Adopted: 18 April 2024

DOI: 10.2903/j.efsa.2024.8799

efsa JOURNAL

SCIENTIFIC OPINION

Safety and efficacy of a feed additive consisting of an essential oil obtained from the wood of *Juniperus deppeana* Steud. (cedarwood Texas oil) for use in 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 obtained from the wood of *Juniperus deppeana* Steud. (cedarwood Texas oil), when used as a sensory additive for all animal species. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that the essential oil under assessment is safe up to the maximum proposed use levels in complete feed of 15 mg/kg for veal calves (milk replacer), cattle for fattening, sheep, goats, horses, dogs, salmonids and ornamental fish. For the other species, the calculated safe concentrations in complete feed were 5 mg/kg for chickens for fattening, 8 mg/kg for laying hens, 7 mg/kg for turkeys for fattening, 10 mg/kg for piglets, 12 mg/kg for pigs for fattening, 14 mg/kg for sows and dairy cows, 8.5 mg/kg for rabbits and 4 mg/kg for cats. These conclusions were extrapolated to other physiologically related species. For any other species, the additive was considered safe at 4 mg/kg complete feed. The use of cedarwood Texas oil in water for drinking was considered safe provided that the total daily intake of the additive does not exceed the daily amount that is considered safe when consumed via feed. No concerns for consumers and the environment were identified following the use of the additive up to the maximum proposed use level in feed. The additive under assessment should be considered as irritant to skin and eyes, and as a skin and respiratory sensitiser. Since the individual components of cedarwood Texas 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 was considered necessary.

KEYWORDS

cedarwood Texas oil, component-based approach, flavouring compounds, *Juniperus deppeana* Steud., safety, sensory additives

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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 ten additives (namely juniper oil, juniper berry extract (water-based, wb) and juniper tincture from *Juniper communis* L., cedarwood Texas oil from *Juniperus mexicana* Schiede, pine oil and pine tincture from *Pinus pinaster* Soland., pine oil white from *Pinus* spp., e.g. *P. sylvestris* L., pine needle oil from *Abies alba* Mill., Abies sibirica Ledeb., gingko extract (wb) and gingko tincture from *Gingko biloba* L.) belonging to botanically defined group (BDG) 18 - Gymnosperms (Coniferales, Ginkgoales) when used as feed additives for all animal species (category: sensory additives; functional group: flavourings). During the assessment, the applicant withdrew the application for three additives.[3] These additives 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 seven remaining additives under application: cedarwood Texas oil from the wood of *Juniperus deppeana* Steud (synonym: *Juniperus mexicana* Schiede).[5] for all animal species.

The remaining six additives belonging to botanically defined group (BDG) 18 - Gymnosperms (Coniferales, Ginkgoales) 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 11 February 2019.

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 cedarwood Texas oil from the wood of *J. deppeana*, when used under the proposed conditions of use (see Section 3.2.4).

1.2 | Additional information

'Cedarwood Texas oil' from *Juniperus mexicana* Schiede (syn: *Juniperus mexicana* Schiede) 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 cedarwood Texas oil from the wood of *J. deppeana* as a feed additive. The dossier was received on 11 February 2019 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2010-01516.[7]

The FEEDAP Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) 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. The applicant submitted a written agreement to use the data submitted for the

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2]On 13/3/2013, EFSA was informed by the applicant that the applicant company changed to FEFANA asbl, Avenue Louise 130 A, Box 1, 1050 Brussels, Belgium.
[3]Juniper berry extract (wb), pine oil (27 February 2019); pine needle oil (18 March 2021).
[4]Register of feed additives, Annex II, withdrawn by OJ L162, 10.05.2021, p. 5.
[5]Accepted name: *Juniperus deppeana* Steud., synonym *Juniperus mexicana* Schiede ex Schltdl. & Cham.
[6]FEED dossier reference: FAD-2010-0320.
[7]The original application EFSA-Q-2010-01516 was split and the EFSA-Q-2010-01516 remained associated to cedarwood Texas oil.

assessment of chemically defined flavourings (dossiers, publications and unpublished reports) for the risk assessment of the preparations belonging to BDG 18, including the 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 the group BDG 18 (Ginkgoales). In particular, for the characterisation of cedarwood Texas oil, the EURL recommended a method based on gas chromatography with flame ionisation detection (GC-FID) for the quantification of the phytochemical marker *cis-thujopsene* in *cedarwood Texas oil*.[9]

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of cedarwood Texas oil from the wood of *J. deppeana* is in line with the principles laid down in Regulation (EC) No 429/2008[10] 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, 2012a), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018), Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019), Guidance on the assessment of the safety of feed additives for the users (EFSA FEEDAP Panel, 2023), Guidance document on harmonised methodologies for human health, animal health and ecological risk assessment of combined exposure to multiple chemicals (EFSA Scientific Committee, 2019a), Statement on the genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019b), Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment (EFSA Scientific Committee, 2019c).

3 | ASSESSMENT

The additive under assessment, cedarwood Texas oil, is obtained from the wood of *Juniperus deppeana* Steud. It 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

Juniperus deppeana Steud. (syn. *Juniperus mexicana* Schiede.) is a medium-sized conifer belonging to the Cupressaceae (Cypress) family, native to Mexico and the southern USA. It is commonly referred to as the alligator juniper or checkerbark juniper because of the characteristic pattern of its bark. Other than its use as timber, this species finds practical application as a source of essential oil. There are no recognised medicinal uses associated with this species.

The term 'cedarwood oil' may give rise to confusion since its original use has extended beyond the essential oils derived from cedar species (*Cedrus libani* A.Rich., *Cedrus atlantica* (Endl.) Manetti ex Carriere and *Cedrus deodora* (Roxb.ex D.Don) G.Don) to encompass essential oils derived from other conifers whose sensory properties resemble those of the true cedarwood oils. These include Virginian cedarwood oil obtained from *Juniperus virginiana* L. and Chinese cedarwood oils from *Cupressus funebris* Endl. or *Juniperus chinensis* L. in addition to the Texas oil under application.

The raw material for the production of the cedarwood Texas essential oil is wood of *J. deppeana* originating from the USA. After milling, the volatile constituents are extracted from the wood by steam distillation, condensed and then separated from the water by decantation.

[8]Technical dossier/Supplementary information/Letter dated 31/1/2023.

[9]The full report is available on the EURL website: https://joint-research-centre.ec.europa.eu/publications/fad-2010-0320_en.

[10]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 | Characterisation

3.2.1 | Characterisation of the additive

Cedarwood Texas oil is a pale yellow clear mobile liquid, with a characteristic aroma. In five batches of the additive, the refractive index ranged between 1.5050 and 1.5053 (specification: 1.500–1.510).[11] Cedarwood Texas oil is identified with the single Chemical Abstracts Service (CAS) number 91772-61-1 and the European Inventory of Existing Chemical Substances (EINECS) number 294-461-7.

The product specifications used by the applicant are based on those developed by the International Organisation for Standardization (ISO) 4725:2004(E) for oil of cedarwood, Texas (*Juniperus mexicana* Schiede),[12] adapted to reflect the concentrations of the main volatile components of the essential oil. Four components contribute to the specifications as shown in Table 1, with *cis*-thujopsene selected as phytochemical marker. Analysis of five batches of the additive showed compliance with these specifications when analysed by GC-FID and expressed as percentage of the gas chromatographic peak area (% GC area).[13] GC-FID analysis also detected the presence of cuparene (1.37%–1.47%) and widdrol (1.19%–1.62%) in the same batches.

