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Safety and efficacy of a feed additive consisting of an essential oil derived from the leaves of *Origanum majorana* L. (marjoram oil) for use in all animal species (FEFANA asbl)

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Safety and efficacy of a feed additive consisting of an essential oil derived from the leaves of *Origanum majorana* L. (marjoram 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://open.efsa.europa.eu/experts>.

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 leaves of *Origanum majorana* L. (marjoram 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 use of marjoram oil is very unlikely to induce adverse effects in long-living and reproductive animals and is of no safety concern for short-living animals (species for fattening) when used at the proposed use level of 10 mg/kg complete feed. The FEEDAP Panel considered that the use of marjoram oil in water for drinking alone or in combination with use in feed should not exceed the daily amount that is considered very unlikely to induce adverse effects in long-living and reproductive animals and of no safety concern for short-living animals (species for fattening) when consumed via feed alone. No safety concerns were identified for the consumer and the environment from the use of the additive in animal feed. Regarding user safety, the essential oil under assessment should be considered as irritant to skin and eyes and as dermal and respiratory sensitiser. When handling the essential oil, exposure of unprotected users to estragole, a genotoxic carcinogen, may occur. Exposure of users by any route is considered a risk and should be minimised. Since the leaves of *O. majorana* and their 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

4-terpinenol, efficacy, flavouring compounds, marjoram oil, *Origanum majorana* L., safety, sensory additives, α -Terpineol

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1 | INTRODUCTION

1.1 | Background and Terms of Reference

Regulation (EC) No 1831/2003¹ 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 feed additive shall submit an application in accordance with Article 7. In particular, 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 7 years after the entry into force of this Regulation.

The European Commission received a request from the Feed Flavoursings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)² for authorisation/re-evaluation of 41 additives (king of bitter extract, thyme leaved gratiola tincture, devils claw extract, devils 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, savory summer oil, savory 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 12 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 29 additives under application: marjoram oil from *Origanum majorana* L.⁵ for use in all animal species.

The remaining 28 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 (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). 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 marjoram oil from *O. majorana*, when used under the proposed conditions of use (see **Section 3.3.3**).

1.2 | Additional information

Marjoram oil from *Origanum majorana* L. is currently authorised 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) under the name 'marjoram oil sweet'. 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 dossier⁶ in support of the authorisation request for the use of marjoram oil from *O. majorana* as a feed additive. The dossier was received on 26/6/2025 and the general information and supporting documentation are available on Open.EFSA at <https://open.efsa.europa.eu/questions/EFSA-Q-2025-00407>.⁷

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.

¹Regulation (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.

²On 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.

³Thyme leaves gratiola tincture, spike lavender oil, melissa oil, pennyroyal oil, basil oil and savoury summer oil (27 February 2019); Spanish marjoram oil (28 September 2023); lilac chastetree extract and savory summer tincture (8 July 2024); devils claw extract (wb), balm leaves extract (sb), olive extract (sb) (16 December 2024).

⁴Register of feed additives, Annex II, withdrawn by OJ L162, 10.05.2021, p. 5.

⁵Accepted name: *Origanum majorana* L.; synonym: *Majorana ortensis* Moench.

⁶Dossier reference: FAD-2010-0137.

⁷The original application EFSA-Q-2010-0137 was split on 26/6/2025 and a new EFSA-Q-2025-00407 was generated.

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 preparations belonging to BDG 01, including the current one under assessment.⁸

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. During the assessment, upon request of EFSA, the EURL issued two partial reports.⁹ The additive under assessment is included in the second partial report. In particular, the EURL recommended a method based on gas chromatography with flame ionisation detection (GC–FID) for the quantification of the phytochemical markers 4-terpinenol and α -terpineol in marjoram oil.¹⁰

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of marjoram oil from *O. majorana* is in line with the principles laid down in Regulation (EC) No 429/2008¹¹ 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,¹² Guidance for the preparation of dossiers for sensory additives (EFSA FEEDAP Panel, 2012a), 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, 2019a), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2024), Guidance on the assessment of the safety of feed additives for the users (EFSA FEEDAP Panel, 2023a), Guidance document on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals (EFSA Scientific Committee et al., 2019a), Statement on the genotoxicity assessment of chemical mixtures (EFSA Scientific Committee et al., 2019b), Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment (EFSA Scientific Committee et al., 2019c), General approach to assess the safety for the target species of botanical preparations which contain compounds that are genotoxic and/or carcinogenic (EFSA FEEDAP Panel, 2021a).¹³

3 | ASSESSMENT

The additive under assessment, marjoram oil, is an essential oil obtained from the dried leaves of *O. majorana* L. 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

O. majorana L. is a perennial herb belonging to the family Lamiaceae. It is native to Cyprus and Turkey but subsequently introduced into most of Europe and to India because of its value as a culinary herb. Although considered as a perennial, marjoram is not cold hardy and consequently may be treated as an annual in more northern regions. *O. majorana* is closely related to and resembles oregano (*Origanum vulgare* L.). While the leaves of *O. majorana* are described as generally smaller and more grey/green than those of *O. vulgare*, the two species are distinguished botanically by the shape of the calyx.

O. majorana is most commonly called marjoram, but in some regions the names sweet marjoram or knotted marjoram may be used to distinguish it from oregano. It may also be referred to as pot marjoram, but this name is also associated with a number of other species of *Origanum*, notably *Origanum onites* L. The name wild marjoram and winter marjoram are also used to describe *O. vulgare* and its sub-species.

The additive is extracted from the dried leaves of *O. majorana* by steam distillation. The volatile constituents are condensed and then separated from the aqueous phase by decantation. The applicant indicates that volatile fraction mixing may be used to achieve a specification.

⁸Technical dossier/Supplementary information August 2024/Letter dated 27/8/2024.

⁹Additives included in the first partial report: Spanish sage oil, peppermint oil, thymus origanum oil, patchouli oil, clary sage oil, lavender oil and sage oil; additives included in the second partial report: cornmint oil, spearmint oil, thyme oil, rosemary oil, marjoram oil, rosemary tincture, basil tincture, lavender tincture, peppermint tincture, sage tincture and wild thyme tincture.

