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Safety and efficacy of a feed additive consisting of an essential oil derived from *Eucalyptus globulus* Labill. (eucalyptus oil) for all animal species (FEFANA asbl)

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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 and twigs of *Eucalyptus globulus* Labill. (eucalyptus oil) when used as a sensory additive in feed and water for drinking for all animal species. The FEEDAP Panel concluded that the use of eucalyptus oil is safe at the following concentrations in complete feed: 12 mg/kg for chickens for fattening, 18 mg/kg for laying hens, 16 mg/kg for turkeys for fattening, 22 mg/kg for piglets, 26 mg/kg for pigs for fattening, 32 mg/kg for sows, 55 mg/kg for veal calves (milk replacer), 48 mg/kg for cattle for fattening, sheep, goats and horses, 31 mg/kg for dairy cows, 19 mg/kg for rabbits, 55 mg/kg for salmonids, 58 mg/kg for dogs, 10 mg/kg for cats and 75 mg/kg for ornamental fish. These conclusions were extrapolated to other physiologically related species. For any other species, the additive was considered safe at 10 mg/kg complete feed. No concerns for consumers were identified following the use of eucalyptus oil up to the highest safe level in feed. The additive under assessment should be considered as irritant to skin and eyes and the respiratory tract and as a skin sensitiser. The use of eucalyptus oil at the proposed use level in feed was not expected to pose a risk for the environment. Since *E. globulus* and its preparations were recognised to flavour food and its function in feed would be essentially the same as that in food, no further demonstration of efficacy was considered necessary.

Keywords: sensory additives, flavouring compounds, *Eucalyptus globulus* Labill., eucalyptus oil, 1,8-cineole

Requestor: European Commission

Question number: EFSA-Q-2010-01282 (New EFSA-Q-2023-00395)

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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 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 7 years after the entry into force of this Regulation.

The European Commission received a request from the Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)[2] for authorisation/re-evaluation of 18 preparations (namely geranium oil, geranium rose oil, eucalyptus oil, eucalyptus tincture, clove oil, clove tincture, broom tea tree oil, purple loosestrife tincture, tea tree oil, melaleuca cajuputi oil, niaouli oil, allspice oil, bay oil, pomegranate bark extract, bambusa tincture, citronella oil, lemongrass oil and vetiveria oil) belonging to botanically defined group (BDG) 07 – *Geraniales, Myrtales, Poales* when used as feed additives for all animal species (category: sensory additives; functional group: flavourings). During the assessment, the applicant withdrew the application for four preparations (namely broom tea tree oil, geranium oil, bay oil and vetiveria oil[3]). These preparations were deleted from the register of feed additives.[4] During the course of the assessment, this application was split and the present opinion covers only one out of the initial 18 preparations under application: an essential oil from the leaves and twigs of *Eucalyptus globulus* Labill.[5] (eucalyptus oil) for all animal species.

The remaining 11 preparations belonging to botanically defined group (BDG) 07 – *Geraniales, Myrtales, Poales* 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 21 December 2010.

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 product eucalyptus oil (*E. globulus*), when used under the proposed conditions of use (see **Section 3.2.3**).

1.2. Additional information

Eucalyptus oil from *Eucalyptus globulus* Labill. (eucalyptus oil) 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.

There is no specific EU authorisation for any *E. globulus* preparation when used to provide flavour in food. However, according to Regulation (EC) No 1334/2008[6] 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.'

[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] On 27 February 2019, EFSA was informed by the applicant about the withdrawal of the applications on broom teatree oil, geranium oil, bay oil and vetiveria oil.
[4] Register of feed additives, Annex II, withdrawn by OJ L162, 10.05.2021, p. 5.
[5] Accepted name.
[6] 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.

'Eucalyptus leaf (Eucalypti folium)' are described in a monograph of the European Pharmacopoeia 11.0 (PhEur, 2022a). They are defined as the whole or cut dried leaves of older branches of *Eucalyptus globulus* Labill. with a content of minimum 20 mL/kg of essential oil for the whole drug (anhydrous drug) and minimum 15 mL/kg of essential oil for the cut drug (anhydrous drug).

'Eucalyptus oil (Eucalypti aetheroleum)' is described in a monograph of the European Pharmacopoeia 11.0 (PhEur, 2022b). It is defined as the essential oil obtained by steam distillation and rectification from the fresh leaves or the fresh terminal branchlets of various species of *Eucalyptus* rich in 1,8-cineole. The species mainly used are *Eucalyptus globulus* Labill., *Eucalyptus polybractea* R.T.Baker and *Eucalyptus smithii* R.T.Baker.

In 1998, the Committee for Veterinary Medicinal Products of the European Medicines Agency (EMA) published a report on Eucalypti aetheroleum, the oil obtained by steam distillation of twigs and leaves of *Eucalyptus globulus* Labill. and other *Eucalyptus* species (EMA, 1998).

For *Eucalyptus globulus* Labill., folium, the European Medicines Agency (EMA) issued an assessment report (EMA, 2013a) with an addendum (EMA, 2022) and a community herbal monograph for human medicinal use (EMA, 2013b).

For *Eucalyptus globulus* Labill., *Eucalyptus polybractea* R.T.Baker and/or *Eucalyptus smithii* R.T.Baker, aetheroleum, the European Medicines Agency (EMA) issued an assessment report (EMA, 2014a) and a community herbal monograph for human medicinal use (EMA, 2014b).

Many of the individual components of the essential oils have been already assessed as chemically defined flavourings for use in feed and food by the FEEDAP Panel, the EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food (AFC), the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) and the EFSA Panel on Food Additives and Flavourings (FAF). The flavouring compounds currently authorised for feed[7] and/or food[8] use, together with the EU Flavour Information System (FLAVIS) number, the chemical group as defined in Commission Regulation (EC) No 1565/2000[9], and the corresponding EFSA opinion are listed in Table 1.

