2010). For these compounds, for which there is no concern for genotoxicity, EFSA requested additional sub-chronic toxicity data (EFSA CEF Panel, 2011b). In the absence of such toxicological data, the CEF Panel was unable to complete its assessment (EFSA CEF Panel, 2015a). As a result, these compounds are no longer authorised for use as flavours in food. For these compounds, in the absence of toxicity data, the FEEDAP Panel applies the threshold of toxicological concern (TTC) approach or read-across from structurally related substances, as recommended in the Guidance document on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals (EFSA Scientific Committee, 2019a).

The oil under assessment contains up to 0.19% α-thujone and 0.03% of β-thujone. These substances have been evaluated by the FEEDAP Panel as components of expressed lemon oil (EFSA FEEDAP Panel, 2021).

[26]Commission Implementing Regulation (EU) No 872/2012 of 1 October 2012 adopting the list of flavouring substances provided for by Regulation (EC) No 2232/96 of the European Parliament and of the Council, introducing it in Annex I to Regulation (EC) No 1334/2008 of the European Parliament and of the Council and repealing Commission Regulation (EC) No 1565/2000 and Commission Decision 1999/217/EC. OJ L 267, 2.10.2012, p. 1.

[27]European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003. https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed-eu-reg-comm_register_feed_additives_1831-03.pdf.

[28]The FEEDAP Panel concluded that the 'The flavouring compounds included in CG 25 are calculated to be safe for all animal species at a maximum level of 5 mg/kg complete feed. The high use levels proposed for thymol and carvacrol (125 mg/kg) could not be confirmed as safe' (EFSA FEEDAP Panel, 2012d).

Eighteen compounds have not been previously assessed for use as flavourings. The FEEDAP Panel notes that 10 of them[29] accounting for 1.1% of the GC–MS area are aliphatic monoterpenes or sesquiterpenes structurally related to flavourings already assessed in CG 31 and a similar metabolic and toxicological profile is expected. Because of their lipophilic nature, they are expected to be rapidly absorbed from the gastro-intestinal tract, oxidised to polar oxygenated metabolites, conjugated and excreted (EFSA FEEDAP Panel, 2015b, 2016c).

The genotoxic potential for eight compounds (*trans*-p-2-menthen-1-ol, 4-terpinenyl acetate, spathulenol, viridiflorol, carvenone, 2-methyl-5-(propan-2-ylidene)cyclohexane-1,4-diol, carvacryl acetate, thymohydroquinone) was predicted with the Organisation for Economic Co-operation and Development (OECD) QSAR Toolbox.[30] No alerts were identified for in vitro mutagenicity, genotoxic and non-genotoxic carcinogenicity, or other toxicity endpoints for spathulenol, viridiflorol and 2-methyl-5-(propan-2-ylidene)cyclohexane-1,4-diol. For the other components, structural alerts were due to the presence of a vinyl/allyl alcohol group for *trans-p*-2-menthen-1-ol, an ester group for 4-terpinyl acetate, a ketone group for carvenone, an activated (di)aryl ester for carvacryl acetate and a phenol/hydroquinone group for thymohydroquinone. In all cases, predictions of mutagenicity by Ames test (with and without S9 mix) were made by 'read-across' analyses of data available for similar substances to the target compounds (i.e. analogues obtained by categorisation). Categories were defined using general mechanistic and endpoint profilers as well as empirical profilers. Subcategorisation was performed in order to exclude analogues less similar to the target compounds. Mutagenicity read-across-based predictions were found consistently negative for all categories of analogues. On this basis, the alerts raised were discounted.[31]

3.4.1 | Safety for the target species

Tolerance studies in the target species and/or toxicological studies in laboratory animals made with the essential oil under assessment were not submitted.

In the absence of these data, the approach to the safety assessment of a mixture whose individual components are known is based on the safety assessment of each individual component (component-based approach). This approach requires that the mixture is sufficiently characterised and that the individual components can be grouped into assessment groups, based on structural and metabolic similarity. The combined toxicity can be predicted using the dose addition assumption within an assessment group, taking into account the relative toxic potency of each component (EFSA Scientific Committee, 2019a).

As the additive under assessment is a fully defined mixture (the identified components represent > 99% of the % GC area, see Section 3.3.1), the FEEDAP Panel applied a component-based approach to assess the safety for target species of the essential oil. The oil under assessment contains by specification up to 75% of carvacrol and up to 5% of thymol, which are assessed separately from the other components of the oil.

