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Safety and efficacy of 26 compounds belonging to chemical group 3 (α,β -unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids and esters) when used as flavourings for all animal species and categories

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Abstract

Following a request from the European Commission, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of 26 compounds belonging to chemical group 3 (α,β -unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids and esters). They are all currently authorised as flavours in food. The FEEDAP Panel was unable to perform the assessment of non-2(*cis*)-en-1-ol [02.112] in the absence of data on its purity. The FEEDAP Panel concludes that hex-2-en-1-ol [02.020], pent-2-en-1-ol [02.050], 2-dodecenal [05.037], nona-2,4-dienal [05.071], *trans*-2-nonenal [05.072], hex-2(*trans*)-enal [05.073], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], deca-2(*trans*),4(*trans*)-dienal [05.140], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], *tr*-2, *tr*-4-nonadienal [05.194], *tr*-2, *tr*-4-undecadienal [05.196], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396] are safe at the proposed maximum use level of 5 mg/kg feed for all animal species; nona-2,6-dien-1-ol [02.049], *trans*-2, *cis*-6-nonadien-1-ol [02.231], nona-2(*trans*),6(*cis*)-dienal [05.058], nona-2(*trans*),6(*trans*)-dienal [05.172], allyl heptanoate [09.097] and allyl hexanoate [09.244] are safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species. No safety concern would arise for the consumer from the use of these compounds up to the highest safe levels in feed. In the absence of studies to assess the safety for the user, the FEEDAP Panel cannot conclude on the safety for the users when handling the additives. No environmental risk is foreseen for these compounds at the concentrations considered safe for the target species. Since the 25 compounds are used in food as flavourings and their function is essentially the same as that in food, no further demonstration of efficacy is necessary.

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Keywords: sensory additives, flavourings, α,β -unsaturated straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids/esters, chemical group 3, safety

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Table of contents

Abstract.....	1
1. Introduction.....	4
1.1. Background and Terms of Reference.....	4
1.2. Additional information.....	5
2. Data and methodologies.....	5
2.1. Data.....	5
2.2. Methodologies.....	5
3. Assessment.....	6
3.1. Characterisation.....	6
3.1.1. Characterisation of flavouring substances.....	6
3.1.2. Shelf-life.....	9
3.1.3. Conditions of use.....	9
3.2. Safety.....	9
3.2.1. Absorption, distribution, metabolism and excretion.....	9
3.2.2. Toxicological studies.....	10
3.2.3. Safety for the target species.....	10
3.2.3.1. Conclusions on safety for the target species.....	11
3.2.4. Safety for the consumer.....	11
3.2.5. Safety for the user.....	12
3.2.6. Safety for the environment.....	12
3.3. Efficacy.....	12
4. Conclusions.....	12
Documentation provided to EFSA.....	13
Chronology.....	13
References.....	13
Abbreviations.....	15
Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Chemically Defined Flavourings – Group 03 α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes.....	16

1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003¹ establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of 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 7 years after the entry into force of this Regulation.

The European Commission received a request from the Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)² for authorisation of 43 substances (geraniol, hex-2-en-1-ol, 3,7,11-trimethyldodeca-2,6,10-trien-1-ol, nona-2,6-dien-1-ol, pent-2-en-1-ol, nerol, non-2(*cis*)-en-1-ol, *tr*-2, *cis*-6-nonadien-1-ol, citral (mixture of geraniol and neral), 2-dodecenal, nona-2(*trans*),6(*cis*)-dienal, nona-2,4-dienal, *trans*-2-nonenal, hex-2(*trans*)-enal, 2,4-decadienal, 2,4-heptadienal (or hepta-2,4-dienal), deca-2(*trans*),4(*trans*)-dienal, dodec-2(*trans*)-enal, hept-2(*trans*)-enal, non-2-enal, nona-2(*trans*),6(*trans*)-dienal, undec-2(*trans*)-enal, *trans*-2-octenal, *trans*-2-decenal, *tr*-2, *tr*-4-nonadienal, *tr*-2, *tr*-4-undecadienal, 2-methyl-2-pentenoic acid, 2-methylcrotonic acid, geranyl acetate, geranyl butyrate, geranyl formate, allyl heptanoate, geranyl propionate, neryl propionate, neryl formate, neryl acetate, allyl hexanoate, ethyldeca-2(*trans*),4(*cis*)-dienoate, hex-2(*trans*)-enyl acetate, hex-2-enyl butyrate, neryl isobutyrate, geranyl isobutyrate and prenyl acetate) belonging to chemical group (CG) 3, when used as a feed additive for all animal species (category: sensory additives; functional group: flavourings). CG 3 for flavouring substances is defined in Commission Regulation (EC) No 1565/2000³ as ‘ α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohol and acetal containing α,β -unsaturated alcohols or aldehydes. No aromatic or heteroaromatic moiety as a component of an ester or acetal.’ During the course of the assessment, this application was split and the present opinion covers 26 out of the 43 substances under application (see Section 1.2).

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). During the course of the assessment, the applicant withdrew the application for the use of chemically defined flavourings in water for drinking.⁴ EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 1 December 2010.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of hex-2-en-1-ol [EU Flavour Information System (FLAVIS) number 02.020], nona-2,6-dien-1-ol [02.049], pent-2-en-1-ol [02.050], non-2(*cis*)-en-1-ol [02.112], *trans*-2, *cis*-6-nonadien-1-ol [02.231], 2-dodecenal [05.037], nona-2(*trans*),6(*cis*)-dienal [05.058], nona-2,4-dienal [05.071], *trans*-2-nonenal [05.072], hex-2(*trans*)-enal [05.073], 2,4-decadienal [05.081], hepta-2,4-dienal [05.058], deca-2(*trans*),4(*trans*)-dienal [05.140], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], nona-2(*trans*),6(*trans*)-dienal [05.172], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], *tr*-2, *tr*-4-nonadienal [05.194], *tr*-2, *tr*-4-undecadienal [05.196], allyl heptanoate [09.097], allyl hexanoate [09.244], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396] when used under the proposed conditions of use (see Section 3.1.3).

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 Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG), Avenue Louise 130A, B-1050, Brussels, Belgium.

³ 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.

⁴ On 10 March 2016, EFSA was informed by the European Commission on the withdrawal of the application for re-authorisation of chemically defined flavourings – use in water.

1.2. Additional information

The initial application concerned 43 compounds assigned to this CG, intended to be used as feed flavourings for all animal species. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) has already delivered an opinion on 17 out of the 43 compounds (EFSA FEEDAP Panel, 2016).

