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SCIENTIFIC OPINION

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Safety and efficacy of feed additives consisting of ginkgo tinctures obtained from the leaves of *Ginkgo biloba* L. 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 tinctures obtained from the dried leaves of *Ginkgo biloba* L. (ginkgo tinctures) when used as sensory additives. The tinctures are water/ethanol solutions with a dry matter content of 5.7% (tincture A) and 3.0% (tincture B). The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that the additives under assessment are safe for the target species at the following concentrations in complete feed: (i) ginkgo tincture A at 240 mg/kg for horses and 750 mg/kg for dogs; (ii) ginkgo tincture B at 600 mg/kg for horses and 50 mg/kg for all other animal species. No safety concern would arise for the consumer from the use of ginkgo tinctures up to the maximum proposed use level in feed for the target species. The tinctures should be considered as irritants to skin and eyes, and as dermal and respiratory sensitisers. The use of ginkgo tinctures at the proposed use levels in feed for the target species is not considered to be a risk to the environment. While the available data indicate that Ginkgo preparations have a distinctive flavour profile, there is no evidence that ginkgo tinctures would impart flavour to a food or feed matrix. Therefore, the FEEDAP Panel cannot conclude on the efficacy of the additives.

KEYWORDS

efficacy, flavouring compounds, *Ginkgo biloba* L., ginkgo tincture, 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 feed additive shall submit an application in accordance with Article 7 and 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 the authorisation/re-evaluation of ten additives (namely juniper oil, juniper berry extract (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., ginkgo extract (water-based, wb) and ginkgo tincture from *Ginkgo 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 one out of the seven remaining additives under application: ginkgo tincture (*Ginkgo biloba* L.) 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). 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 feed additives consisting of the product ginkgo tincture (*G. biloba* L.), when used under the proposed conditions of use (see Section 3.3.1.3).

1.2 | Additional information

Ginkgo tincture from *G. biloba* L. is currently authorised as a feed additive according to the entry in the European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003 (2b natural products – botanically defined). It has not been previously assessed by EFSA as a feed additive.

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[5] in support of the authorisation request for the use of ginkgo tincture as feed additive. The dossier was received on 27/3/2024 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2024-00194.[6]

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.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the phytochemical marker in the additives. In particular, for the characterisation of ginkgo tincture the EURL recommended a method based on high-performance liquid chromatography with ultraviolet detection (HPLC-UV) for the determination of the phytochemical marker total flavone glycosides in ginkgo tincture. In addition, the EURL recommended

[1]Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2]On 13/3/2013, EFSA was informed by the applicant that the applicant company changed to FEFANA asbl, Avenue Louise 130 A, Box 1, 1050 Brussels, Belgium.
[3]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, 10.5.2021, p. 5.
[5]FEED dossier reference: FAD-2010-0320.
[6]The original application EFSA-Q-2010-01516 was split on 27/03/2024 and a new EFSA-Q-2024-00194 was generated.

a method based on high-performance thin-layer chromatography (HPTLC) for the determination of total flavonoids in ginkgo tincture.[7]

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of ginkgo tincture is in line with the principles laid down in Regulation (EC) No 429/2008[8] 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, 2012), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the 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, 2019), Statement on the genotoxicity assessment of chemical mixtures (EFSA Scientific Committee, 2019) and Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment (EFSA Scientific Committee, 2019).

3 | ASSESSMENT

This application covers two tinctures, ginkgo tinctures A and B, derived from the dried leaves of *G. biloba* L. They are intended for use as sensory additives (functional group: flavouring compounds). Ginkgo tincture A is intended for use in feed for horses and dogs, tincture B is intended for use in feed and water for drinking for all animal species.

3.1 | Origin and extraction

G. biloba L. is a dioecious tree species commonly called the maidenhair tree or simply ginkgo. It is the only living member of the Ginkgoaceae, a family of gymnosperms now extinct and, for this reason, it is often referred to as a 'living fossil'. The fossil records of the Ginkgoaceae indicate a world-wide distribution, but it seems likely that the modern relatives of *G. biloba* originated in China. It is now widely cultivated as an ornamental species in temperate parts of the world.

Tincture A is obtained by extraction of dried leaves (whole or cut) of *G. biloba* L. (originating from China) using a water/ethanol mixture (1:1, v:v). The ratio of dry raw material to solvent is 1:5 (w:v). Following maceration for 21 days, the tincture is obtained by pressing to remove solid material, and filtration.[9]

Tincture B is produced from the dried leaves of *G. biloba* L. (originating from China, Morocco or France) by extended extraction for [redacted] under ambient conditions with a [redacted]. The ratio of dry raw material to solvent is [redacted] The tincture is then recovered by pressing to separate solid and liquid phases and the extracted solution is then clarified by filtration.[10]

3.2 | Uses other than feed flavouring

Ginkgo leaf (Ginkgonis folium) and Ginkgo dry extract, refined and quantified (Ginkgonis extractum siccum raffinatum et quantificatum) from *Ginkgo biloba* L., are described in monographs of the European Pharmacopoeia 11.0 (PhEur, 2022a, 2022b) and of the European Medicines Agency (EMA, 2015a, 2015b) for medicinal uses.

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

[8]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.

[9]Technical dossier/Supplementary information March 2021/SIn reply_Ginkgo tincture_final.

[10]Technical dossier/Supplementary information March 2021 /SIn_data_Ginkgo tincture_Manghebati_SAS.