¹⁰Evaluation report received on 18/6/2025 and available on the EU Science Hub https://joint-research-centre.ec.europa.eu/reports-and-technical-documentation/fad-2010-0137_en.

¹¹Commission 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.

¹²Online version: <https://www.efsa.europa.eu/en/data-report/compendium-botanicals>.

¹³<https://www.efsa.europa.eu/sites/default/files/2021-05/general-approach-assessment-botanical-preparations-containing-genotoxic-carcinogenic-compounds.pdf>.

3.2 | Uses other than feed flavouring

There is no specific EU authorisation for any *O. majorana* preparation when used to provide flavour in food. However, according to Regulation (EC) No 1334/2008¹⁴ 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.’

‘*O. majorana* L. herba’ is described in monographs of the European Medicines Agency (EMA, 2016a, 2016b, 2023) for medicinal uses.

3.3 | Characterisation

3.3.1 | Characterisation of marjoram oil

The essential oil is obtained from the dried leaves of *O. majorana* sourced from Egypt. It is a yellow to yellow-greenish liquid with characteristic odour. Marjoram oil is identified with the single Chemical Abstracts Service (CAS) number 8015-01-8, the European Community (EC) number 282-004-4,¹⁵ the Flavor Extract Manufacturers Association (FEMA) number 2663 and the Council of Europe (CoE) number 316. In five batches of the additive, the refractive index (20°C) fell within the range 1.4725–1.4730, the density (20°C) ranged between 890 and 893 kg/m³ and the optical rotation (20°C) between +21.5° and +22.3°.¹⁶

For marjoram oil, six components contribute to the specifications as shown in Table 1, with 4-terpinenol and α-terpineol 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).¹⁷

TABLE 1 Constituents of marjoram oil as defined by specifications, and 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			% GC area		
EU register name	CAS no	FLAVIS no	Specification ¹	Mean	Range
4-Terpinenol	562-74-3	02.072	14–32	21.86	20.94–22.68
γ-Terpinene	99-85-4	01.020	11–18	13.88	13.50–14.16
α-Terpinene	99-86-5	01.019	6–12	8.65	8.41–8.81
Sabinene (4(10)-thujene)	3387-41-5	01.059	4–10	8.32	8.03–8.54
trans-Sabinene hydrate	17699-16-0	–	1.5–7.5	3.77	3.56–4.01
α-Terpineol	98-55-5	02.014	1–5	3.10	2.89–3.21
Total				59.57 ²	58.60–60.71 ³

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

¹Specification defined based on GC–FID analysis.
²The value given for the Total (mean) is the mean of the sum of the constituents in the individual batches analysed.
³The values given for the Total (range) are the lowest and the highest values of the sum of the constituents in the individual batches analysed.

The applicant provided a full analysis of the same five batches using GC–FID.¹⁸ In total, up to 40 peaks were detected in the chromatograms, all of which were identified and accounted for on average 99.99% (99.93%–100.0%) of the GC area. The six specified compounds accounted for 59.6% on average (range 58.6%–60.7%) of the % GC area (**Error! Reference source not found.**). Besides the six compounds indicated in the product specification, 24 compounds were detected at individual levels of > 0.1% and are listed in Table 2. These 30 compounds together account on average for 99.6% (range 99.2%–99.9%) of the GC area. The remaining 10 compounds (ranging between 0.09% and 0.05%) and accounting for 0.4% of the GC area

¹⁴Regulation (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.
¹⁵The following entries were found at <https://echa.europa.eu/home>: ‘Marjoram oil’ EC 616–979-8; CAS 8016-33-9; ‘Marjoram oil’. EC 916-955-7, CAS 8015-01-8. ‘Marjoram, sweet, ext.’ (extractives obtained from *Origanum majorana* L. including essential oils): EC 282-004-4; CAS 84082-58-6; ‘MARJORAM (*Origanum majorana* L.) Extract’ (defined as extracts from *Origanum majorana* L. including essential oils): EINECS 918-348-5’.
¹⁶Technical dossier/Supplementary information October 2024/Annex_II_SIn_reply_Marjoram_oil_CoAs_chrom_Conf.
¹⁷Technical dossier/Supplementary information October 2024/Annex_II_SIn_reply_Marjoram_oil_CoAs_chrom_Conf.
¹⁸Technical dossier/Supplementary information October 2024/Annex_II_SIn_reply_Marjoram_oil_CoAs_chrom_Conf.

are listed in the footnote.¹⁹ Based on the data on the characterisation, marjoram oil is considered a fully characterised mixture, as defined by the EFSA Scientific Committee (2019a).

TABLE 2 Other constituents of marjoram oil accounting for >0.1% of the composition: 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			% GC area	
EU register name	CAS no	FLAVIS no	Mean	Range
cis-Sabinene hydrate	15537-55-0	–	15.92	15.19–16.82
Terpinolene	586-62-9	01.005	3.16	3.09–3.21
β-Caryophyllene	87-44-5	01.007	2.59	2.49–2.66
Myrcene	123-35-3	01.008	2.17	2.12–2.24
d-Limonene ¹	5989-27-53	01.045	2.00	1.93–2.05
β-Phellandrene	555-10-2	01.055	1.94	1.87–1.98
Linalyl acetate	115-95-7	09.013	1.67	1.39–1.88
cis-p-2-Menthen-1-ol	29803-82-5	–	1.52	1.48–1.55
Bicyclogermacrene	67650-90-2	–	1.49	1.30–1.64
Linalool	78-70-6	02.013	1.39	0.91–2.80
p-Cymene (1-isopropyl-4-methylbenzene)	99-87-6	01.002	0.99	0.84–1.20
trans-p-2-menthen-1-ol	29803-81-4	–	0.92	0.89–0.94
α-Pinene (pin-2(3)-ene)	80-56-8	01.004	0.80	0.77–0.84
α-Thujene	2867-05-2	–	0.68	0.63–0.72
trans-Sabinyl acetate	71327-37-2	–	0.50	0.33–0.60
trans-Piperitol	16721-39-4	–	0.48	0.47–0.49
β-Pinene (pin-2(10)-ene)	127-91-3	01.003	0.46	0.44–0.48
α-Phellandrene	99-83-2	01.006	0.37	0.35–0.40
cis-Piperitol	16721-38-3	–	0.31	0.31–0.32
Estragole ²	140-67-0	–	0.18	0.06–0.29 ³
1,8-Cineole	470-82-6	03.001	0.16	0.15–0.19
4-Terpinenyl acetate	4821-04-9	–	0.15	0.13–0.18
3,7,10-Humulatriene	6753-98-6	01.043	0.12	0.11–0.13
cis-Dihydrocarvone	3792-53-8	–	0.12	0.09–0.15
Total			39.99 ⁴	38.94–40.62 ⁵

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

¹Stereochemistry not given, however considering that the naturally occurring limonene is typically *d*-limonene, it is assumed that this form also occurs in marjoram oil (Bina and Rahimi, 2017).