Thymol and carvacrol

The tolerance trials carried out in chickens for fattening, piglets, cattle for fattening and salmons with a mixture of flavourings containing thymol [04.005] and carvacrol [04.031] ('Herbal mixture') showed that both compounds are safe up to 125 mg/kg complete feed with a margin of safety of 10 (EFSA FEEDAP Panel, 2023b). The FEEDAP Panel considers that the conclusions reached for carvacrol can be extrapolated to the ester carvacryl acetate.

The concentration of carvacrol (11.3–93.8 mg/kg complete feed) and thymol (0.8–6.3 mg/kg complete feed) resulting from the use of the additive at the proposed conditions of use for the different target animal categories are shown in Table 5. The corresponding concentration of carvacryl acetate would be 0.018–0.15 mg/kg complete feed.

TABLE 5 Concentration of thymol and carvacrol in complete feed (mg/kg) for the different target animal categories at the proposed use levels of Spanish type origanum oil.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg complete feed)[a]	Concentration of carvacrol (mg/kg complete feed)[a,b]	Concentration of thymol (mg/kg complete feed)[a,c]
Chickens for fattening	79	15	11.3	0.8
Laying hens	53	15	11.3	0.8
Turkeys for fattening	59	15	11.3	0.8
Pig for fattening	44	30	22.5	1.5
Piglets	37	30	22.5	1.5
Sows lactating	30	30	22.5	1.5
Veal calves (milk replacer)	19	20	15.0	1.0

[29] *trans*-3,7-dimethyl-1,3,6-octatriene, *(E)*-alpha-bisabolene, abietatriene, α-thujene, aromadendrene, viridiflorene, γ-cadinene, (+)-δ-cadinene, palustradiene and γ-muurolene (CG 31).

[30] Technical dossier/Supplementary information July 2023/Annex_VII_SIn_reply_thymus_origanum_oil_QSAR.

[31] Technical dossier/Supplementary information July 2023/BDG_01_SIn-reply_thymus_origanum oil.

TABLE 5 (Continued)

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg complete feed)[a]	Concentration of carvacrol (mg/kg complete feed)[a,b]	Concentration of thymol (mg/kg complete feed)[a,c]
Cattle for fattening	20	20	15.0	1.0
Dairy cows	31	20	15.0	1.0
Sheep/goats	20	20	15.0	1.0
Horses	20	30	22.5	1.5
Rabbits	50	25	18.8	1.3
Salmonids	18	125	93.8	6.3
Dogs	17	25	18.8	1.3
Cats[d]	20	25	18.8	1.3
Ornamental fish	5	25	18.8	1.3

[a]Complete feed containing 88% DM, milk replacer 94.5% DM.

[b]Based on the highest proposed specification (75% of the GC area) of carvacrol in the additive.

[c]Based on the highest proposed specification (5% of the GC area) of thymol in the additive.

Considering that carvacrol and thymol are safe up to 125 mg/kg complete feed (EFSA FEEDAP Panel, 2023b), the FEEDAP Panel concludes that the use of Spanish type origanum oil at the maximum proposed use levels in complete feed (see Table 5) is safe for all animal species with regards its content of thymol and carvacrol.

l-Carvone

The concentration of *l*-carvone resulting from the use of the additive at the proposed conditions of use for the different target animal categories would range between 0.007 and 0.058 mg/kg complete feed.

Considering that *l*-carvone is safe up to 10 mg/kg complete feed (EFSA FEEDAP Panel, 2023b), the FEEDAP Panel concludes that the use of Spanish type origanum oil at the maximum proposed use levels in complete feed is safe for all animal species with regards its content of *l*-carvone.

Components other than thymol, carvacrol and l-carvone

Based on considerations related to structural and metabolic similarities, the components were allocated to 14 assessment groups, corresponding to the chemical groups (CGs) 1, 3, 4, 5, 6, 8, 10, 13, 16, 18, 25, 26, 31 and 32, as defined in Annex I of Regulation (EC) No 1565/2000. For CG 31 (aliphatic and aromatic hydrocarbons), sub-assessment groups as defined in Flavouring Group Evaluation 25 (FGE.25) and FGE.78 were established (EFSA CEF Panel, 2015a, 2015b). The allocation of the components to the (sub-) assessment groups is shown in Table 6 and in the corresponding footnote.