Table 1: 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 (common name)	FLAVIS no	EFSA opinion,* year
02	Branched-chain primary aliphatic alcohols/ aldehydes/ acids, acetals and esters with esters containing branched-chain alcohols and acetals containing branched-chain aldehydes	3-Methyl 3-methylbutyrate	09.463	2012a
04	Non-conjugated and accumulated unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals and esters	Citronellol	02.011	2016a
05	Saturated and unsaturated aliphatic secondary alcohols, ketones and esters with esters containing secondary alcohols	Isopulegol	02.067	2020
		3-Methylpent-3-en-2-one[(a)]	07.101	2013, CEF

[7] 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.

[8] 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.

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

CG	Chemical group	Product – EU register name (common name)	FLAVIS no	EFSA opinion,* year
06	Aliphatic, alicyclic and aromatic saturated and unsaturated tertiary alcohols and esters with esters containing tertiary alcohols ethers	Linalool	02.013	2012b
		α-Terpineol	02.014	
		4-Terpinenol	02.072	
		2,6-Dimethyloct-7-en-2-ol[(a)]	02.144	2011a, CEF
08	Secondary alicyclic saturated and unsaturated alcohols, ketones, ketals and esters with ketals containing alicyclic alcohols or ketones and esters containing secondary alicyclic alcohols	Fenchyl alcohol	02.038	2016b
		Isoborneol	02.059	
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	07.165	2011b, CEF
13	Furanones and tetrahydrofurfuryl derivatives	Linalool oxide[(b)]	13.140	2012c
16	Aliphatic and alicyclic ethers	1,8-Cineole	03.001	2012d, 2021
31	Aliphatic and aromatic hydrocarbons and acetals containing saturated aldehydes	Limonene	01.001	2008, EFSA (AFC)
		1-Isopropyl-4-methylbenzene (p-cymene)	01.002	2015
		Terpinolene	01.005	
		α-Phellandrene	01.006	
		1-Isopropenyl-4-methylbenzene	01.010	
		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	
		Myrcene	01.008	
		Camphene	01.009	
		β-Ocimene[(c)] (3,7-Dimethyl-1,3,6-octatriene)	01.018	2015a, CEF
		β-Phellandrene[(a),(d)]	01.055	2011c, CEF

*: FEEDAP opinion unless otherwise indicated.
(a): Evaluated for use in food only. According to Regulation (EC) 1565/2000, flavourings evaluated by JECFA before 2000 are not required to be re-evaluated by EFSA.
(b): EFSA evaluated linalool oxide [13.140], a mixture of cis- and trans-linalool oxide (5-ring).
(c): EFSA evaluated β-ocimene [01.018], a mixture of *(E)*- and *(Z)*-isomers (EFSA CEF Panel, 2015a).
(d): Evaluated applying the 'Procedure' described in the Guidance on the data required for the risk assessment of flavourings to be used in or on food (EFSA CEF Panel, 2010). No longer authorised for use as flavours in food, as the additional toxicity data requested (EFSA CEF Panel, 2011c) were not submitted and the CEF Panel was unable to complete its assessment (EFSA CEF Panel, 2015b).

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[10] in support of the authorisation request for the use of eucalyptus oil from *E. globulus* as a

[10] FEED dossier reference: FAD-2010-0219.

feed additive. The dossier was received on 8 June 2023 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2023-00395.[11]

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.

Some 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 use the data submitted for the assessment of chemically defined flavourings (dossiers, publications and unpublished reports) for the risk assessment of preparations belonging to BDG 07, including the current one under assessment.[12]

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 additives. The evaluation report is related to the methods of analysis for each feed additive included the group BDG 07 (Geraniales, Myrtales, Poales). During the assessment, upon request from EFSA, the EURL issued a first amendment of the original report, which included the additive under assessment, *eucalyptus oil*.[13] In particular, the EURL recommended a method based on gas chromatography coupled with flame ionisation detection (GC-FID) for the determination of the phytochemical marker *1,8-cineole* in *eucalyptus oil*.[14]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of eucalyptus oil from *E. globulus* is in line with the principles laid down in Regulation (EC) No 429/2008[15] 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 for the preparation of dossiers for sensory additives (EFSA FEEDAP Panel, 2012e), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012f), 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 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, eucalyptus oil, is derived from the leaves and twigs of *Eucalyptus globulus* Labill. and is intended for use as sensory additive (functional group: flavouring compounds) in feed and water for drinking for all animal species.

3.1. Origin and extraction

Eucalyptus globulus Labill. is a fast-growing evergreen tree native to Australia belonging to the myrtle (Myrtaceae) family. The species is commonly known as the southern blue gum tree or simply the blue gum tree in reference to the glaucous colour of the adult leaves. There are four recognised subspecies arising from different geographical locations within Australia, each with a locally associated name (e.g. Tasmanian blue gum, Maidan's gum). Other than a herbal tea prepared from the leaf, there

[11] The original application EFSA-Q-2010-01282 was split on 07/06/2023 and a new EFSA-Q-2023-00395 was generated.
[12] Technical dossier/Supplementary information February 2023/Letter dated 31/01/2023.
[13] Preparations included in the first amendment: geranium rose oil, eucalyptus oil, lemongrass oil and clove oil.
[14] The full report is available on the EURL website: https://joint-research-centre.ec.europa.eu/publications/fad-2010-0219_en.
[15] 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.

are no food uses for *E. globulus* itself. However, an essential oil produced from the leaves is used to flavour food, in perfumery, in domestic products and in some medicinal products. For this reason, *E. globulus* is now grown commercially in many countries.

The present additive is extracted by steam distillation from the leaves (either fresh or dried) and twigs of *E. globulus* sourced from China and India. The volatile constituents are condensed and then separated from the aqueous phase by decantation. The essential oil may be rectified by distillation to obtain 1,8-cineole content higher than 70%.