²Substance which shall not be added as such to food (Annex III), maximum level in food is set by Regulation (EC) No 1334/2008, including dairy products (50 mg/kg), processed fruits, vegetables (incl. mushrooms, fungi, roots, tubers, pulses and legumes), nuts and seeds (50 mg/kg), fish products (50 mg/kg) and non-alcoholic beverages (10 mg/kg).

³Detected in two batches.

⁴The value given for the Total (mean) is the mean of the sum of the constituents in the individual batches analysed.

⁵The values given for the Total (range) are the lowest and the highest values of the sum of the constituents in the individual batches analysed.

The EFSA Compendium of botanicals²⁰ reports as substances of potential concern for human and animal health the occurrence of (–)-camphor (5.61%) and myrcene (1.3–2.08%) in the essential oil from the leaves of *O. majorana*.

The applicant carried out an extensive literature search to identify data related to the chemical composition of *O. majorana* and its botanical preparations and the possible presence of substances of concern.²¹ Four cumulative databases (LIVIVO, NCBI, OVID and ToxInfo) were searched. The keywords used covered different aspects of safety and the inclusion and exclusion criteria were provided by the applicant. The literature search (no time limits specified) retrieved 26 references investigating the composition of marjoram oil. The results of the literature search confirmed the information in the EFSA Compendium. In addition, one reference reported the presence of low concentrations of myristicin (0.34% as % GC

¹⁹Additional constituents: constituents (*n* = 10) between <0.1% and ≥0.05%: 2-(4-methylphenyl)propan-2-ol, *trans*-p-2-menthene-1,4-diol, citronellol, δ-cadinene, pseudolimonene, pinocarveol, β-caryophyllene epoxide, spathulenol, neryl acetate, *d,l*-bornyl acetate.

²⁰Online version: <https://www.efsa.europa.eu/en/data-report/compendium-botanicals>, accessed on 13 June 2025.

²¹Technical dossier/Supplementary information October 2024/Literature search_marjoram_oil.

area) in an essential oil obtained by steam distillation of the dried leaves of *O. majorana* (Prabu et al., 2020). Myristicin was below the limit of detection (LOD) in the oil under assessment (LOD 0.001%).

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 marjoram 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).²² However, no data supporting this statement were provided.

3.3.3 | Conditions of use

Marjoram oil is intended to be added to feed and water for drinking for all animal species without a withdrawal period. The maximum use level in complete feed proposed for all animal species and categories is 10 mg/kg. No use level has been proposed for the use of the additive in water for drinking.

3.4 | Safety

No studies to support the safety for target animals, consumers and users were performed with the additive under assessment.

In line with the recommendation of the EFSA Scientific Committee for the genotoxicity assessment of fully defined chemical mixtures (EFSA Scientific Committee, 2019b), the assessment of genotoxicity is based on the identified components.

Twenty-five of the individual components of the essential oil, accounting on average for 74% of the GC peak areas, have been already assessed as chemically defined flavourings for use in feed and food by the FEEDAP Panel and the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). The flavouring compounds together with the EU Flavour Information System (FLAVIS) number, the chemical group as defined in Commission Regulation (EC) No 1565/2000,²³ and the corresponding EFSA opinion are listed in Table 3.

TABLE 3 Flavouring components of marjoram oil already assessed by EFSA 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 opinion,* year
03	α, β-Unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/ acids, acetals and esters	Neryl acetate	09.213	2016a
04	Non-conjugated and accumulated unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals and esters	Citronellol	02.011	2016b
06	Aliphatic, alicyclic and aromatic saturated and unsaturated tertiary alcohols and esters with esters containing tertiary alcohols ethers	Linalool	02.013	2012a
		α-Terpineol	02.014	
		2-(4-Methylphenyl)propan-2-ol	02.042	
		4-Terpinenol	02.072	
		Linalyl acetate	09.013	
(Continues)				

²²Technical dossier/Section II.
²³Commission 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 3 (Continued)

CG	Chemical group	Product (EU register name)	FLAVIS No	EFSA opinion,* year
08	Secondary alicyclic saturated and unsaturated alcohols, ketones, ketals and esters with ketals containing alicyclic alcohols or ketones and esters containing secondary alicyclic alcohols	Pinocarveol ¹	02.015	2012, CEF
		<i>d,l</i> -Bornyl acetate	09.017	2016c
16	Aliphatic and alicyclic ethers	1,8-Cineole	03.001	2012b, 2012b
31	Aliphatic and aromatic hydrocarbons and acetals containing saturated aldehydes	1-Isopropyl-4-methylbenzene (<i>p</i> -Cymene)	01.002	2015
		Terpinolene	01.005	
		α -Phellandrene	01.006	
		α -Terpinene	01.019	
		γ -Terpinene	01.020	
		<i>d</i> -Limonene	01.045	
		Pin-2(10)-ene (β -pinene)	01.003	2016d
		Pin-2(3)-ene (α -pinene)	01.004	
		β -Caryophyllene	01.007	
		Myrcene	01.008	
		δ -Cadinene ^{1,2}	01.021	2011, CEF
		3,7,10-Humulatriene ^{1,2}	01.043	
		β -Phellandrene ^{1,2}	01.055	
		4(10)-Thujene (sabinene) ¹	01.059	2015a, CEF
32	Epoxides	β -Caryophyllene epoxide ¹	16.043	2014, CEF

*FEEDAP opinion unless otherwise indicated.