The remaining 26 compounds were excluded from the previous assessment because the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) was not in the position to conclude on the genotoxicity of this group of compounds and expressed the need for additional data to complete the assessment (EFSA CEF Panel, 2014a,b). Subsequently, the EFSA CEF Panel delivered two opinions on the 26 compounds, concluding that there are no genotoxicity concerns (EFSA CEF Panel, 2018; EFSA FAF Panel, 2018).

Consequently, this opinion deals with 26 compounds, namely hex-2-en-1-ol [02.020], nona-2,6-dien-1-ol [02.049], pent-2-en-1-ol [02.050], non-2(*cis*)-en-1-ol [02.112], *trans*-2, *cis*-6-nonadien-1-ol [02.231], 2-dodecenal [05.037], nona-2(*trans*),6(*cis*)-dienal [05.058], nona-2,4-dienal [05.071], *trans*-2-nonenal [05.072], hex-2(*trans*)-enal [05.073], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], deca-2(*trans*),4(*trans*)-dienal [05.140], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], nona-2(*trans*),6(*trans*)-dienal [05.172], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], *tr*-2, *tr*-4-nonadienal [05.194], *tr*-2, *tr*-4-undecadienal [05.196], allyl heptanoate [09.097], allyl hexanoate [09.244], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396], excluded from the previous opinion.

The 26 compounds are currently listed in the European Union (EU) database of flavouring substances (also named Union list)⁵ and in the EU Register of Feed Additives,⁶ and thus authorised for use in food and feed in the EU. They have not been previously assessed by EFSA as feed additives.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁷ in support of the authorisation request for the use of ' α,β -unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids and esters' as feed additives.

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 EU Reference Laboratory (EURL) report as it relates to the methods used for the control of the ' α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids, acetals and esters with esters containing α,β -unsaturated alcohol and acetal containing α,β -unsaturated alcohols or aldehydes. No aromatic or heteroaromatic moiety as a component of an ester or acetal in animal feed.' The Executive Summary of the EURL report can be found in Annex A.⁸

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of 26 compounds belonging to CG 3 is in line with the principles laid down in Regulation (EC) No 429/2008⁹ and the relevant guidance documents: Guidance for the preparation of dossiers for sensory additives (EFSA FEEDAP Panel, 2012a), Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008), Guidance for the preparation of dossiers for additives already authorised for use in food (EFSA FEEDAP Panel, 2012b), Guidance for establishing the safety of additives for the

⁵ 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.

⁶ https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed-eu-reg-comm_register_feed_additives_1831-03.pdf

⁷ FEED dossier reference: FAD-2010-0416.

⁸ The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/default/files/FiniRep-FAD-2010-0124.pdf>

⁹ 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.

consumer (EFSA FEEDAP Panel, 2012c), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012d).

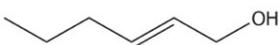
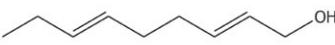
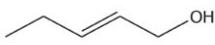
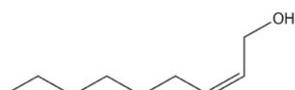
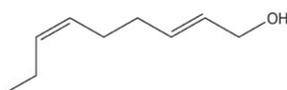
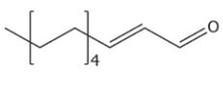
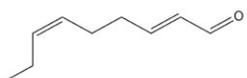
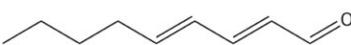
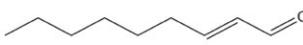
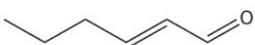
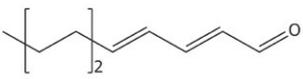
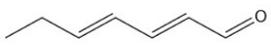
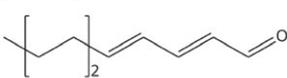
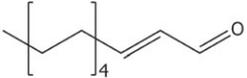
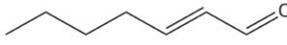
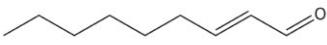
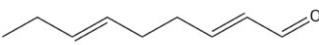
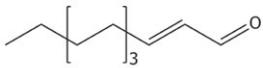
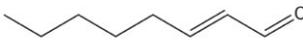
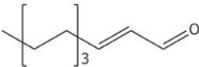
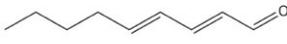
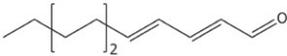
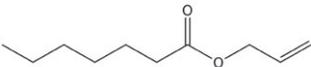
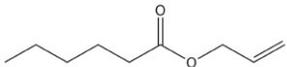
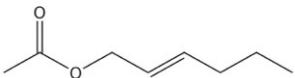
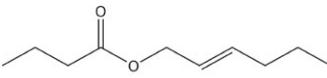
3. Assessment

The additives under assessment are 26 compounds belonging to CG 3 – ‘ α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohol and acetal containing α,β -unsaturated alcohols or aldehydes’, intended for use as sensory additives (functional group: flavouring compounds) in feed for all animal species.

3.1. Characterisation

3.1.1. Characterisation of flavouring substances

The molecular structures of the 26 additives under assessment are shown in Figure 1 and their physicochemical characteristics in Table 1.

Hex-2-en-1-ol ^(a) [02.020] 	Nona-2,6-dien-1-ol ^(a) [02.049] 	Pent-2-en-1-ol ^(a) [02.050] 
Non-2(<i>cis</i>)-en-1-ol [02.112] 	<i>trans</i> -2, <i>cis</i> -6-Nonadien-1-ol [02.231] 	2-Dodecenal ^(a) [05.037] 
Nona-2(<i>trans</i>),6(<i>cis</i>)-dienal [05.058] 	Nona-2,4-dienal ^(a) [05.071] 	<i>trans</i> -2-Nonenal [05.072] 
Hex-2(<i>trans</i>)-enal [05.073] 	2,4-Decadienal ^(a) [05.081] 	Hepta-2,4-dienal ^(a) [05.084] 
Deca-2(<i>trans</i>),4(<i>trans</i>)-dienal [05.140] 	Dodec-2(<i>trans</i>)-enal [05.144] 	Hept-2(<i>trans</i>)-enal [05.150] 
Non-2-enal ^(a) [05.171] 	Nona-2(<i>trans</i>),6(<i>trans</i>)-dienal [05.172] 	Undec-2(<i>trans</i>)-enal [05.184] 
<i>trans</i> -2-Octenal [05.190] 	<i>trans</i> -2-Decenal [05.191] 	<i>tr</i> -2, <i>tr</i> -4-Nonadienal [05.194] 
<i>tr</i> -2, <i>tr</i> -4-Undecadienal [05.196] 	Allyl heptanoate [09.097] 	Allyl hexanoate [09.244] 
Hex-2(<i>trans</i>)-enyl acetate [09.394] 	Hex-2-enyl butyrate ^(a) [09.396] 	

(a): mixture of *cis/trans* isomers, the *trans*-isomer or the *trans, trans*-isomer is shown.