TABLE 1 Main constituents of the essential oil from the wood of *Juniperus deppeana* Steud. as defined by specification: 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 percent 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**	**Mean**	**Range**
cis-Thujopsene	470-40-6	–	25–35	29.8	26.8–31.0
(+)-Cedrol	77-53-2	02.120	≥ 20	22.0	20.9–23.8
α-Cedrene	469-61-4	01.122	15–25	16.9	15.8–19.3
β-Cedrene	546-28-1	–	3–8	5.80	4.73–6.19

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

The applicant provided the full characterisation of the volatile constituents of the same five batches obtained by gas chromatography coupled with mass spectrometry (GC–MS).[14] In total, up to 92 constituents were detected, 82 of which were identified and accounted on average for 97.8% (97.3%–98.2%) of the % GC area. The four compounds indicated in the product specification accounted for 78.0% on average (range 74.2%–79.8%) of the % GC area. Besides 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 at levels > 0.5%, together account on average for 92.3% (87.5%–93.9%) of the % GC area. The remaining 63 compounds (ranging between 0.001% and 0.5%) and accounting together for about 5.5% are listed in the footnote.[15] Ten unidentified compounds accounting together for 1.55% on average (range 1.11%–1.84%) of the % GC area were detected in different batches of cedarwood Texas oil. Based on the chromatographic profile, the molecular weight and fragmentation patterns, they were tentatively identified as terpene ketones or terpene alcohols (with formulas $C_{15}H_{24}O$; $C_{14}H_{24}O$ or $C_{15}H_{22}O$). Based on the available data on the characterisation, cedarwood Texas oil is considered a fully defined mixture (EFSA Scientific Committee, 2019).

[11]Technical dossier/Supplementary information October 2021/Annex_II_ SIn_Reply_cedarwood_Texas_oil_CoA_chrom.

[12]Technical dossier/Supplementary information October 2021/Annex_III_SIn_reply_cedarwood_Texas_oil_ISO.

[13]Technical dossier/Supplementary information October 2021/SIn reply_ BDG18_cedarwood_Texas_oil/Table 2.

[14]Technical dossier/Supplementary information October 2021/ Annex_II_ SIn_Reply_cedarwood_Texas_oil_CoA_chrom.

[15]Additional constituents:constituents ($n = 20$) between < 0.5% and ≥ 0.1%: 2-epi-α-funebrene, himachalol, *l*-di-epi-α-cedrene, 10-epi-γ-eudesmol, α-calacorene, β-selinene, γ-cuprenene, γ-maaliene, α-curcumene, β-chamigrene, α-cadinol, γ-cadinene, α-terpineol, *(Z)*-α-bergamotene, *(Z)*-β-farnesene, δ-cadinene, α-funebrene, α-terpinyl acetate, 1,10-di-epi-cubenol and *(I)*-α-bisabolol; constituents ($n = 8$) between < 0.1 and ≥ 0.05%: junenol, α-chamipinene, 1-epi-cubenol, cedranone, (–)-α-elemol, α-pinene, cedr-8-en-15-ol and cedryl acetate;constituents ($n = 19$) between < 0.05% and > 0.01%: β-calacorene, terpinolene, α-neocallitropsene, 1-isopropenyl-4-methylbenzene, cadalene, 1-isopropyl-2-methoxy-4-methylbenzene, α-copaene, pin-2-en-4-one, 7-epi-α-selinene, α-cadinene, 4-terpinenol, *(E)*-nerolidol, camphor, caryophyllenol I, δ-3-carene, *d,l*-bornyl acetate, α-ylangene, α-fenchene and *p*-cymene;constituents ($n = 16$) < 0.01%: pinocarveol, limonene, *(Z)*-ocimenol, thymol, nootkatone, α-methylstyrene, myrtenal, 2,4-thujadiene, myrtenol, methyl geranate, camphene, fenchyl alcohol, pinocamphone, β-pinene, *trans*-β-terpinyl acetate and pinocarvone.

TABLE 2 Other constituents of the essential oil from the wood of *Juniperus deppeana* Steud. accounting for > 0.5% of the composition (based on the analysis of five batches) not included in the specifications. The content of each constituent is expressed as the area percent of the corresponding chromatographic peak (% GC area), assuming the sum of chromatographic areas of all detected peaks as 100%.

Constituent			% GC area	
EU register name	**CAS no**	**FLAVIS no**	**Mean**	**Range**
cis-Thujopsene	470-40-6	–	26.9	25.7–28.1
(+)-Cedrol	77-53-2	02.120	25.5	24.4–27.2
α-Cedrene	469-61-4	01.122	19.0	17.9–19.6
β-Cedrene	546-28-1	–	6.56	5.51–7.10
β-Himachalene	1461-03-6	–	2.40	2.27–2.57
Cuparene	16982-00-6	–	1.86	1.74–1.96
α-Acorenol	28296-85-7	–	1.29	0.92–1.48
β-Elemene	33880-83-0	–	1.09	0.69–1.25
α-Alaskene	28400-12-6	–	0.92	0.86–0.97
epi-Cedrol	19903-73-2	–	0.83	0.24–1.85
α-Chamigrene	19912-83-5	–	0.83	0.73–0.89
γ-Selinene	515-17-3	–	0.81	n.d.–1.04
10-epi-β-Acoradiene	43219-80-3	–	0.79	0.74–0.98
α-Duprezianene	–	–	0.68	0.57–0.75
Allocedrol	50657-30-2	–	0.58	0.50–0.75
α-Himachalene	3853-83-6	–	0.57	0.52–0.60
δ-Amorphene	189165-79-5	–	0.56	n.d.–0.73
β-Acorenol	28400-11-5	–	0.56	0.48–0.62
β-Alaskene	28908-21-6	–	0.52	0.47–0.57
Total			92.3	87.5–93.9[a]

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

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

The applicant performed a literature search (see Section 3.3) for the chemical composition of *J. deppeana* and its preparations to identify the presence of any recognised substances of concern.[16] The few studies investigating the composition of cedarwood oil from *J. deppeana* and *J. virginiana* did not report the presence of substances of concern.

3.2.2 | 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), organo-chloride pesticides, organo-phosphorous pesticides, aflatoxins (B1, B2, G1, G2) and ochratoxin A. However, no data have been provided on the presence of these impurities. Since cedarwood Texas 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.

3.2.3 | Shelf-life

The typical shelf-life of cedarwood Texas 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).[17] However, no data supporting this statement were provided.

[16]Technical dossier/Supplementary information October 2021/Literature search_cedarwood_Texas_oil.

[17]Technical dossier/Section II.

3.2.4 | Conditions of use

Cedarwood Texas oil is intended to be added to feed and water for drinking for all animal species without a withdrawal time. The maximum proposed use level is 15 mg/kg complete feed. No use level has been proposed by the applicant for use in water for drinking.

3.3 | Safety

The assessment of safety of cedarwood Texas oil is based on the maximum use levels proposed by the applicant in complete feed (15 mg/kg).

No studies to support the safety for target animals, consumers and users were performed with the additive under assessment. The applicant carried out a structured database search to identify data related to the chemical composition and the safety of preparations obtained from *J. mexicana* and *J. virginiana*.[18] Three cumulative databases (LIVIVO, OVID and ToxNet) and 15 single databases including PubMed and Web of Science were used. The literature search (no time limits) was conducted in 2021. The keywords used covered different aspects of safety and the inclusion and exclusion criteria were provided by the applicant.