3.3 | Ginkgo tinctures

3.3.1 | Characterisation of tincture A

Tincture A has a density of 951–964 kg/m^3 (956 kg/m^3 on average). The additive is an ethanol/water (50/50, v/v) solution, which contains by specification 6% ±1% of plant derived compounds, including ≤ 200 mg/L total bisflavones, ≤ 100 mg/L total ginkgolic acids, ≤ 400 mg/L total terpene lactones and ≤ 500 mg/L total flavonol glycosides.[11]

Table 1 summarises the results of proximate analysis of five batches of the tincture A (of Chinese origin) expressed as % of the tincture (w/w).[12] The solvent represents on average 94.29% of the additive, leaving a dry matter (DM) content of 5.71% (w/w).[13]

TABLE 1 Proximate analysis of ginkgo tincture A (*Ginkgo biloba* L.) based on the analysis of five batches (mean and range).

Constituent	Mean % (w/w)	Range % (w/w)
Dry matter	5.71	5.56–5.89
Lipids	0.1	< 0.1–0.1
Protein	0.24	0.2–0.3
Ash	0.44	0.4–0.5
Fibre	< 0.5	< 0.5
Total sugar	1.22	1.1–1.3
Solvent	94.29	94.11–94.44

The fraction of secondary metabolites was characterised in the same batches of the additive and the results are summarised in Table 2. Total phenolic compounds determined by spectrophotometry (at 760 nm) are expressed as gallic acid equivalents.[14] Individual compounds were determined by high-performance liquid chromatography (HPLC) with an ultraviolet (UV) or evaporative light scattering (ELSD) detector: bisflavones,[15] ginkgolic acids,[16] flavonol glycosides[17] (as quercetin equivalents), organic acids other than ginkgolic acids[18] (UV) and terpene lactones (ELSD).[19]

TABLE 2 Characterisation of the fraction of secondary metabolites of ginkgo tincture A (*Ginkgo biloba* L.) based on the analysis of five batches (mean and range).

Constituent	CAS no	Mean µg/mL	Range µg/mL
Total phenolic compounds	–	2091	1958–2300
Ginkgolic acids		53.1	43.7–60.7
C13:0 and C15:1 (coeluted)	20261-38-5 22910-60-7	37.3	31.7–43.0
C17:1	22910-60-7	15.3	12.0–17.6
Bisflavones		73.3	41.5–98.0
Bilobetin	521-32-4	11.7	5.5–17.9
Ginkgetin+isoginkgetin	481-46-9 548-19-6	52.7	31.7–70.9
Sciadopitysin	521-34-6	8.2	4.3–12.5

(Continues)

[11]Technical dossier/Supplementary information March 2021/ SIn reply_Ginkgo tincture_final.
[12]Technical dossier/Supplementary information March 2021/Annex_II_Nutritional_Analysis_and_Microbiology_Ginkgo.
[13]Technical dossier/Supplementary information March 2021/Annex_III_Determination_of_Dry_Weight_Ginkgo.
[14]Technical dossier/Supplementary information March 2021/Annex_VIII_Photometric_Analysis_Total_Phenols_Ginkgo.
[15]Technical dossier/Supplementary information March 2021/Annex_IV_HPLC_Bisflavones_Ginkgo.
[16]Technical dossier/Supplementary information March 2021/Annex_VI_HPLC Ginkgolic Acids_Ginkgo.
[17]Technical dossier/Supplementary information March 2021/Annex_I_Flavone Glycosides_Ginkgo.
[18]Technical dossier/Supplementary information March 2021/Annex_XII_HPLC_Total Organic Acids.
[19]Technical dossier/Supplementary information March 2021/Annex_V_HPLC_Ginkgolides.

TABLE 2 (Continued)

Constituent	CAS no	Mean µg/mL	Range µg/mL
Flavonoid glycosides		971	853–1154
Quercetin glycoside	–	433	368–519
Kaempferol glycoside	–	429	379–516
Isorhamnetin glycoside	–	89.5	78.6–95.4
Luteolin glycoside	–	19.8	14.9–25.4
Ginkgolides and derivatives (terpene lactones)		352	347–355
Ginkgolide A	15291-75-5	107	94–116
Ginkgolide B	15291-77-7	56.5	43.6–65.0
Ginkgolide C	15291-76-6	55.4	41.6–66.2
Bilobalide	33570-04-6	132	122–144
Organic acids other than ginkgolic acids		29,567	27,635–31,776
Quinic acid	77-95-2	169	124–219
Malic acid	6915-15-7	331	212–396
Shikimic acid	138-59-0	28,774	27,064–31,053
Other acids	–	294	192–375
Total identified		33,107	31,549–35,279

Tincture A was shown to contain 'organic acids other than ginkgolic acids' up to 3.34% (w/w)[20] (3.10% on average), accounting for 55.3% of the DM (53.1% on average). Terpene lactones (ginkgolides and bilobalide) accounted for up to 0.04% (w/w) corresponding to 0.7% of the DM. Total phenolic compounds accounted for up to 0.24% (w/w) (0.22% on average) corresponding to 4.3% of the DM (3.8% on average). The phenolic fraction included ginkgolic acids up to 0.006% (w/w) (corresponding to 0.1% of the DM), and flavonoids, mainly flavonol glycosides up to 0.12% (w/w) (corresponding to 2.2% of the DM), the flavone luteolin glycoside up to 0.003% (w/w) (corresponding to 0.06% of the DM) and bisflavones up to 0.01% (w/w) (corresponding to 0.2% of the DM). The fraction of secondary metabolites accounted on average for 57% of the DM fraction of the tincture (range: 55%–59%) and the other plant constituents for about 43%.

