Adopted: 26 November 2024

DOI: 10.2903/j.efsa.2024.9135

efsa JOURNAL

SCIENTIFIC OPINION

Safety and efficacy of a feed additive consisting of an essential oil derived from the leaves of *Salvia officinalis* L. (sage 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 *Salvia officinalis* L. (sage 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 sage oil is considered safe up to the maximum proposed use levels in complete feed of 20 mg/kg for ornamental fish. For the other species, the calculated safe concentrations in complete feed were 3 mg/kg for chickens for fattening and turkeys for fattening, 4 mg/kg for laying hens and rabbits, 5 mg/kg for piglets, 6 mg/kg for pigs for fattening, 7 mg/kg for sows and dairy cows, 11 mg/kg for veal calves (milk replacers) and salmonids, 10 mg/kg for cattle for fattening, sheep/goats and horses, 12 mg/kg for dogs and 2 mg/kg for cats. These conclusions were extrapolated to other physiologically related species. For any other species, the additive is safe at 2 mg/kg complete feed. The FEEDAP Panel considered that the use of sage oil 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 sage oil in animal feed under the proposed conditions of use is safe for the consumer and the environment. Regarding user safety, sage oil should be considered as an irritant to skin and eyes and as a dermal and respiratory sensitiser. Since the oil of the leaves of *S. officinalis* is 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

camphor, flavouring compounds, sage oil, *Salvia officinalis* L., sensory additives, α-thujone, β-thujone

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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, 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 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: sage oil from *S. officinalis*[5] 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 (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 sage oil from the leaves of *S. officinalis* when used under the proposed conditions of use (see Section 3.3.3).

1.2 | Additional information

Sage oil from *Salvia officinalis* 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). 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[6] in support of the authorisation request for the use of sage oil from *S. officinalis* as a feed additive. The dossier was received on 19 June 2024 and the general information and supporting documentation are available at https://open.efsa.europa.eu/questions/EFSA-Q-2024-00406.[7]

[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 13/03/2013, 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, 10.05.2021, p. 5.
[5]Accepted name: *Salvia officinalis* L.
[6]Dossier reference: FAD-2010-0137.
[7]The original application EFSA-Q-2010-01307 was split on 19/06/2024 and a new EFSA-Q-2024-00406 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 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. The evaluation report is related to the methods of analysis for each feed additive included in BDG 01 – Lamiales. During the assessment, upon request of EFSA, the EURL issued a partial report,[9] 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 *camphor, α-thujone and β-thujone* in *sage oil*.[10]

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of sage oil from *S. officinalis* is in line with the principles laid down in Regulation (EC) No 429/2008[11] 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, 2023a), 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, sage oil, is an essential oil obtained from the fresh leaves of *Salvia officinalis* 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

Salvia officinalis L. is a small perennial shrub belonging to the family Lamiaceae. It is characterised by its grey-green leaves and its lavender-like flower borne on short spikes. The species is native to the northern parts of the Mediterranean but has been introduced into many other temperate regions of the world. It is referred to as the common sage (sometimes the garden sage) and is distinguished from other sage plants such as Spanish sage (*Salvia officinalis* subsp. *lavandulifolia* (Vahl) Gams) or Clary sage (*Salvia sclarea* L.) with which it has a long history of use as a culinary herb in common.

The additive is extracted from the fresh leaves of *S. officinalis* by steam distillation. The volatile constituents are condensed and then separated from the aqueous phase by decantation.

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

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

[10]Evaluation report 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.

[11]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 flavourings

While there is no specific EU authorisation for any *S. officinalis* preparation when used to provide flavour in food, according to Regulation (EC) No 1334/2008[12] 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.'

'Sage leaf (*Salvia officinalis* L. folium)' is described in a monograph of the European Pharmacopoeia 11.0 (PhEur, 2022) and '*Salvia officinalis* L., folium and *Salvia officinalis* L., aetheroleum' in monographs of the European Medicines Agency (EMA, 2016a, 2016b) for medicinal uses.

3.3 | Characterisation

3.3.1 | Characterisation of sage oil

The essential oil is obtained from *S. officinalis* sourced from Ukraine and is a colourless to yellow liquid with a characteristic camphoraceous odour, with a spicy note. Sage oil is identified with the single Chemical Abstracts Service (CAS) number 8022-56-6, the European Inventory of Existing Commercial Chemical Substances (EINECS) number 283-291-0, the Flavor Extract Manufacturers Association (FEMA) number 3001 and the Council of Europe (CoE) number 414. In five batches of the additive, the specific gravity (20°C) ranged between 915 and 916 kg/m^3, the refractive index (20°C) between 1.4572 and 1.4698 and the optical rotation (20°C) between 7.0 and −8.44.[13]

For sage oil, the specifications used by the applicant are based on those developed by the International Organisation for Standardization (ISO) 9909:1997 for the oil of Dalmatian sage (*Salvia officinalis* L.),[14] which were adapted to reflect the concentrations of selected volatile components. Four components contribute to the specifications as shown in Table 1, with camphor,[15] α-thujone and β-thujone selected as the phytochemical markers. The analysis of three batches of the additive showed compliance with these specifications when analysed by GC-FID and expressed as percentage of gas chromatographic peak area (% GC area).[16]

TABLE 1 Constituents of sage oil 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**	**Specifications[1]**	**Mean**	**Range**
α-Thujone[2]	546-80-5	–	18–27	24.96	23.54–26.00
Camphor[3]	76-22-2	–	4–24.5	18.74	18.50–18.87
1,8-Cineole	470-82-6	03.001	5.5–13	10.70	10.33–10.99
β-Thujone[2]	1125-12-8	–	3–7	5.60	4.98–6.16
Total				59.99[4]	59.42–60.39[5]

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

[1]Specifications defined based on GC-FID analysis.

[2]Substance which shall not be added as such to food (Annex III), maximum level in food is set by Regulation (EC) No1334/2008, 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 produced from Artemisia species (0.5 mg/kg).

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

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

[5]The 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 by gas chromatography–mass spectrometry (GC–MS).[17] In total, up to 52 peaks were detected in the chromatogram, which were all identified and accounted on average for 99.2% (99.0%–99.4%) of the % GC area. The four specified compounds accounted on average for 54.3% (range 53.1%–56.0%) of the % GC area when measured with GC–MS (Table 2). In addition to the four compounds indicated in the product specifications, 15 other compounds were detected at individual levels >0.5% and are listed in Table 2. These 19 compounds

[12]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.

[13]Technical dossier/Supplementary information April 2024/Annex_II_SIn_reply_Sage_oil_COA_Chrom.