For each component in the assessment group, exposure in target animals was estimated considering the use levels in feed, the percentage of the component in the oil and the default values for feed intake according to the guidance on the safety of feed additives for target species (EFSA FEEDAP Panel, 2017b). Default values on body weight (bw) are used to express exposure in terms of mg/kg bw per day. The intake levels of the individual components calculated for chickens for fattening, the species with the highest ratio of feed intake/body weight per day, are shown in Table 6.

For hazard characterisation, each component of an assessment group was first assigned to the structural class according to Cramer classification using Toxtree (version 3.1.0, May 2018[32]). For some components in the assessment group, toxicological data were available to derive no observed adverse effect levels (NOAEL). Structural and metabolic similarity among the components in the assessment groups were assessed to explore the application of read-across, allowing extrapolation from a known NOAEL of a component of an assessment group to the other components of the group with no available NOAEL or, if sufficient evidence were available for members of a (sub-) assessment group, to derive a (sub-) assessment group NOAEL.

Toxicological data from sub-chronic studies, from which NOAEL values could be derived, were available for citral [05.020], a mixture of neral and geranial, in CG 3 (EFSA FEEDAP Panel, 2016a), oct-1-en-3-one [07.081] in CG 5 (EFSA FEEDAP Panel, 2020), linalool [02.013] and terpineol [02.230][33] in CG 6 (EFSA FEEDAP Panel, 2012a), 1,8-cineole [03.001] in CG 16 (EFSA FEEDAP Panel, 2021), eugenol [04.003] in CG 18 (EFSA FEEDAP Panel, 2011), myrcene [01.008], *p*-cymene [01.002] and β-caryophyllene [01.007] in CG 31 (EFSA FEEDAP Panel, 2015b, 2016c) and β-caryophyllene epoxide [16.043] in CG 32 (EFSA CEF Panel, 2014).

For α-terpinene [01.019], the FEEDAP Panel identified a NOAEL of 60 mg/kg bw per day based on maternal toxicity (reduced body weight gain) in a teratogenicity study in rats (Araujo et al., 1996; also reported in ECHA, 2018). An uncertainty

[32]Toxtree includes both the original Cramer rule base with the 33 structural rules (Cramer et al., 1978) and an extended rule base with five additional rules which were introduced to overcome misclassification (in Class I or Class II) of several substances with low NOAELs. https://toxtree.sourceforge.net/.

[33]Terpineol is a mixture of four structural isomers: α-terpineol [02.014], β-terpineol, γ-terpineol and 4-terpinenol [02.072]. α-terpineol [02.014], is defined as a mixture of *(R)*-(+)-α-terpineol and *(S)*-(−)-α-terpineol.

factor (UF) of 2 was applied to the NOAEL of 60 mg/kg bw per day to take into account the nature of the study. The FEEDAP Panel applied a $BMDL_{10}$ of 8 mg/kg bw per day to α-thujone (EFSA FEEDAP Panel, 2021), which is also extended to β-thujone despite its lower neurotoxicity.

Read-across was applied using the NOAEL of 345 mg/kg bw per day for citral [05.020] to extrapolate to *(Z)*-nerol [02.058], neral [05.170], geranial [05.188] and geranyl acetate in CG 3. Similarly, the NOAEL of 6.7 mg/kg bw per day for oct-1-en-3-one [07.081] was extrapolated to oct-1-en-3-ol [02.023] in CG 5.

Considering the structural and metabolic similarities, for the subgroup of terpinyl derivatives in CG 6, i.e. 4-terpinenol [02.072] and 4-terpinenyl acetate, the reference point was selected based on the NOAEL of 250 mg/kg bw per day available for terpineol [02.230]. An uncertainty factor (UF) of 2 was applied to the NOAEL of 250 mg/kg bw per day to take into account the short duration (35 days) of the study with terpineol (EFSA FEEDAP Panel, 2012a).

Since a compound-specific NOAEL has been identified for α-terpinene [01.019], which is lower than that of *d*-limonene [01.045], the representative compound in CG 31, III, the FEEDAP Panel considered the need to review the read-across applied within this group. The assessment group 'cyclohexene derivatives' includes compounds characterised by the presence of at least two double bonds, which can be either isolated (as in *d*-limonene) or conjugated (as in α-terpinene). For the two subgroups of compounds, a refinement in read-across is applied as follows: the NOAEL of 250 mg/kg bw per day for *d*-limonene is applied to the compounds with isolated double bonds and the NOAEL of 60 mg/kg bw per day for α-terpinene to the compounds with conjugated double bonds.