¹Evaluated 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.

²Evaluated 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.

Three compounds listed in Table 3, δ -cadinene [01.021], 3,7,10-humulatriene [01.043] and β -phellandrene [01.055] have been evaluated in Flavouring Group Evaluations 25 Revision 2 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, 2011). In the absence of this 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 remaining 22 components of marjoram oil listed in Table 3, accounting on average for 72% of the GC peak areas, have been previously assessed and considered safe for use as flavourings. They are currently authorised for use in food²⁴ without limitations and for use in feed²⁵ at individual use levels higher than those resulting from the intended use in feed of the essential oil under assessment.

Fourteen volatile compounds have not been previously assessed for use as flavourings. The FEEDAP Panel notes that 12 of them²⁶ accounting for about 26% of the GC peak areas, are aliphatic monoterpenes or sesquiterpenes structurally related to flavourings already assessed in CG 6, 8 and 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, and not to accumulate in animal tissues and products (EFSA FEEDAP Panel, 2012a, 2015, 2016c, 2016d).

The genotoxic potential of two of the remaining compounds, spathulenol and *trans*-*p*-2-menthene-1,4-diol, was predicted using the Organisation for Economic Co-operation and Development (OECD) QSAR Toolbox.²⁷ No alerts were identified for in vitro mutagenicity, genotoxic and non-genotoxic carcinogenicity or other toxicity endpoints for spathulenol.

²⁴Commission 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.

²⁵European 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.

²⁶*trans*-Sabinene hydrate, *cis*-sabinene hydrate, *trans*-sabinyl acetate, *cis*-*p*-2-menthen-1-ol, 4-terpinenyl acetate, *trans*-*p*-2-menthen-1-ol (CG 6); *cis*-dihydorcarvone, *cis*-piperitol, *trans*-piperitol (CG 8); pseudolimonene, α -thujene, bicyclogermacrene.

²⁷Technical dossier/Supplementary information October 2024/Annex_VI_Sin_reply marjoram_oil_QSAR.

For *trans-p*-2-menthene-1,4-diol structural alerts were identified due to the presence of the vinyl/allyl alcohol group. For all substances, predictions of mutagenicity by Ames test (with and without S9) were made by 'read-across' analyses of data available for similar substances to the target compounds (i.e. analogues obtained by categorisation). Read-across-based predictions were found consistently negative for all categories of analogues. On this basis, the alerts raised were discounted by the FEEDAP Panel.

Two batches of the additive under assessment contained low concentrations of estragole (0.06% and 0.29%).

The applicant provided one paper by Dantas et al. (2016) on the genotoxicity of preparations obtained from the leaves of *O. majorana*. The study was performed with an essential oil from the dried leaves of *O. majorana*, containing most of the components²⁸ identified in the oil under assessment, which did not induce gene mutations in bacteria (*Salmonella* Typhimurium strains TA98, TA97a, TA100, TA102 and TA1535) and in mammalian cells (V79 Chinese hamster lung fibroblast cells). The FEEDAP Panel noted that the negative results obtained with the mixture could be biased by the dilution or absence of components of interest; thus, this study was not considered further for the assessment.

For the absorption, distribution, metabolism and excretion (ADME) and the toxicology of estragole, reference is made to the safety evaluation made by the FEEDAP Panel in the EFSA opinion on olibanum extract and fennel oil (EFSA FEEDAP Panel, 2022, 2023b).

3.4.1 | Safety for the target species

Tolerance studies in the target species and/or toxicological studies in laboratory animals 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 on average 99.9% 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. Estragole, a substance for which a concern for genotoxicity has been identified, is assessed separately.

3.4.1.1 | Components other than estragole

Based on considerations related to structural and metabolic similarities, the components were allocated to six assessment groups, corresponding to the chemical groups (CGs) 3, 4, 8, 16, 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 4 and in the corresponding footnote.

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 2018²⁹). For some components in the assessment group, toxicological data were available to identify no observed adverse effect levels (NOAELs). 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 of sub-chronic studies, from which NOAEL values could be identified, were available for the following components: 345 mg/kg bw per day for citral [05.020] the representative compound in CG 3 (EFSA FEEDAP Panel, 2016a), 50 mg/kg bw per day for citronellol [02.011] in CG 4 (EFSA FEEDAP Panel, 2016b), 117 mg/kg bw per day for linalool [02.013] and 250 mg/kg bw per day for terpineol [02.230]³⁰ in CG 6 (EFSA FEEDAP Panel, 2012a), 15 mg/kg bw per day for *d,l*-isobornyl acetate [09.218] in CG 8 (EFSA FEEDAP Panel, 2016c), 100 mg/kg bw per day for 1,8-cineole [03.001] in CG 16 (EFSA FEEDAP Panel, 2021b), 44 mg/kg bw per day for myrcene [01.008], 154 mg/kg bw per day for *p*-cymene [01.002], 250 mg/kg bw per day for *d*-limonene [01.046] and 222 mg/kg bw per day for β -caryophyllene [01.007] in CG 31 (EFSA FEEDAP Panel, 2015, 2016d) and 109 mg/kg bw per day for 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 body weight (bw) per day based on maternal toxicity (reduced body weight gain) in a teratogenicity study in rats. The NOAEL of 60 mg/kg bw per day was divided by a factor of 2 to take account of the nature of the study (see Araujo et al., 1996; ECHA, 2018).

²⁸Composition of the test item: γ -terpinene (25.73%), α -terpinene (17.35%), terpinen-4-ol (17.24%) and sabinene (10.8%).

²⁹Toxtree 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/>.

³⁰Terpineol 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.

In CG 3, the NOAEL of 345 mg/kg bw per day identified for citral [05.020] was applied to neryl acetate [09.213] (EFSA FEEDAP Panel, 2016a).

In CG 6, a NOAEL of 250 mg/kg bw per day was identified for terpineol [02.230] and divided by a factor of 2 to take account of the nature of the study (EFSA FEEDAP Panel, 2012a). The resulting value of 125 mg/kg bw per day was used as the reference point for terpinyl derivatives, α -terpineol [02.014], 4-terpinenol [02.072], 4-terpinenyl acetate, and for *cis*-*p*-2-menthen-1-ol and *trans*-*p*-2-menthen-1-ol.