[14]Technical dossier/Supplementary information April 2024/Annex_III_SIn_reply_sage_oil_ISO_9909_1997.

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

[16]Technical dossier/Supplementary information April 2024/Annex V SIn_reply_Sage_oil_raw_data.

[17]Technical dossier/Supplementary information April 2024/Annex_II_SIn_reply_Sage_oil_COA_Chrom.

accounted on average for 95.8% (95.3%–96.4%) of the % GC area. The remaining 33 compounds (ranging between 0.009% and 0.44%) and accounting on average for 3.4% (3.0%–3.7%) of the % GC area are listed in the footnote.[18] Based on these data, sage oil is considered a fully defined mixture (EFSA Scientific Committee, 2019a).

TABLE 2 Constituents of sage oil, accounting for > 0.5% of the composition: Batch to batch variation based on the analysis of 10 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**
α-Thujone[1]	546-80-5	–	20.48	19.97–21.36
Camphor[2]	76-22-2	–	17.58	17.58–17.97
1,8-Cineole	470-82-6	03.001	10.63	10.16–11.17
β-Thujone[1]	1125-12-8	–	5.61	5.61–6.17
3,7,10-Humulatriene	6753-98-6	01.043	7.28	6.89–7.56
β-Caryophyllene	87-44-5	01.007	6.75	6.48–7.20
Camphene	79–92-5	01.009	5.80	5.50–6.14
α-Pinene (pin-2(3)-ene)	80–56-8	01.004	5.38	5.13–5.70
d,l-Borneol	507–70-0	02.016	4.15	3.95–4.42
β-Pinene (pin-2(10)-ene)	127–91-3	01.003	2.86	2.62–3.15
d,l-Bornyl acetate	76–49-3	09.017	2.08	1.90–2.36
d-Limonene[3]	5989-27-5	01.045	1.58	1.43–1.75
γ-Terpinene	99–85-4	01.020	1.50	1.38–1.62
p-Cymene (1-isopropyl-4-methylbenzene)	99–87-6	01.002	0.75	0.39–1.30
Myrcene	123–35-3	01.008	0.73	0.67–0.79
Terpinolene	586–62-9	01.005	0.72	0.64–0.86
α-Thujene	2867-05-2	–	0.67	0.63–0.71
Linalool	78–70-6	02.013	0.64	0.46–0.84
4-Terpinenol	562–74-3	02.072	0.63	0.56–0.66
Total			95.83[4]	95.30–96.40[5]

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

[1]Substance 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 produced from Artemisia species (0.5 mg/kg).

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

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

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

[5]The 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 carried out an extensive database search (no time limits) to identify data related to the chemical composition and the safety of preparations obtained from *S. officinalis*.[19] Four cumulative databases (LIVIVO, NCBI, OVID and ToxInfo), 13 single databases and 11 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. The literature search on the chemical composition of *Salvia officinalis* L. and its preparations was aimed at identifying the presence of any recognised substances of concern. The EFSA Compendium of botanicals (EFSA, 2012)[20] reports the presence of following substances of possible concern: 1,8-cineole in the aerial parts of *S. officinalis*, and α-thujone, β-thujone, camphor and estragole in the essential oil from the aerial parts of the plant. All these compounds have been analysed in the additive under assessment and the results are reported in Tables 1 and 2. Estragole was not detected in the essential oil under assessment (limit of detection (LOD), 0.001%).

No other substances of concern were identified in the literature provided by the applicant.

[18]Additional constituents: constituents ($n = 11$) between < 0.5% and ≥ 0.1%: aromadendrene, 1,1,7-trimethyltricyclo[2.2.1.0.(2.6)]heptane (tricyclene), viridiflorol, α-terpinene, β-caryophyllene epoxide, α-fenchene, humulene oxide II, 4(10)-thujene (sabinene), α-terpineol, alloaromadendrene, and *(Z)*-3,7-dimethyl-1,3,6-octatriene (*(Z)*-ocimene); constituents ($n = 19$) between < 0.1% and ≥ 0.02%: isocadinene, calamenene, pinocamphone, myrtenol, *trans*-sabinene hydrate, pseudolimonene, camphene hydrate, α-copaene, manool, hex-3*(cis)*-en-1-ol, carvacrol, isocaryophyllene, 2-(4-methylphenyl)propan-2-ol, hexan-1-ol, *d,l*-isoborneol, 4-hydroxy-4-methylpentan-2-one, α-phellandrene, δ-3-Carene, and *(E)*-3,7-dimethyl-1,3,6-octatriene (*(E)*-β-ocimene); constituents ($n = 3$) between < 0.02% and ≥0.005%: carvotan acetone, α-cubebene and myrtenyl acetate.

[19]Technical dossier/Supplementary information April 2024/Literature search_sage oil.

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

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 sage 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

Sage 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 sage oil in complete feed.

Animal category	Maximum use level (mg/kg complete feed)
Chickens for fattening	10
Laying hens	10
Turkeys for fattening	10
Piglets	15
Pigs for fattening	15
Sows	15
Veal calves (milk replacers)	15
Cattle for fattening	15
Dairy cows	15
Sheep/goats	15
Horses	20
Rabbits	20
Salmon and other fin fish	20
Dogs	40
Cats	40
Ornamental fish	20
Other species	20

3.4 | Safety

The assessment of the safety of sage 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.

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) and the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF). The flavouring compounds currently authorised for food[22] and/or feed[23] use, together with the EU Flavour Information

[21]Technical dossier/Section II.

[22]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.

[23]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.

System (FLAVIS) number, the chemical group as defined in Commission Regulation (EC) No 1565/2000,[24] and the corresponding EFSA opinion are listed in Table 4.

TABLE 4 Flavouring compounds 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 opinion.