Figure 1: Molecular structures, EU register names and [FLAVIS numbers] of the 26 flavouring compounds under assessment

Table 1: Chemical Abstracts Service (CAS) and FLAVIS numbers and some characteristics of the chemically defined flavourings under assessment

EU Register name	CAS No	FLAVIS No	Molecular formula	Molecular weight	Physical state	Log $K_{ow}^{(a),(b)}$
Hex-2-en-1-ol	2305-21-7	02.020	C ₆ H ₁₂ O	100.16	Liquid	1.61
Nona-2,6-dien-1-ol	7786-44-9	02.049	C ₉ H ₁₆ O	140.23	Liquid	2.87
Pent-2-en-1-ol	20273-24-9	02.050	C ₅ H ₁₀ O	86.13	Liquid	1.12
Non-2(<i>cis</i>)-en-1-ol	41453-56-9	02.112	C ₉ H ₁₈ O	142.23	Liquid	3.08
<i>trans</i> -2, <i>cis</i> -6-Nonadien-1-ol	28069-72-9	02.231	C ₉ H ₁₆ O	140.22	Liquid	2.87
2-Dodecenal	4826-62-4	05.037	C ₁₂ H ₂₂ O	182.31	Liquid	4.53
Nona-2(<i>trans</i>),6(<i>cis</i>)-dienal	557-48-2	05.058	C ₉ H ₁₄ O	138.21	Liquid	2.84
Nona-2,4-dienal	6750-03-4	05.071	C ₉ H ₁₄ O	138.21	Liquid	2.84
<i>trans</i> -2-Nonenal	18829-56-6	05.072	C ₉ H ₁₆ O	140.22	Liquid	3.06
Hex-2(<i>trans</i>)-enal	6728-26-3	05.073	C ₆ H ₁₀ O	98.14	Liquid	1.58
2,4-Decadienal	2363-88-4	05.081	C ₁₀ H ₁₆ O	152.24	Liquid	3.33
Hepta-2,4-dienal	4313-03-5	05.084	C ₇ H ₁₀ O	110.16	Liquid	1.86
Deca-2(<i>trans</i>),4(<i>trans</i>)-dienal	2363-88-4	05.140	C ₁₀ H ₁₆ O	152.24	Liquid	3.33
Dodec-2(<i>trans</i>)-enal	20407-84-5	05.144	C ₁₂ H ₂₂ O	182.31	Liquid	4.53
Hept-2(<i>trans</i>)-enal	18829-55-5	05.150	C ₇ H ₁₂ O	112.17	Liquid	2.07
Non-2-enal	2463-53-8	05.171	C ₉ H ₁₆ O	140.22	Liquid	3.06
Nona-2(<i>trans</i>),6(<i>trans</i>)-dienal	17587-33-6	05.172	C ₇ H ₁₂ O	138.21	Liquid	2.84
Undec-2(<i>trans</i>)-enal	53448-07-0	05.184	C ₁₁ H ₂₀ O	168.27	Liquid	4.04
<i>trans</i> -2-Octenal	2548-87-0	05.190	C ₈ H ₁₄ O	126.20	Liquid	2.57
<i>trans</i> -2-Decenal	3913-81-3	05.191	C ₁₀ H ₁₈ O	154.25	Liquid	3.55
<i>tr</i> -2, <i>tr</i> -4-Nonadienal	5910-87-2	05.194	C ₉ H ₁₄ O	138.21	Liquid	2.84
<i>tr</i> -2, <i>tr</i> -4-Undecadienal	30361-29-6	05.196	C ₁₁ H ₁₈ O	166.26	Liquid	3.82
Allyl heptanoate	142-19-8	09.097	C ₁₀ H ₁₈ O ₂	170.25	Liquid	3.67
Allyl hexanoate	123-68-2	09.244	C ₉ H ₁₆ O ₂	156.22	Liquid	3.18
Hex-2(<i>trans</i>)-enyl acetate	2497-18-9	09.394	C ₈ H ₁₄ O ₂	142.20	Liquid	2.61
Hex-2-enyl butyrate	53398-83-7	09.396	C ₁₀ H ₁₈ O ₂	170.25	Liquid	3.60

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

(a): Logarithm of octanol–water partition coefficient.

(b): Taken from Pubchem or Generated from EPI-Suite 4.01.

The 26 compounds are all synthetically produced. Typical routes of synthesis are described for each compound.¹⁰

Data were provided on the batch to batch variation in five batches of each additive except five compounds. Owing to the low use volume (< 2 kg/year), data on two batches were provided for nona-2,6-dien-1-ol [02.049] and hex-2-enyl butyrate [09.396], data on one batch only for nona-2,4-dienal [05.071], 2,4-decadienal [05.081] and allyl heptanoate [09.097].¹¹ For non-2(*cis*)-en-1-ol [02.112], no data on the purity were provided. Therefore, this compound was excluded from further assessment. For the remaining 25 compounds, the content of the active substance exceeded the JECFA specifications (Table 2).

¹⁰ Technical dossier/Section II.

¹¹ Technical dossier/Section II/Annex 2.1 and Supplementary information May 2011.

