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## Safety and efficacy of eight compounds belonging to different chemical groups when used as flavourings for cats and dogs

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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 23 compounds belonging to different chemical groups. This opinion concerns eight out of the 23 compounds, which are currently authorised for use as flavours in food. The Panel concludes that the eight additives are safe for cats and dogs at the proposed use level: phenylmethanethiol [12.005] and benzyl methyl sulfide [12.077] at 0.05 mg/kg complete feed; 2-pentylthiophene [15.096] at 0.1 mg/kg complete feed; tridec-2-enal [05.078] and 12-methyltridecanal [05.169] at 0.5 mg/kg complete feed; 2,5-dimethylphenol [04.019] at the 1 mg/kg complete feed; hexa-2(*trans*),4(*trans*)-dienal [05.057] at 1.5 mg/kg complete feed; 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084] at 2.25 mg/kg complete 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. Since all eight 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.

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# 1 Introduction

## 1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003<sup>1</sup> 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 and in addition, Article 10(2) of that Regulation also 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 Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)<sup>2</sup> for the authorisation/re-evaluation of 23 compounds belonging to different chemical Groups, when used as feed additives for cats and dogs (category: sensory additives; functional group: flavouring compounds).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive) and under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application. During the course of the assessment, the applicant withdrew the application for the use of chemically defined flavourings in water for drinking.<sup>3</sup> The particulars and documents in support of the application were considered valid by EFSA as of 19 March 2018.

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 and user and on the efficacy of the 23 compounds belonging to different CGs, namely 2,5-dimethylphenol [04.019], hexa-2(*trans*),4(*trans*)-dienal [05.057], oct-2-enal [05.060], dec-2-enal [05.076], tridec-2-enal [05.078], 12-methyltridecanal [05.169], 2-hexenal [05.189], 3,5-octadiene-2-one [07.247], dec-2-enoic acid [08.073], phenethyl propionate [09.137], methyl decanoate [09.251], ethyl dec-2-enoate [09.283], ethyl dec-4-enoate [09.284], butylamine [11.003], phenylmethanethiol [12.005], benzyl methyl sulfide [12.077], 3-methylbutane-1-thiol [12.171], 2-methylfuran [13.030], 2-acetyl-5-methylfuran [13.083], 2-ethyl-4-hydroxy-5-methyl-3(*2H*)-furanone [13.084], 2-acetyl-3-methylpyrazine [14.082], picoline beta (3-methylpyridine) [14.135] and 2-phenylthiophene [15.096], when used under the proposed conditions of use (see Section 3.1.2).

During the assessment, the applicant expressed the intention to withdraw the application for 15 out of the 23 compounds.<sup>4</sup>

## 1.2. Additional information

The present opinion concerns only eight compounds, namely 2,5-dimethylphenol [04.019], hexa-2(*trans*),4(*trans*)-dienal [05.057], tridec-2-enal [05.078], 12-methyltridecanal [05.169], phenylmethanethiol [12.005], benzyl methyl sulfide [12.077], 2-ethyl-4-hydroxy-5-methyl-3(*2H*)-furanone [13.084] and 2-phenylthiophene [15.096].

The eight compounds under assessment have been assessed by Joint Food and Agriculture Organization of the United Nations (FAO/WHO) Expert Committee on Food Additives (JECFA) and were considered of no safety concern (WHO, 2000, 2004, 2005, 2012). For five out of the eight compounds, namely 2,5-dimethylphenol [04.019], 12-methyltridecanal [05.169], phenylmethanethiol [12.005], benzyl methyl sulfide [12.077] and 2-pentylthiophene [15.096] (previously named 'sec-pentylthiophene'), EFSA agreed with JECFA conclusions that there is 'no safety concern at the

<sup>1</sup> 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.

<sup>2</sup> On 13/3/2013, EFSA was informed by the applicant that FFAC EEIG was liquidated on 19/12/2012 and their rights as applicant were transferred to FEFANA Asbl (EU Association of Specialty Feed Ingredients and their Mixtures), Avenue Louise 130A, Box 1, 1050 Brussels, Belgium.