Many of the individual components of the essential oil have been already assessed as chemically defined flavourings for use in feed and food by the FEEDAP Panel, the EFSA Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food (AFC), the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) or the EFSA Panel on Food Additives and Flavourings (FAF). The flavouring compounds currently authorised for feed[19] and/or food[20] use, together with the EU Flavour Information System (FLAVIS) number, the chemical group as defined in Commission Regulation (EC) No 1565/2000[21] and the corresponding EFSA opinion are listed in Table 3.

TABLE 3 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
01	Straight-chain primary aliphatic alcohols/ aldehydes/acids, acetals and esters with esters containing saturated alcohols and acetals containing saturated aldehydes	Methyl geranate[a]	09.643	2013, CEF
06	Aliphatic, alicyclic and aromatic saturated and unsaturated tertiary alcohols and esters with esters containing tertiary alcohols ethers	α-Terpineol	02.014	2012b
		Nerolidol[b]	02.018	
		4-Terpinenol	02.072	
		α-Terpinyl acetate	09.015	
		(+)-Cedrol[a]	02.120	2011a, CEF
		(l)-α-Bisabolol[a]	02.129	
		(–)-α-Elemol[a]	02.149	
07	Primary alicyclic saturated and unsaturated alcohols, aldehydes, acids, acetals esters with esters containing alicyclic alcohols	Myrtenol[a]	02.091	2017, CEF
		Myrtenal[a]	05.106	2019, FAF
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	2016a
		Nootkatone	07.089	
		d-Camphor[c]	07.215	
		d,l-Bornyl acetate	09.017	
		Pinocarveol	02.100	2012a, CEF
		Pin-2-en-4-one[a]	07.196	2012b, CEF
		Cedryl acetate	09.171	2011a, CEF

(Continues)

[18]Technical dossier/Supplementary information October 2021/Literature_search_cedrawoood_Texas_oil.

[19]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.

[20]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.

[21]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 180, 19.7.2000, p. 8.

TABLE 3 (Continued)

CG	Chemical group	Product – EU register name (common name)	FLAVIS no	EFSA opinion,* year
25	Phenol derivatives	Thymol	04.006	2012c
26	Aromatic ethers	1-Isopropyl-2-methoxy-4-methylbenzene	04.043	2012d
31	Aliphatic and aromatic hydrocarbons	Limonene[a,d]	01.001	2008a, AFC
		1-Isopropyl-4-methylbenzene (*p*-cymene)	01.002	2015
		Terpinolene	01.005	
		1-Isopropenyl-4-methylbenzene	01.010	
		Pin-2(10)-ene (β-pinene)	01.003	2016b
		Pin-2(3)-ene (α-pinene)	01.004	
		β-Caryophyllene	01.007	
		Camphene	01.009	
		δ-3-Carene	01.029	
		δ-Cadinene[a,e]	01.021	2011b, CEF
		α-Cedrene[a,e]	01.022	

*FEEDAP opinion unless otherwise indicated.

[a]Evaluated for use in food. According to Regulation (EC) 1565/2000, flavourings evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) before 2000 are not required to be re-evaluated by EFSA.

[b]EFSA evaluated nerolidol [02.018] as a mixture of isomers (34%–44% *cis*-nerolidol and 54%–64% *trans*-nerolidol) was evaluated for use in food and feed (EFSA FEEDAP Panel, 2012b).

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

[d]JECFA and EFSA evaluated *d*-limonene [01.045] (EFSA, 2008a). *d*-Limonene [01.045] and *l*-limonene [01.046] were also evaluated for use in feed (EFSA FEEDAP Panel, 2015).

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

The additive under assessment is a fully defined mixture (Section 3.2.1), with 82 identified components (accounting for > 97.3% of the % GC area) and 10 tentatively identified components (accounting together for 1.55% on average of the % GC area).

As shown in Table 3, a number of components (29) of cedarwood Texas oil, accounting for about 45% of the % GC peak area, have been previously assessed and considered safe for use as flavourings, and are currently authorised for food[22] and feed[23] uses at individual use levels higher than those resulting from the intended use of the essential oil in feed.

For (+)-cedrol [02.120], one of the major components of the additive, metabolism studies and genotoxicity studies have been assessed by the EFSA CEF Panel (EFSA CEF Panel, 2011a). Two metabolism studies with (+)-cedrol [02.120] given orally to the rabbit and dog (Bang & Ourisson, 1975; Trifilieff et al., 1975, as referenced in EFSA CEF Panel, 2011a) indicated that it is hydroxylated and excreted in urine as the respective conjugates. Only a minor portion of (+)-cedrol is directly conjugated and excreted. (+)-Cedrol was not mutagenic in Salmonella typhimurium TA97a, TA98, TA100, TA102, TA1535, TA1537 up to 5000 μg/plate, without and with metabolic activation by rat liver S9 and was not considered to have genotoxic potential. Other genotoxicity endpoints were evaluated by quantitative structure–activity relationship (QSAR) analysis (see Section 3.3.1). No adverse effects were observed when (+)-cedrol (~ 8.4 mg/kg bw per day, the only dose tested) was administered to rats for 32 days by gavage (IOFI, 2006, as referenced in EFSA CEF Panel, 2011a). Considering that the dietary intake of (+)-cedrol as a food flavouring substance belonging to Cramer Class I was below the respective TTC value, the EFSA CEF Panel concluded that it does not give rise to safety concerns.

Two additional compounds listed in Table 3, δ-cadinene [01.021] and α-cedrene [01.022], were evaluated in FGE25.Rev2 (EFSA CEF Panel, 2011b) 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 these compounds, for which there was no concern for genotoxicity, EFSA requested additional subchronic toxicity data (EFSA CEF Panel, 2011b). In the absence of such toxicological data, the EFSA CEF Panel was unable to complete its assessment (EFSA CEF Panel, 2015a). As a result, these compounds are not authorised for use as flavours in food. In the absence of toxicity data, the FEEDAP Panel applied the threshold of toxicological concern (TTC) approach or read-across from structurally related substances, following the approach recommended

[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. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed-eu-reg-comm_register_feed_additives_1831-03.pdf.

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).

A large number (53) of the identified components of cedarwood Texas oil accounting for about 55% of the GC area have not been previously assessed for use as flavourings. The majority of them (46) are structurally related to compounds already authorised for use in food and feed in CG 6 (nine compounds), CG 8 (one compound) and CG 31 (36 compounds).[24] The FEEDAP Panel notes that the majority of the compounds not previously assessed are aliphatic mono- or sesquiterpenes structurally related to flavourings already assessed in CG 31 (36 compounds) and a similar metabolic and toxicological profile may be expected. These lipophilic compounds accounting for about 47.2% of the GC % area are expected to be rapidly absorbed from the gastro-intestinal tract, oxidised to polar oxygenated metabolites, conjugated and excreted (EFSA FEEDAP Panel, 2016a, 2016b). The compounds belonging to CG 6 (nine compounds) are hydroxylated metabolites of compounds belonging to CG 31, and therefore, a similar metabolic and toxicological profile is expected (including genotoxicity). The compound belonging to CG 8 (cedranone) is structurally and metabolically related to (+)-cedrol. For these components, based on the structural similarity with compounds already authorised for use in food and feed it unlikely that they would raise a concern for genotoxicity (see Section 3.3.1). The 10 additional compounds tentatively identified as terpene ketones or terpene alcohols are expected to behave in a similar way.