Table 2: Identity of the substances and data on purity

EU Register name	FLAVIS No	JECFA minimum specification % ^(a)	Assay % ⁽ⁱ⁾	
			Average	Range
Hex-2-en-1-ol ^(b)	02.020	95	96.1	95.8–96.5
Nona-2,6-dien-1-ol ^(b)	02.049	95 ^(c)	99.2	98.8–99.6
Pent-2-en-1-ol ^(b)	02.050	95	99.8 ^(d)	99.4–99.9
Non-2(<i>cis</i>)-en-1-ol	02.112	96	–	–
<i>trans</i> -2, <i>cis</i> -6-Nonadien-1-ol	02.231	92	95.5	92.5–99.5
2-Dodecenal ^(b)	05.037	93 ^{(b),(e)}	96.2	94.0–99.8
Nona-2(<i>trans</i>),6(<i>cis</i>)-dienal	05.058	92 ^(f)	96.3	96.0–96.9
Nona-2,4-dienal ^(b)	05.071	89 ^{(c),(g)}	90.0	90.0–90.0
<i>trans</i> -2-Nonenal	05.072	92 ^(h)	96.9	95.9–98.6
Hex-2(<i>trans</i>)-enal	05.073	92 ⁽ⁱ⁾	98.9	98.1–99.3
2,4-Decadienal ^(b)	05.081	89 ^{(c),(j)}	93.0	93.0–93.0
Hepta-2,4-dienal ^(b)	05.084	92 ^(k)	93.2	90.2–99.4
Deca-2(<i>trans</i>),4(<i>trans</i>)-dienal	05.140	89 ^(l)	97.4	94.7–98.5
Dodec-2(<i>trans</i>)-enal	05.144	89 ^(m)	98.5	94.7–99.6
Hept-2(<i>trans</i>)-enal	05.150	97	97.8	97.0–98.6
Non-2-enal ^(b)	05.171	92 ^{(c),(n)}	97.2	96.0–98.0
Nona-2(<i>trans</i>),6(<i>trans</i>)-dienal	05.172	97	97.5	96.8–98.2
Undec-2(<i>trans</i>)-enal	05.184	95	98.5	96.7–98.7
<i>trans</i> -2-Octenal	05.190	92 ^(o)	96.5	95.0–98.1
<i>trans</i> -2-Decenal	05.191	92 ^(p)	96.6	96.1–97.3
<i>tr</i> -2, <i>tr</i> -4-Nonadienal	05.194	89 ^(q)	97.6	89.0–100
<i>tr</i> -2, <i>tr</i> -4-Undecadienal	05.196	91 ^(r)	98.2	97.6–99.1
Allyl heptanoate	09.097	97 ^{(c),(s)}	99.9	99.9
Allyl hexanoate	09.244	98 ^(s)	99.7	99.0–99.9
Hex-2(<i>trans</i>)-enyl acetate	09.394	90 ^(t)	97.8	96.0–99.0
Hex-2-enyl butyrate ^(b)	09.396	90 ^(c)	98.0	98.0–98.0

EU: European Union; FLAVIS number: EU Flavour Information System numbers; JECFA: The Joint FAO/WHO Expert Committee on Food Additives.

(a): FAO (2006).

(b): Sum of *cis/trans* isomers.

(c): production volume < 2 kg/year

(d): (Z)-isomer representing on average 97.7% (97.0–98.4%).

(e): secondary components: 3–4% 2-dodecenoic acid.

(f): secondary component: 4–7% (E,E)-2,6-nonadienal.

(g): at least 89% (predominantly E,E); secondary components 5–6% 2,4-nonadien-1-ol and 1–2% 2-nonen-1-ol (EFSA CEF Panel, 2018).

(h): secondary component: 3–4% 2-nonenic acid.

(i): secondary component: 3–4% 2-hexenoic acid.

(j): secondary components: mixture of the (*cis, cis*)-, (*cis, trans*)- and (*trans, cis*)-2,4-decadienals (sum of all isomers 95%); acetone and isopropanol (EFSA CEF Panel, 2018).

(k): at least 92% (predominantly E,E); secondary components 2–4% (E,Z)-2,4-heptadienal and 2–4% 2,4-heptadienoic acid (EFSA CEF Panel, 2018).

(l): secondary components: 4–5% deca-2(*trans*),4(*cis*)-dienal, < 1% deca-2(*cis*),4(*cis*)-dienal, < 0.5% deca-2(*cis*),4(*trans*)-dienal and < 0.1% 2,4-decadienoic acid (EFSA CEF Panel, 2018).

(m): secondary component: 2–3% 2-dodecenoic acid.

(n): secondary component: 3–4% 2-nonenic acid.

(o): secondary components: 3–4% 2-octenoic acid and ethyl octanoate.

(p): secondary component: 3–4% 2-decenoic acid

(q): name in the Union List to be changed to (2E, 4E)-nona-2,4-dienal. At least 89%; secondary components at least 5% 2,4-nonadien-1-ol and 2-nonen-1-ol and other isomers of 2,4-nonadienal (EFSA CEF Panel, 2018).

(r): name in the Union List to be changed to (2E, 4E)-undeca- 2,4-dienal. 90–95% E,E with 0.1–8% E,Z (EFSA CEF Panel, 2018).

(s): allyl alcohol 0.1% max.

(t): secondary components: 5–6% (Z)-2-hexenyl acetate.

Potential contaminants are considered as part of the product specification and are monitored as part of the Hazard Analysis and Critical Control Point procedure applied by all consortium members. The parameters considered include residual solvents, heavy metals and other undesirable substances. However, no evidence of compliance was provided for these parameters.

3.1.2. Shelf-life

The shelf-life of the compounds under assessment is stated to range from 8 to 36 months, when stored in closed containers under recommended conditions. This assessment is made on the basis of compliance with the original specification over this storage period.

3.1.3. Conditions of use

The applicant proposes the use of all of the 25 compounds under assessment in feed for all animal species without withdrawal time. For all the additives, the applicant proposes a normal use level of 1 mg/kg feed and a high use level of 5 mg/kg complete feed.

3.2. Safety

The assessment of safety is based on the high use level proposed by the applicant (5 mg/kg complete feed).

The compounds under assessment have been recently evaluated by EFSA as food flavourings (EFSA CEF Panel, 2018; EFSA FAF Panel, 2018).

3.2.1. Absorption, distribution, metabolism and excretion

The compounds of CG 3 under assessment in the present opinion are primary unsaturated alcohols, aldehydes (enals and dienals) and esters. In general, compounds belonging to CG 3 are rapidly absorbed, distributed, metabolised and excreted (WHO, 1997, 1999, 2004a,b, 2005, 2006; EFSA CEF Panel, 2010, 2013).

In 2016, the FEEDAP Panel delivered an opinion on 17 compounds belonging to CG 3 and summarised the metabolic pathways involved in their biotransformation (EFSA FEEDAP Panel, 2016). The 25 compounds under assessment are metabolised via the same metabolic pathways: (i) hydrolysis of esters; (ii) oxidation of linear alcohols and aldehydes to acids by high capacity NAD⁺/NADP-dependent enzymes; (iii) reduction of aldehydes to alcohols by NAD(P)H-dependent reductases; (iv) conjugation of alcohols with glucuronic acid; (v) β -oxidation of carboxylic acids. The α,β -unsaturated enals and dienals are expected to be oxidised to the corresponding acid which is completely metabolised in the fatty acid β -oxidation pathway (β -oxidative cleavage and complete metabolism via the tricarboxylic acid cycle). Due to their electrophilic characteristics, they can also be detoxified by conjugation with glutathione, directly or enzyme mediated, and excreted as mercapturic acid derivatives (WHO, 2004b, 2006).