CG	Chemical group	Product (EU register name)	FLAVIS No.	EFSA* opinion, year
01	Straight-chain primary aliphatic alcohols/aldehydes/acids, acetals and esters with esters containing saturated alcohols and acetals containing saturated aldehydes	Hexan-1-ol	02.005	2013
04	Non-conjugated and accumulated unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals and esters	Hex-3(*cis*)-en-1-ol	02.056	2016a
05	Saturated and unsaturated aliphatic secondary alcohols, ketones and esters with esters containing secondary alcohols	6-Methylhept-5-en-2-one	07.015	2015a
06	Aliphatic, alicyclic and aromatic saturated and unsaturated tertiary alcohols and esters with esters containing tertiary alcohol ethers	Linalool	02.013	2012a
		α-Terpineol	02.014	
		2-(4-Methylphenyl)propan-2-ol	02.042	
		4-Terpinenol	02.072	
07	Primary alicyclic saturated and unsaturated alcohols/aldehydes/acids/acetals/esters with esters containing alicyclic alcohols	Myrtenol[1]	02.091	2017, CEF
		Myrtenyl acetate[1]	09.302	
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
		d,l-Isoborneol	02.059	
		d,l-Bornyl acetate	09.017	
		d-Camphor	07.215	2016b, 2023b
10	Secondary aliphatic saturated or unsaturated alcohols, ketones, ketals and esters with a second secondary or tertiary oxygenated functional group	4-Hydroxy-4-methylpentan-2-one[1]	07.165	2008, AFC
16	Aliphatic and alicyclic ethers	1,8-Cineole	03.001	2012b, 2021
25	Phenol derivatives containing ring-alkyl, ring-alkoxy and side chains with an oxygenated functional group	Carvacrol	04.031	2012c
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[1,2]	01.043	2011, CEF
		1,1,7-trimethyltricyclo [2.2.1.0.(2.6)] heptane Tricyclene[1,2]	01.060	
		4(10)-Thujene (sabinene)[1]	01.059	2015a, CEF
		cis-3,7-Dimethyl-1,3,6-octatriene *(Z)*-β-Ocimene[1]	01.064	
32	Epoxides	β-Caryophyllene epoxide[1]	16.043	2014, CEF

*FEEDAP opinion unless otherwise indicated.

[1]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.

[2]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 shown in Table 4, a number of components of sage oil, accounting for about 53% of the % GC peak areas, have been previously assessed by EFSA and considered safe for use as flavourings. They are currently authorised for use in food[25] without limitations and for use in feed[26] at individual use levels higher than those resulting from the intended use in feed of the essential oil under assessment.

Two compounds, listed in Tables 1, 3, and 7,10-humulatriene [01.043] and tricyclene [01.060] have been evaluated in Flavouring Group Evaluations 25 Revision 2 (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 subchronic 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).

Twenty-one compounds have not been previously assessed for use as flavourings. The FEEDAP Panel notes that 13 additional components[27] accounting for 1.8% of the GC–MS area are aliphatic monoterpenes or sesquiterpenes structurally related to flavourings already assessed in CG 6 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 no significant accumulation in animal tissues and products is expected (EFSA FEEDAP Panel, 2012a, 2015b, 2016c). Humulene oxide II is structurally related to β-caryophyllene epoxide and a similar behaviour is expected.

The oil under assessment contains by specification up to 27% α-thujone, up to 7% β-thujone and up to 24.5% camphor. α-Thujone and β-thujone have been evaluated by the FEEDAP Panel as components of expressed lemon oil (EFSA FEEDAP Panel, 2021).

Camphor (as a mixture of isomers) has not been evaluated for use as a flavouring but is closely related to the flavouring compound *d*-camphor [07.215] already assessed in CG 8 (EFSA FEEDAP Panel, 2016b). Subsequently, *d*-camphor was assessed in tolerance studies with a mixture of flavourings referred to as 'Herbal mixture' in chickens for fattening, piglets, cattle for fattening and salmons. Based on the results of the tolerance studies the FEEDAP Panel concluded that *d*-camphor was safe up to 5 mg/kg complete feed (EFSA FEEDAP Panel, 2023b).

The genotoxic potential of four compounds (viridiflorol, manool, pinocamphone and carvotan acetone) was predicted by the applicant using the Organisation for Economic Co-operation and Development (OECD) Quantitative Structure–Activity relationship (QSAR) Toolbox. No alerts were identified for in vitro mutagenicity by Ames test (with and without S9 mix), for genotoxic and non-genotoxic carcinogenicity and for other toxicity endpoints for viridiflorol. For the other compounds, structural alerts were due to the presence of (i) a vinyl/allyl alcohol group for manool, (ii) an alpha and beta unsaturated vinyl/allyl ketone group for carvotan acetone and (iii) ketone groups (nucleophilic addition) for pinocamphone. 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. For all compounds, mutagenicity read-across-based predictions were found negative.[28] On this basis, the alerts raised were discounted by the FEEDAP Panel. These four compounds are terpenoids belonging to CG 6 (viridiflorol and manool) and CG 8 (pinocamphone and carvotan acetone) and they are expected to follow the same metabolic pathways described above.

The following sections focus on the evidence provided by the applicant in the form of literature searches for α-thujone and β-thujone, as substances of concern.

3.4.1 | Absorption, distribution, metabolism and excretion

α-Thujone and β-thujone

The toxicokinetics of α-thujone in male and female F344/N rats and B6C3F1 mice was investigated in the framework of the National Toxicology Program (NTP) studies on thujone (Waidyanatha et al., 2013). Following gavage administration of a single dose of α-thujone or α- and β-thujone mixture (20- or 50 mg/kg body weight (bw) in rats, 40–80 mg/kg bw in mice), α-thujone was rapidly absorbed without any species, sex or dosage effect. The absolute bioavailability of α-thujone

[25]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.

[26]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.

[27]*trans*-sabinene hydrate, camphene hydrate (CG 6); *trans*-3,7-dimethylocta-1,3,6-octatiene (*(E)*-β-ocimene), pseudolimonene, calamenene, α-thujene, α-fenchene, α-cubebene, α-copaene, isocaryophyllene, aromadendrene, alloaromadendrene and isocadinene, (CG 31).

[28]Technical dossier/Supplementary information April 2024/Annex VII_SIn_reply_sage_oil_QSAR.

was higher in rats than in mice. In rats but not in mice, the bioavailability of α-thujone was four-fold higher in females than males. The AUC for both test items was several folds higher in rats than in mice; the AUC for α-thujone was higher in female than in male rats. Both test items are rapidly distributed to brain; females of both species showed a higher brain: plasma ratio than males and female rats displayed longer brain half-lives with respect to their mice counterparts. Finally, particularly for α-thujone, plasma clearance was higher in male than in female rats.