3.3.1.1 | *Impurities*

Data on impurities were provided for three batches of ginkgo tincture A. Lead (0.007–0.011 mg/kg) was detected in all batches, arsenic (0.0054 mg/kg) and cadmium (0.011 mg/kg) were detected in one batch and were below the corresponding limit of quantification (LOQ) in the other batches. Mercury was below the LOQ in all batches. In the same batches mycotoxins (aflatoxins B1, B2, G1 and G2) were below the LOQ and pesticides were below the LOQ in a multiresidue analysis.[21] When specifically analysed, diethyltoluamide (DEET, 0.90–1.6 mg/L) was detected in all three batches and piperonylbutoxide (0.011 mg/kg) in one batch. Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), dioxin-like polychlorinated biphenyls (DL-PCBs) and non-DL-PCBs were analysed in the same batches. The calculated upper bound (UB) concentration was in the range of 4.24–7.64 pg WHO_{2005}-PCDD/F-TEQ/L for the sum of PCCD/F, and was in the range 4.74–8.05 pg WHO_{2005}-PCCD/F + PCB TEQ/L for the sum of PCCD/F and DL-PCBs.[22]

Analysis of microbial contamination of five batches of ginkgo tincture A indicated that *Salmonella* spp. was absent in 25 g. *E. coli* was < 10 colony forming units (CFU)/g and *Enterobacteriaceae* were not detected.[23]

The FEEDAP Panel considers that the level of microbial contamination and detected impurities do not raise safety concerns.

[20]For each batch, the values analysed in each individual batch and expressed as µg/mL were converted into g/100 g or % (w/w) considering the value of the density determined for each individual batch. The values expressed as g/100 g are then related to the DM content determined in the corresponding batch. The values reported in the text are the average and the highest value of the range calculated for the five batches.

[21]Technical dossier/Supplementary information March 2021/Annex_VIII_Mycotoxins, Heavy Metals, Pesticides, Ginkgo. LOQ for heavy metals and arsenic: < 0.005 mg/kg for arsenic, < 0.002 mg/kg for mercury and < 0.0004 mg/kg for cadmium; LOQ for individual pesticides: 0.001–0.005 mg/L; LOQ for mycotoxins: < 0.1 µg/kg for aflatoxins B1, B2, G1 and G2 and ochratoxin A, < 2 µg/kg for zearalenone, α- and β-zearalenone, HT2-toxin, T2-toxin cytrochalasin E and sterigmatocystin, < 5 µg/kg for nivalenol, fusarenon X and diacetoxyscirpenol, and < 10 for deoxynivalenol, deoxynivalenol-3-glycoside, 3-acetyldeoxynivalenol, 15-acetyldeoxynivalenol, citrinin, patulin and fumonisins B1, B2 and B3.

[22]Technical dossier/Supplementary information March 2021/Annex_IX_Dioxins and PCBs residues_Ginkgo. Upper bound concentrations are calculated on the assumption that all values of the different congeners below the limit of quantification are equal to the limit of quantification. TEQ = toxic equivalency factors for dioxins, furans and dioxin-like PCBs established by WHO in 2005 (van den Berg et al., 2006).

[23]Technical dossier/Supplementary information March 2021/Annex_II_ Nutritional_Analysis_and_Microbiology_Ginkgo.

3.3.1.2 | *Shelf-life*

The applicant states that the typical shelf-life of tincture A is at least 12 months, when stored in tightly closed containers under standard conditions. However, no data supporting this statement were provided.

3.3.1.3 | *Conditions of use*

Ginkgo tincture A is intended for use in feed for horses and dogs at maximum proposed use levels of 240 and 750 mg/kg complete feed,[24] respectively.

3.3.2 | Characterisation of tincture B

Tincture B is a yellow to clear brown liquid, with a characteristic green soft odour. It has an average density of 978 kg/m^3 (range: 974–981 kg/m^3) and a pH of 4.2 (4.08–4.42). It is a water/ethanol ([redacted]) solution, which contains [redacted].[25]

Table 3 summarises the results of the analysis of five batches of the additive expressed as % of the tincture (w/w). The solvent represents about 97.0% of the additive leaving a DM content of about 3.0%. The DM consists of ash (0.29% on average) and a plant-derived organic fraction (2.69%). The additive contains hexane extractable compounds (0.024%), total phenolic compounds (0.1141%) expressed as gallic acid equivalents, and separately determined nine flavonoids (0.1038%) expressed as rutin equivalents. Rutin content is on average 0.0103%.

TABLE 3 Major constituents of tincture B (*Ginkgo biloba* L.) based on the analysis of five batches.

Constituent	Method	Mean % (w/w)	Range % (w/w)
Proximate analysis			
Dry matter	Gravimetry	2.979	2.907–3.035
Ash	Gravimetry	0.293	0.269–0.305
Organic fraction	By difference	2.686	2.638–2.736
Hexane extractable fraction	LLE-gravimetry	0.0024	0.0013–0.0031
Solvent	100%-dry matter	97.02	96.97–97.09
Characterisation of the organic fraction			
Total phenolic compounds	Folin–Ciocalteu	0.1141	0.0818–0.1505
Total flavonoids	HPTLC	0.1038	0.0922–0.1185
Rutin	HPTLC	0.0103	0.0090–0.0117

Abbreviations: HPTLC, high-performance thin-layer chromatography; LLE, liquid-liquid extraction.

The secondary metabolites were not characterised as for tincture A. However, tincture B is produced similarly but more diluted than tincture A, as it was obtained with a lower ratio plant parts:solvent ([redacted] vs. 1:5) and less ethanol in the extraction mixture (water/ethanol [redacted] vs. 1:1, tincture B vs. tincture A). This is reflected in the content of total phenolic compounds (0.12% vs. 0.21%). Analytical data on the concentration of ginkgolic acid were not available for tincture B. Considering the similarity in the manufacturing process and that tincture B is more diluted in ethanol and in the content of total phenolic compounds than tincture A, it is assumed that the highest concentration of ginkgolic acids of 0.006% analysed in tincture A (w/w) is not exceeded.