In CG 8, the NOAEL of 15 mg/kg bw per day for *d,l*-isobornyl acetate [09.218] was applied to *d,l*-bornyl acetate [09.017]. In the same group, the benchmark dose (BMD) lower confidence limit for a benchmark response of 10% (BMDL₁₀) of 60 mg/kg bw per day for *d*-carvone [07.146] was applied to *cis*-dihydrocarvone (EFSA FEEDAP Panel, 2016c; EFSA Scientific Committee, 2014).

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 follow: 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.

Considering the structural and metabolic similarities, the NOAELs for the representative compounds in CG 31, *d*-limonene [01.045] and β -caryophyllene [01.007] were applied, respectively, using read-across to the compounds within sub-assessment groups III (γ -terpinene [01.020], terpinolene [01.005] and β -phellandrene [01.055]), and V (sabinene [01.059], bicyclogermacrene, α -pinene [01.004], α -thujene, β -pinene [01.003], δ -cadinene [01.021]),³¹ respectively (EFSA FEEDAP Panel, 2015, 2016d). In the current assessment, the NOAEL of 60 mg/kg bw per day for α -terpinene [01.019] and divided by a factor of 2 to take account of the nature of the study, is applied to α -phellandrene [01.006].

The NOAEL of 222 mg/kg bw per day for β -caryophyllene [01.007] was also applied to *cis*-sabinene hydrate, *trans*-sabinene hydrate, *trans*-sabinyl acetate and spathulenol in CG 6 and 3,7,10-humulatriene [01.043] in CG 31, VI.³² For spathulenol, the NOAEL of β -caryophyllene [01.007] was divided by a factor of 2 to take account of the uncertainty in read-across due to the presence of an additional cyclopropane ring. Similarly for 3,7,10-humulatriene, the NOAEL of β -caryophyllene was divided by a factor of 2 to take account of the uncertainty in read-across due to differences in the structure (extrapolation from a tricyclic to a macrocyclic non-aromatic compound) (EFSA FEEDAP Panel, 2023c).

For the remaining compounds,³³ toxicity studies performed with the compounds under assessment were not available and read-across was not possible. Therefore, the 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 4.

For each component in the assessment group, exposure of target animals (expressed as mg/kg bw per day) was estimated considering the maximum proposed use level of 10 mg marjoram oil/kg complete feed, the percentage of the component in the oil and the default values for body weight and feed intake according to the guidance on the safety of feed additives for target species (EFSA FEEDAP Panel, 2017b). For those compounds covered by specifications (4-terpinenol, γ -terpinene, α -terpinene, sabinene, *trans*-sabinene hydrate and α -terpineol, see Table 1), the indicated maximum specified concentration is used for the calculation of exposure. For the other components the highest analysed concentration in the additive is used.

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, (i) when a group reference point is available, a group MOE was calculated for the combined intake; (ii) when different reference points are available for the components, the combined (total) margin of exposure (MOET) was calculated as the reciprocal of the sum of the reciprocals of the MOE for the individual substances (EFSA Scientific Committee, 2019a). A MOE(T) > 100 allowed for interspecies- and intra-individual variability. 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.³⁴

The approach to the safety assessment of marjoram oil is shown in Table 4 for chickens for fattening, which is the species with the highest ratio of feed intake/body weight and represents the worst-case scenario among the target species.

³¹Some of these compounds are not listed in Table 4 because their individual margin of exposure (MOE) was > 50,000.

³²Grouping the components *cis*-sabinene hydrate, *trans*-sabinene hydrate, *trans*-sabinyl acetate, spathulenol (CG 6) and 3,7,10-humulatriene [01.043] (CG 31, VI) with β -caryophyllene [01.007] and the other components assessed based on the same NOAEL of 222 mg/kg bw per day in CG 31, V had no impact on the outcome of the assessment (MOET 592).

³³CC I (3 mg/kg bw per day): 2-(4-methylphenyl)propan-2-ol (CG 6); *trans*-piperitol, *cis*-piperitol, pinocarveol (CG 8); CC II (0.91 mg/kg bw per day): *trans*-*p*-2-menthene-1,4-diol (CG 6).

³⁴Compounds included in the assessment groups but not reported in the table: neryl acetate [09.213] (CG 3); citronellol [02.011] (CG 4); 4-terpinenyl acetate, spathulenol (CG 6); 1,8-cineole (CG 16); pseudolimonene (CG 31, III); β -pinene [01.003], δ -cadinene [01.021] (CG 31, V); 3,7,10-humulatriene [01.043] (CG 31, VI); β -caryophyllene epoxide [16.043] (CG 32).