The evidence on the metabolism and the toxicity of thujone (α- and β-thujone) has been described by the European Medicines Agency (EMA) in the public statement on the use of herbal medicinal products containing thujone (EMA, 2012). The FEEDAP Panel reviewed and summarised the available evidence in the opinion on expressed lemon oil (EFSA FEEDAP Panel, 2021) as follows: 'Metabolism of thujone has been investigated in mouse, rat and human liver preparations in vitro and in mice, rats and (partially) rabbits in vivo. Hydroxylation occurs at various positions, mainly at 7- and 4-positions, followed to a different extent by glucuronidation, and reductions as minor reactions are principal metabolic pathways, although in vitro and in vivo metabolic profiles do not necessarily agree with each other (Höld et al., 2000, 2001; Ishida et al., 1989). After in vitro liver microsomal incubations with α-thujone, 7-hydroxy-α-thujone seems to be a major metabolite in mice, rats and humans, whereas with β-thujone, formation of 4-hydroxy-β-thujone exceeded that of the 7-hydroxymetabolite in all species. 2-Hydroxy-thujone was observed only in mouse liver microsomes.' (...) 'In mice, treated orally with α-thujone in vivo, 2-hydroxy-α-thujone (mostly as a glucuronide) was the principal metabolite in urine, whereas 7-hydroxy-β-thujone was by far the most abundant urinary metabolite after β-thujone administration. In the rat, 4-hydroxythujones were the principal urinary metabolites after administration of thujones (Höld et al., 2001).'

In summary, in orally treated rats and mice, α-thujone was rapidly absorbed with no apparent species- and sex-related differences. In liver, it undergoes CYP-mediated hydroxylation at different positions. The bioavailability of α-thujone was higher in rats than in mice. Sex-related differences were consistently observed in rats. Female rats displayed a higher bioavailability, a higher AUC, a lower plasma clearance, a higher brain:plasma ratio as compared to males. According to NTP, 'these results may provide a partial explanation for the increased sensitivity of females compared to males to the neurotoxic effects of thujone' (NTP, 2011).

3.4.2 | Toxicology

3.4.2.1 | *Genotoxicity and carcinogenicity*

For fully defined mixtures, the EFSA Scientific Committee (EFSA SC) recommends applying a component-based approach, i.e. assessing all components individually for their genotoxic potential (EFSA Scientific Committee, 2019b).

α-Thujone and β-thujone

The genotoxicity and carcinogenicity data of thujone (α- and β-thujone) have been summarised in the EMA public statement on the use of herbal medicinal products containing thujone (EMA, 2012). Thujone was tested in the framework of the NTP of the US Department of Health and Human Services (NTP, 2011).

As summarised by EMA (2012), 'In connection with the NTP study (NTP, 2011, TR No. 570), the genotoxic potential of racemic thujone[29] (used in the carcinogenicity study) and α-thujone were investigated according to the NTP protocols. The Ames test results of both compounds were negative in the presence or absence of the activating enzyme system. In vivo, daily exposure by gavage to racemic thujone (6.25, 12.5, 25, 50, or 75 mg α,β-thujone/kg bw) for 3 months did not result in an increase in micronucleated erythrocytes in the peripheral blood of male B6C3F1 mice. However, female mice had a small but significant increase in micronucleated erythrocytes in the peripheral blood at the end of the 3-month study. Racemic thujone did not induce bone marrow toxicity.' Although the micronucleus rate at the highest dose in female mice fulfilled the criteria for positive results, the FEEDAP Panel has doubts in the relevance of the results because of the unusually low values of the concurrent control.

According to the NTP report (NTP, 2011) on 2-year gavage studies with rats (dose levels 12.5, 25, 50 mg/kg) and mice (dose levels 3, 6, 12, 25 mg/kg), 'there was some evidence of carcinogenic activity of α, β-thujone in male F344/N rats based on increased incidences of preputial gland neoplasms at the dose level of 25 mg/kg (all rats at 50 mg/kg died before the end of the study);[30] increased incidences of benign phaeochromocytoma of the adrenal medulla may have been related to administration of α,β-thujone in male F344/N rats administered 12.5 or 25 mg/kg.[31] There was no evidence of carcinogenic activity of α,β-thujone in female F344/N rats administered 12.5 or 25 mg/kg. There was no evidence of carcinogenic activity of α,β-thujone in male or female B6C3F1 mice administered 3, 6, or 12 mg/kg.

The FEEDAP Panel noted that both lesions are of limited relevance. Preputial gland tissues are unique to rodents (Maronpot et al., 2004), and therefore, the tumours at this site are not relevant to other species. Phaeochromocytomas are known to occur naturally at high frequency in male rats (Greim et al., 2009).

[29]According to the NTP report, the mixture tested in the 3 month and 2-year carcinogenicity study was not racemic thujone but an α,β-thujone mixture containing 70% α-thujone, 11% β-thujone, 16% fenchone, 2% camphor and 0.5% of unidentified impurities.

[30]Preputial gland: incidences of carcinoma (1/49, 0/49, 5/50); adenoma or carcinoma (3/49, 1/49, 9/50).

[31]Adrenal medulla: incidences of benign phaeochromocytoma (6/50, 8/50, 12/49).

3.4.2.2 | *Repeated dose toxicity studies*

As summarised by EMA (2012), thujone was tested in the framework of the NTP of the US Department of Health and Human Services (NTP, 2011).

'α-Thujone and an isomeric mixture[32] were administered by gavage to B6C3F1 mice and to Fischer 344 rats at doses of 0, 1, 3, 10, 30 or 100 mg/kg for 14 days. In both species, the increased mortality observed in the top dose group was associated with indications of neurotoxicity (hyperactivity, tremors, tonic seizures). In the 3-month NTP, α-thujone and the isomeric mixture were administered by gavage to B6C3F1 mice and to Fischer 344 rats at doses of 0, 6.25, 12.5, 25, 50 or 100 mg/kg for 13 weeks. In both species the increased mortality observed in the higher dose groups (from 25 or 50 and greater) was associated with seizures.'

In the chronic study, 'an isomeric mixture of thujone[33] was administered by gavage to B6C3F1 mice at doses of 0, 3, 6, 12, and 25 mg/kg body weight/day and to Fischer 344 rats at doses of 0, 12.5, 25, and 50 mg/kg body weight/day for 2 years. In both species, increased mortality was observed in the top dose group, and in the rat also in the middle dose group. Clonic and tonic seizures were observed in the middle and top dose groups in rats[34] and in the top dose group in mice.[35] A small increase in clonic seizures was observed also in the low dose group in rats.' All of the rats in the high-dose groups (50 mg/kg bw) and most of the rats in the mid-dose (25 mg/kg bw) groups had clonic seizures (43/50 males and 47/50 females). Seizures first occurred on days 694, 612, 109 and 73 for male rats in the vehicle control, 12.5, 25 and 50 mg/kg bw groups, respectively. In female rats, seizures first occurred on days 304, 308, 47 and 21 for the vehicle control, 12.5, 25 and 50 mg/kg bw groups, respectively. For mice, clonic seizures were seen only in the top dose tested (25 mg/kg bw, 41/50 males and 50/50 females). 'The administration of α,β-thujone resulted in increased incidences of non-neoplastic lesions in the brain[36] and spleen[37] of male and female F344/N rats, the kidneys[38] of male F344/N rats and the pituitary gland[39] of female F344/N rats usually at the two highest dose levels. In the rat, the no observed effect level (NOEL) value was 12.5 mg/kg bw for mortality and tonic seizures (no NOEL for clonic seizures). In the mouse, the NOEL was 12 mg/kg bw for seizures and mortality.'