The following sections focus on the seven compounds[25] not previously assessed or not structurally related to flavourings previously assessed, based on the evidence provided by the applicant in the form of several literature searches, and QSAR analysis to screen for substances raising potential genotoxicity concern.

3.3.1 | 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). Therefore, the potential genotoxicity of identified constituents is first considered. Then, in vitro genotoxicity studies performed with the mixture under assessment (in the present assessment the essential oil) or an essential oil similar to the additive under assessment are described.

The genotoxic potential of seven compounds (*(Z)*-ocimenol, cedr-8-en-15-ol, pinocamphone, pinocarvone, caryophyllenol I, allocedrol and junenol) was predicted by the applicant using the Organisation for Economic Co-operation and Development (OECD) QSAR Toolbox.[26] No structural alerts were found for *(Z)*-ocimenol, pinocamphone and allocedrol. Structural alerts were due to the presence of vinyl/allyl group for cedr-8-en-15-ol and caryophyllenol I, vinyl/allyl group and unsaturated ketones for pinocarvone, and to the presence of menthol moiety for junenol. In all cases, predictions of Ames mutagenicity 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. Mutagenicity read-across-based predictions were found consistently negative for all categories of analogues. On this basis, the alerts raised were discounted.

For all the 53 compounds not previously assessed for use as flavours in food and/or feed, EFSA has verified the results of the QSAR analysis with all the profilers contained in the OECD QSAR Toolbox. This was confirmed by applying other freely available QSAR models, VEGA and Janus. Overall, the QSAR analysis did not point to a concern for genotoxicity.

Genotoxicity studies with an essential oil from Juniperus virginiana

The applicant provided genotoxicity studies performed with a cedarwood Texas oil obtained from *Juniperus virginiana* (NTP, 2016), which is considered similar to the additive under assessment. The test item contained higher percentage of α-cedrene compared to the additive under assessment (27% vs. 17%) and lower % of *cis*-thujopsene (20% vs. 30%), but similar % of β-cedrene (6%) and (+)-cedrol (1%). Cedarwood Texas oil (0.33–333 μg/plate) did not induce gene mutations in S. typhimurium strains TA98, TA100 and TA102 when tested in the presence and absence of metabolic activation (NTP, 2016).

3.3.2 | Considerations on read across for the major components of cedarwood Texas oil

Four compounds indicated in the product specification, *cis*-thujopsene, (+)-cedrol, α-cedrene and β-cedrene, account for 78.0% on average (range 74.2%–79.8%) of the % GC area.

[24]CG 6 (9 compounds, accounting for 3.8%): *trans*-β-terpinyl acetate, epi-cedrol, 10-epi-γ-eudesmol, 1-epi-cubenol, α-acorenol, β-acorenol, 1,10-di-epi-cubenol, himachalol and α-cadinol; CG 8 (1 compound, 0.08%): cedranone; CG 31, II (1 compound, 0.15%): *(Z)*-β-farnesene; CG 31, III (1 compound, 1.1%): β-elemene; CG 31, IV (6 compounds, 2.4%): cuparene, α-curcumene, α-calacorene, β-calacorene, cadalene and α-methylstyrene; CG 31, V (28 compounds, 47.2%): *cis*-thujopsene (27%), β-cedrene (6.6%), β-himachalene (2.4%), γ-selinene (0.8%), β-chamigrene (0.2%), β-acoradiene, 10-epi; α-alaskene, α-chamigrene, α-duprezianene, δ-amorphene, α-himachalene, β-alaskene, 2-epi-α-funebrene, γ-cadinene, *l*-di-epi-α-cedrene, γ-cuprenene, β-selinene, γ-maaliene, *(Z)*-α-bergamotene, α-funebrene, α-neocallitropsene, 7-epi-α-selinene, α-chamipinene, α-cadinene, α-copaene, α-ylangene, α-fenchene and 2,4-thujadiene.

[25]*(Z)*-Ocimenol, cedr-8-en-15-ol, pinocamphone, pinocarvone, caryophyllenol I, allocedrol and junenol.

[26]Technical dossier/Supplementary information October 2021/Annex VI_SIn_reply_cedarwood Texas oil_QSAR.

Two compounds *cis*-thujopsene and β-cedrene have not been evaluated for use as flavourings in food and α-cedrene [01.122] is no longer authorised for use in food (EFSA CEF Panel, 2015a). For (+)-cedrol [02.120], a limited data set on the metabolism and the toxicity has been evaluated by the EFSA CEF Panel (EFSA CEF Panel, 2011a). For all the compounds, there was no concern for genotoxicity found by QSAR and experimental data in the case of (+)-cedrol.

The FEEDAP Panel evaluated the possibility to read-across from the representative compound of CG 31, subgroup V, β-caryophyllene [01.007] to these major components of cedarwood Texas oil.

In the next paragraphs, specific considerations on the structural and metabolic similarity of the candidate compounds with the representative compound β-caryophyllene [01.007] are discussed. The structures of the compounds are given in Figure 1.

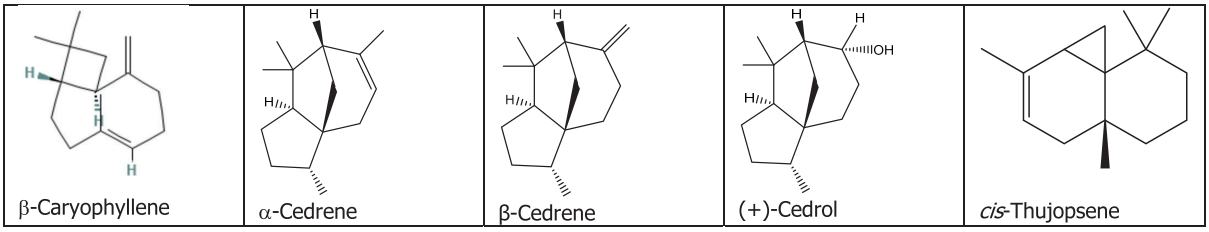

FIGURE 1 Molecular structures of the representative compound β-caryophyllene [01.007] and of the compounds candidate for read across, α-cedrene, β-cedrene, (+)-cedrol and *cis*-thujopsene.

β-Caryophyllene

β-Caryophyllene is a bicyclic sesquiterpene characterised by the presence of two double bonds, one in the 9-membered ring (endocyclic) and another as terminal double bond (exocyclic). Owing to its complex structure and its reactivity, due to the presence of a terminal double bond, β-caryophyllene was selected for testing as representative substance for CG 31 ('aliphatic and aromatic hydrocarbons'), subgroup V ('bi-, tricyclic, non-aromatic hydrocarbons') as defined in Flavouring Group Evaluation 25 (FGE.25) and FGE.78 (EFSA CEF Panel, 2015a, 2015b).

Data on the metabolism of β-caryophyllene [01.007] have been evaluated by the EFSA CEF Panel (EFSA CEF Panel, 2011b): 'In rabbits, β-caryophyllene [01.007] undergoes epoxidation of the endocylic 5,6-double bond to yield a stable epoxide metabolite and hydroxylation at the gem-dimethyl group. The resulting metabolite 14-hydroxycaryophyllene-5,6-epoxide and its C14-acetylated conjugate could be detected in the urine. A second epoxidation of the 5,6-epoxide's exocyclic 2,12-double bond, ultimately resulting in the 14-hydroxycaryophyllene-5,6-epoxide-2,12-diol, was also reported.'