3.3.2.1 | *Impurities*

No information on the concentrations of undesirable compounds in tincture B is given. The applicant controls contamination at the level of the raw material. Specifications are set with suppliers covering cadmium (< 1 mg/kg), mercury (< 0.1 mg/kg) and lead (< 5 mg/kg), polycyclic aromatic hydrocarbons (< 50 μg/kg for the sum of benzo[a]pyrene, benzo[a]anthracene, benzo[b]fluorantene and crysene, and < 10 μg/kg for benzo[a]pyrene). Pesticides should comply with Regulation (EC) No 396/2005.[26]

[24]Concentrations in complete feed based on the maximum proposed use levels of 2.0 and 0.20 mL tincture/head per day for horses and dogs, respectively, tincture/head and day, respectively.

[25]Technical dossier/Supplementary information March 2021 /SIn_data_Ginkgo tincture_Manghebati_SAS.

[26]Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC Text with EEA relevance. OJ L 70, 16.3.2005, p. 1–16.

For microbial contamination specifications include total count ($< 5 \times 10^7$/g), yeast and mould ($< 5 \times 10^5$/g), *E. coli* ($< 10^3$/g) and *Salmonella* (absent in 25 g). Four certificates of analysis of the raw material (ginkgo leaves) showing compliance were provided.[27]

Analysis of impurities in the tincture apparently is made on irregular basis and does not form part of the Hazard Analysis and Critical Control Points (HACCP) plan.

3.3.2.2 | *Shelf-life*

The shelf-life of tincture B is declared by the applicant to be at least 36 months when stored in tightly closed containers under standard conditions. However, no data supporting this statement were provided.

3.3.2.3 | *Conditions of use*

Ginkgo tincture B is intended for use in feed for all animal species. The applicant proposes a maximum concentration of 50 mg ginkgo tincture/kg complete feed or water for drinking for all animal species except horses for which the proposed use level is 600 mg/kg complete feed.

3.3.3 | Safety

The assessment of safety is based on the maximum use levels in complete feed proposed by the applicant of 750 mg/kg for dogs, 240 mg/kg for horses (for tincture A) and 50 mg/kg for all animal species, except horses (600 mg/kg) for tincture B.

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

Ginkgo tincture A consists of 94.3% (w/w) of a water/ethanol (1:1, v/v) mixture. The concentration of plant derived compounds is about 5.7% (w/w) of the tincture. The dry matter includes ash, protein, lipids and carbohydrates, which are not of concern, and are not further considered. The additive contains 'other organic acids' (3.34%, w/w), mainly shikimic acid, quinic acid and malic acid, which are ubiquitous plant components with low toxicity and are not further considered.

Among the secondary metabolites of ginkgo tincture A, up to 0.04% (w/w) consisted of terpene lactones (ginkgolides and bilobalide) and up to 0.24% (w/w) of total phenolic compounds. Within the phenolic fraction, up to 0.006% of tincture A consists of ginkgolic acids and up to 0.13% consists of flavonoids, flavonol glycosides (0.12%, w/w), the flavone luteolin glycoside (0.003%, w/w) and bisflavones (0.01%, w/w) which were identified and quantified individually.

Ginkgo tincture B consists of 97% (w/w) of a [redacted]) mixture, with a content of total phenolic compounds of 0.11%, mostly consisting of flavonoids (0.10%) not further identified. In the absence of analytical data on the secondary metabolites, read-across is applied from tincture A to tincture B. Considering the similarity in the manufacturing process and considering that tincture B is more diluted in ethanol and in the content of total phenolic compounds than tincture A, it is assumed that the highest concentrations of terpene lactones (ginkgolides and bilobalide), ginkgolic acids, bisflavones, flavonol glycosides and luteolin glycoside quantified in tincture A are not exceeded in tincture B.

Secondary plant metabolites (phenolic compounds including flavonoids, ginkgolic acids and terpene lactones) will be assessed based on considerations at the level of the assessment group (see Sections 3.3.4.1–3.3.4.3).

The absorption, distribution, metabolism, excretion (ADME) and the toxicology of the main components of ginkgo tinctures, i.e. flavonol glycosides (quercetin, kaempferol, isorhamnetin) and terpene lactones (ginkgolides A, B, C and J, and bilobalide) have been assessed by the FEEDAP Panel in an opinion on ginkgo extract (EFSA FEEDAP Panel, 2024).

Briefly, the pharmacokinetic study in rats orally exposed to 90 mg/kg body weight (bw) per day of a standardised *Ginkgo biloba* extract (GBE50) showed that the absorbed flavonoids were metabolised and excreted. Similarly, the terpene lactones (ginkgolides and bilobalide) were found to be eliminated from the body very rapidly (Chen et al., 2013).

Based on the available literature submitted by the applicant on the safety of *G. biloba* leaves, their preparations and on their constituents, in particular quercetin and kaempferol, the FEEDAP Panel concluded that the genotoxicity of *Ginkgo biloba* leaf extracts observed in vitro is not expressed in vivo. The tumours observed in the long-term study with GBE50 (NTP, 2013) similar to the feed additive ginkgo extract, are most probably the result of a thresholded carcinogenic mode of action due to oxidative stress and/or enzyme induction via constitutive androstane receptors and not due to a direct DNA reactive mode of action.

In the assessment of the feed additive ginkgo extract, the FEEDAP Panel identified a reference point of 6.25 mg/kg bw per day from a 90-day study with GBE50 as part of the NTP toxicology and carcinogenicity studies (NTP, 2013). The reference point for GBE50 was derived by applying an overall uncertainty factor (UF) of 10 to the lowest observed adverse effect level (LOAEL), which was based on effects seen on liver changes in male rats at all doses. The UF was considered adequate to extrapolate from the LOAEL to a no observed adverse effect level (NOAEL) and to account for the effects seen in the long-term studies and the uncertainty in the relevance of mode of action (liver and thyroid enzyme induction) in the target species (EFSA FEEDAP Panel, 2024).