ADME studies in laboratory animals were made available for *trans*-2-nonenal [05.072] and *trans*-2-hexenal [05.073]. They are shortly described below.

Male Wistar rats ($n = 10$) were given by gavage *trans*-2-nonenal or *trans*-2-hexenal as a single dose of 100 mg/kg body weight (bw). Analyses of urine by proton nuclear magnetic resonance spectroscopy (¹H-NMR) confirmed that *trans*-2-nonenal is absorbed from the gastrointestinal tract into the systemic circulation and excreted in the urine mainly as C3 mercapturate conjugates within 24 h. Trace amounts of *trans*-2-nonenal were detected in the faeces. The analysis of the stomach contents of rats 16 h after administration of *trans*-2-nonenal showed that approximately 15% of the administered dose had been oxidised to *trans*-2-nonenic acid (Grootveld et al., 1998, as referenced in WHO, 2006). The major urinary metabolite isolated from the urine of male Wistar rats given *trans*-2-pentenal or *trans*-2-nonenal was the mercapturic acid conjugate of the corresponding alcohol, 3-S-(*N*-acetylcysteinyl)pentan-1-ol or 3-S-(*N*-acetylcysteinyl)nonan-1-ol, respectively. Low concentrations of glucuronic acid conjugates were also detected in the urine. The authors suggested that these conjugates arose from a sequential pathway involving thiol conjugation, oxidation or reduction of the aldehyde functional group, followed by glucuronic acid conjugation of the resulting carboxylic acid or alcohol, respectively (Grootveld et al., 1998, as referenced in WHO, 2006).

Studies of metabolism of compounds belonging to CG 3 in animals other than rodents are lacking in the scientific literature.¹² However, the enzymes involved in the biotransformation pathways of these

¹² Technical dossier/Section III.

compounds are present in all target species (reviewed in EFSA FEEDAP Panel, 2016). Therefore, food-producing animals, including fish and birds, as well as non-food-producing animals can also be assumed to have the ability to metabolise and excrete the 25 flavourings under assessment.

3.2.2. Toxicological studies

Toxicological data (subchronic studies or other repeated-dose studies with multiple doses tested) were submitted only for hex-2(*trans*)-enal [05.073] and deca-2(*trans*),4(*trans*)-dienal [05.140].

In a subchronic study in rats (males/females, 15 animals/sex and group), hex-2(*trans*)-enal [05.073] was administered with the diet at doses of 0, 260, 640, 1,600 and 4,000 mg/kg for 13 weeks. The study examined body weight, feed intake, haematology (at weeks 6 and 13), gross pathology and histopathological changes. At the highest dose tested, a slight but not significant reduction in growth was observed associated with reduced feed intake, most probably due to reduced palatability. A relatively low specific gravity and a large urinary volume observed in males at 4,000 mg/kg suggested a minimal degree of renal dysfunction, not supported by urine analysis, kidney weight and histology. A no observed adverse effect level (NOAEL) of 1,600 mg/kg corresponding to 80 mg/kg bw per day was identified by the authors of the study for hex-2(*trans*)-enal (Gaunt et al., 1971). The FEEDAP Panel agrees with the NOAEL of 80 mg/kg bw per day identified for hex-2(*trans*)-enal from this study.

Because of similarity in structure and metabolism, the FEEDAP Panel considers that the NOAEL identified for hex-2(*trans*)-enal [05.073] can be extrapolated to hex-2-en-1-ol [02.020], pent-2-en-1-ol [02.050], 2-dodecenal [05.037], *trans*-2-nonenal [05.072], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396].

The subchronic toxicity of deca-2(*trans*),4(*trans*)-dienal [05.140] was tested in rats (males/females, 6 animals/sex and group) for 13 weeks. The test item was administered with the diet at doses 0, 3.39, 10.70 and 33.90 mg/kg bw per day. The study examined mortality, body weight, haematology, clinical chemistry and urinalysis (at weeks 6 and 12), gross pathology and histopathology. No adverse effects associated with the treatment were observed. The NOAEL identified by the authors of the study was 34 mg/kg bw per day, the highest dose tested (Damske et al., 1980). The FEEDAP Panel agrees with the NOAEL of 34 mg/kg bw per day identified for deca-2(*trans*),4(*trans*)-dienal from this study.

Because of similarity in structure and metabolism, the FEEDAP Panel considers that the NOAEL identified for deca-2(*trans*),4(*trans*)-dienal [05.140] can be extrapolated to nona-2,4-dienal [05.071], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], *tr*-2, *tr*-4-nonadienal [05.194] and *tr*-2, *tr*-4-undecadienal [05.196].

3.2.3. Safety for the target species

The maximum feed concentration which can be considered safe for the target animals can be derived from the lowest NOAEL identified if suitable data are available (EFSA FEEDAP Panel, 2012a).

Toxicological data derived from a subchronic study were only available for hex-2(*trans*)-enal [05.073] and deca-2(*trans*),4(*trans*)-dienal [05.140]. The NOAEL of 80 mg/kg bw per day for hex-2(*trans*)-enal [05.073] is considered to apply also to hex-2-en-1-ol [02.020], pent-2-en-1-ol [02.050], 2-dodecenal [05.037], *trans*-2-nonenal [05.072], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396] (see Section 3.2.2). Similarly, the NOAEL of 34 mg/kg bw per day for deca-2(*trans*),4(*trans*)-dienal [05.140] can be applied to all compounds sharing the same 2-*trans*, 4-*trans*-dienal structure, i.e. nona-2,4-dienal [05.071], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], *tr*-2, *tr*-4-nonadienal [05.194] and *tr*-2, *tr*-4-undecadienal [05.196] (see Section 3.2.2). Applying an uncertainty factor (UF) of 100 to the NOAELs derived from subchronic studies, the maximum safe intake for the target species was derived following the EFSA Guidance on sensory additives (EFSA FEEDAP Panel, 2012a), and thus, the maximum safe feed concentration was calculated (see Table 3).