Lachenmeier and Uebelacker (2010) performed a re-evaluation of the available evidence using the benchmark dose (BMD) approach instead of the NOEL. The application of the dose–response modelling on the long-term chronic toxicity study of the NTP in rats, using clonic seizures as a response, yielded a BMD lower confidence limit for a benchmark response of 10% ($BMDL_{10}$) as 11 mg/kg body weight per day in male rats.[40] Since no clear differences between sexes were apparent from the modelling results, the FEEDAP Panel concluded that the sex-related differences observed in toxicokinetic studies were not reflected in the selected endpoint for $BMDL_{10}$ calculation' (see Section 3.4.1 for sex-related differences in kinetics). Considering that the mixture tested contained 70% of α-thujone, the FEEDAP Panel calculated a $BMDL_{10}$ of 8 mg/kg bw per day for α-thujone (EFSA FEEDAP Panel, 2021). Despite β-thujone having been reported to have a much lower neurotoxicity compared to α-thujone (NTP, 2011), the FEEDAP Panel applied the $BMDL_{10}$ of 8 mg/kg bw per day also for β-thujone (EFSA FEEDAP Panel, 2022).

3.4.3 | Safety for the target species

Tolerance studies in the target species and/or toxicological studies in laboratory animals made with the essential oil under application 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 98.9% 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. The oil under assessment contains by specification up to 24.5% of an isomeric mixture of camphor, which is assessed separately from the other components of the oil.

[32]α,β-Thujone mixture containing 70% α-thujone, 11% β-thujone, 16% fenchone, 2% camphor and 0.5% of unidentified impurities.

[33]α,β-Thujone mixture containing 70% α-thujone, 11% β-thujone, 16% fenchone, 2% camphor and 0.5% of unidentified impurities.

[34]Male rats: clonic seizures (1/50, 5/50, 43/50, 50/50), tonic seizures (0/50, 0/50, 2/50, 18/50); females rats: clonic seizures (1/50, 3/50, 47/50, 50/50), tonic seizures (0/50, 0/50, 15/50, 2/50).

[35]Male mice: clonic seizures (0/50, 0/50, 0/50, 0/50, 41/50), tonic seizures (0/50, 0/50, 0/50, 0/50, 35/50); females mice: clonic seizures (1/50, 1/50, 0/50, 0/50, 50/50), tonic seizures (0/50, 0/50, 0/50, 0/50, 40/50).

[36]Male rats: necrosis (0/50, 0/50, 1/50, 3/50), pigmentation (0/50, 1/50, 0/50, 3/50); female rats: pigmentation (1/50, 3/50, 5/50, 19/50).

[37]Male rats: pigmentation (19/50, 24/50, 30/49, 46/48); female rats: pigmentation (39/48, 40/49, 39/48, 45/50).

[38]Male rats: mineralisation (17/48, 33/48, 41/44, 38/49).

[39]Female rats: pars distalis, atrophy (0/50, 0/49, 2/49, 12/48); Rathke's cleft, dilatation (7/50, 1/49, 13/49, 26/48).

[40]The value of 11 mg/kg bw per day for male rat was confirmed by recalculating the $BMDL_{10}$ using the EFSA Bayesian BMD tool (EFSA Scientific Committee, 2022).

Camphor

The tolerance trials carried out in chickens for fattening, piglets, cattle for fattening and salmons with a mixture of flavourings containing *d*-camphor ('Herbal mixture') showed that *d*-camphor is safe up to 5 mg/kg complete feed for all animal species with a margin of safety of 10 (EFSA FEEDAP Panel, 2023b). The FEEDAP Panel considers that the conclusions reached for *d*-camphor can be extrapolated to *l*-camphor by applying read-across.

At the proposed conditions of use for sage oil (see Section 3.3.3), the concentration of camphor in feed would range from 2.5 mg/kg for poultry species to 9.8 mg/kg for dogs and cats, considering that camphor is present in the essential oil under assessment at the highest specification of 24.5% (see Table 5).

TABLE 5 Concentration of camphor (isomeric mixture) in complete feed resulting from the use of sage oil at the proposed conditions of use and calculated maximum safe concentrations of sage oil in complete feed (mg/kg) to ensure a safe level of camphor for the different target animal categories.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg complete feed)[1]	Concentration of camphor (mg/kg complete feed)[2]	Maximum safe use level (mg/kg complete feed)[1,3]
Chickens for fattening	79	10	2.5	–
Laying hens	53	10	2.5	–
Turkeys for fattening	59	10	2.5	–
Pig for fattening	44	15	3.7	–
Piglets	37	15	3.7	–
Sows lactating	30	15	3.7	–
Veal calves (milk replacer)	19	15	3.7	–
Cattle for fattening	20	15	3.7	–
Dairy cows	31	15	3.7	–
Sheep/goats	20	15	3.7	–
Horses	20	20	4.9	–
Rabbits	50	20	4.9	–
Salmonids	18	20	4.9	–
Dogs	17	40	9.8	20
Cats	20	40	9.8	20
Ornamental fish	5	20	4.9	–

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

[2]Based on the highest proposed specification (24.5% of the GC area) of camphor in the additive.

[3]Maximum safe use level calculated to ensure a maximum concentration of ≤ 5 mg camphor/kg complete feed.

Considering that *d*-camphor is tolerated up to 5 mg/kg complete feed and considering a concentration of camphor (isomeric mixture) in sage oil corresponding to the highest specification of 24.5%, the FEEDAP Panel concludes that, with regard to the presence of camphor, the use of sage oil is safe at the maximum proposed use levels for all animal species except dogs and cats, for which a maximum safe use level of 20 mg/kg complete feed is calculated.