[27]Technical dossier/Supplementary information March 2021/Annex_01_Ginkgo tincture Manghebati.

From the reference point of 6.25 mg/kg bw per day for ginkgo extract, the FEEDAP Panel derived reference points of 2.0 and 1.0 mg/kg bw per day for flavonol glycosides and terpene lactones (ginkgolides and bilobalide) respectively, considering that they represent 31.3% and 15.4% of the GBE50 tested by NTP, respectively.

Luteolin glycoside has been detected in low concentrations in ginkgo tincture A and is evaluated by applying read-across from hesperidin (EFSA FEEDAP Panel, 2021).

3.3.4 | Safety for the target species

Tolerance studies and/or toxicological studies made with the tinctures under application were not submitted.

In the absence of tolerance studies and/or toxicity data from repeated dose studies in laboratory animals performed with the additive under assessment, the approach to the safety assessment of the mixture is based on its individual components or groups of components (EFSA Scientific Committee, 2019). For flavonol glycosides and terpene lactones, the estimated reference points of 2.0 and 1.0 mg/kg bw per day, respectively, were derived from sub-chronic studies with GBE50 (see Section 3.3.1), considering that they represent, respectively, 31.3% and 15.4% of the test item. For the flavone luteolin glycoside a NOAEL of 500 mg/kg bw was set by read-across from hesperidin (EFSA FEEDAP Panel, 2021). For the group assessment of phenolic compounds, bisflavones and ginkgolic acids, in the absence of toxicological data from which a NOAEL can be derived, the threshold of toxicological concern (TTC) is applied to derive maximum safe feed concentrations for the whole groups in ginkgo tinctures (EFSA FEEDAP Panel, 2017b).

In the next paragraphs, for each group of components, the feed concentration is calculated at the highest proposed use levels in complete feed of 750 mg ginkgo tincture A/kg for dogs, 600 mg ginkgo tincture B/kg for horses and 50 mg ginkgo tincture B/kg for the other species. The calculated maximum safe concentrations in feed for the target species are also reported in the corresponding Tables.

In the absence of analytical data on the concentration of individual components or group of components in tincture B, in a worst-case scenario it is assumed that the same components identified and quantified in tincture A are present in tincture B at the same concentrations as in tincture A.

3.3.4.1 | *Total phenolic compounds including flavonoids*

Among the secondary metabolites, 0.24% are total phenolic compounds including 0.13% flavonoids. In the flavonoid fraction, four bisflavones and four flavonol glycosides were identified and quantified accounting for ≤ 0.01% and ≤ 0.12% of tincture A, respectively. Considering the different structures, bisflavones and flavonol glycosides are assessed in two separate groups. Tincture A also contains the flavone luteolin glycoside in a low concentration (≤ 0.003%), which is separately assessed.

Polyphenols other than flavonoids

In both tinctures, the highest concentration of the fraction of polyphenols after subtraction of values for flavonoids is ≤ 0.11%.

The feed concentrations of polyphenols calculated at the highest proposed use levels in complete feed are reported in Table 4. Although the individual compounds were not identified (with the exception of ginkgolic acids, representing 0.006% of the fraction), the occurrence of phenolic acids, such as hydroxycinnamic acids and its glycosides, have to be expected in the leaves of *G. biloba* according to literature (see EFSA FEEDAP Panel, 2024). These compounds are assigned to Cramer Class I.

TABLE 4 Highest feed concentration of **polyphenols other than flavonoids** from ginkgo tinctures (*Ginkgo biloba* L.) calculated at the highest proposed use levels in complete feed and maximum safe concentrations in feed for the target species calculated by applying the threshold of toxicological concern for Cramer Class I compounds.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration polyphenols (mg/kg complete feed)[b]	Maximum safe concentration polyphenols (mg/kg complete feed)[b]
Chickens for fattening	79	50	0.06	0.3
Laying hens	53	50	0.06	0.5
Turkeys for fattening	59	50	0.06	0.5
Piglets	44	50	0.06	0.6
Pigs for fattening	37	50	0.06	0.7
Sows lactating	30	50	0.06	0.9
Veal calves (milk replacer)	19	50	0.06	1.5
Cattle for fattening	20	50	0.06	1.3
Dairy cows	31	50	0.06	0.9

(Continues)

TABLE 4 (Continued)

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration polyphenols (mg/kg complete feed)[b]	Maximum safe concentration polyphenols (mg/kg complete feed)[b]
Sheep/goats	20	50	0.06	1.3
Horses	20	600	0.70	1.3
Rabbits	50	50	0.06	0.5
Salmonids	18	50	0.06	1.5
Dogs	17	750	0.88	1.6
Cats	20	50	0.06	1.3
Ornamental fish	5	50	0.06	5.9

Abbreviations: bw, body weight; DM, dry matter.

[a]The use levels reported are for tincture B, except dogs, for which the use level for tincture A is reported.

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

The results shown in Table 4 indicate that the feed concentration of polyphenols would be well below the maximum acceptable feed concentration for Cramer Class I (EFSA FEEDAP Panel, 2017b). Therefore, no concern for the target species arises from polyphenols other than flavonoids in ginkgo tinctures A and B.

Bisflavones

Four bisflavones were identified and quantified in tincture A, accounting together for ≤ 0.01%. Tincture B is assumed to contain the same concentration of bisflavones (0.01%).

The feed concentrations of bisflavones calculated at the highest proposed use levels in complete feed were compared to maximum acceptable concentration in feed for Cramer Class III (EFSA FEEDAP Panel, 2017b). The results are shown in Table 5.