Based on the data available on the metabolism of β-caryophyllene and other terpenes, α-pinene, β-pinene, δ-3-carene, camphene and (+)-longifolene, the compounds belonging to CG 31, subgroup V are expected to be metabolised either by side chain oxidation or epoxidation of the exocyclic or endocyclic double bonds. The hydroxylated metabolites (i.e. alcohol) are excreted as conjugates, probably with glucuronic acid (EFSA CEF Panel, 2011b).

For β-caryophyllene [01.007], the EFSA CEF Panel derived a no adverse effect level (NOAEL) of 222 mg/kg bw per day (the lowest dose tested) from a 90-day study in rats based on several adverse effects[27] observed at the middle and high doses (EFSA CEF Panel, 2015a). In its assessment of β-caryophyllene as feed a flavouring, the FEEDAP Panel agreed with the conclusions of the CEF Panel (EFSA FEEDAP Panel, 2016b).

α-Cedrene and β-cedrene

α-Cedrene and β-cedrene are tri-cyclic sesquiterpenes, characterised by the presence of one double bond on the seven-membered ring, either endocyclic (α-cedrene) or exocyclic (β-cedrene) and by the presence of methyl substituent groups on both rings. The structure of α-cedrene and β-cedrene is therefore considered similar to that of the representative compound β-caryophyllene.

No toxicological data were available for cedrenes. However, the FEEDAP Panel considers that the reactivity of cedrenes is sufficiently represented by β-caryophyllene.

Based on structural and metabolic similarity, the FEEDAP Panel considered that the NOAEL of 222 mg/kg bw per day for β-caryophyllene can be applied using read-across to α-cedrene and β-cedrene.

(+)-Cedrol

(+)-Cedrol is a cedrane sesquiterpenoid and a tertiary alcohol. (+)-Cedrol shares the same ring skeleton of cedrene, without the double bond (either endocyclic or exocyclic).

(+)-Cedrol is formed from cedrene by oxidation of the double bond (either endocyclic or exocyclic) and represents an intermediate metabolite in the detoxification of the sesquiterpene. The hydroxy group of cedrol can be conjugated and

[27]Haematological parameters in males showed a dose-dependent increase in white blood cells and several changes in other blood cells. Pathology and histopathology revealed an increase in the absolute and relative liver weight associated with hepatocellular hypertrophy in both sexes, the presence of erythrocytes in the sinuses of the mesenteric lymph nodes in both sexes and an increase in relative kidney weight in females, not associated with microscopically alterations.

the compound excreted as glucuronide. Metabolism studies with cedrol [02.120] in rabbit and dog (Bang & Ourisson, 1975; Trifilieff et al., 1975, as referenced in EFSA CEF Panel, 2011a) indicated that only a minor portion of (+)-cedrol is directly conjugated and excreted and that (+)-cedrol is further hydroxylated and excreted in urine as such or as conjugates.

When (+)-cedrol (approximately 8.4 mg/kg bw per day) was administered to rats for 32 days by gavage, no adverse effects were observed (IOFI, 2006, as referenced in EFSA CEF Panel, 2011a). Higher doses were not tested. The FEEDAP Panel notes that the study was not designed to derive a NOAEL value for (+)-cedrol but was rather aimed at demonstrating the absence of adverse effects in animals at a dietary intake exceeding of at least 100 times the maximum estimated human intake. The FEEDAP Panel considers that the limited toxicological data available for (+)-cedrol would not prevent to apply read-across from a structurally related compound, for which more reliable and complete toxicological data are available. When comparing (+)-cedrol with the corresponding sesquiterpene cedrene and the representative compound β-caryophyllene, a lower reactivity is expected because of the absence of the double bond(s).

Based on structural and metabolic similarity and considering the lower expected reactivity of (+)-cedrol, the FEEDAP Panel considered that the NOAEL of 222 mg/kg bw per day for β-caryophyllene can be applied using read-across to (+)-cedrol.

cis-Thujopsene

cis-Thujopsene is a tri-cyclic sesquiterpene characterised by the presence of a cyclopropane ring fused with a six-membered ring. Under mild acidic conditions, the opening of the cyclopropane ring has been reported to occur with the rearrangement of the cyclopropane ring into a seven-membered ring. As a result, transformation of *cis*-thujopsene into widdrol occurs (Dauben & Aoyagi, 1972; Dauben & Friedrich, 1964). The structure of widdrol, characterised by fused six- and seven-membered rings, with methyl ring substituent groups and an endocyclic double bond, is considered similar to the representative compound β-caryophyllene. Widdrol is one of the primary components included in the ISO specifications for cedarwood oil from either *J. mexicana* or *J. virginiana* and has been detected in the additive under assessment by GC-FID.

Like (+)-cedrol, the hydroxy group of widdrol can be conjugated and the compound excreted as glucuronide. Further side chain oxidation or epoxidation of the endocyclic double bond is likely to occur and the resulting hydroxylated metabolites (i.e. alcohol) are excreted as conjugates, probably with glucuronic acid.

Based on structural and metabolic similarity, the FEEDAP Panel considered that the NOAEL of 222 mg/kg bw per day for β-caryophyllene can be applied using read-across to *cis*-thujopsene. The NOAEL of 222 mg/kg bw per day was halved to take into account the uncertainty in read-across due to the presence of a cyclopropane ring.

Minor constituents

The read-across from β-caryophyllene [01.007] was applied to the other minor constituents of cedarwood Texas oil, which share the same structural features (bi- or tricyclic sesquiterpenes with fused rings, with the presence of one or two double bonds, endocyclic and/or exocyclic).[28] The compounds which contain spirocycles, two rings that share a common atom, namely α-alaskene, β-alaskene, 10-epi-β-acoradiene, α-neocallitropsene, α- chamigrene, β-chamigrene were excluded from the read-across. The read-across was extended to the corresponding oxygenated derivatives belonging to CG 6 and 8.

3.3.3 | Safety for the target species

Tolerance studies in 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.

As the additive under assessment is a fully defined mixture (the identified components represent > 97.3% 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 nine assessment groups, corresponding to the chemical groups (CGs) 1, 6, 7, 8, 25, 26 and 31, 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, 2015b). The allocation of the components to the (sub-)assessment groups is shown in Table 4.

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

[28] α-himachalene, β-himachalene, γ-selinene, α-duprezianene, δ-amorphene, δ-cadinene, α-himachalene, 2-epi-α-funebrene, γ-cadinene, *l*-di-epi-α-cedrene, β-selinene, γ-maaliene, α-funebrene, 7-epi-α-selinene, α-chamipinene, α-cadinene, α-pinene, α-copaene, α-ylanglene, δ-3-carene, α-fenchene, camphene and β-pinene.

feed additives for target species (EFSA FEEDAP Panel, 2017b). 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 calculated for chickens for fattening, the species with the highest ratio of feed intake/body weight per day are shown in Table 4 and in the corresponding footnote.

For hazard characterisation, each component of an assessment group was first assigned to the structural class according to Cramer Class 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 allowing extrapolation from a known NOAEL of a component of an assessment group to the other components of the group with no available NOAEL or, if sufficient evidence were available for members of a (sub-)assessment group, to derive a (sub-)assessment group NOAEL.