3.2. Characterisation

3.2.1. Characterisation of eucalyptus oil

The essential oil under assessment is a clear slightly mobile liquid with a characteristic odour. In five batches of the additive, the refractive index (20°C) is between 1.460 and 1.461 (specification: 1.458–1.470).[16] Eucalyptus oil is identified with the single Chemical Abstracts Service (CAS) number 8000-48-4, the European Inventory of Existing Chemical Substances (EINECS) number 283-406-2, the Flavor Extract Manufacturers Association (FEMA) number 2466, and the Council of Europe (CoE) number 185.[17]

For eucalyptus oil, the product specifications are based on the standard developed by the International Organization for Standardization (ISO) 770:2002(E) for crude or rectified oils of Eucalyptus globulus (*Eucalyptus globulus* Labill.),[18] adapted to reflect the concentrations of selected volatile components of the essential oil. Three components contribute to the specification as shown in Table 2, with 1,8-cineole selected as the phytochemical marker, that was confirmed by analysis of two batches of the additive by GC-FID.[19] The applicant provided the full characterisation of the seven batches by gas chromatography–mass spectrometry (GC–MS). The three compounds account for 90.01% on average (range 83.94–96.09%) of the GC area (Table 2).[20]

Table 2: Major constituents of the essential oil from the leaves and twigs of *Eucalyptus globulus* Labill. as defined based on ISO standard (770:2002): batch to batch variation based on the analysis of seven batches by gas chromatography–mass spectrometry. 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	CAS no	FLAVIS no	% GC area		
EU register name			Specification[(a)]	Mean	Range
1,8-Cineole	470-82-6	03.001	≥ 70	79.53	72.5–86.9
d-Limonene	138-86-3	01.045	2–15	8.03	4.16–11.12
α-Pinene (pin-2(3)-ene)	80-56-8	01.004	1–10	2.45	1.28–3.28
Total				90.01	83.94–96.09[(b)]

EU: European Union; CAS no: Chemical Abstracts Service number; FLAVIS no: EU Flavour Information System numbers.
(a): Specifications defined based on GC-FID analysis.
(b): The values given for the total are the lowest and the highest values of the sum of the components in the batches analysed.

In total, up to 41 constituents were detected, 40 of which were identified and accounted on average for 99.99% (99.94–100.04%) of the % GC area. Besides the three compounds indicated in the product specifications, 10 other compounds were detected at individual levels > 0.1% and are listed in Table 3. These 13 compounds together account on average for 99.69% (99.50–99.90%) of the % GC area. The remaining 28 compounds (ranging between 0.01% and 0.09%) and accounting

[16] Technical dossier/Supplementary information November 2022/Annex_IIa_SIn_Reply_eucalyptus_oil_COA_chrom_batches_1–3 and Annex_IIb_SIn_ Reply_eucalyptus_oil_COA_chrom_batches_4–7.
[17] The following entries were found at https://echa.eurpa.eu/home: 'Eucalyptus globulus oil': EINECS 616–775-9; CAS 8000-48-4; 'Eucalyptus globulus, ext.' (extracts from Eucalyptus globulus including essential oils): EINECS 283–406-2; CAS 84625–32-1.
[18] Technical dossier/Supplementary information November 2022/Annex_III_SIn_reply_eucalyptus_oil_ ISO_770_2002(en).
[19] Technical dossier/Supplementary information November 2022/EURL_Appendix_eucalyptus_oil. GC-FID analysis: 1,8-cineole (81.0%), limonene (5.9%) and α-pinene (3.1%).
[20] Technical dossier/Supplementary information November 2022/Annex_IIa_SIn_Reply_eucalyptus_oil_COA_chrom_batches_1-3 and Annex_IIb_SIn_ Reply_eucalyptus_oil_COA_chrom_batches_4-7.

for 0.30% of the % GC area are listed in the footnote.[21] Based on the available data on the characterisation, eucalyptus oil is considered a fully defined mixture (EFSA Scientific Committee, 2019a).

Table 3: Constituents of the essential oil from the leaves and twigs of *Eucalyptus globulus* Labill. accounting for > 0.1% of the composition (based on the analysis of seven batches by gas chromatography–mass spectrometry) not included in the specifications. 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	CAS no	FLAVIS no	% GC area	
EU register name			Mean	Range
p-Cymene (1-isopropyl-4-methylbenzene)	99-87-6	01.002	5.57	4.70–6.91
γ-Terpinene	99-85-4	01.020	4.30	1.94–7.06
α-Phellandrene	99-83-2	01.006	0.77	0.59–1.03
Myrcene	123-35-3	01.008	0.48	0.35–0.78
α-Terpineol	98-55-5	02.014	0.47	0.33–0.83
β-Pinene (pin-2(10)-ene)	127-91-3	01.003	0.25	0.15–0.37
4-Terpinenol	562-74-3	02.072	0.19	0.16–0.28
Terpinolene	586-62-9	01.005	0.18	0.07–0.23
α-Terpinene	99-86-5	01.019	0.14	0.08–0.21
4-Hydroxy-4-methylpentan-2-one	123-42-2	07.165	0.14	0.13–0.14
Total			9.68	3.75–15.56[(a)]

EU: European Union; CAS no: Chemical Abstracts Service number; FLAVIS no: EU Flavour Information System numbers.
(a): The values given for the Total are the lowest and the highest values of the sum of the components in the seven batches analysed.

3.2.1.1. Substances of concern

The applicant performed a literature search for information on the chemical composition of *E. globulus* and its preparations and the presence of compounds of known concern.[22] The presence of 1,8-cineole (the main constituent of the oil under assessment) was identified as potential substance of toxicological concern in the EFSA compendium (EFSA, 2012).[23] The applicant also consulted the online database on volatile compounds in food (VCF).[24] One reference (Chalchat et al., 1995) reported the presence of methyleugenol (0.15–0.51%) in four samples of eucalyptus oil (origin: Spain and Montenegro) characterised by concentrations of 1,8-cineole ranging between 4.1% and 50.3%, therefore not comparable with the oil under assessment. Two out of the 33 references retrieved by the applicant reported the presence of methyleugenol. Methyleugenol (6.23%) was detected in a eucalyptus oil with a content of 1,8-cineole ranging between 7.71% and 13.23% and obtained from aerial parts of Tunisian *E. globulus* only when collected during the vegetative stage, not comparable to the product under assessment. The oils produced from aerial parts collected during other developmental stages (full flowering and fructification) did not contain methyleugenol (limit of detection (LOD), not given) (Salem et al., 2018). In another publication, an essential oil from *E. globulus* Labill. ssp. *globulus* (origin: Portugal) was shown to contain 74.6% 1,8-cineole and 3.5% methyleugenol. The different components of the essential oil were identified by their retention indices by GC-FID (Vieira et al., 2017).