The NOAELs of 44, 250 and 222 mg/kg bw per day for the representative compounds of CG 31, myrcene [01.008], *d*-limonene [01.045] and β-caryophyllene [01.007] were applied, respectively, using read-across to the compounds within sub-assessment groups II (*cis*-3,7-dimethyl-1,3,6-octatriene [01.064] and *trans*-3,7-dimethyl-1,3,6-octatriene), III (γ-terpinene [01.020], β-phellandrene [01.055], terpinolene [01.005] β-bisabolene and *(E)*-α-bisabolene), V (α-thujene, α-pinene [01.004], β-pinene [01.003], δ-3-carene [01.029], aromadendrene, viridiflorene, γ-cadinene, (+)-δ-cadinene and γ-muurolene),[34] respectively (EFSA CEF Panel, 2015a, 2015b). In the current assessment, the NOAEL of 60 mg/kg bw per day for α-terpinene [01.019] is applied to α-phellandrene, with an UF of 2 to take into account the nature of the study carried out with α-terpinene.

The NOAEL of 222 mg/kg bw per day for β-caryophyllene [01.007] was also applied to sabinene hydrate and viridiflorol in CG 6. Read-across was also applied from β-caryophyllene [01.007] to 3,7,10-humulatriene [01.043]. For 3,7,10-humulatriene, an UF of 2 was applied to the NOAEL of 222 mg/kg bw per day for β-caryophyllene [01.007] to take into account the uncertainty in read-across (EFSA FEEDAP Panel, 2023c).

For the remaining compounds,[35] toxicity studies performed with the compounds under assessment and NOAEL values derived from toxicity studies were not available and read-across was not possible. Therefore, the threshold of toxicological concern (TTC) approach was applied (EFSA FEEDAP Panel, 2017b; EFSA Scientific Committee, 2019c).

As the result of the hazard characterisation, a reference point was identified for each component in the assessment group based on the toxicity data available (NOAEL from in vivo toxicity study or read-across) or from the 5th percentile of the distribution of NOAELs of the corresponding Cramer Class (i.e. 3, 0.91 and 0.15 mg/kg bw per day, respectively, for Cramer Class I, II and III compounds, Munro et al., 1996). Reference points selected for each compound are shown in Table 6.

For risk characterisation, the margin of exposure (MOE) was calculated for each component as the ratio between the reference point and the exposure. For each assessment group, the combined (total) margin of exposure (MOET) was calculated as the reciprocal of the sum of the reciprocals of the MOE of the individual substances (EFSA Scientific Committee, 2019a). A MOET > 100 allowed for interspecies- and intra-individual variability (as in the default 10 × 10 uncertainty factor). The compounds resulting individually in an MOE > 50,000 were not further considered in the assessment group as their contribution to the MOE(T) is negligible. They are listed in the footnote.[36]

The approach to the safety assessment of Spanish type origanum oil for the target species is summarised in Table 6. The calculations were done for chickens for fattening, the species with the highest ratio of feed intake/body weight and represent the worst-case scenario.

[34]Some of these compounds are not listed in Table 5 because their individual margin of exposure (MOE) was > 50,000.

[35]Methyl citronellate (CG 1); lavandulyl acetate (CG 4); octan-3-one and octan-3-ol (CG 5); *trans-p*-2-menthen-1-ol, 2-(4-methylphenyl)propan-2-ol, 4-terpinenyl acetate and spathulenol (CG 6); camphor, dihydrocarvone and carvenone (CG 8); thymohydroquinone (CG 25); abietatriene (CG 31, IV); camphene and palustradiene (CG 31,V).

[36]Compounds included in the assessment groups but not reported in the table: *(Z)*-nerol, neral, geranial and geranyl acetate (CG 3); terpineol, sabinene hydrate, 4-terpinenyl acetate, linalyl acetate and viridiflorol (CG 6); *l*-carvone (CG 8); eugenol (CG 18); *cis*-3,7-dimethyl-1,3,6-octatriene and *trans*-3,7-dimethyl-1,3,6-octatriene (CG 31, II); β-phellandrene, terpinolene, β-bisabolene and *(E)*-α-bisabolene (CG 31, III); β-pinene, δ-3-carene, aromadendrene, viridiflorene, γ-cadinene, (+)-δ-cadinene and γ-muurolene (CG 31, V), 3,7,10-humulatriene (CG 31, VI).