TABLE 4 Compositional data, intake values (calculated for chickens for fattening at 10 mg/kg complete feed), reference points, margin of exposure (MOE) for the individual components of marjoram 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 concentration in the oil	Highest concentration in feed	Daily intake ¹	Cramer class ²	NOAEL ³	MOE ⁴	MOET ⁵
Constituent	–	%	mg/kg	mg/kg bw per day	–	mg/kg bw per day	–	–
CG 6								
4-Terpinenol	02.072	32.0	3.200	0.2873	(I)	125 ⁶	435	
<i>cis</i> -Sabinene hydrate	–	16.82	1.682	0.1510	(I)	222	1470	
<i>trans</i> -Sabinene hydrate	–	7.5	0.750	0.0673	(I)	222	3297	
α-Terpineol	02.014	5.0	0.500	0.0449	(I)	125 ⁶	2785	
Linalool	02.013	2.80	0.280	0.0251	(I)	117	4655	
Linalyl acetate	09.013	1.88	0.188	0.0169	(I)	117	6936	
<i>cis</i> - <i>p</i> -2-menthen-1-ol	–	1.55	0.155	0.0139	(I)	125 ⁶	9001	
<i>trans</i> - <i>p</i> -2-menthen-1-ol	–	0.94	0.094	0.0084	(I)	125 ⁶	14,797	
<i>trans</i> -Sabinyl acetate	–	0.60	0.060	0.0054	(I)	222	41,147	
2-(4-Methylphenyl) propan-2-ol	02.042	0.10	0.010	0.0009	I	3	3410	
<i>trans</i> - <i>p</i> -2-menthene-1,4-diol	–	0.10	0.010	0.0009	II	0.91	1034	
MOET CG 6								183
CG 8								
<i>trans</i> -Piperitol	–	0.49	0.049	0.0044	I	3	682	
<i>cis</i> -Piperitol	–	0.32	0.032	0.0029	I	3	1051	
<i>cis</i> -Dihydrocarvone	–	0.15	0.015	0.0013	(II)	60	46,093	
Pinocarveol	02.100	0.07	0.007	0.0006	I	3	4988	
<i>d,l</i> -Bornyl acetate	09.017	0.05	0.005	0.0005	(I)	15	31,526	
MOET CG 8								374
CG 31, II (Acyclic alkanes)								
Myrcene	01.008	2.24	0.224	0.0201	(I)	44	2193	
CG 31, III (Cyclohexene hydrocarbons)								
γ-Terpinene	01.020	18.0	1.800	0.1616	(I)	250	1547	
α-Terpinene	01.019	12.0	1.200	0.1077	(I)	30 ⁷	379	
Terpinolene	01.005	3.21	0.321	0.0288	(I)	250	8667	
<i>d</i> -Limonene	01.046	2.05	0.205	0.0184	(I)	250	13,584	
β-Phellandrene	01.055	1.98	0.198	0.0178	(I)	250	14,072	
α-Phellandrene	–	0.40	0.040	0.0036	(I)	30 ⁷	8272	
MOET CG 31, III								217
CG 31, IVe (Benzene hydrocarbons, alkyl)								
<i>p</i> -Cymene	01.002	1.20	0.120	0.0108	(I)	154	14,295	
CG 31, V (Bi-, tricyclic, non-aromatic hydrocarbons)								
Sabinene	01.059	10.0	1.000	0.0898	(I)	222	2473	
β-Caryophyllene	01.007	2.66	0.266	0.0239	(I)	222	9283	
Bicyclogermacrene	–	1.64	0.164	0.0147	(I)	222	15,051	
α-Pinene	01.004	0.84	0.084	0.0076	(I)	222	29,369	
α-Thujene	–	0.72	0.072	0.0065	(I)	222	34,251	

(Continues)

TABLE 4 (Continued)

Essential oil composition			Exposure		Hazard characterisation		Risk characterisation	
Assessment group	FLAVIS no	Highest concentration in the oil	Highest concentration in feed	Daily intake ¹	Cramer class ²	NOAEL ³	MOE ⁴	MOET ⁵
Constituent	–	%	mg/kg	mg/kg bw per day	–	mg/kg bw per day	–	–
Group MOE CG 31, V							1558	

Abbreviations: MOE, margin of exposure; MOET, combined (total) MOE; NOAEL, no observed adverse effect level.

¹Rounded intake values are shown in the Table.

²When a NOAEL value is available or read-across is applied, the allocation to the Cramer class is put into parentheses.

³Values **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.

⁴The MOE for each component is calculated as the ratio of the reference point (no observed adverse effect level, NOAEL) to the intake (non-rounded values are used in the calculations). When a group reference point is available, a group MOE is calculated for the combined intake. Group MOE values are reported **in bold**.

⁵The combined margin of exposure (MOET) is calculated for each assessment group as the reciprocal of the sum of the reciprocals of the MOE for the individual substances. MOET values are reported **in bold**.

⁶A factor of 2 was applied to the NOAEL of 250 mg/kg bw per day for terpineol because of nature of the study.

⁷A factor of 2 was applied to the NOAEL of 60 mg/kg bw per day for α -terpinene because of nature of the study.

As shown in Table 4, for all assessment groups the MOE(T) calculated for chickens for fattening at the proposed use level of 10 mg/kg complete feed was > 100. The lowest MOET of 183 was calculated for CG 6, the assessment group which includes the major components. The MOET for CG 6 compounds calculated for the other target species at 10 mg/kg complete feed are summarised in Table 5.

TABLE 5 Combined margin of exposure (MOET) for the assessment group CG 6 calculated for the different target animal species/categories at the proposed use level of 10 mg/kg complete feed.

Animal species/category	Daily feed intake (g DM/kg bw)	Use level (mg/kg complete feed) ¹	Lowest MOET CG 6
Chickens for fattening	79	10	182
Laying hens	53	10	273
Turkeys for fattening	59	10	245
Pigs for fattening	44	10	329
Piglets	37	10	391
Sows	30	10	482
Veal calves (milk replacer)	19	10	817
Cattle for fattening	20	10	723
Dairy cows	31	10	466
Sheep/goats	20	10	723
Horses	20	10	723
Rabbits	50	10	289
Salmonids	18	10	803
Dogs	17	10	850
Cats	20	10	723
Ornamental fish	5	10	2891

¹Complete feed containing 88% DM, milk replacer 94.5% DM.

At the maximum proposed use level of 10 mg/kg complete feed, the MOET exceeds the value of 100 for all animal species. 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 for aromatic compounds (Court & Greenblatt, 1997; Lautz et al., 2021), the use of marjoram oil as an additive in cat feed needs a wider margin of exposure. A MOET of 500 is considered adequate. For all the animal species and categories listed in Table 5, marjoram oil is considered safe when used as feed additive at 10 mg/kg complete feed (without considering the presence of estragole).

3.4.1.2 | Estragole

Estragole (0.06% and 0.29%) was detected in two batches of the oil under assessment (see Section 3.3.1).

Estragole belongs to the assessment group *p*-allylalkoxybenzenes and is genotoxic and carcinogenic. According to the General approach to assess the safety for the target species of botanical preparations which contain compounds that are genotoxic and/or carcinogenic (EFSA FEEDAP Panel, 2021a), different reference points and a different magnitude of the MOE are applied for long-living and reproductive animals (including those animals reared for laying/breeding/reproduction) and for short-living animals. Short-living animals are defined as those animals raised for fattening whose lifespan under farming conditions makes it very unlikely that they develop cancer as a result of the exposure to genotoxic and/or carcinogenic substances in the diet.