The presence of perillaldehyde (0.1%) has been reported in an eucalyptus leaf oil from Ecuador containing 67% 1,8-cineole in one publication (Pino et al., 2021). Since the presence of perillaldehyde

[21] Additional constituents: constituents (n = 17) between < 0.1 and ≥ 0.2%: trans-3,7-dimethyl-1,3,6-octatriene, linalool, laevo-pinocarveol, citronellol, 1-isopropenyl-4-methylbenzene, 2,6-dimethyloct-7-en-2-ol, isopulegol, (Z)-dehydroxylinalool oxide, aromadendrene, β-phellandrene, 2-((1R,4R)-4-hydroxy-4-methylcyclohex-2-enyl)propan-2-yl acetate, δ-terpineol, 3-methylbutyl 3-methylbutyrate, α-thujene, camphene, linalool oxide and (E,Z)-alloocimene, constituents (n = 11) between < 0.2 and ≥ 0.1%: fenchyl alcohol, 4-methylpent-3-en-2-one, isoborneol, 2-(adamantan-1-yl)-N-methylacetamide, 3,7-dimethylocta-2E,4E-diene, (E,E)-2,6-alloocimene, cyclohexane, 1-methyl-4-(1-methylethylidene), β-thujene, isoledene and limonene dioxide.
[22] Technical dossier/Supplementary information November2022/Literature search_eucalyptus_oil.
[23] Online version: https://www.efsa.europa.eu/en/data-report/compendium-botanicals.
[24] https://www.vcf-online.nl/VcfHome.cfm

in eucalyptus oil was not confirmed by other authors, the findings of a single report were considered of limited relevance.

Methyleugenol and perillaldehyde were not detected by GC–MS in the essential oil under assessment (LOD, 0.01%).

3.2.1.2. Impurities

The applicant referred to the 'periodic testing' of some representative flavourings premixtures for mercury, cadmium and lead, arsenic, fluoride, dioxins and polychlorinated biphenyls (PCBs), organochloride pesticides, organophosphorus pesticides, aflatoxins (B1, B2, G1, G2) and ochratoxin A. However, no data have been provided on the presence of these impurities. Since eucalyptus oil is produced by steam distillation, the likelihood of any measurable carry-over of all the above-mentioned elements is considered low, except for mercury.

3.2.2. Shelf-life

The typical shelf-life of eucalyptus 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).[25] However, no data supporting this statement were provided.

3.2.3. Conditions of use

Eucalyptus oil is intended to be added to feed and water for drinking for all animal species without a withdrawal period. Maximum use levels in complete feed and in water for drinking were proposed for the animal species and categories listed in Table 4.

Table 4: Conditions of use for eucalyptus oil obtained from the leaves and twigs of *Eucalyptus globulus* Labill.: maximum proposed use levels in feed and in water for drinking for certain animal categories

	Use level in feed (mg/kg feed)	Use level in water (mg/kg)
Chicken for fattening	400	60
Laying hens	400	60
Turkey for fattening	400	60
Piglet	400	50
Pig for fattening	400	50
Sow lactating	400	50
Veal calf (milk replacer)	450	70
Cattle for fattening	400	40
Dairy cow	400	10
Sheep/goat	400	70
Horse	400	10
Rabbit	400	50
Salmon	100	–
Dogs	160	–(a)
Cats	160	–(a)
Ornamental fish	75	–
Other minor species	75	–(a)

(a): The additive is not intended for use in water for drinking.

3.3. Safety

The assessment of the safety of eucalyptus oil is based on the maximum use levels proposed by the applicant in complete feed for the species listed above (see Table 4).

Many of the components of eucalyptus oil, accounting for more than 99% of the % GC peak areas, have been previously assessed and considered safe for use as flavourings, and are currently authorised

[25] Technical dossier/Section II.

for use in food[26] without limitations and for use in feed[27] at individual use levels higher than those resulting from the intended use of the essential oil in feed. The list of the compounds already evaluated by the EFSA Panels is given in Table 1 (see Section 1.2).

One compound listed in Table 1, β-phellandrene [01.055] has been evaluated in Flavouring Group Evaluation 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 food (EFSA CEF Panel, 2010). For this compound, for which there is no concern for genotoxicity, EFSA requested additional subchronic toxicity data (EFSA CEF Panel, 2011c). In the absence of such data, the EFSA CEF Panel was unable to complete its assessment (EFSA CEF Panel, 2015b). As a result, this compound is not authorised for use as flavour in food. For this compound, 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).

Fifteen components of eucalyptus oil, each accounting for < 0.1% of the % GC area, have not been previously assessed for use as flavourings. The FEEDAP Panel notes that 12 of them[28] are aliphatic mono- or sesquiterpenes structurally related to flavourings already assessed in CG 6, 8, 16 and 31 and for which a similar metabolic and toxicological profile is expected. These lipophilic compounds, accounting together for about 0.3% of the GC area, are expected to be rapidly absorbed from the gastrointestinal tract, oxidised to polar oxygenated metabolites, conjugated and excreted (EFSA FEEDAP Panel, 2012b,d, 2015, 2016b,c).