TABLE 6 Compositional data, intake values (calculated for chickens for fattening at 15 mg/kg complete feed), reference points and margin of exposure (MOE) for the individual components of Spanish type origanum oil classified according to assessment groups, and combined margin of exposure (MOET) for each assessment group.

Essential oil composition			Exposure		Hazard characterisation		Risk characterisation	
Assessment group	**FLAVIS-No**	**Highest conc. in the oil**	**Highest feed conc.**	**Intake[a]**	**Cramer Class[b]**	**NOAEL[c]**	**MOE[d]**	**MOET[e]**
Constituent	–	%	mg/kg	mg/kg bw per day	–	mg/kg bw per day	–	–
CG 1								
Methyl citronellate	09.517	0.01	0.0017	0.00015	I	*3*	20,253	
CG 4								
Lavandulyl acetate	09.612	0.06	0.0083	0.00074	I	*3*	4051	
CG 5								
Oct-1-en-3-ol	02.023	0.34	0.0503	0.00451	(I)	6.7	1485	
Octan-3-one	07.062	0.20	0.0296	0.00265	II	*0.91*	343	
Octan-3-ol	02.098	0.03	0.0047	0.00042	I	*3*	7187	
MOET CG 5								268
CG 6								
Linalool	02.042	1.34	0.2004	0.01799	(I)	117	6503	
4-Terpinenol	02.072	0.82	0.1230	0.01104	(I)	125[f]	11,320	
2-(4-Methylphenyl) propan-2-ol	02.042	0.03	0.0041	0.00039	I	*3*	7682	
trans-p-2-Menthen-1-ol	–	0.02	0.0035	0.00031	I	*3*	9686	
Spathulenol	–	0.02	0.0027	0.00024	I	*3*	12,377	
MOET CG 06								1798
CG 8								
d,l-Borneol	02.016	0.46	0.0693	0.00622	(I)	**15**	2411	
Camphor	–	0.22	0.0329	0.00295	II	*0.91*	309	
Dihydrocarvone	07.128	0.04	0.0062	0.00055	II	*0.91*	1648	
Carvenone	–	0.02	0.0029	0.00026	II	*0.91*	3557	
MOET CG 08								220
CG 10								
2-Methyl-5-(propan-2-ylidene) cyclohexane-1,4-diol	–	0.12	0.0183	0.00164	I	*3*	1826	
CG 13								
Linalool oxide	13.140	0.01	0.0021	0.00019	II	*0.91*	4827	
CG 16								
1,8-Cineole	03.001	0.28	0.0422	0.00378	(II)	**100**	26,428	
CG 25								
Thymohydroquinone	–	0.20	0.0300	0.00269	I	3	1114	
CG 26								
1-Isopropyl-2-methoxy-4-methylbenzene	04.043	0.25	0.0375	0.00337	I	3	891	
CG 31, II (Acyclic alkanes)								
Myrcene	01.008	1.25	0.1869	0.01678	(I)	**44**	2622	
CG 31, III (Cyclohexene hydrocarbons)								
γ-Terpinene	01.020	5.72	0.8580	0.07703	(I)	250	3246	
α-Terpinene	01.019	1.45	0.2178	0.01955	(I)	**30**[g]	1534	

(Continues)

TABLE 6 (Continued)

Essential oil composition			Exposure		Hazard characterisation		Risk characterisation	
Assessment group	**FLAVIS-No**	**Highest conc. in the oil**	**Highest feed conc.**	**Intake[a]**	**Cramer Class[b]**	**NOAEL[c]**	**MOE[d]**	**MOET[e]**
d-Limonene	01.045	0.39	0.0588	0.00528	(I)	**250**	47,361	
α-Phellandrene	01.006	0.26	0.0393	0.00353	(I)	30[g]	8503	
MOET CG 31, III								910
CG 31, IVe (Benzene hydrocarbons, alkyl)								
p-Cymene	01.002	8.28	1.2425	0.11154	(I)	**154**	1381	
Abietatriene	–	0.03	0.0047	0.00044	I	*3*	7187	
MOET CG 31, IVe								1158
CG 31, V (Bi-, tricyclic, non-aromatic hydrocarbons)								
β-Caryophyllene	01.007	3.69	0.5540	0.04973	(I)	**222**	4464	
α-Thujene	–	0.88	0.1322	0.01186	(I)	222	18,713	
α-Pinene	01.004	0.88	0.1322	0.01186	(I)	222	18,713	
Camphene	01.009	0.15	0.0224	0.00201	I	*3*	1495	
Palustradiene	–	0.06	0.0092	0.00082	I	*3*	3652	
MOET CG 31, V								785
CG 32								
β-Caryophyllene epoxide	16.043	0.57	0.0852	0.00765	(III)	**119**	15,558	
Thujones								
α-Thujone	–	0.19	0.0287	0.00257	(III)	**8**	3110	
β-Thujone	–	0.03	0.0047	0.00042	(III)	8	19,164	
								2676