Toxicological data of subchronic studies, from which NOAEL values could be derived, were available for few components of the essential oil, i.e. terpineol[29] [02.230] in CG 6 (EFSA FEEDAP Panel, 2012b), thymol [04.006] in CG 25 (EFSA FEEDAP Panel, 2012c), d-limonene [01.045] in CG 31 (EFSA FEEDAP Panel, 2015). In addition, NOAEL values were available for other compounds structurally related to those present in cedarwood Texas oil, i.e. for several compounds in CG 1 (EFSA FEEDAP Panel, 2013), for linalool [02.013] in CG 6 (EFSA FEEDAP Panel, 2012b), *d,l*-isobornyl acetate [09.218] in CG 8 (EFSA FEEDAP Panel, 2016a), myrcene [01.008], *p*-cymene [01.002] and β-caryophyllene [01.007] in CG 31 (EFSA FEEDAP Panel, 2015, 2016b).

For CG 1, a group NOAEL of 120 mg/kg bw was derived from the toxicological data available and selected as reference point for methyl geranate [09.643]. For the compounds in CG 6, a 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] and was aplied to all terpineol derivatives, and to 10-epi-γ-eudesmol, 1,10-epi-cubenol, 1-epi-cubenol, α-cadinol and l-α-bisabolol. The NOAEL of 117 mg/kg bw per day for linalool was applied to *(E)*-nerolidol [02.232].

Read-across was applied using the NOAEL of 15 mg/kg bw per day for *d,l*-isobornyl acetate [09.218] to extrapolate to *d,l*-borneol [02.016] in CG 8.

The NOAELs of 44 and 250 mg/kg bw per day for the representative compounds in CG 31, myrcene [01.008] and d-limonene [01.045] were applied, respectively, using read-across to the compounds within sub-assessment group II (*(Z)*-β-farnesene) and group III (β-elemene and terpinolene [01.005]). The NOAEL of 44 mg/kg bw per day for myrcene [01.008] was also applied to *(Z)*-ocimenol in CG 6 (EFSA CEF Panel, 2015a, 2015b). The NOAEL of 222 mg/kg bw per day for β-caryophyllene was applied using read-across to the compounds within subassessment group V[30] sharing the same structural features (bi- or tricyclic sesquiterpenes with fused rings with the presence of double bonds, either internal or terminal) but not to compounds which contain spirocycles (EFSA CEF Panel, 2015a, 2015b). For *cis*-thujopsene, the NOAEL of 222 mg/kg bw per day was halved to take into account the uncertainty in read-across due to the presence of a cyclopropane ring. The NOAEL of 222 mg/kg bw per day for β-caryophyllene [01.007] was also extrapolated to the oxygenated derivatives, sharing the same structure (bi- or tricyclic sesquiterpenes with fused rings with the presence of double bonds, either internal or terminal) i.e. (+)-cedrol [02.120], epi-cedrol and himachalol in CG 6, and to cedranone, cedryl acetate [09.171] and caryophyllenol I in CG 8.

For the remaining compounds,[31] NOAEL values were not available and read-across was not possible. Therefore, the threshold of toxicological concern (TTC) approach was applied (EFSA FEEDAP Panel, 2012a, 2017a, 2017b, 2017c).

As the result of the hazard characterisation, a reference point was identified for each component in the assessment group based on the toxicity data available (NOAEL from in vivo toxicity study or read-across) or from the 5th percentile of the distribution of NOAELs of the corresponding Cramer Class (i.e. 3, 0.91 and 0.15 mg/kg bw per day, respectively, for Cramer Class I, II and III compounds, Munro et al., 1996). Reference points selected for each compound are shown in Table 4.

For 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, 2019b, 2019c). An 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.[32]

The approach to the safety assessment of cedarwood Texas oil for chickens for fattening is summarised in Table 4. 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 15 mg/kg in feed.

[29]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.

[30]Compounds in sub-assessment group V in which read-across from β-caryophyllene [01.007] was applied: α-cedrene [01.022], β-cedrene, β-himachalene, γ-selinene, α-duprezianene, δ-amorphene, δ-cadinene, α-himachalene, 2-epi-α-funebrene, γ-cadinene, l-di-epi-α-cedrene, β-selinene, γ-maaliene, α-funebrene, 7-epi-α-selinene, α-chamipinene, α-cadinene, α-pinene, α-copaene, α-ylanglene, δ-3-carene, α-fenchene, camphene and β-pinene.

[31]α-acorenol, β-acorenol and (−)-α-elemol (CG 6); cedr-8-en-15-ol, myrtenal and myrtenol (CG 7); allocedrol, junenol, cedarnone, pin-2-en-4-one, camphor, pinocarveol, nootkatone, fenchyl alcohol, pinocamphone and pinocarvone (CG 8); 1-isopropyl-2-methoxy-4-methylbenzene (CG 26); cuparene, α-chalacorene, β-chalacorene, cadalene 1-isopropenyl methylbenzene and α-methylstyrene (CG 31; IVe); β-chamigrene,10-epi-β-acoradiene, α-alaskene, α-chamigrene, β-alaskene, γ-cuprenene, α-neocallitropsene, and 2,4-thujadiene (CG 31, V).

[32]Compounds included in the assessment groups but not reported in Table 4: methyl geranate (CG 1); l-α-bisabolol, α-terpineol, α-terpinyl acetate, *(E)*-nerolidol, *(Z)*-ocimenol, 4-terpinenol and trans-β-terpinyl acetate (CG 6); cedranone, cedryl acetate, caryophyllenol I, *d,l*-bornyl acetate and fenchyl alcohol (CG 08); thymol (CG 25); terpinolene and limonene (CG 31, III); *p*-cymene (CG 31, IVe); β-selinene, γ-maaliene, *(Z)*-α-bergamotene, α-funebrene, 7-epi-α-selinene, α-chamipinene, α-cadinene, α-pinene, α-copaene, α-ylangene, δ-3-carene, α-fenchene, camphene and β-pinene (CG 31, V).

TABLE 4 Compositional data, intake values (calculated for chickens for fattening at 15 mg/kg complete feed), reference points and margin of exposure (MOE) for the individual components of cedarwood Texas 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 Constituent	FLAVIS-no –	Highest conc. in the oil %	Highest feed conc. mg/kg	Intake[a] mg/kg bw/day	Cramer class[b] –	NOAEL[c] mg/kg bw/day	MOE –	MOET –
CG 6								
(+)-Cedrol	02.120	27.24	4.086	0.3668	(I)	222	605	
epi-Cedrol	–	1.85	0.277	0.0249	(I)	222	8921	
10-epi-γ-Eudesmol	–	1.75	0.263	0.0236	(I)	250	10,597	
α-Acorenol	–	1.48	0.222	0.0200	I	*3*	150	
β-Acorenol	–	0.62	0.093	0.0083	I	*3*	359	
1,10-di-epi-Cubenol	–	0.59	0.088	0.0079	(I)	250	31,520	
Himachalol	–	0.42	0.064	0.0057	(I)	222	38,882	
α-Cadinol	–	0.41	0.061	0.0055	(I)	250	45,840	
1-epi-Cubenol	–	0.40	0.060	0.0054	(I)	250	46,414	
(–)-α-Elemol	–	0.13	0.020	0.0018	I	*3*	1701	
MOET CG 6								83
CG 7								
Cedr-8-en-15-ol	–	0.27	0.041	0.0036	I	*3*	822	
Myrtenal	05.106	0.02	0.003	0.0003	II	*0.91*	3379	
Myrtenol	02.091	0.02	0.002	0.0002	I	*3*	14,852	
MOET CG 7								633
CG 8								
Allocedrol	–	0.75	0.113	0.0101	I	*3*	296	
Junenol	–	0.44	0.066	0.0059	I	*3*	507	
Nootkatone	07.089	0.04	0.005	0.0005	II	*0.91*	1877	
Pin-2-en-4-one	02.038	0.03	0.004	0.0004	II	*0.91*	2414	
Camphor	–	0.02	0.003	0.0003	II	*0.91*	2938	
Pinocarveol	02.100	0.01	0.002	0.0001	I	*3*	22,278	
Pinocamphone	–	0.004	0.001	0.0001	III	*0.15*	2785	
Pinocarvone	–	0.003	0.0005	0.00004	III	*0.15*	3713	
MOET CG 8								136
CG 26								
1-Isopropyl-2-methoxy-4-methylbenzene	04.043	0.03	0.005	0.0004	I	*3*	6751	
CG 31, II (Acyclic alkanes)								
(Z)-β-Farnesene	–	0.19	0.028	0.0025	(I)	44	17,288	
CG 31, III (Cyclohexene hydrocarbons)								
β-Elemene	–	1.25	0.187	0.0168	(I)	*250*	14,488	
CG 31, IVe (Benzene hydrocarbons, alkyl)								
Cuparene	–	1.96	0.294	0.0264	I	*3*	114	
α-Calacorene	–	0.36	0.059	0.0053	I	*3*	29,067	
β-Calacorene	–	0.18	0.053	0.0048	I	*3*	626	
Cadalene	–	0.15	0.027	0.0024	III	*0.15*	1259	
1-Isopropenyl-4-methylbenzene	01.002	0.07	0.023	0.0020	I	*3*	73	
α-Methylstyrene	–	0.01	0.001	0.0001	I	*3*	24,754	
MOET CG 31, IVe								40