For long-living and reproductive animals a MOE with a magnitude > 10,000, when comparing the estimated exposure to genotoxic and/or carcinogenic substances with a BMDL₁₀ from a rodent carcinogenicity study, is considered of low concern. The FEEDAP Panel identified the BMDL₁₀ of 22.2 mg/kg bw per day derived from rodent carcinogenicity studies with methyleugenol (NTP, 2000; Suparmi et al., 2019), as the reference point for the entire group of *p*-allylalkoxybenzenes (EFSA FEEDAP Panel, 2022). In the current assessment this reference point is applied to assess the exposure of long-living and reproductive animals to estragole.

For short-living animals, genotoxicity and carcinogenicity endpoints are not considered relevant, therefore a lower magnitude of the MOE (> 100) when comparing estimated exposure with a reference point based on non-neoplastic end-points is considered adequate (EFSA FEEDAP Panel, 2021a). The FEEDAP Panel identified a NOAEL of 10 mg/kg bw per day for non-neoplastic lesions from a 90-day study in mice with methyleugenol (NTP, 2000). In the current assessment this reference point is applied to assess the exposure of short-living animals to estragole.

The highest daily intake of estragole was calculated for the different animal categories considering the maximum proposed use level of 10 mg marjoram oil/kg complete feed and the highest analysed concentration in the additive (0.29%). The intake values are reported in Table 6, together with the corresponding MOE. This is calculated considering the relevant reference point for long-living and reproductive animals or for short-living animals (species for fattening).

TABLE 6 Target animal intake of estragole and margin of exposure (MOE) calculated at the maximum proposed use level of 10 mg/kg of in complete feed.

Animal category	Daily feed intake g DM/kg bw	Use level in feed ¹ mg/kg	Estragole intake ² µg/kg bw per day	MOE ^{3,4} –
Long-living and reproductive animals				
Laying hens	53	10	1.7	12,596
Piglets	44	10	1.5	15,172
Sows	30	10	1.0	22,126
Dairy cows	31	10	1.0	21,697
Sheep/goats	20	10	0.7	33,379
Horses	20	10	0.7	33,379
Rabbits	50	10	1.6	13,352
Dogs	17	10	0.5	40,055
Cats	20	10	0.7	33,379
Ornamental fish			0.1	148,352
Short-living animals (species for fattening)				
Chickens for fattening	79	10	2.6	3841
Turkeys for fattening	59	10	1.9	5172
Pigs for fattening	37	10	1.2	8276
Veal calves (milk replacer)	19	10	0.6	17,241
Cattle for fattening	20	10	0.7	15,172
Sheep/goats for meat production	20	10	0.7	15,172
Horses for meat production	20	10	0.7	15,172
Rabbits for meat production	50	10	1.6	6069
Salmonids	18	10	0.6	17,340

Abbreviations: bw, body weight; DM, dry matter; MOE, margin of exposure.

¹Complete feed containing 88% DM, milk replacer 94.5% DM.

²The intake value of estragole is calculated at the highest analysed concentration of 0.29%.

³The MOE for long-living and reproductive animals is calculated as the ratio of the reference point (BMDL₁₀ of 22.2 mg/kg bw per day) to the intake.

⁴The MOE for short-living animals (species for fattening) is calculated as the ratio of the reference point (NOAEL of 10 mg/kg bw per day) to the intake.

When the estimated exposures for long-living and reproductive animals are compared to the BMDL₁₀ of 22.2 mg methyleugenol/kg bw per day (Suparmi et al., 2019), a MOE > 10,000 is obtained for all long-living and reproductive animals (Table 6). In accordance with the EFSA Statement on the MOE (EFSA Scientific Committee, 2012), the use of an additive

in feed is considered of low concern for long-living and reproductive animals if the MOE is $> 10,000$. Consequently, the FEEDAP Panel considers it very unlikely that the use of the feed additive will induce adverse effects during their lifetime.

For short-living animals (species for fattening), the magnitude of the MOE is > 100 (Table 6) and is of no safety concern, when comparing the exposure to the reference point of 10 mg/kg bw per day for non-neoplastic endpoints.

3.4.1.3 | Overall evaluation

No concern has been identified for the components other than estragole at the maximum proposed use level of 10 mg/kg complete feed (see Section 3.4.1.1 and Table 5). At this use level, the presence of estragole is considered very unlikely to induce adverse effects in long-living and reproductive animals and of no safety concern for short-living animals (species for fattening). These conclusions are extrapolated to all animal species.

No specific proposals have been made by the applicant for the use in water for drinking. The FEEDAP Panel considers that the use in water for drinking alone or in combination with the use in feed should not exceed the daily amount resulting from the use of the additive at 10 mg/kg complete feed.

3.4.1.4 | Conclusions on the safety for the target species

The FEEDAP Panel concludes that the use of marjoram oil is very unlikely to induce adverse effects in long-living and reproductive animals and is of no safety concern for short-living animals (species for fattening) when used at the maximum proposed use level of 10 mg/kg complete feed.

The FEEDAP Panel considers that the use of marjoram oil in water for drinking alone or in combination with use in feed should not exceed the daily amount that is considered very unlikely to induce adverse effects in long-living and reproductive animals and of no safety concern for short-living animals (species for fattening) when consumed via feed alone.

3.4.2 | Safety for the consumer

Marjoram oil 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 0.345 mg/kg per day for marjoram and for marjoram oil of 0.001 mg/kg bw per day (Burdock, 2009). Fenaroli's handbook reports use levels ranging from 114 to 9945 mg/kg for marjoram and from 1 to 300 mg/kg in food and beverages for marjoram oil.

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 production (see Table 3, 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 marjoram oil are expected to be extensively metabolised and excreted in the target species. For the major components, 4-terpinenol, γ -terpinene, α -terpinene, sabinene, *trans*-sabinene hydrate and α -terpineol, the available data in laboratory animals and humans indicate that they are absorbed, metabolised and excreted and are not expected to accumulate in animal tissues and products (EFSA FEEDAP Panel, 2012a, 2015, 2016d).