The remaining three compounds, 2-((1R,4R)-4-hydroxy-4-methylcyclohex-2-enyl)propan-2-yl acetate, 2-(adamantan-1-yl)-N-methylacetamide and limonene dioxide, were screened with the Organization for Economic Co-operation and Development (OECD) Quantitative Structure–Activity Relationship (QSAR) Toolbox. No alert was identified for *in vitro* mutagenicity, for genotoxic and non-genotoxic carcinogenicity and for other toxicity endpoints for 2-(adamantan-1-yl)-N-methylacetamide, whereas for 2-((1R,4R)-4-hydroxy-4-methylcyclohex-2-enyl)propan-2-yl acetate structural alerts were due to the presence of ester group and for limonene dioxide to the presence of epoxides. For these 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). Mutagenicity read-across-based relevant predictions were found negative for both substances.[29] On this basis, the alerts raised were discounted.

3.3.1. Safety for the target species

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

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

As the additive under assessment is a fully defined mixture (the identified components represent > 99.5% of the % GC area, see Section 3.2.1), the FEEDAP Panel applied a component-based approach to assess the safety for target species of the essential oil.

Based on considerations related to structural and metabolic similarities, the components were allocated to 11 assessment groups, corresponding to the chemical groups (CGs) 2, 4, 5, 6, 8, 10, 13,

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

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

[28] δ-Terpineol (CG 6); laevo-pinocarveol (CG 8); (Z)-dehydroxylinalool oxide (CG 16); trans-3,7-dimethyl-1,3,6-octatriene; (E,Z)-2,6-alloocimene; 3,7-dimethylocta-2E,4E-diene; (E,E)-2,6-alloocimene; cyclohexane, 1-methyl-4-(1-methylethylidene)-; α-thujene; β-thujene; isoledene and aromadendrene (CG 31).

[29] Technical dossier/Supplementary information December 2022/Annex VI_SIn_reply_eucalyptus_oil_QSAR.

16, 19, 31 and 32, as defined in Annex I of Regulation (EC) No 1565/2000. For chemical group 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,b). The allocation of the components to the (sub-)assessment groups is shown in Table 5 and in the corresponding footnote.

For each component in the assessment group, exposure of target animals was estimated considering the use levels in feed, the percentage of the component in the oil and the default values for feed intake according to the guidance on the safety of feed additives for target species (EFSA FEEDAP Panel, 2017b). Default values on body weight (bw) are used to express exposure in terms of mg/kg bw per day. The intake levels of the individual components calculated for chickens for fattening, the species with the highest ratio of feed intake/body weight per day, are shown in Table 5.

For hazard characterisation, each component of an assessment group was first assigned to the structural class according to Cramer classification (Cramer et al., 1978). For some components in the assessment group, toxicological data were available to derive no observed adverse effect level (NOAEL) values. Structural and metabolic similarity among the components in the assessment groups were assessed to explore the application of read-across. If justified, extrapolation from a known NOAEL of a component of an assessment group to the other components of the group with no available NOAEL was made. If sufficient evidence was available for the members of a (sub-) assessment group, a (sub-)assessment group NOAEL was derived.

Toxicological data of subchronic studies, from which NOAEL values could be derived, were available for citronellol [02.011] in CG 4 (EFSA FEEDAP Panel, 2016a), for isopulegol [02.067] in CG 5 (EFSA FEEDAP Panel, 2020), terpineol[30] [02.230] and linalool [02.013] in CG 6 (EFSA FEEDAP Panel, 2012b), isoborneol in CG 8 (EFSA FEEDAP Panel, 2016b), 1,8-cineole in CG 16 (EFSA FEEDAP Panel, 2012d, 2021), and for the representative compounds for subassessment groups of CG 31, myrcene [01.008], d-limonene [01.045], p-cymene [01.002] and β-caryophyllene [01.007] (EFSA FEEDAP Panel, 2015, 2016c).

For the terpinyl derivatives in CG 6, namely α-terpineol [02.014], 4-terpinenol [02.072] and δ-terpineol in CG 6, the reference point was selected based on the NOAEL of 250 mg/kg bw per day available for terpineol [02.230] and d-limonene [01.045].

The NOAELs of 44, 250 and 222 mg/kg bw per day for the representative compounds of CG 31, myrcene [01.008], d-limonene [01.045] and β-caryophyllene [01.007] were applied, respectively, using read-across to the compounds within subassessment group II (trans-3,7-dimethyl-1,3,6-octatriene, *(E,Z)*-alloocimene, 3,7-dimethylocta-2E,4E-diene and *(E,E)*-2,6-alloocimene), III ((γ-terpinene [01.020], α-phellandrene [01.006], α-terpinene [01.019], β-phellandrene [01.055] and terpinolene [01.005]) and V (α-pinene [01.004], β-pinene [01.003], α-thujene, camphene [01.009], β-thujene and aromadendrene)[31] (EFSA CEF Panel, 2015a,b).

For the remaining compounds,[32] 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). All these compounds belong to Cramer class I except fenchone and carvenone (Cramer class II).

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 5.

For risk characterisation, the margin of exposure (MOE) was calculated for each component as the ratio between the reference point and the exposure. For each assessment group, the combined (total) margin of exposure (MOET) was calculated as the reciprocal of the sum of the reciprocals of the MOE of the individual substances (EFSA Scientific Committee, 2019a). An MOET > 100 allowed for interspecies and intra-individual variability (as in the default 10 × 10 uncertainty factor).

[30] Terpineol is a mixture of four isomers: α-terpineol [02.014], a mixture of *(R)*-(+)-α-terpineol and *(S)*-(–)-α-terpineol, β-terpineol, γ-terpineol and 4-terpinenol [02.072] (or δ-terpineol). The specification for terpineol [02.230] covers α-, β-, γ– and δ-terpineol. Composition of mixture: 55–75% α-terpineol, 16–23% γ-terpineol, 1–10% cis-β-terpineol, 1–13% trans-β-terpineol and 0–1% δ-terpineol (EFSA CEF Panel, 2015c) FGE.18Rev 3.