[a]Intake calculations for the individual components are based on the use level of 15 mg/kg in feed for chickens for fattening, the species with the highest ratio of feed intake/body weight.

[b]When a NOAEL value is available or read-across is applied, the allocation to the Cramer class is put into parentheses.

[c]Values **in bold** refer to those components for which the NOAEL value was available, values *in italics* are the 5th percentile of the distribution of NOAELs of the corresponding Cramer Class, other values (plain text) are NOAELs extrapolated by using read-across.

[d]The MOE for each component is calculated as the ratio of the reference point (no observed adverse effect level, NOAEL) to the intake.

[e]The combined margin of exposure (MOET) is calculated for each assessment group as the reciprocal of the sum of the reciprocals of the MOE of the individual substances.

[f]An uncertainty factor of 2 was applied to the NOAEL of 250 mg/kg bw per day for terpineol (short duration of the study).

[g]An uncertainty factor of 2 was applied to the NOAEL of 60 mg/kg bw per day for α-terpinene (nature of the study).

As shown in Table 6, the MOET calculated at the proposed use level (15 mg/kg complete feed) was > 100 for all assessment groups. The lowest MOET was calculated for CG 8. From the lowest MOET of 220 for chickens for fattening, the MOET for CG 8 compounds was calculated for the other target species considering the respective daily feed intake and conditions of use. The results are summarised in Table 7.

TABLE 7 Combined margin of exposure (MOET) for the assessment group CG 8 calculated for the different target animal categories at the proposed use level in feed.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg feed)[a]	Lowest MOET CG 8
Chickens for fattening	79	15	220
Laying hens	53	15	328
Turkeys for fattening	59	15	295
Piglets	44	30	198
Pigs for fattening	37	30	235
Sows lactating	30	30	290
Veal calves (milk replacer)	19	20	686
Cattle for fattening	20	20	652

TABLE 7 (Continued)

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg feed)[a]	Lowest MOET CG 8
Dairy cows	31	20	420
Sheep/goats	20	20	652
Horses	20	30	435
Rabbits	50	25	209
Salmonids	18	125	116
Dogs	17	25	613
Cats[b]	20	25	521
Ornamental fish	5	25	2086

[a]Complete feed containing 88% DM, milk replacer 94.5% DM.

[b]The MOET for cats is increased to 500 because of the reduced capacity of glucuronidation.

Table 7 shows that for all animal species the MOET exceeds the value of 100 at the proposed use levels in complete feed. Because glucuronidation is an important metabolic pathway to facilitate the excretion of the components of the essential oil and considering that cats have an unusually low capacity for glucuronidation, particularly of aromatic compounds (Court & Greenblatt, 1997; Lautz et al., 2021), the use of Spanish type origanum oil as an additive in cat feed needs a wider margin of exposure. A MOET of 500 is considered adequate. For all target species listed in Table 7, Spanish type origanum oil is considered safe at the proposed use levels in complete feed. These levels are extrapolated to physiologically-related minor species. For the other species not considered, the lowest value of 15 mg/kg complete feed is applied.

Use in water for drinking

No specific proposals have been made by the applicant for the use level in water for drinking. The FEEDAP Panel considers that the use in water for drinking alone or in combination with use in feed should not exceed the daily amount that is considered safe when consumed via feed alone.

3.4.1.1 | *Conclusions on safety for the target species*

The FEEDAP Panel concludes that the use of Spanish type origanum oil up to the respective maximum proposed use levels in complete feed, as detailed in Table 8, is safe for the target species.

TABLE 8 Maximum use levels of Spanish type origanum oil (mg/kg complete feed) considered safe for the target species.