The physiologically-based kinetic (PBK) model simulations in target species indicated that the carry-over of estragole and its 1'-hydroxy metabolite to tissues and products (e.g. eggs, milk) is limited due to rapid elimination and a decline in concentrations in edible tissues (Noorlander et al., 2024). Since estragole occurs in the additive at low concentrations, relevant residues in food products of animal origin are unlikely.

Considering the above and the reported human exposure due to the direct use of marjoram and marjoram oil in food (Burdock, 2009), the FEEDAP Panel considers that it is unlikely that the consumption of products from animals given marjoram oil at the maximum use level proposed by the applicant would lead to a significant increase of human background exposure.

Therefore, no safety concern would be expected for the consumers from the use of marjoram oil up to the maximum proposed use level in feed.

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 provided a safety data sheet³⁵ for marjoram oil, which identified hazards for dermal and eye irritation and dermal and respiratory sensitisation.

The FEEDAP Panel concludes that marjoram oil should be considered as irritant to skin and eyes and as dermal and respiratory sensitiser. When handling the essential oil, exposure of unprotected users to estragole, a genotoxic carcinogen, may occur. Exposure of users by any route is considered a risk and should be minimised.

³⁵Technical dossier/Supplementary information October 2024/Annex_VII_SIn_reply_marjoram_oil_MSDS. Aspiration toxicity (H304, category 1), skin irritation (H315, category 2), eye irritation (H319, category 2), skin sensitisation (H317, category 1), in accordance with the criteria outlined in Annex I of 1272/2008/EC (CLP/EU-GHS).

3.4.4 | Safety for the environment

O. majorana L. is native to and widely distributed in Europe and cultivated in many European countries. The use of marjoram oil in animal feed under the proposed conditions of use is not expected to pose a risk to the environment.

3.5 | Efficacy

Marjoram and marjoram oil from *O. majorana* L. are listed in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2009) and by FEMA with the reference numbers 2662 and 2663.

Since the leaves of *O. majorana* L. and their preparations are recognised to flavour food and their function in feed would be essentially the same as that in food, no further demonstration of efficacy is considered necessary.

4 | CONCLUSIONS

Marjoram oil from *O. majorana* L. may be produced from plants of different origins and by various processes resulting in preparations with different composition and toxicological profiles. Thus, the following conclusions apply only to marjoram oil which contains $\leq 0.29\%$ estragole and is produced by steam distillation from the leaves of *O. majorana*.

The FEEDAP Panel concludes that the use of marjoram oil is very unlikely to induce adverse effects in long-living and reproductive animals and is of no safety concern for short-living animals (species for fattening) when used at the proposed use level of 10 mg/kg complete feed.

No specific proposals have been made by the applicant for the use in water for drinking. The FEEDAP Panel considers that the use in water for drinking alone or in combination with the use in feed should not exceed the daily amount resulting from the use of the additive at 10 mg/kg complete feed.

No safety concerns were identified for the consumer and the environment from the use of the additive in animal feed under the proposed conditions of use.

Regarding user safety, the essential oil under assessment should be considered as irritant to skin and eyes and as dermal and respiratory sensitiser. When handling the essential oil, exposure of unprotected users to estragole, a genotoxic carcinogen, may occur. Exposure of users by any route is considered a risk and should be minimised.

Since the leaves of *O. majorana* L. and their preparations are recognised to flavour food and their function in feed would be essentially the same as that in food, no further demonstration of efficacy is considered necessary.

5 | RECOMMENDATION

The specifications should ensure that marjoram oil contains $\leq 0.29\%$ estragole.

6 | DOCUMENTATION PROVIDED TO EFSA/CHRONOLOGY

Date	Event
23/11/2010	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. <i>Issues: analytical methods</i>
08/01/2013	Reception of supplementary information from the applicant - Scientific assessment remains suspended
26/02/2013	EFSA informed the applicant (EFSA ref. 7,150,727) 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 savory summer oil
30/06/2021	EFSA informed the applicant that the evaluation process restarted
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. <i>Issues: characterisation, safety for target species, safety for the consumer, safety for the user and environment</i>

Date	Event
28/09/2023	Partial withdrawal of the application for the following additive: Spanish majoram oil
08/07/2024	Partial withdrawal of the application for the following additives: lilac chastetree extract and savory summer tincture
26/08/2024	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives. Partial report related to seven additives: 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)
30/10/2024	Reception of supplementary information from the applicant (partial dataset: marjoram oil) - Scientific assessment remains suspended
16/12/2024	Partial withdrawal of the application for the following additives: devils claw extract (wb), balm leaves extract (sb), olive extract (sb)
18/06/2025	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives. Partial report related to 11 additives: cornmint oil, spearmint oil, thyme oil, rosemary oil, marjoram oil, rosemary tincture, basil tincture, lavender tincture, peppermint tincture, sage tincture and wild thyme tincture
26/06/2025	The application was split and a new EFSA-Q-2025-00407 was assigned to the additive included in the present assessment
18/11/2025	Opinion adopted by the FEEDAP Panel on marjoram oil (EFSA-Q-2025-00407). 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

ADME	absorption, distribution, metabolism and excretion
BDG	botanically defined group
BMD	benchmark dose
BMDL ₁₀	benchmark dose lower confidence limit for a benchmark response of 10%
BW	body weight
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
ECHA	European Chemicals Agency
EMA	European Medicines Agency
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
FEMA	Flavor Extract Manufacturers Association
FFAC	Feed Flavourings authorisation Consortium of FEFANA (EU Association of Specialty Feed Ingredients and their Mixtures)
FGE	food group evaluation
FLAVIS	The EU Flavour Information System
FL-no	FLAVIS number
GC-FID	gas chromatography-flame ionisation detection
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LOD	limit of detection
MOE	margin of exposure
MOET	combined (total) margin of exposure
NOAEL	no observed adverse effect level
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
PhEur	European Pharmacopoeia
QSAR	Quantitative Structure Activity Relationship
TTC	threshold of toxicological concern
WHO	World Health Organization

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REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2010-01307 (new EFSA-Q-2025-00407).

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