TABLE 5 Highest feed concentration of **bisflavones** from ginkgo tinctures (*Ginkgo biloba* L.) calculated at the highest proposed use levels in complete feed and maximum safe concentrations in feed for the target species calculated by applying the threshold of toxicological concern for Cramer Class III compounds.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration bisflavones (mg/kg complete feed)[b]	Maximum safe concentration bisflavones (mg/kg complete feed)[b]
Chickens for fattening	79	50	0.005	0.02
Laying hens	53	50	0.005	0.02
Turkeys for fattening	59	50	0.005	0.02
Piglets	44	50	0.005	0.03
Pigs for fattening	37	50	0.005	0.04
Sows lactating	30	50	0.005	0.05
Veal calves (milk replacer)	19	50	0.005	0.08
Cattle for fattening	20	50	0.005	0.07
Dairy cows	31	50	0.005	0.04
Sheep/goats	20	50	0.005	0.07
Horses	20	600	0.062	0.07
Rabbits	50	50	0.005	0.03
Salmonids	18	50	0.005	0.08
Dogs	17	750	0.077	0.08
Cats	20	50	0.005	0.07
Ornamental fish	5	50	0.005	0.29

Abbreviations: bw, body weight; DM, dry matter.

[a]The use levels reported are for tincture B, except dogs, for which the use level for tincture A is reported.

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

The results shown in Table 5 indicate that bisflavones would be near or below the maximum acceptable feed concentration for Cramer Class III. Therefore, the presence of bisflavones in ginkgo tinctures A and B is not considered of concern for the target species.

Flavonol glycosides

The flavonol glycosides in ginkgo tincture A have been identified and are the same detected in the ginkgo extract evaluated by the FEEDAP Panel (EFSA FEEDAP Panel, 2024) and in GBE50. Flavonol glycosides represent ≤ 0.12% of tincture A. In the current assessment it is assumed that the same flavonol glycosides are present in tincture B and that, in a worst-case scenario, they are present in tincture B at the same concentration as in tincture A.

The feed concentrations of flavonol glycosides calculated at the highest proposed use levels in complete feed are reported in Table 6. Applying an uncertainty factor of 100 to the estimated reference point of 2.0 mg/kg bw per day for the sum of flavonol glycosides (see Section 3.2.3), the safe concentrations of flavonols glycosides in complete feed for the target species were calculated according to the FEEDAP Guidance on the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b). Generally, for cats, an additional UF of 5 is applied, considering their unusually low capacity for glucuronidation of compounds (Court & Greenblatt, 1997; Lautz et al., 2021). Because the reference point was derived applying an additional UF of 10 to the LOAEL for GBE50 (EFSA FEEDAP Panel, 2024), the resulting UF of 1000 was considered adequate. The calculated safe concentrations of flavonol glycosides in feed for the target species are shown in Table 6.

TABLE 6 Highest feed concentration of **flavonol glycosides** from ginkgo tinctures (*Ginkgo biloba* L.) calculated at the highest proposed use levels in complete feed and maximum safe concentrations in feed for the target species calculated using the reference point of 2.0 mg/kg bw per day for flavonol glycosides.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration flavonol glycosides (mg/kg complete feed)[b]	Maximum safe concentration flavonol glycosides (mg/kg complete feed)[b]
Chickens for fattening	79	50	0.06	0.2
Laying hens	53	50	0.06	0.3
Turkeys for fattening	59	50	0.06	0.3
Piglets	44	50	0.06	0.4
Pigs for fattening	37	50	0.06	0.5
Sows lactating	30	50	0.06	0.6
Veal calves (milk replacer)	19	50	0.06	1.0
Cattle for fattening	20	50	0.06	0.9
Dairy cows	31	50	0.06	0.6
Sheep/goats	20	50	0.06	0.9
Horses	20	600	0.71	0.9
Rabbits	50	50	0.06	0.4
Salmonids	18	50	0.06	1.0
Dogs	17	750	0.89	1.1
Cats	20	50	0.06	0.9
Ornamental fish	5	50	0.06	3.9

Abbreviations: bw, body weight; DM, dry matter.

[a]The use levels reported are for tincture B, except dogs, for which the use level for tincture A is reported.

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

The calculated safe concentrations of flavonol glycosides are higher or close to the concentrations of flavonol glycosides in feed resulting from the use of ginkgo tinctures at the proposed use levels in feed. Therefore, the presence of flavonol glycosides in ginkgo tinctures A and B is not considered of concern for the target species.

Luteolin glycoside

Luteolin glycoside is present in the tinctures (A and B) in lower concentrations (≤ 0.003%) than the flavonol glycosides, resulting in feed concentrations of 0.001 mg/kg for all species except dogs and horses, for which the concentration in feed is 0.02 mg/kg. These concentrations are several orders of magnitude below the safe concentrations of luteolin glycoside in feed calculated using the NOAEL of 500 mg/kg bw derived by read-across from hesperidin (EFSA FEEDAP Panel, 2017b). The safe concentrations in feed for the target species ranges between 56 mg/kg in chickens for fattening and 978 mg/kg in ornamental fish.

Overall, no concern for the target species arises from the phenolic fraction and the presence of flavonoids.

3.3.4.2 | *Ginkgolic acids*

Ginkgolic acids represent ≤ 0.006% of tincture A. Tincture B is assumed to contain the same concentration of ginkgolic acids (0.006%). The feed concentrations of ginkgolic acids calculated at the highest proposed use levels in complete feed

were compared to maximum acceptable concentration in feed for Cramer Class III (EFSA FEEDAP Panel, 2017b). The results are shown in Table 7.