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

[32] 3-Methylbutyl 3-methylbutyrate (CG 2); 4-methylpent-3-en-2-one (CG 5); 2-((1R,4R)-4-Hydroxy-4-methylcyclohex-2-enyl) propan-2-yl acetate (CG 6); laevo-pinocarveol and isoborneol (CG 8); 4-hydroxy-4-methylpentan-2-one (CG 10); linalool oxide (CG 13); cyclohexane, 1-methyl-4-(1-methylethylidene)- (CG 31, III); isopropenyl-4-methylbenzene (CG 31, IVe); isoledene (CG 31, V); limonene dioxide (CG 32).

The approach to the safety assessment of eucalyptus oil for the target species is summarised in Table 5. 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 400 mg/kg complete feed.

Table 5: Compositional data, intake values (calculated for chickens for fattening at 400 mg/kg complete feed), reference points and margin of exposure (MOE) for the individual components of eucalyptus oil classified according to assessment groups

Essential oil composition			**Exposure**		**Hazard characterisation**		**Risk characterisation**	
Assessment group	**FLAVIS no**	**Highest conc. in the oil**	**Highest feed conc.**	**Intake[a]**	**Cramer class[b]**	**NOAEL[c]**	**MOE**	**MOET**
Constituent	–	**%**	**mg/kg**	**mg/kg bw per day**	–	**mg/kg bw per day**	–	–
CG 2								
3-Methylbutyl 3-methylbutyrate	09.463	0.02	0.08	0.0072	I	*3*	418	
CG 4								
Citronellol	02.011	0.05	0.180	0.0162	(I)	**50**	3,094	
CG 5								
4-Methylpent-3-en-2-one	07.101	0.01	0.040	0.0036	II	*0.91*	253	
Isopulegol	02.067	0.03	0.120	0.0108	(I)	**38**	3,527	
MOET CG 5								236
CG 6								
α-Terpineol	02.014	0.83	3.320	0.2980	(I)	250	839	
4-Terpinenol	02.072	0.28	1.120	0.1005	(I)	250	2,486	
2,6-Dimethyloct-7-en-2-ol	02.144	0.04	0.156	0.0140	(I)	10	714	
Linalool	02.042	0.07	0.268	0.0241	(I)	117	4,863	
δ-Terpineol	–	0.02	0.092	0.0083	(III)	250	30,270	
2-((1R,4R)-4-Hydroxy-4-methylcyclohex-2-enyl) propan-2-yl acetate	–	0.02	0.080	0.0072	(III)	250	34,810	
MOET CG 06								307
CG 8								
laevo-Pinocarveol	–	0.06	0.240	0.0215	I	*3*	139	
Fenchyl alcohol	02.038	0.02	0.060	0.0054	I	*3*	557	
Isoborneol	02.059	0.01	0.040	0.0036	(I)	**15**	4,177	
MOET CG 08								108
CG 10								
4-Hydroxy-4-methylpentan-2-one	07.165	0.14	0.560	0.0503	I	*3*	60	
CG 13								
Linalool oxide	13.140	0.02	0.080	0.0052	II	*0.91*	127	
CG 16								
1,8-Cineole	03.001	86.85	347.40	31.187	(II)	**100**	3	
(Z)-Dehydroxylinalool oxide	–	0.03	0.120	0.0108	II	**0.91**	84	
								3
CG 19								
2-(Adamantan-1-yl)-N-methylacetamide	–	0.01	0.040	0.0036	III	*0.15*	42	

Essential oil composition			Exposure		Hazard characterisation		Risk characterisation	
Assessment group	**FLAVIS no**	**Highest conc. in the oil**	**Highest feed conc.**	**Intake[a]**	**Cramer class[b]**	**NOAEL[c]**	**MOE**	**MOET**
Constituent	–	**%**	**mg/kg**	**mg/kg bw per day**	–	**mg/kg bw per day**	–	–
CG 31, II (Acyclic alkanes)								
Myrcene	01.008	0.78	3.120	0.2801	(I)	**44**	157	
tr-3,7-Dimethyl-1,3,6-octatriene	–	0.17	0.680	0.0610	(I)	44	721	
(E,Z)-2,6-Alloocimene	–	0.02	0.064	0.0057	(I)	44	7,658	
3,7-Dimethylocta-2E,4E-diene	–	0.01	0.040	0.0036	(I)	44	12,253	
(E,E)-2,6-Alloocimene	–	0.01	0.040	0.0036	(I)	44	12,253	
MOET CG 31, II								124
CG 31, III (Cyclohexene hydrocarbons)								
Limonene	01.001	11.12	44.48	3.9931	(I)	**250**	63	
γ-Terpinene	01.020	7.06	28.24	2.5352	(I)	250	99	
α-Phellandrene	01.006	1.03	4.120	0.3699	(I)	250	676	
α-Terpinene	01.019	0.21	0.840	0.0754	(I)	250	3,315	
β-Phellandrene	01.055	0.03	0.120	0.0108	(I)	250	23,207	
Terpinolene	01.055	0.23	0.924	0.0830	(I)	250	3,014	
Cyclohexane, 1-methyl-4-(1-methylethylidene)-	–	0.01	0.040	0.0036	I	*3*	835	
MOET CG 31, III								34
CG 31, IVe (Benzene hydrocarbons, alkyl)								
p-Cymene	01.002	6.91	27.64	2.4813	(I)	**154**	62	
Isopropenyl-4-methylbenzene	01.010	0.05	0.200	0.0180	I	*3*	167	
MOET CG 31, IVe								45
CG 31, V (Bi-, tricyclic, non-aromatic hydrocarbons)								
α-Pinene	01.004	3.28	13.10	1.1760	(I)	222	189	
β-Pinene	01.003	0.37	1.480	0.1329	(I)	222	1,671	
α-Thujene	–	0.02	0.072	0.0065	(I)	222	34,346	
Camphene	01.009	0.02	0.096	0.0086	(I)	222	25,759	
β-Thujene	–	0.01	0.040	0.0036	I	222	61,823	
Isoledene	–	0.01	0.040	0.0036	I	*3*	835	
Aromadendrene	–	0.03	0.120	0.0108	I	222	20,608	
MOET CG 31, V								138
CG 32								
Limonene dioxide	–	0.01	0.040	0.0036	III	*0.15*	42	

(a): Intake calculations for the individual components are based on the use level of 400 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 (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.