(Continues)

TABLE 4 (Continued)

Essential oil composition			Exposure		Hazard characterisation		Risk characterisation	
Assessment group Constituent	**FLAVIS-no –**	**Highest conc. in the oil %**	**Highest feed conc. mg/kg**	**Intake[a] mg/kg bw/day**	**Cramer class[b] –**	**NOAEL[c] mg/kg bw/day**	**MOE –**	**MOET –**
CG 31, V (Bi-, tricyclic, non aromatic hydrocarbons)								
cis-Thujopsene	–	28.14	4.220	0.3789	(I)	111	293	
α-Cedrene	01.022	19.57	2.936	0.2636	(I)	222	842	
β-Cedrene	–	7.10	1.064	0.0956	(I)	222	2323	
β-Himachalene	–	2.57	0.385	0.0346	(I)	222	6422	
γ-Selinene	–	1.04	0.157	0.0141	(I)	222	15,791	
β-Chamigrene	–	1.00	0.149	0.0134	I	*3*	224	
β-Acoradiene, 10-epi	–	0.98	0.147	0.0132	I	*3*	228	
α-Alaskene	–	0.97	0.146	0.0131	I	*3*	229	
α-Chamigrene	–	0.89	0.134	0.0120	I	*3*	250	
α-Duprezianene	–	0.75	0.112	0.0101	I	222	22,070	
δ-Amorphene	–	0.73	0.110	0.0098	I	222	22,553	
δ-Cadinene	01.021	0.70	0.104	0.0094	(I)	222	23,687	
α-Himachalene	–	0.60	0.090	0.0081	(I)	222	27,386	
β-Alaskene	–	0.57	0.086	0.0077	I	*3*	391	
2-epi-α-Funebrene	–	0.55	0.082	0.0074	(I)	222	30,139	
γ-Cadinene	–	0.42	0.063	0.0056	(I)	222	39,535	
l-di-epi-α-Cedrene	–	0.40	0.060	0.0054	(I)	222	40,908	
γ-Cuprenene	–	0.35	0.052	0.0046	I	*3*	646	
α-Neocallitropsene	–	0.16	0.024	0.0022	I	*3*	1384	
2,4-Thujadiene	–	0.01	0.001	0.0001	III	*0.15*	1392	
								36

[a]Intake calculations for the individual components are based on the use level of 15 mg/kg in feed for chickens for fattening, the species with the highest ratio of feed intake/body weight. 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 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 4, for several assessment groups, the MOET was < 100, with the lowest MOET calculated for the assessment group 'Bi-, tricyclic, non aromatic hydrocarbons' (CG 31, V). From the lowest MOET of 36 for chickens for fattening, the MOET for CG 31,V was calculated for the other target species considering the respective daily feed intake and conditions of use. The results are summarised in Table 5.

TABLE 5 Combined margin of exposure (MOET) for (Bi-, tricyclic, non aromatic hydrocarbons (CG 31, V) calculated for the different animal categories at the proposed use level in feed and maximum safe use levels in feed calculated to ensure an MOET ≥ 100 (500 for cats).

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg complete feed)[a]	Lowest MOET CG31,V	Maximum safe use level (mg/kg complete feed)[a]
Chickens for fattening	79	15	36	5
Laying hens	53	15	54	8
Turkeys for fattening	59	15	48	7
Piglets	44	15	65	10
Pigs for fattening	37	15	77	12
Sows lactating	30	15	95	14
Veal calves (milk replacer)	19	15	161	–
Cattle for fattening	20	15	142	–
Dairy cows	31	15	92	14
Sheep/goats	20	15	142	–
Horses	20	15	142	–

TABLE 5 (Continued)

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level (mg/kg complete feed)[a]	Lowest MOET CG31,V	Maximum safe use level (mg/kg complete feed)[a]
Rabbit	50	15	57	8.5
Salmonids	18	15	158	–
Dogs	17	15	167	–
Cats[b]	20	15	142	4
Ornamental fish	5	15	569	–

[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.

At the proposed use levels in complete feed, the MOET exceeds the value of 100 for veal calves (milk replacer), cattle for fattening, sheep/goats, horses, dogs, salmonids and ornamental fish (Table 5). For the other species, the maximum safe use levels in feed were calculated in order to ensure a MOET ≥ 100. Because glucuronidation is an important metabolic reaction to facilitate the excretion of the components of the essential oil, the use of cedarwood Texas oil as additive in cat feed needs a wider margin of exposure. Considering that cats have an unusually low capacity for glucuronidation (Court & Greenblatt, 1997; Lautz et al., 2021), an MOET of 500 is considered adequate. The maximum proposed use level of 15 is safe for veal calves (milk replacer), cattle for fattening, sheep/goats, horses, dogs, salmonids and ornamental fish. For the other species/categories, the calculated maximum safe levels are shown in Table 5. These levels are extrapolated to physiologically related minor species. For the other species not considered, the lowest value of 4 mg/kg complete feed is applied.

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.

3.3.3.1 | *Conclusions on safety for the target species*

The FEEDAP Panel considers that the levels of cedarwood Texas oil summarised in Table 6 are safe for the respective target species.

TABLE 6 Safe concentrations of cedarwood Texas oil in complete feed (mg/kg) for all animal species and categories.

Animal categories	Safe concentration (mg/kg complete feed)[a]
Turkeys for fattening	7
Chickens for fattening, other poultry for fattening or reared for laying/reproduction and ornamental birds	5
Laying hens and other laying/reproductive birds	8
Pigs for fattening	12
Piglets and other Suidae species for meat production or reared for reproduction	10
Sows and other Suidae species for reproduction	14
Veal calves (milk replacer)	15
Sheep/goats	15
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction and camelids at the same physiological stage	15
Dairy cows and other ruminants and camelids for milk production or reproduction	14
Horses and other Equidae	15
Rabbits	8.5
Salmonids and minor fin fish	15
Dogs	15
Cats	4
Ornamental fish	15
Other species	4

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

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.