Animal categories	Maximum use level (mg/kg complete feed)[a]
Turkeys for fattening	15
Chickens for fattening, other poultry for fattening or reared for laying/reproduction and ornamental birds	15
Laying hens and other laying/reproductive birds	15
Pigs for fattening	30
Piglets and other porcine species for meat production or reared for reproduction	30
Sows and other porcine species for reproduction	30
Veal calves (milk replacer)	20
Sheep/goats	20
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction, cervids and camelids at the same physiological stage	20
Dairy cows and other ruminants, cervids and camelids for milk production or reproduction	20
Horses and other equines	30
Rabbits and other leporids	25
Salmonids and minor fin fish	125
Dogs	25
Cats	25
Ornamental fish	25
Other species	15

[a]Complete feed containing 88% DM, milk replacer 94.5% DM.

The FEEDAP Panel considers that the use in water for drinking alone or in combination with use in feed should not exceed the daily amount that is considered safe when consumed via feed alone.

3.4.2 | Safety for the consumer

T. capitata (L.) Cav. (synonym: *T. capitatus* (L.) Hoffmanns. & Link) is included in the general term 'thyme' in the Fenaroli's handbook of flavour ingredients (Burdock, 2009) and is added to a wide range of food categories for flavouring purposes. Although individual consumption figures are not available, the Fenaroli's handbook of flavour ingredients cites intake values of 0.65 mg/kg per day for 'thyme' (FEMA 3063).

Most of the individual constituents of the essential oil under assessment are currently authorised as food flavourings without limitations and have been already assessed for consumer safety when used as feed additives in animal feed (see Table 4, Section 3.3).

No data on residues in products of animal origin were made available for any of the constituents of the essential oil. However, the Panel recognises that the constituents of Spanish type origanum oil are expected to be extensively metabolised and excreted in the target species.

The FEEDAP Panel considers that it is unlikely that the consumption of products from animals given Spanish origanum oil at the maximum proposed use levels would increase human background exposure to its constituents. The use of Spanish type origanum oil in animal nutrition under the proposed conditions of use is considered safe for human consumers of animal products.

3.4.3 | Safety for the user

No specific data were provided by the applicant regarding the safety of the additive for users.

The applicant made a literature search aimed at retrieving studies related to the safety of preparations obtained from *T. capitata* for users.[37] A publication (Alabdullatif et al., 2017) reported eye irritation studies in rabbits for several essential oils including one derived from *T. capitata*. The study was said to be conducted according to the recommendations of US EPA. All of the oils tested showed evidence of dermal irritation in treated rabbits, thus the additive Spanish type origanum oil should be considered to be a dermal irritant.

The applicant also provided a safety data sheet[38] for Spanish type origanum oil, where hazards for users have been identified.

The FEEDAP Panel considers the essential oil as irritant to skin and eyes, and as a dermal and respiratory sensitiser.

3.4.4 | Safety for the environment

T. capitata occurs wild and cultivated in many European countries.

The use of Spanish type origanum oil in animal feed under the proposed conditions of use is not expected to pose a risk to the environment.

3.5 | Efficacy

Origanum oil Spanish type from *T. capitata* is listed by FEMA with the reference number 2828.

Since *T. capitata* and its preparations are recognised to flavour food (see Section 3.4.2) and the function in feed would be essentially the same as that in food, no further demonstration of efficacy is considered necessary.

4 | CONCLUSIONS

The FEEDAP Panel concludes that Spanish type origanum oil is safe for the target species at the respective maximum proposed use levels detailed in the table below:

[37]Technical dossier/Supplementary information July 2023/Literature search_Thymus origanum oil.

[38]Technical dossier/Supplementary information July 2023/Annex_VIII_Sin_reply_thymus_origanum_oil_MSDS. Aspiration hazard (H304, category 1), serious eye damage/eye irritation (H302, category 4), skin corrosion/irritation (H315, category 2), sensitisation (H317, category 1), in accordance with the criteria outlined in Annex I of 1272/2008/EC (CLP/EU-GHS).

Animal categories	Maximum use level (mg/kg complete feed)[a]
Turkeys for fattening	15
Chickens for fattening, other poultry for fattening or reared for laying/reproduction and ornamental birds	15
Laying hens and other laying/reproductive birds	15
Pigs for fattening	30
Piglets and other porcine species for meat production or reared for reproduction	30
Sows and other porcine species for reproduction	30
Veal calves (milk replacer)	20
Sheep/goats	20
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction, cervids and camelids at the same physiological stage	20
Dairy cows and other ruminants, cervids and camelids for milk production or reproduction	20
Horses and other equines	30
Rabbits and other leporids	25
Salmonids and minor fin fish	125
Dogs	25
Cats	25
Ornamental fish	25
Other species	15

[a] Complete feed containing 88% DM, milk replacer 94.5% DM.