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

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

As shown in Table 5, for several assessment groups, the MOET was < 100 at the proposed use levels (400 mg/kg feed). The lowest MOET was calculated for CG 16. From the lowest MOE of 3 for chickens for fattening, the MOE for the assessment group 'aliphatic and alicyclic ethers' (CG 16) was calculated for the other target species considering the respective daily feed intake and conditions of use. The results are summarised in Table 6.

Table 6: Combined margin of exposure (MOET) for CG 16 calculated for the different target animal categories at the proposed use level in feed

Animal category	Body weight (kg)	Feed intake (g DM/day)	Proposed use level (mg/kg feed)	Lowest MOET CG 16	Maximum safe use level (mg/kg feed)[(a)]
Chicken for fattening	2	158	400	3	12
Laying hen	2	106	400	5	18
Turkey for fattening	3	176	400	4	16
Piglet	20	880	400	5	22
Pig for fattening	60	2,200	400	6	26
Sow lactating	175	5,280	400	8	32
Veal calf (milk replacer)	100	1,890	450	12	55
Cattle for fattening	400	8,000	400	12	48
Dairy cows	650	20,000	400	8	31
Sheep/goat	60	1,200	400	12	48
Horse	400	8,000	400	12	48
Rabbit	2	100	400	5	19
Salmon	0.12	2.1	100	13	55
Dog	15	250	160	54	58
Cat	3	60	160	30[(b)]	10
Ornamental fish	0.012	0.054	75	253	75

(a): Complete feed containing 88% DM, milk replacer 94.5% DM.
(b): The MOET for cats is increased to 500 because of the reduced capacity of glucuronidation of compounds.

Table 6 shows that the MOET exceeds the value of 100 only 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 pathway to facilitate the excretion of the components of the essential oil and considering that cats have a low capacity for glucuronidation (Court and Greenblatt, 1997; Lautz et al., 2021), the use of eucalyptus oil as additive in cat feed needs a wider margin of exposure. An MOET of 500 is considered adequate. The maximum safe levels in feed are shown in Table 6.

In poultry, pigs and rabbits, the daily consumption of water by drinking is about two to three times the amount of feed DM ingested (EFSA FEEDAP Panel, 2010). For ruminants, the ratio water intake/dry matter intake could be much higher than for poultry and pigs, but a precise value for the different ruminant species and categories cannot be estimated. The applicant proposed a maximum use level in water for drinking of 60 mg/kg water for poultry, 50 mg/kg water for pigs and rabbits, 70 mg/kg for veal calves, sheep/goats, 40 mg/kg for cattle for fattening and 10 mg/kg or dairy cows and horses, which would result in an exposure higher than that which is considered safe when consumed via feed.

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

3.3.1.1. Conclusions on safety for the target species

The conclusions of the FEEDAP Panel on the maximum safe concentrations in complete feed of eucalyptus oil are summarised in Table 7.

Table 7: Maximum safe concentrations of eucalyptus oil in complete feed (mg/kg) for all animal species and categories

Animal categories	Maximum safe concentration (mg/kg feed)[(a)]
Chickens for fattening, other poultry for fattening or reared for laying/ reproduction, ornamental birds and other avian species at the same physiological stage	12
Laying hens and other laying/reproductive birds	18
Turkeys for fattening	16
Pigs for fattening	26
Piglets and other Suidae species for meat production or reared for reproduction	22
Sows and other Suidae species for reproduction	32
Veal calves (milk replacer)	55
Sheep/goat	48
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction and camelids at the same physiological stage	48
Dairy cows and other ruminants and camelids for milk production or reproduction	31
Horses and other Equidae	48
Rabbits	19
Salmonids and minor fin fish	55
Dogs	58
Cats	10
Ornamental fish	75
Any other species	10

(a): Complete feed containing 88% DM, milk replacer 94.5% DM.

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

3.3.2. Safety for the consumer

Eucalyptus oil obtained from the leaves of *E. globulus* 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 (Burdock, 2009) cites values of 0.0022 mg/kg bw per day for eucalyptus oil (FEMA 2466). Fenaroli also reports use levels in food and beverages in the range of 0.70 mg/kg up to 18.02 mg/kg (meat products) and up to 1,958 mg/kg in hard candies.

Many 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 1, Section 1.2).

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 eucalyptus oil are expected to be extensively metabolised and excreted in the target species. Also for the major component, 1,8-cineole, the available data indicate that it is absorbed, metabolised by oxidation and excreted and it is not expected to accumulate in animal tissues and products. Consequently, relevant residues in food products are unlikely (EFSA FEEDAP Panel, 2012d).

Considering the above and the reported human exposure due to the direct use of preparations of Eucalyptus leaves in food (Burdock, 2009), it is unlikely that the consumption of products from animals given eucalyptus oil at the proposed maximum use level would increase human background exposure.

No safety concern would be expected for the consumer from the use of eucalyptus oil up to the highest safe level in feed.

3.3.3. Safety for the user

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

The applicant produced a safety data sheet[33] for eucalyptus oil, where hazards for users have been identified.

The applicant made a literature search aimed at retrieving studies related to the safety of preparations obtained from *E. globulus* for the users.[34] There is limited evidence from the literature that eucalyptus oil may be a potential skin irritant and skin sensitiser (reviewed by Tisserand and Young, 2014; Infante et al., 2022; Moreira et al., 2022).

The hazards identified include skin irritation and sensitisation. Eucalyptus globulus oil has been notified to ECHA and studies submitted also indicate skin irritancy and skin sensitisation. One rabbit study of eye irritation concludes that it is not irritant to eyes.