Table 3: Maximum safe concentration in feed for different target animals for (A) hex-2(*trans*)-enal [05.073] and 13 structurally related compounds and (B) deca-2(*trans*),4(*trans*)-dienal [05.140] and five structurally related compounds

Target animal	Default values		Maximum safe intake/feed concentration			
	Body weight (kg)	Feed intake (g/day) ⁽¹⁾	Intake (mg/day)		Concentration (mg/kg feed) ⁽²⁾	
			A	B	A	B
Salmonids	2	40	1.6	0.7	40	17
Veal calves (milk replacer)	100	2,000	80	34	40	17
Cattle for fattening	400	8,000	320	136	35	15
Dairy cows	650	20,000	520	221	23	10
Piglets	20	1,000	16	6.8	16	7
Pigs for fattening	100	3,000	80	34	27	11
Sows	200	6,000	160	68	27	11
Chickens for fattening	2	120	1.6	0.7	13	6
Laying hens	2	120	1.6	0.7	13	6
Turkeys for fattening	12	400	9.6	4.1	24	10
Dogs	15	250	12	5.1	42	18
Cats	3	60	2.4	1.0	35	15

(1): Complete feed with 88% DM, except milk replacer for veal calves (94.5% dry matter (DM)), and for cattle for fattening, dairy cows, dogs and cats for which the values are DM intake.

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

(A): hex-2(*trans*)-enal [05.073], hex-2-en-1-ol [02.020], pent-2-en-1-ol [02.050], 2-dodecenal [05.037], *trans*-2-nonenal [05.072], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396].

(B): deca-2(*trans*),4(*trans*)-dienal [05.140], nona-2,4-dienal [05.071], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], *tr*-2, *tr*-4-nonadienal [05.194] and *tr*-2, *tr*-4-undecadienal [05.196].

Since individual reliable NOAELs could not be found for the six remaining compounds, the threshold of toxicological concern (TTC) approach was followed to derive the maximum safe feed concentration (EFSA FEEDAP Panel, 2012a).

For Cramer class I compounds, i.e. nona-2,6-dien-1-ol [02.049], *trans*-2, *cis*-6-nonadien-1-ol [02.231], nona-2(*trans*),6(*cis*)-dienal [05.058], nona-2(*trans*),6(*trans*)-dienal [05.172], allyl heptanoate [09.097] and allyl hexanoate [09.244], the calculated safe use level is 1.5 mg/kg complete feed for cattle, salmonids and non-food producing animals and 1.0 mg/kg complete feed for pigs and poultry.

3.2.3.1. Conclusions on safety for the target species

The FEEDAP Panel concludes that:

- hex-2-en-1-ol [02.020], pent-2-en-1-ol [02.050], 2-dodecenal [05.037], nona-2,4-dienal [05.071], *trans*-2-nonenal [05.072], hex-2(*trans*)-enal [05.073], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], deca-2(*trans*),4(*trans*)-dienal [05.140], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], *tr*-2, *tr*-4-nonadienal [05.194], *tr*-2, *tr*-4-undecadienal [05.196], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396] are safe at the proposed maximum use level of 5 mg/kg complete feed for all animal species;
- nona-2,6-dien-1-ol [02.049], *trans*-2, *cis*-6-nonadien-1-ol [02.231], nona-2(*trans*),6(*cis*)-dienal [05.058], nona-2(*trans*),6(*trans*)-dienal [05.172], allyl heptanoate [09.097] and allyl hexanoate [09.244] are safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species.

3.2.4. Safety for the consumer

The safety for the consumer of the 25 compounds used as food flavours has been already assessed by JECFA (WHO, 1999, 2004a,b, 2005) and EFSA (EFSA CEF Panel, 2018; EFSA FAF Panel, 2018). All compounds are currently authorised in the EU as food flavourings without limitations.

Although deposition and residue studies of the compounds in farm animals are not available, the FEEDAP Panel considers that the use of these flavourings in animal feed would not appreciably increase the human exposure to these compounds. This is based on the low use levels to be applied in feed and the expected extensive metabolism and excretion in target animals (see Section 3.2.1). Consequently, no safety concern would arise for the consumer from the use of these 25 compounds up to the highest levels considered safe for target animals (1 or 5 mg/kg complete feed).

3.2.5. Safety for the user

The applicant as required produced a safety data sheet¹³ for each compound where hazards for users have been identified. No studies to assess the safety for the user were submitted. Therefore, the FEEDAP Panel cannot conclude on the safety for the users when handling the additive.

3.2.6. Safety for the environment

The compounds under assessment are naturally occurring in the environment¹⁴ or expected to be fully metabolised to carbon dioxide and water either in the animal (see Section 3.2.1) or subsequently in the environment. Consequently, their use in animal nutrition at the concentrations in feed considered safe for the target species is also considered safe for the environment.

3.3. Efficacy

Since the 25 compounds are used in food as flavourings, and their function in feed is essentially the same as that in food, no further demonstration of efficacy is necessary (EFSA FEEDAP Panel, 2012a).

4. Conclusions

The FEEDAP Panel was unable to perform an assessment of non-2(*cis*)-en-1-ol [02.112] in the absence of data on its purity.

The FEEDAP Panel concludes that hex-2-en-1-ol [02.020], pent-2-en-1-ol [02.050], 2-dodecenal [05.037], nona-2,4-dienal [05.071], *trans*-2-nonenal [05.072], hex-2(*trans*)-enal [05.073], 2,4-decadienal [05.081], hepta-2,4-dienal [05.084], deca-2(*trans*),4(*trans*)-dienal [05.140], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], *trans*-2-octenal [05.190], *trans*-2-decenal [05.191], *tr*-2, *tr*-4-nonadienal [05.194], *tr*-2, *tr*-4-undecadienal [05.196], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396] are safe at the proposed maximum use level of 5 mg/kg complete feed for all animal species; nona-2,6-dien-1-ol [02.049], *trans*-2, *cis*-6-nonadien-1-ol [02.231], nona-2(*trans*),6(*cis*)-dienal [05.058], nona-2(*trans*),6(*trans*)-dienal [05.172], allyl heptanoate [09.097] and allyl hexanoate [09.244] are safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species.

No safety concern would arise for the consumer from the use of these compounds up to the highest safe levels in feed.

In the absence of studies to assess the safety for the user, the FEEDAP Panel cannot conclude on the safety for the users when handling the additives.

No environmental risk is foreseen for these compounds at the concentrations considered safe for the target species.

Since all of the compounds under assessment are used in food as flavourings and their function in feed is essentially the same as that in food, no further demonstration of efficacy is necessary.