Components other than camphor

Based on considerations related to structural and metabolic similarities, the components were allocated to 10 assessment groups, corresponding to the chemical groups (CGs) 1, 4, 6, 7, 8, 10, 16, 25, 31 and 32, as defined in Annex I of Regulation (EC) No 1565/2000. For CG 31 ('aliphatic and aromatic hydrocarbons'), subassessment 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 5 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 2018[41]). For some components in the assessment group, toxicological data were available to derive no observed adverse effect levels (NOAELs). Structural and metabolic similarity among the components in the assessment groups were evaluated to explore the application of read-across. If justified, extrapolation can be made from a known NOAEL of a component in an assessment group to the other components of the group with no available NOAEL. If sufficient evidence is available for the components of a (sub)assessment group, a (sub)assessment group NOAEL can be derived.

[41]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/.

Toxicological data of subchronic studies, from which NOAEL values could be derived, were available for several compounds in CG 1 (EFSA FEEDAP Panel, 2013), for hex-3(cis)-en-1-ol [02.056] in CG 4 (EFSA FEEDAP Panel, 2016a), 6-methylhept-5-en-2-one [07.015] in CG 5 (EFSA FEEDAP Panel, 2015a), linalool [02.013] and terpineol [02.230][42] in CG 6 (EFSA FEEDAP Panel, 2012a), *d,l*-isobornyl acetate [09.218] in CG 8 (EFSA FEEDAP Panel, 2016b), 1,8-cineole [03.001] in CG 16 (EFSA FEEDAP Panel, 2012b, 2021), carvacrol [04.031] in CG 25 (EFSA FEEDAP Panel, 2012c), myrcene [01.008], *d*-limonene [01.045] and β-caryophyllene [01.007] in CG 31 (EFSA FEEDAP, 2015b, 2016c), and β-caryophyllene epoxide [16.043] for 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). The NOAEL of 60 mg/kg bw per day was divided by a factor of 2 to take into account the nature of the study.

The FEEDAP Panel applied a $BMDL_{10}$ of 8 mg/kg bw per day for α-thujone (EFSA FEEDAP Panel, 2021), which is also extended to β-thujone despite its lower neurotoxicity.

For CG 1, a group NOAEL of 120 mg/kg was derived from the toxicological data available and was extrapolated to hexan-1-ol [02.005].

For the subgroup of terpinyl derivatives in CG 6, i.e., α-terpineol [02.072] and 4-terpinenol [02.072], the reference point was selected based on the NOAEL of 250 mg/kg bw per day available for terpineol [02.230]. The NOAEL of 250 mg/kg bw per day was divided by a factor of 2 to take into account the short duration (35 days) of the study with terpineol (EFSA FEEDAP Panel, 2012a).

For *d,l*-borneol [02.016], *d,l*-isoborneol [02.059] and *d,l*-bornyl acetate [09.218] in CG 8, a NOAEL of 15 mg/kg bw per day was extrapolated from *d,l*-isobornyl acetate [09.218].

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], limonene [01.001] and β-caryophyllene [01.007] were applied, respectively, using read-across to the compounds within subassessment groups II (*cis*-3,7-dimethyl-1,3,6-octatriene and *trans*-3,7-dimethyl-1,3,6-octatriene), III (γ-terpinene [01.020] and terpinolene [01.055]) and V (camphene [01.009], α-pinene [01.004], β-pinene [01.003], α-thujene, aromadendrene, tricyclene [01.060], α-fenchene, alloaromadendrene, α-copaene, δ-3-carene [01.029], isocaryophyllene, sabinene [01.059] and α-cubebene),[43] respectively (EFSA CEF Panel, 2015a, 2015b). Read-across was also applied from β-caryophyllene [01.007] to viridiflorol in CG 6 and 3,7,10-humulatriene [01.043] in CG 31,VI. For viridiflorol and 3,7,10-humulatriene, the NOAEL of 222 mg/kg bw per day for β-caryophyllene [01.007] was divided by a factor of 2 to take into account the differences in the structures (the presence of an additional cyclopropane ring in viridiflorol and extrapolation from a tricyclic to a macrocyclic non-aromatic compound for 3,7,10-humulatriene) (EFSA FEEDAP Panel, 2023c). In the current assessment, the NOAEL of 60 mg/kg bw per day for α-terpinene [01.019] is applied to α-phellandrene, divided by a factor of 2 to take into account the nature of the study carried out with α-terpinene.

The NOAEL of 109 mg/kg bw per day for β-caryophyllene epoxide [16.043] was applied to humulene oxide II in CG 32.

For the remaining compounds,[44] 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 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). For those compounds covered by specifications (camphor, α-thujone, β-thujone and 1,8-cineole, see Table 1), the maximum limit is used for the calculation of exposure. For the other components, the highest analysed concentration is used. Default values on body weight are used to express exposure in terms of mg/kg bw per day. The intake levels of the individual components are calculated for chickens for fattening, the species with the highest ratio of feed intake/body weight per day 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, 2019).

[42]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.

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

[44]CC I (3 mg/kg bw per day): camphene hydrate, 2-(4-methylphenyl)propan-2-ol, myrtenol, myrtenyl acetate, 4-hydroxy-4-methylpentan-2-one, pseudolimonene, calamenene, isocadinene; CC II (0.91 mg/kg bw per day): carvotan acetone; CC III (0.15 mg/kg bw per day): manool, pinocamphone.

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.[45]

The approach to the safety assessment of sage 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 at the use level of 10 mg/kg complete feed.

TABLE 6 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 sage 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.**	**Daily Intake[1]**	**Cramer class[2]**	**NOAEL/ $BMDL_{10}$[3]**	**MOE[4]**	**MOET[5]**
Constituent	**–**	**%**	**mg/kg**	**mg/kg bw per day**	**–**	**mg/kg bw per day**	**–**	**–**
CG 6								
Linalool	02.013	0.84	0.084	0.0076	(I)	117	15,479	
4-Terpinenol	02.072	0.66	0.066	0.0059	(I)	125[6]	21,193	
Viridiflorol	02.215	0.39	0.039	0.0035	(I)	111[7]	32,116	
Camphene hydrate	–	0.06	0.006	0.0005	I	*3*	5762	
2-(4-Methylphenyl) propan-2-ol	02.042	0.05	0.005	0.0004	I	*3*	7426	
Manool	–	0.04	0.004	0.0004	III	*0.15*	389	
MOET CG 6								331
CG 7								
Myrtenol	02.091	0.54	0.005	0.0005	I	*3*	6188	
Myrtenyl acetate	09.302	0.02	0.002	0.0002	I	*3*	17,588	
								4578
CG 8								
d,l-Borneol	02.016	4.42	0.442	0.0397	(I)	15	378	
d,l-Bornyl acetate	09.218	2.36	0.236	0.0212	(I)	15	708	
Pinocamphone	–	0.12	0.012	0.0010	III	*0.15*	145	
d,l-Isoborneol	02.059	0.03	0.003	0.0003	(I)	15	49,144	
Carvotan acetone	–	0.03	0.003	0.0002	II	*0.91*	3754	
MOET CG 8								89
CG 10								
4-Hydroxy-4-methylpentan-2-one	07.165	0.03	0.003	0.0002	I	*3*	12,853	
CG 16							857	
1,8-Cineole	03.001	13	1.300	0.1167	II	**100**	997	
CG 31, II (Acyclic alkanes)								
Myrcene	01.008	0.79	0.079	0.0071	(I)	**44**	6212	
(Z)-β-Ocimene	01.064	0.12	0.012	0.0011	(I)	44	40,174	
MOET CG 31, II								5380
CG 31, III (Cyclohexene hydrocarbons)								