The essential oil under assessment should be considered as irritant to skin and eyes, and as a dermal and respiratory sensitiser.

3.3.4. Safety for the environment

Although *E. globulus* is not a species native to Europe, the blue gum is among the most extensively planted eucalypts because of its uses and its adaptability to a range of climatic conditions. It is particularly suited to areas with a Mediterranean climate and so is found widely distributed in southern parts of Europe. Therefore, the use of the eucalyptus oil in animal feed under the proposed conditions of use is not expected to pose a risk to the environment.

3.4. Efficacy

E. globulus and its leaf oil are listed in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2009) and by FEMA with the reference number 2466 (eucalyptus oil).

Since preparations of the leaves of *E. globulus* including its oil 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

Eucalyptus oil from *Eucalyptus globulus* may be produced from plants of different geographical origins and by various processes resulting in preparations with different composition and toxicological profiles. Therefore, the following conclusions apply only to eucalyptus oil, in which methyleugenol was not detected (limit of detection 0.005%) and is produced by steam distillation from the leaves and twigs of *E. globulus* and rectified by distillation to obtain 1,8-cineole content higher than 70%.

The conclusions of the FEEDAP Panel on the maximum safe concentrations in complete feed of eucalyptus oil are summarised as following:

Animal categories	Maximum safe concentration (mg/kg feed)[(a)]
Chickens for fattening, other poultry for fattening or reared for laying/ reproduction, ornamental birds and other avian species at the same physiological stage	12
Laying hens and other laying/reproductive birds	18
Turkeys for fattening	16
Pigs for fattening	26
Piglets and other Suidae species for meat production or reared for reproduction	22
Sows and other Suidae species for reproduction	32
Veal calves (milk replacer)	54
Sheep/goat	47

[33] Technical dossier/Supplementary Information November 2022/Annex_VII_SIn reply_eucalyptus oil_MSDS. Aspiration hazard (H304, category 1), Hazards for skin corrosion/irritation (H315, category 2), skin sensitisation (H317, category 1) in accordance with the criteria outlined in Annex I of 1272/2008/EC (CLP/EU-GHS).

[34] Technical dossier/Supplementary information November 2022/Literature search_eucalyptus oil.

Animal categories	Maximum safe concentration (mg/kg feed)[(a)]
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction and camelids at the same physiological stage	47
Dairy cows and other ruminants and camelids for milk production or reproduction	31
Horses and other Equidae	47
Rabbits	19
Salmonids and minor fin fish	53
Dogs	56
Cats	10
Ornamental fish	75
Any other species	10

(a): Complete feed containing 88% DM, milk replacer 94.5% DM.

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

No concerns for consumers were identified following the use of the additive at the use level considered safe in feed for the target animals.

The essential oil under assessment should be considered as irritant to skin and eyes, and as a skin and respiratory sensitiser.

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

Eucalyptus oil is recognised to flavour food. Since its function in feed would be essentially the same as that in food, no further demonstration of efficacy is considered necessary.

5. Recommendations

The specification should ensure that methyleugenol is not detected in eucalyptus oil from *Eucalyptus globulus*.

6. Documentation provided to EFSA/chronology

Date	Event
28/10/2010	Dossier received by EFSA. Botanically defined flavourings from Botanical Group 07 – Geraniale, Myrtales, Poales for all animal species and categories. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)
09/11/2010	Reception mandate from the European Commission
21/12/2010	Application validated by EFSA – Start of the scientific assessment
22/03/2011	Comments received from Member States
01/04/2011	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: analytical methods*
08/01/2013	Reception of supplementary information from the applicant – Scientific assessment remains suspended
26/02/2013	EFSA informed the applicant (EFSA ref. 7150727) that, in view of the workload, the evaluation of applications on feed flavourings would be re-organised by giving priority to the assessment of the chemically defined feed flavourings, as agreed with the European Commission
20/01/2014	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
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
17/12/2019	EFSA informed the applicant that the evaluation process restarted
18/12/2019	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*

Date	Event
29/11/2022	Reception of supplementary information from the applicant (partial dataset: eucalyptus oil) – Scientific assessment remains suspended
06/06/2023	Reception of an amendment of the Evaluation report of the European Union Reference Laboratory for Feed Additives related to geranium rose oil, eucalyptus oil, lemongrass oil and clove oil
07/06/2023	The application was split and a new EFSA-Q-2023-00395 was assigned to the preparation included in the present assessment
08/06/2023	Scientific assessment re-started for the preparation included in the present assessment
04/07/2023	Opinion adopted by the FEEDAP Panel on eucalyptus oil (EFSA-Q-2023-00395). End of the Scientific assessment for the preparation included in the present assessment. The assessment of other preparations in BGD 07 is still ongoing

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Abbreviations

AFC	EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food
BDG	Botanically defined group
bw	body weight
CAS	Chemical Abstracts Service
CDG	Chemically defined group
CEF	EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CG	chemical group
CLP	Classification, Labelling and Packaging
CoE	Council of Europe
EEIG	European economic interest grouping
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
FEMA	Flavor Extract Manufacturers Association
FFAC	Feed Flavourings authorisation Consortium of (FEFANA) the EU Association of Specialty Feed Ingredients and their Mixtures

FGE	Flavouring Group Evaluation
FLAVIS	the EU Flavour Information System
FLAVIS no	FLAVIS number
GC	gas chromatography
GC-FID	gas chromatography with flame ionisation detector
GC–MS	gas chromatography–mass spectrometry
ISO	International standard organisation
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
MOE	margin of exposure
MOET	combined margin of exposure (total)
NOAEL	no observed adverse effect level
OECD	Organization for Economic Co-operation and Development
PhEur	European Pharmacopoeia
QSAR	Quantitative Structure–Activity Relationship
SC	EFSA Scientific Committee
TTC	threshold of toxicological concern
UV	ultraviolet
WHO	World Health Organization