¹³ Technical dossier/Section II/Annex II.3. Hazards for skin and eye contact are recognised for *trans*-2, *cis*-6-nonadien-1-ol [02.231], 2-dodecenal [05.037], nona-2,4-dienal [05.071], *trans*-2-nonenal [05.072], hex-2(*trans*)-enal [05.073], 2,4-decadienal [05.081], deca-2(*trans*),4(*trans*)-dienal [05.140], dodec-2(*trans*)-enal [05.144], hept-2(*trans*)-enal [05.150], non-2-enal [05.171], undec-2(*trans*)-enal [05.184], and allyl heptanoate [09.097]. Hazard for respiratory exposure is recognised for *trans*-2-nonenal [05.072], deca-2(*trans*),4(*trans*)-dienal [05.140], hex-2(*trans*)-enyl acetate [09.394] and hex-2-enyl butyrate [09.396]. Hex-2(*trans*)-enal [05.073] and hept-2(*trans*)-enal [05.150] are also reported to be skin sensitisers.

¹⁴ Technical dossier/Supplementary information May 2011.

Documentation provided to EFSA

- 1) Chemically Defined Group 03 – α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes. September 2010. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 2) Chemically Defined Group 03 – α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes. July 2011. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 3) Chemically Defined Group 03 – α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes. July 2012. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 4) Chemically Defined Group 03 – α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes. January 2019. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 5) Evaluation report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Chemically Defined Group 03 – α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes.
- 6) Comments from Member States.

Chronology

Date	Event
17/9/2010	Dossier received by EFSA
26/10/2010	Reception mandate from the European Commission
1/12/2010	Application validated by EFSA – Start of the scientific assessment
24/2/2011	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: characterisation, safety for target species, safety for the consumer, safety for the user and efficacy</i>
1/3/2011	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
2/3/2011	Comments received from Member States
11/11/2011	Request of supplementary/complementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 (addendum) – Scientific assessment remains suspended <i>Issues: Safety for the consumer</i>
10/3/2016	Partial withdrawal from EC: use in water (Art. (4))
18/5/2016	The applicant was informed that the application was split into two separate questions with two different EFSA-Q-numbers. The initial EFSA-Q-2010-01219 was assigned to the 32 compounds for which EFSA has completed the evaluation as food flavours, whereas the new EFSA-Q-2016-00344 was assigned to the 26 compounds, for which the assessment was pending
29/1/2019	Reception of supplementary information from the applicant – Scientific assessment re-started
28/2/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

References

- Damske DR, Mechler FJ, Beliles RP and Liverman JL, 1980. 90-Day toxicity study in rats. 2,4-Decadienal. Final report. LBI Project No. 21130-02. June 1980. Unpublished report submitted by EFFA to FLAVIS Secretariat.
- EFSA (European Food Safety Authority), 2008. Technical Guidance of the Scientific Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) for assessing the safety of feed additives for the environment. EFSA Journal 2008;6(10):842, 28 pp. <https://doi.org/10.2903/j.efsa.2008.842>
- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2010. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF); Flavouring Group Evaluation 5, Revision 2 (FGE.05Rev2): branched- and straight-chain unsaturated carboxylic acids and esters of these with aliphatic saturated alcohols from chemical groups 1, 2, 3 and 5. EFSA Journal 2010;8(10):1400, 84 pp. <https://doi.org/10.2903/j.efsa.2010.1400>

- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2013. Scientific Opinion on Flavouring Group Evaluation 06, Revision 4 (FGE.06Rev4): straight- and branched-chain aliphatic unsaturated primary alcohols, aldehydes, carboxylic acids and esters from chemical groups 1, 3 and 4. EFSA Journal 2013;11(2):3091, 94 pp. <https://doi.org/10.2903/j.efsa.2013.3091>
- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2014a. Scientific Opinion on Flavouring Group Evaluation 203 Revision 1 (FGE.203Rev1): a,b-Unsaturated aliphatic aldehydes and precursors from chemical subgroup 1.1.4 of FGE.19 with two or more conjugated double-bonds and with or without additional non-conjugated double-bonds. EFSA Journal 2014;12(4):3626, 31 pp. <https://doi.org/10.2903/j.efsa.2014.3626>
- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2014b. Scientific Opinion on Flavouring Group Evaluation 200 (FGE.200): 74 a,b-unsaturated aldehydes and precursors from subgroup 1.1.1 of FGE.19. EFSA Journal 2014;12(6):3709, 57 pp. <https://doi.org/10.2903/j.efsa.2014.3709>
- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), Silano V, Bolognesi C, Castle L, Chipman K, Cravedi J-P, Engel K-H, Fowler P, Franz R, Grob K, Husøy T, Kärenlampi S, Mennes W, Milana MR, Pfaff K, Riviere G, Srinivasan J, Tavares Poças MF, Tlustos C, Wölfle D, Zorn H, Binderup M-L, Marcon F, Marzin D, Mosesso P, Anastassiadou M, Carfi M and Gürtler R, 2018. Scientific Opinion on Flavouring Group Evaluation 203, Revision 2 (FGE.203Rev2): a,b-unsaturated aliphatic aldehydes and precursors from chemical subgroup 1.1.4 of FGE.19 with two or more conjugated double-bonds and with or without additional non-conjugated double-bonds. EFSA Journal 2018;16(7):5322, 39 pp. <https://doi.org/10.2903/j.efsa.2018.5322>
- EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings), Younes M, Aquilina G, Castle L, Engel K-H, Fowler P, Frutos Fernandez MJ, Fürst P, Gundert-Remy U, Husøy T, Mennes W, Moldeus P, Oskarsson A, Rainieri S, Shah R, Waalkens-Berendsen I, Wölfle D, Binderup M-L, Bolognesi C, Marcon F, Marzin D, Mosesso P, Carfi M, Vianello G and Gürtler R, 2018. Scientific Opinion on Flavouring Group Evaluation 200, Revision 1 (FGE.200 Rev.1): 74 α,β -unsaturated aliphatic aldehydes and precursors from chemical subgroup 1.1.1 of FGE.19. EFSA Journal 2018;16(10):5422, 60 pp. <https://doi.org/10.2903/j.efsa.2018.5422>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012a. Guidance for the preparation of dossiers for sensory additives. EFSA Journal 2012;10(1):2534, 26 pp. <https://doi.org/10.2903/j.efsa.2012.2534>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012b. Guidance for the preparation of dossiers for additives already authorised for use in food. EFSA Journal 2012;10(1):2538, 4 pp. <https://doi.org/10.2903/j.efsa.2012.2538>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012c. Guidance for establishing the safety of additives for the consumer. EFSA Journal 2012;10(1):2537, 12 pp. <https://doi.org/10.2903/j.efsa.2012.2537>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012d. Guidance on studies concerning the safety of use of the additive for users/workers. EFSA Journal 2012;10(1):2539, 5 pp. <https://doi.org/10.2903/j.efsa.2012.2539>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2016. Scientific opinion on the safety and efficacy of a,b-unsaturated straight-chain and branched-chain aliphatic primary alcohols, aldehydes, acids and esters belonging to chemical group 3 when used as flavourings for all animal species. EFSA Journal 2016;14(6):4512, 21 pp. <https://doi.org/10.2903/j.efsa.2016.4512>
- FAO (Food and Agricultural Organization of the United Nations), 2006. FAO JECFA Monographs 1: Combined Compendium of Food Additive Specifications—Joint FAO/WHO Expert Committee on Food Additives—All specifications monographs from the 1st to the 65th meeting (1956–2005). Volume 4. Analytical methods, test procedures and laboratory solutions used by and referenced in the food additive specifications. Food and Agricultural Organization of the United Nations, Rome, Italy.
- Gaunt IF, Colley J, Wright MG, Creasey M, Grasso P and Gangolli SD, 1971. Acute and short-term toxicity studies on trans-2-hexenal. Food and Cosmetic Toxicology, 9, 775–786.
- Grootveld M, Atherton MD, Sheerin AN, Hawkes J, Blake DR, Richens TE, Silwood CJL, Lynch E and Claxson AWD, 1998. *In vivo* absorption, metabolism, and urinary excretion of α,β -unsaturated aldehydes in experimental animals. Journal of Clinical Investigation, 101, 1210–1218.
- WHO (World Health Organization), 1997. Evaluation of certain food additives and contaminants. Forty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives. Geneva, 6-15 February 1996. WHO Technical Report Series, no. 868. WHO, Geneva, Switzerland.
- WHO (World Health Organization), 1999. Evaluation of certain food additives and contaminants. Forty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, no. 884. Rome, 17–26 June 1997. WHO, Geneva, Switzerland.
- WHO (World Health Organization), 2004a. Evaluation of certain food additives. Sixty-first report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, no. 922. Rome, 10–19 June 2003. WHO, Geneva, Switzerland.