[45]Compounds included in the assessment groups but not reported in the table: hexan-1-ol (CG 1); hex-3(*cis*)-en-1-ol (CG 4); α-terpineol and *trans*-sabinene hydrate β (CG 6); *d,l*-isoborneol (CG 8); carvacrol (CG 25); *(E)*-β-ocimene (CG 31,II); α-phellandrene (CG 31, III); tricyclene, α-fenchene, alloroaromadenderene, α-copaene, δ-3-carene, isocaryophyllene, sabinene and α-cubebene (CG 31,V).

TABLE 6 (Continued)

Essential oil composition			Exposure		Hazard characterisation		Risk characterisation	
Assessment group	**FLAVIS-No**	**Highest conc. In the oil**	**Highest feed conc.**	**Daily Intake[1]**	**Cramer class[2]**	**NOAEL/ $BMDL_{10}$[3]**	**MOE[4]**	**MOET[5]**
Constituent	**–**	**%**	**mg/kg**	**mg/kg bw per day**	**–**	**mg/kg bw per day**	**–**	**–**
d-Limonene	01.045	1.75	0.175	0.0157	(I)	**250**	15,895	
γ-Terpinene	01.020	1.62	0.162	0.0146	(I)	250	17,180	
Terpinolene	01.005	0.86	0.086	0.0077	(I)	250	32,533	
α-Terpinene	01.019	0.32	0.032	0.0028	(I)	**30**[8]	10,542	
Pseudolimonene	–	0.06	0.006	0.0005	I	*3*	5967	
MOET CG 31, III								2414
CG 31, IV (Benzene hydrocarbons, alkyl)								
p-Cymene	01.002	1.30	0.130	0.0117	(I)	**154**	13,155	
Calamenene	–	0.09	0.009	0.0008	I	*3*	3672	
MOET CG 31, IVe								2871
CG 31, V (Bi-, tricyclic, non-aromatic hydrocarbons)								
β-Caryophyllene	01.007	7.20	0.720	0.0647	(I)	**222**	3433	
Camphene	01.009	6.14	0.614	0.0551	(I)	222	4028	
α-Pinene	01.004	5.70	0.570	0.0512	(I)	222	4338	
β-Pinene	01.003	3.15	0.315	0.0283	(I)	222	7841	
α-Thujene	–	0.71	0.071	0.0064	(I)	222	34,732	
Aromadendrene	–	0.68	0.068	0.0061	(I)	222	36,636	
Isocadinene	–	0.09	0.009	0.0009	I	*3*	3755	
MOET CG 31, V								820
CG 31, VI (macrocyclic non-aromatic hydrocarbons)								
3,7,10-Humulatriene	01.043	7.56	0.756	0.0679	(I)	111[7]	1636	
CG 32								
β-Caryophyllene epoxide	16.043	0.41	0.041	0.0036	(III)	**109**	29,980	
Humulene oxide II	–	0.31	0.031	0.0028	(III)	109	38,916	
								16,934
Thujones								
α-Thujone	–	27	2.700	0.2424	(III)	**8**	33	
β-Thujone	–	7	0.700	0.0628	(III)	8	127	
								26

[1]Intake calculations for the individual components are based on the use level of 10 mg/kg in feed for chickens for fattening, the species with the highest ratio of feed intake/body weight. The MOE for each component is calculated as the ratio of the reference point (no observed adverse effect level, NOAEL) to the intake. 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.

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

[3]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.

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

[5]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.

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

[7]A factor of 2 was applied to the NOAEL of 222 mg/kg bw per day for β-caryophyllene because of differences in the structures.

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

As shown in Table 6, for all assessment groups except for thujones and CG 8, the MOET was > 100 at the proposed use level of 10 mg/kg complete feed in chickens for fattening. From the lowest MOET of 26 for chickens for fattening, the MOET for thujones was calculated for the other target species considering the respective daily feed intake/kg bw and the proposed use levels in feed. The results are summarised in Table 7.

TABLE 7 Combined margin of exposure (MOET) for the assessment group thujones for the different target animal categories at the proposed use levels in feed and maximum safe use level in feed.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg complete feed)[1]	Lowest MOET Thujones[2]	Maximum safe use level (mg/kg complete feed)[1]
Chickens for fattening	79	10	26	3
Laying hens	53	10	39	4
Turkeys for fattening	59	10	35	3
Piglets	44	15	31	5
Pigs for fattening	37	15	37	6
Sows lactating	30	15	46	7
Veal calves (milk replacer)	19	15	77	12
Cattle for fattening	20	15	68	10
Dairy cows	31	15	44	7
Sheep/goats	20	15	68	10
Horses	20	20	51	10
Rabbits	50	20	21	4
Salmonids	18	20	57	11
Dogs	17	40	30	12
Cats[3]	20	40	26	2
Ornamental fish	5	20	205	–[4]

[1]Complete feed containing 88% DM, milk replacer 94.5% DM.
[2]Based on the highest proposed specification of α-thujone and β-thujone (27% and 7% of the GC area) in the additive.
[3]The MOET for cats is increased to 500 because of the reduced capacity of glucuronidation.
[4]For the species for which the MOET is > 100, the proposed use level is considered safe.

At the proposed use levels in complete feed, the MOET exceeds the value of 100 for ornamental fish. For the other species, the maximum safe use levels in feed were calculated to ensure an MOET ≥ 100. Because glucuronidation is an important metabolic reaction 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 sage oil as additive in cat feed needs a wider margin of exposure. An MOET of 500 is considered adequate. The maximum proposed use level of 20 mg/kg is safe for ornamental fish. For the other species, the resulting maximum safe levels in feed are shown in Table 7. These levels are extrapolated to physiologically related minor species. For the other species not considered, the lowest value of 2 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 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.