The FEEDAP Panel considers that the use in water for drinking alone or in combination with use in feed should not exceed the daily amount that is considered safe when consumed via feed alone.

The use of Spanish type origanum oil in animal feed under the proposed conditions of use is safe for the consumer and the environment.

Regarding user safety, the essential oil under assessment should be considered as irritant to skin and eyes, and as a dermal and respiratory sensitiser.

Since *T. capitata* (L.) Cav. and its preparations are recognised to flavour food and the function in feed would be essentially the same as that in food, no further demonstration of efficacy is considered necessary.

5 | DOCUMENTATION PROVIDED TO EFSA/CHRONOLOGY

Date	Event
29/09/2010	Dossier received by EFSA. Botanically defined flavourings from Botanical Group 01 – Lamiales for all animal species and categories. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)
03/01/2011	Reception mandate from the European Commission
06/01/2011	Application validated by EFSA – Start of the scientific assessment
01/04/2011	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: analytical methods*
08/01/2013	Reception of supplementary information from the applicant - Scientific assessment remains suspended
26/02/2013	EFSA informed the applicant (EFSA ref. 7150727) that, in view of the workload, the evaluation of applications on feed flavourings would be re-organised by giving priority to the assessment of the chemically defined feed flavourings, as agreed with the European Commission
24/06/2015	Technical hearing during risk assessment with the applicant according to the "EFSA's Catalogue of support initiatives during the life-cycle of applications for regulated products": data requirement for the risk assessment of botanicals
27/02/2019	Partial withdrawal by applicant (EC was informed) for the following additives: thyme leaves gratiola tincture, spike lavender oil, melissa oil, pennyroyal oil, basil oil and savoury summer oil
30/06/2021	EFSA informed the applicant that the evaluation process restarted

Date	Event
08/07/2021	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation, safety for target species, safety for the consumer, safety for the user and environment*
14/07/2023	Reception of supplementary information from the applicant (partial dataset: thymus origanum oil) - Scientific assessment remains suspended
08/07/2024	Partial withdrawal of the application for the following additives: lilac chastetree extract and savoury summer tincture
26/08/2024	Reception of a partial evaluation report of the European Union Reference Laboratory for Feed Additives. Scientific assessment re-started for the additives included in the partial report: Spanish sage oil, peppermint oil, thymus origanum oil, patchouli oil, clary sage oil, lavender oil and sage oil
27/08/2024	Reception of supplementary information from the applicant (letter of agreement)
30/08/2024	The application was split and a new EFSA-Q-2024-00541 was assigned to the preparation included in the present assessment
17/09/2024	Opinion adopted by the FEEDAP Panel on Spanish type origanum oil (EFSA-Q-2024-00541). End of the Scientific assessment for the additive included in the present assessment. The assessment of other additives in BGD 01 is still ongoing

ABBREVIATIONS

AFC	EFSA Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food
bw	body weight
BDG	Botanically defined group
CAS	Chemical Abstracts Service
CDG	Chemically defined group
CEF	EFSA Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CG	chemical group
CLP	Classification, Labelling and Packaging
CoE	Council of Europe
DM	dry matter
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EINECS	European Inventory of Existing Chemical Substances
EMA	European Medicines Agency
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
FFAC	Feed Flavourings authorisation Consortium of FEFANA (EU Association of Specialty Feed Ingredients and their Mixtures)
FEMA	Flavour Extract Manufacturers Association
FGE	food group evaluation
FLAVIS	The EU Flavour Information System
FLAVIS No	FLAVIS number
GC	gas chromatography
GC–MS	gas chromatography–mass spectrometry
GC-FID	gas chromatography-flame ionisation detection
ISO	International Organisation for Standardisation
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LOD	limit of detection
MOE	margin of exposure
MOET	total margin of exposure
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PCBs	polychlorinated biphenyls
PhEur	European Pharmacopoeia
QSAR	quantitative structure activity relationship
TTC	threshold of toxicological concern
UF	uncertainty factor
WHO	World Health Organization

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REQUESTOR

European Commission

QUESTION NUMBER

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