TABLE 7 Highest feed concentration of **ginkgolic acids** from ginkgo tinctures (*Ginkgo biloba* L.) calculated at the highest proposed use levels in complete feed and maximum safe concentrations in feed for the target species calculated by applying the threshold of toxicological concern for Cramer Class III compounds.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration ginkgolic acids (mg/kg complete feed)[b]	Maximum safe concentration ginkgolic acids (mg/kg complete feed)[b]
Chickens for fattening	79	50	0.003	0.02
Laying hens	53	50	0.003	0.02
Turkeys for fattening	59	50	0.003	0.02
Piglets	44	50	0.003	0.03
Pigs for fattening	37	50	0.003	0.04
Sows lactating	30	50	0.003	0.05
Veal calves (milk replacer)	19	50	0.003	0.08
Cattle for fattening	20	50	0.003	0.07
Dairy cows	31	50	0.003	0.04
Sheep/goats	20	50	0.003	0.07
Horses	20	600	0.038	0.07
Rabbits	50	50	0.003	0.03
Salmonids	18	50	0.003	0.08
Dogs	17	750	0.048	0.08
Cats	20	50	0.003	0.07
Ornamental fish	5	50	0.003	0.29

Abbreviations: bw, body weight; DM, dry matter.

[a]The use levels reported are for tincture B, except dogs, for which the use level for tincture A is reported.

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

The results shown in Table 7 indicate that ginkgolic acids would be below the maximum acceptable feed concentration. Therefore, the presence of ginkgolic acids in ginkgo tinctures A and B is not considered of concern for the target species.

3.3.4.3 | *Terpene lactones*

Among the secondary metabolites, terpene lactones (ginkgolides and bilobalide) represent 0.04% of tincture A. In the current assessment, it is assumed that terpene lactones are present in tincture B at the same concentration as in tincture A.

The feed concentrations of terpene lactones calculated at the highest proposed use levels in complete feed are reported in Table 8. Applying an UF of 100 to the reference point of 1.0 mg/kg bw per day for the sum of terpene lactones (see Section 3.3.3), the safe concentrations of terpene lactones in complete feed for the target species were calculated according to the FEEDAP Guidance on the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b). As mentioned above, for cats an additional UF of 5 is applied, considering their unusually low capacity for glucuronidation of compounds (Court & Greenblatt, 1997; Lautz et al., 2021). Because the reference point was derived applying an additional UF of 10 to the LOAEL, the resulting UF of 1000 was considered adequate. The calculated safe concentrations of ginkgolides in feed for the target species are shown in Table 8.

TABLE 8 Highest feed concentration of **terpene lactones (ginkgolides and bilobalide)** from ginkgo tinctures (*Ginkgo biloba* L.) calculated at the highest proposed use levels in complete feed and maximum safe concentrations in feed for the target species calculated using the reference point of 1.0 mg/kg bw per day for ginkgolides.

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration terpene lactones (mg/kg complete feed)[b]	Maximum safe concentration terpene lactones (mg/kg complete feed)[b]
Chickens for fattening	79	50	0.02	0.1
Laying hens	53	50	0.02	0.2
Turkeys for fattening	59	50	0.02	0.2
Piglets	44	50	0.02	0.2
Pigs for fattening	37	50	0.02	0.2
Sows lactating	30	50	0.02	0.3

TABLE 8 (Continued)

Animal category	Daily feed intake (g DM/kg bw)	Proposed use level in feed[a] (mg additive/kg complete feed)[b]	Highest feed concentration terpene lactones (mg/kg complete feed)[b]	Maximum safe concentration terpene lactones (mg/kg complete feed)[b]
Veal calves (milk replacer)	19	50	0.02	0.5
Cattle for fattening	20	50	0.02	0.4
Dairy cows	31	50	0.02	0.3
Sheep/goats	20	50	0.02	0.4
Horses	20	600	0.22	0.4
Rabbits	50	50	0.02	0.2
Salmonids	18	50	0.02	0.5
Dogs	17	750	0.28	0.5
Cats	20	50	0.02	0.4
Ornamental fish	5	50	0.02	2.0

Abbreviations: bw, body weight; DM, dry matter.

[a]The use levels reported are for tincture B, except dogs, for which the use level for tincture A is reported.

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

The calculated safe concentrations of terpene lactones (ginkgolides and bilobalide) for the target species are higher or close to the concentrations in feed resulting from the use of ginkgo tinctures at the proposed use levels in feed. Therefore, the presence of terpene lactones ginkgo tinctures A and B is not considered of concern for the target species.

3.3.4.4 | *Use in water for drinking*

The FEEDAP Panel considers that for tincture B 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.

3.3.4.5 | *Conclusions on safety for the target species*

The FEEDAP Panel concludes that the ginkgo tinctures are safe at the maximum proposed use levels in complete feed:

- ginkgo tincture A at 240 mg/kg for horses and 750 mg/kg for dogs,
- ginkgo tincture B at 600 mg/kg for horses and 50 mg/kg for all other animal species.

The FEEDAP Panel considers that the use of tincture B 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.

3.3.5 | Safety for the consumer

No data on residues in products of animal origin were made available for any of the constituents of the tinctures.

Considering the low concentration of the constituents of ginkgo tinctures and their expected limited retention in tissues, the FEEDAP Panel considers that it is unlikely that the use of the additives in animal feed would result in a relevant intake of the individual constituents by humans consuming products of animal origin.

The exposure of humans consuming products of animals exposed to the additives will be lower compared to the exposure of the animals, considering absorption, metabolism and excretion of the compounds by target animals. Therefore, no safety concern would arise for the consumer from the use of ginkgo tinctures up to the maximum proposed use level in feed for the target species.

3.3.6 | Safety for the user

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

The additives contain ginkgolic acids, which are considered contact allergens (Hori et al., 1997). The applicant provided information according to Classification, Labelling and Packaging (CLP) Regulation (EC) 1272/2008[28] of ginkgolic acids[29] and ethanol[30] in the tinctures.

The additives should be considered as irritants to skin and eyes, and as dermal and respiratory sensitisers.