- WHO (World Health Organization), 2004b. WHO Food Additives Series, 52 Safety evaluation of certain food additives and contaminants. Prepared by the Sixty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO, Geneva, Switzerland.
- WHO (World Health Organization), 2005. Evaluation of certain food additives. Sixty-third report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series, no. 928. Geneva, 8–17 June 2004. WHO, Geneva, Switzerland.
- WHO (World Health Organization), 2006. WHO Food Additives Series, 54. Safety evaluation of certain food additives. Prepared by the sixty-third meeting of the Joint FAO/WHO Expert Committee on Food Additives. WHO, Geneva, Switzerland.

Abbreviations

bw	body weight
CAS	Chemical Abstracts Service
CDG	chemically defined group
CEF	EFSA Scientific Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids
CG	chemical group
DM	dry matter
EURL	European Union Reference Laboratory
FAO	Food and Agriculture Organization
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
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-MS	gas chromatography-mass spectrometry
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
NMR	nuclear magnetic resonance
NOAEL	no observed adverse effect level
RTL	Retention Time Locking
TTC	threshold of toxicological concern
UF	uncertainty factor
WHO	World Health Organization

Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Chemically Defined Flavourings – Group 03 α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes

The *Chemically Defined Flavourings – Group 03 (α,β -unsaturated (alkene or alkyne) straight-chain and branched-chain aliphatic primary alcohols/aldehydes/acids, acetals and esters with esters containing α,β -unsaturated alcohols or aldehydes)*, in this application comprises 43 substances, for which authorisation as feed additives is sought under the category 'sensory additives', functional group 2(b) 'flavouring compounds', according to the classification system of Annex I of Regulation (EC) No 1831/2003.

In the current application submitted according to Article 4(1) and Article 10(2) of Regulation (EC) No 1831/2003, the authorisation for all species and categories is requested. The flavouring compounds of interest have a purity ranging from 85 to 98%.

Mixtures of flavouring compounds are intended to be incorporated only into *feedingstuffs* or drinking *water*. The Applicant suggested no minimum or maximum levels for the different flavouring compounds in *feedingstuffs*.

For the identification of volatile chemically defined flavouring compounds *CDG03* in the *feed additive*, the Applicant submitted a qualitative multianalyte gas chromatography-mass spectrometry (GC-MS) method, using Retention Time Locking (RTL), which allows a close match of retention times on GC-MS. By making an adjustment to the inlet pressure, the retention times can be closely matched to those of a reference chromatogram. It is then possible to screen samples for the presence of target compounds using a mass spectral database of RTL spectra. The Applicant maintained two FLAVOR2 databases/libraries (for retention times and for MS spectra) containing data for more than 409 flavouring compounds. These libraries were provided to the European Union Reference Laboratory (EURL). The Applicant provided the typical chromatogram for the *CDG03* of interest.

In order to demonstrate the transferability of the proposed analytical method (relevant for the method verification), the Applicant prepared a model mixture of flavouring compounds on a solid carrier to be identified by two independent expert laboratories. This mixture contained 20 chemically defined flavourings belonging to 20 different chemical groups to represent the whole spectrum of compounds in use as feed flavourings with respect to their volatility and polarity. Both laboratories properly identified all the flavouring compounds in all the formulations. Since the substances of *CDG03* are within the volatility and polarity range of the model mixture tested, the Applicant concluded that the proposed analytical method is suitable to determine qualitatively the presence of the substances from *CDG03* in the mixture of *flavouring compounds*.

Based on the satisfactory experimental evidence provided, the EURL recommends for official control for the qualitative identification in the *feed additive* of the individual (or mixture of) flavouring compounds of interest (*) the GC-MS-RTL (Agilent specific) method submitted by the Applicant. However, the method is not able to discriminate between [Nona-2,6-dien-1-ol & tr-2, cis-6-Nonadien-1-ol] or [2-Dodecenal & Dodec-2(trans)-enal] or [Nona-2,4-dienal & tr-2, tr-4-Nonadienal] or [2,4-Decadienal & Deca-2(trans),4(trans)-dienal] or [trans-2-Nonenal & Non-2-enal].

As no experimental data were provided by the Applicant for the identification of the *active substance(s)* in *feedingstuffs* and *water*, no methods could be evaluated. Therefore, the EURL is unable to recommend a method for the official control to identify the *active substance(s)* of interest (*) in *feedingstuffs* or *water*.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005) is not considered necessary.