3.4.3.1 | *Conclusions on safety for the target species*

The FEEDAP Panel considers that the levels of sage oil summarised in Table 8 are safe for the respective target species.

TABLE 8 Safe concentrations of sage oil in complete feed (mg/kg) for all animal species and categories.

Animal categories	Safe concentration (mg/kg complete feed)[1]
Turkeys for fattening	3
Chickens for fattening, other poultry for fattening or reared for laying/reproduction and ornamental birds	3
Laying hens and other laying/reproductive birds	4
Pigs for fattening	6
Piglets and other porcine species for meat production or reared for reproduction	5
Sows and other porcine species for reproduction	7
Veal calves (milk replacer)	11

TABLE 8 (Continued)

Animal categories	Safe concentration (mg/kg complete feed)[1]
Sheep/goats	10
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction, cervids and camelids at the same physiological stage	10
Dairy cows and other ruminants, cervids and camelids for milk production or reproduction	7
Horses and other equines	10
Rabbits and other leporids	4
Salmonids and minor fin fish	11
Dogs	12
Cats	2
Ornamental fish	20
Other species	2

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

3.4.4 | Safety for the consumer

The leaves of *Salvia officinalis* L. (sage) and their oil are 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 (Burdock, 2009) cites intake values of 2.25 mg/kg bw per day for sage (FEMA 3000) and 0.016 mg/kg bw per day for sage oil (FEMA 3001). The Fenaroli handbook also reports use levels in food and beverages in the range of 3 mg/kg up to 225 mg/kg for sage 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 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 sage oil are expected to be extensively metabolised and excreted in the target species. For the major components, the data available for 1,8-cineole, camphor and thujones indicate that they are absorbed, metabolised and rapidly excreted and are not expected to accumulate in animal tissues and products (EFSA FEEDAP Panel, 2012a, 2016b, 2021). Consequently, relevant residues in food products are unlikely.

Considering the above and the reported human exposure due to the direct use of sage oil in food (Burdock, 2009), it is unlikely that the consumption of products from animals given sage oil at the proposed maximum use level would substantially increase human background exposure. The use of sage oil in animal nutrition under the proposed conditions of use is considered safe for human consumers of animal products.

3.4.5 | 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 *S. officinalis* for users.[46] None of the references retrieved were considered relevant to the safety assessment.

The applicant provided a safety data sheet[47] for sage oil, which identified concerns for dermal and eye irritation and dermal and respiratory sensitisation.

The FEEDAP Panel concludes that sage oil should be considered as irritant to skin and eyes, and as a dermal and respiratory sensitiser.

3.4.6 | Safety for the environment

S. officinalis is a species native to Europe where it is also cultivated for culinary and ornamental purposes.

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

[46]Technical dossier/Supplementary information April 2024/Literature search_Sage oil.

[47]Technical dossier/Supplementary information April 2024/Annex VIII_SIn_reply_Sage_oil_MSDS. Aspiration hazard (H304, Category 1), Hazard for skin corrosion/irritation (H315, Category 2), Serious eye damage/eye irritation (H319, Category 2), Skin sensitization (H317, Category 1), in accordance with the criteria outlined in Annex I of 1272/2008/EC (CLP/EU-GHS).

3.5 | Efficacy

The leaves of sage (*Salvia officinalis* L.) and their oil are listed in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2009) and by FEMA with the reference numbers 3000 and 3001.

Since the leaves of *S. officinalis* 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

The conclusions of the FEEDAP Panel on the safe levels in complete feed of sage oil for all animal species are summarised as follows:

Animal categories	Safe concentration (mg/kg complete feed)[1]
Turkeys for fattening	3
Chickens for fattening, other poultry for fattening or reared for laying/reproduction and ornamental birds	3
Laying hens and other laying/reproductive birds	4
Pigs for fattening	6
Piglets and other porcine species for meat production or reared for reproduction	5
Sows and other porcine species for reproduction	7
Veal calves (milk replacer)	11
Sheep/goats	10
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction, cervids and camelids at the same physiological stage	10
Dairy cows and other ruminants, cervids and camelids for milk production or reproduction	7
Horses and other equines	10
Rabbits and other leporids	4
Salmonids and minor fin fish	11
Dogs	12
Cats	2
Ornamental fish	20
Other species	2

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

The FEEDAP Panel considers that the use of sage oil 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 sage 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 the oil of the leaves of *Salvia officinalis* L. is recognised to flavour food and its 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
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. *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. 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

Date	Event
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
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*
28/09/2023	Partial withdrawal of the application for the following additive: Spanish majoram oil
18/04/2024	Reception of supplementary information from the applicant (partial dataset: sage oil) - Scientific assessment remains suspended
19/06/2024	The application was split and a new EFSA-Q-2024-00406 was assigned to the additive included in the present assessment
08/07/2024	Partial withdrawal of the application for the following additives: lilac chastetree extract and savoury summer tincture
26/08/2024	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives. Scientific assessment re-started for the additive included in the present assessment
27/08/2024	Reception of supplementary information from the applicant (letter of agreement)
26/11/2024	Opinion adopted by the FEEDAP Panel on Spanish sage oil (EFSA-Q-2024-00406). 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
CD	Commission Decision
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
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
FL-no	FLAVIS number
GC-MS	Gas chromatography-mass spectrometry
GC-FID	Gas chromatography-flame ionisation detection
ISO	International Organisation for Standardization
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
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
QSAR	Quantitative Structure Activity Relationship
SCF	Scientific Committee on Food
TTC	threshold of toxicological concern
UF	uncertainty factor
WHO	World Health Organization

ACKNOWLEDGEMENTS

The Panel wishes to thank the following for the support provided to this scientific output (in alphabetical order of the last name): Jaume Galobart, Matteo Lorenzo Innocenti and Maria Vittoria Vettori.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2010-01037 (New EFSA-Q-2024-00406)

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How to cite this article: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Villa, R. E., Azimonti, G., Bonos, E., Christensen, H., Durjava, M., Dusemund, B., Gehring, R., Glandorf, B., Kouba, M., López-Alonso, M., Marcon, F., Nebbia, C., Pechová, A., Prieto-Maradona, M., Röhe, I., Theodoridou, K., Bastos, M. d. L., Brantom, P., … Manini, P. (2024). Safety and efficacy of a feed additive consisting of an essential oil derived from the leaves of *Salvia officinalis* L. (sage oil) for use in all animal species (FEFANA asbl). *EFSA Journal*, *22*(12), e9135. https://doi.org/10.2903/j.efsa.2024.9135