3.3.7 | Safety for the environment

The most abundant constituents in ginkgo tincture, flavonols (quercetin, kaempferol, isorhamnetin) and the corresponding flavonol glycosides, as well as organic acids other than ginkgolic acids (malic acid, quinic acid, fumaric acid, shikimic acid, etc.) are ubiquitous compounds naturally present in feed and food and therefore are not expected to be of concern for the environment.

The additive under assessment also contains terpene lactones (ginkgolides and bilobalide). At the proposed use levels in feed for food-producing animals, their concentration in feed would range between 0.02 and 0.09 mg/kg. Because of the very low concentrations in feed and considering the degradation of terpene lactones by the metabolism in the target animals and environmental processes, the use of the ginkgo tinctures at the proposed conditions of use is not considered to be a risk to the environment.

3.4 | Efficacy

G. biloba or its extracts are not listed in Fenaroli's Handbook of Flavour Ingredients (Burdock, 2009) or by the Flavour and Extract Manufactures Association (FEMA). However, infusions of Ginkgo leaves are widely consumed as a tea and other extracts may be used in food supplements. The applicant provided data in the form of sensory evaluations describing the taste and aroma characteristics of such infusions (EFSA FEEDAP Panel, 2024).

While the available data indicate that *Ginkgo* preparations have a distinctive flavour profile, there is no evidence that ginkgo tinctures would impart flavour to a food or feed matrix. Therefore, the FEEDAP Panel cannot conclude on the efficacy of ginkgo tinctures.

4 | CONCLUSION

The following conclusions apply to ginkgo tinctures with ginkgolic acids up to 0.006% (w/w).

Ginkgo tinctures from the dried leaves of *Ginkgo biloba* L. are safe for target species at the maximum proposed use levels in complete feed:

- ginkgo tincture A at 240 mg/kg for horses and 750 mg/kg for dogs,
- ginkgo tincture B at 600 mg/kg for horses and 50 mg/kg for all other animal species.

The FEEDAP Panel considers that the use of tincture B 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 safety concern would arise for the consumer from the use of ginkgo tinctures up to the maximum proposed use level in feed for the target species.

Ginkgo tinctures should be considered as irritant to skin and eyes, and as dermal and respiratory sensitisers.

The use of ginkgo tinctures at the proposed use levels in feed is not expected to pose a risk to the environment.

While the available data indicate that *Ginkgo* preparations have a distinctive flavour profile, there is no evidence that ginkgo tincture(s) would impart flavour to a food or feed matrix. Therefore, the FEEDAP Panel cannot conclude on the efficacy of ginkgo tinctures.

5 | RECOMMENDATIONS

The Panel recommends that the content of ginkgolic acids in ginkgo tinctures should be ≤ 0.006% (w/w).

[28]Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. *OJ L 353, 31.12.2008, p. 1–1355.*

[29]Technical dossier/Supplementary information March 2021/SIn reply Ginkgo tincture final. H319: eye irritation; H315: skin irritation; H317: skin sensitization; H 335: respiratory irritation.

[30]Technical dossier/Supplementary information March 2024/Annex_Qi_Ginkgo Biloba_Tincture_MSDS1 and MSDS2. H319: moderate eye irritation; H315: skin irritation.

6 | 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. 7,150,727) that, in view of the workload, the evaluation of applications on feed flavourings would be re-organised by giving priority to the assessment of the chemically defined feed flavourings, as agreed with the European Commission
24/06/2015	Technical hearing during risk assessment with the applicant according to the "EFSA's Catalogue of support initiatives during the life-cycle of applications for regulated products": data requirement for the risk assessment of botanicals
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*
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
03/03/2021	Reception of supplementary information from the applicant (partial dataset: ginkgo tincture) - Scientific assessment remains suspended
10/03/2023	Reception of supplementary information from the applicant (partial dataset: ginkgo extract) - Scientific assessment remains suspended
14/03/2023	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives- Scientific assessment restarted
25/07/2023	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 the consumer, efficacy*
04/12/2023	Reception of supplementary information from the applicant (partial dataset: ginkgo extract and ginkgo tincture). Scientific assessment restarted
14/03/2024	Reception of supplementary information from the applicant (partial dataset: ginkgo tincture)
27/03/2024	The application was split and a new EFSA-Q-2024-00194 was assigned to the additive included in the present assessment. Scientific assessment re-started for the additive included in the present assessment
18/04/2024	Opinion adopted by the FEEDAP Panel on ginkgo tincture (EFSA-Q-2024-00194). End of the Scientific assessment for the additive included in the present assessment.

ABBREVIATIONS

ADME	absorption, distribution, metabolism and excretion
BW	body weight
CAS	Chemical Abstracts Service
CD	Commission Decision
CDG	chemically defined group
CFU	colony forming unit
DEET	diethyltoluamide
DL	dioxin-like
DM	dry matter
ELSD	evaporative light scattering
EMA	European Medicines Agency
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
FFAC	Feed Flavourings authorisation Consortium of FEFANA (EU Association of Specialty Feed Ingredients and their Mixtures)
HACCP	hazard analysis and critical control points
GBE50	standardised *Ginkgo biloba* extract
HPLC-UV	high-performance liquid chromatography with ultraviolet detection
HPTLC	high-performance thin-layer chromatography
LOAEL	lowest observed adverse effect level
LOQ	limit of quantification
NOAEL	no observed adverse effect level
NTP	National Toxicology Program
PCBs	polychlorinated biphenyls
PCDD	polychlorinated dibenzo-*p*-dioxin
PCDF	polychlorinated dibenzofuran
PhEur	European Pharmacopoeia

TTC threshold of toxicological concern
UB upper bound
UF uncertainty factor
WHO World Health Organization

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REQUESTOR
European Commission

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