3.3.4 | Safety for the consumer

'Cedarwood oil' is added to a wide range of food for flavouring purposes. Although individual consumption figures for the EU are not available, the Fenaroli's handbook of flavour ingredients (Burdock, 2009) cites values of 0.00014 mg/kg bw per day for 'cedarwood oil terpenes'. The FEEDAP Panel notes that the term 'cedarwood oil' is used in Fenaroli in a very unspecific manner not considering the diversity in botanical origin (see Section 3.1).

Several individual constituents of the essential oil under assessment (accounting on average for about 45% of the GC area) are currently authorised as food flavourings without limitations and have been already assessed for consumer safety when used as feed additives in animal production (see Table 3, Section 3.3). A number of identified components of cedarwood Texas oil have not been previously assessed for use as flavourings. However, they are structurally related to flavourings already assessed in CG 31 and a similar metabolic and toxicological profile may be expected (see 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 cedarwood Texas oil are expected to be extensively metabolised and excreted in the target species. Therefore, it is expected that the concentration of any residues of the individual constituents in products of animal origin would be considerably less than the concentrations given by feed to the target species.

No safety concern would be expected for the consumer from the use of cedarwood Texas oil up to the maximum proposed use level in feed.

3.3.5 | 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 sheets[33] for cedarwood Texas oil where hazards for users have been identified. The essential oil under assessment should be considered as irritant to skin and eyes, and as a skin and respiratory sensitiser.

3.3.6 | Safety for the environment

J. deppeana is not a native species to Europe. Therefore, the safety for the environment is assessed based on the individual components of the essential oil.

Several major and minor constituents present in cedarwood Texas oil have not been evaluated by EFSA with respect to its safety for the environment.

At the maximum proposed use level of 15 mg/kg complete feed, 78 identified components of the essential oil will be < 0.5 mg/kg in complete feed, the threshold below which the trigger value for the predicted environmental concentration (PEC_{soil}) of 10 µg/kg is not exceeded.

At the maximum use level of 15 mg/kg, only the four major components, *cis*-thujospene, (+)-cedrol, α-cedrene and β-cedrene, would occur at concentrations > 0.5 mg/kg complete feed. (+)-Cedrol is found in the wood of several conifers, particularly cypress and cedar: *Cedrus atlantica*, *Cupressus sempervirens*, *J. virginiana* and others. The major components *cis*-thujospene, α-cedrene and β-cedrene are structurally similar to the compounds already assessed in CG 31 for which EFSA concluded that they will be 'extensively metabolised by the target species and excreted as innocuous metabolites or carbon dioxide' (EFSA FEEDAP Panel, 2015a, 2016b).

Therefore, the FEEDAP Panel concludes that the use of cedarwood Texas oil as a flavour in animal feed is not expected to pose a risk to the environment.

3.4 | Efficacy

'Cedarwood oil' alcohols and 'cedarwood oil' terpenes, prepared from distillation of cedarwood, are listed in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2009). There is no specific reference number to cedarwood Texas oil made by the Flavour Extract Manufacturers Association (FEMA). The FEEDAP Panel notes that the term 'cedarwood oil' is used in Fenaroli in a very unspecific manner not considering the diversity in botanical origin (see Section 3.1). However, the individual components of the oil are terpenoids and many of them are recognised food and feed flavourings.

Since the individual components of cedarwood Texas 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.

[33]Technical dossier/Supplementary Information November 2020/Annex_VIII_SIn reply_pine_oil_white_MSDS. Aspiration hazard (H304), hazards for skin corrosion/irritation (H315, category 2), skin sensitisation (H317, category 1B).

4 | CONCLUSIONS

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

Animal categories	Safe concentration (mg/kg complete feed)[a]
Turkeys for fattening	7
Chickens for fattening, other poultry for fattening or reared for laying/reproduction and ornamental birds	5
Laying hens and other laying/reproductive birds	8
Pigs for fattening	12
Piglets and other Suidae species for meat production or reared for reproduction	10
Sows and other Suidae species for reproduction	14
Veal calves (milk replacer)	15
Sheep/goats	15
Cattle for fattening, other ruminants for fattening or reared for milk production/reproduction and camelids at the same physiological stage	15
Dairy cows and other ruminants and camelids for milk production or reproduction	14
Horses and other Equidae	15
Rabbits	8.5
Salmonids and minor fin fish	15
Dogs	15
Cats	4
Ornamental fish	15
Other species	4

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

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.

No safety concern would be expected for the consumer from the use of cedarwood Texas oil up to the maximum proposed use level in feed.

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

The use of cedarwood Texas oil at the proposed use level in feed is not expected to pose a risk to the environment.

Since the individual components of cedarwood Texas 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.

5 | DOCUMENTATION PROVIDED TO EFSA/CHRONOLOGY

Date	Event
05/11/2010	Dossier received by EFSA. Botanically defined flavourings from Botanical Group 18 - Gymnosperms (Coniferales, Ginkgoales) for all animal species and categories. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)
14/12/2010	Reception mandate from the European Commission
26/02/2013	EFSA informed the applicant (EFSA ref. 7150727) that, in view of the workload, the evaluation of applications on feed flavourings would be re-organised by giving priority to the assessment of the chemically defined feed flavourings, as agreed with the European Commission
24/06/2015	Technical hearing during risk assessment with the applicant according to the "EFSA's Catalogue of support initiatives during the life-cycle of applications for regulated products": data requirement for the risk assessment of botanicals
11/02/2019	Application validated by EFSA – Start of the scientific assessment
20/02/2019	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*

(Continues)

(Continued)

Date	Event
27/02/2019	Partial withdrawal by applicant (EC was informed) for the following additives: Juniper berry extract (wb), Pine oil
13/05/2019	Comments received from Member States
18/03/2021	Partial withdrawal by applicant (EC was informed) for the following additive: pine needle oil
19/10/2021	Reception of supplementary information from the applicant - (partial dataset: cedarwood Texas oil) - Scientific assessment remains suspended
14/03/2023	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
27/03/2024	The application was split and the EFSA-Q-2010-01516 remained associated to the additive included in the present assessment.
18/04/2024	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment for BDG 18 (EFSA-Q-2010-01516)

ABBREVIATIONS

BDG	Botanically defined group
bw	body weight
CAS	Chemical Abstracts Service
CD	Commission Decision
CEF	EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CG	chemical group
CDG	chemically defined group
DM	dry matter
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	Flavour 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
FL-No	FLAVIS number
GC	gas chromatography
GC-FID	gas chromatography with flame ionisation detector
GC–MS	gas chromatography–mass spectrometry
ISO	International standard organisation
LOD	limit of detection
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
MOET	combined margin of exposure (total)
MOE	margin of exposure
NOAEL	no observed adverse effect level
TTC	threshold of toxicological concern
UF	uncertainty factor
WHO	World Health Organisation

ACKNOWLEDGEMENTS

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

CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2010-01516

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How to cite this article: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis, V., Azimonti, G., Bastos, M. L., Christensen, H., Durjava, M., Kouba, M., López-Alonso, M., López Puente, S., Marcon, F., Mayo, B., Pechová, A., Petkova, M., Ramos, F., Sanz, Y., Villa, R. E., Woutersen, R., Brantom, P., Chesson, A., … Dusemund, B. (2024). Safety and efficacy of a feed additive consisting of an essential oil obtained from the wood of *Juniperus deppeana* Steud. (cedarwood Texas oil) for use in all animal species (FEFANA asbl). *EFSA Journal*, *22*(5), e8799. https://doi.org/10.2903/j.efsa.2024.8799