<sup>3</sup> 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.

<sup>4</sup> Letter dated 29.11.2018. Compounds for withdrawal: oct-2-enal [05.060], dec-2-enal [05.076], 2-hexenal [05.189], 3,5-octadiene-2-one [07.247], dec-2-enoic acid [08.073], phenethyl propionate [09.137], methyl decanoate [09.251], ethyl dec-2-enoate [09.283], ethyl dec-4-enoate [09.284], butylamine [11.003], 3-methylbutane-1-thiol [12.171], 2-methylfuran [13.030], 2-acetyl-5-methylfuran [13.083], 2-acetyl-3-methylpyrazine [14.082] and picoline beta (3-methylpyridine) [14.135].

estimated level of intake based on the Maximised Survey-derived Daily Intake (MSDI) approach' (EFSA, 2008; EFSA CEF Panel, 2010, 2011, 2015a).

For 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084], hexa-2(*trans*),4(*trans*)-dienal [05.057] and tridec-2-enal [05.078], the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) raised a concern for genotoxicity (EFSA, 2009; EFSA CEF Panel, 2014a,b), which was ruled out based on the additional data submitted (EFSA CEF Panel, 2012, 2015b, 2018; EFSA FAF Panel, 2018).

The eight compounds are currently listed in the European Union database of flavouring substances<sup>5</sup> and in the European Union Register of Feed Additives,<sup>5</sup> and thus authorised for use in food and feed in the European Union. 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 dossier<sup>6</sup> in support of the authorisation request for the use of chemically defined flavourings from different chemical groups for use as feed additives in cats and dogs.

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 chemically defined flavourings for use in cats and dogs from different chemical groups in animal feed. The Executive Summary of the EURL report can be found in Annex A.<sup>7</sup>

### 2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of chemically defined flavourings for use in cats and dogs from different chemical groups is in line with the principles laid down in Regulation (EC) No 429/2008<sup>8</sup> and the relevant guidance documents: Guidance for the preparation of dossiers for sensory additives (EFSA FEEDAP Panel, 2012a), Guidance for the preparation of dossiers for additives already authorised for use in food (EFSA FEEDAP Panel, 2012b), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012c), and Guidance on the assessment of additives intended to be used in pets and other non-food-producing animals (EFSA FEEDAP Panel, 2011).

## 3 Assessment

The additives under assessment are eight chemically defined flavourings belonging to six different chemical groups, intended for use as sensory additive (functional group: flavouring compounds) in feed for cats and dogs.

### 3.1. Characterisation

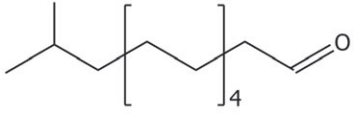
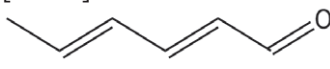
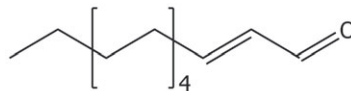
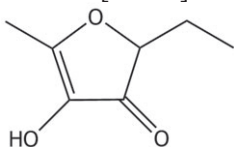
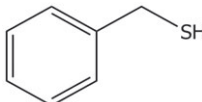
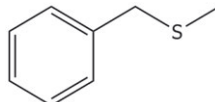
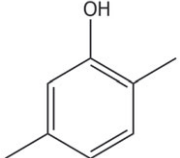
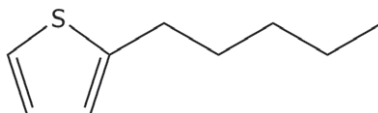
The molecular structures, the corresponding chemical groups and the FLAVIS numbers of the eight additives under application are shown in Figure 1, and their physico-chemical characteristics in Table 1.

<sup>5</sup> [https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed-eu-reg-comm\\_register\\_feed\\_additives\\_1831-03.pdf](https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed-eu-reg-comm_register_feed_additives_1831-03.pdf)

<sup>6</sup> FEED dossier reference: FAD-2010-0355.

<sup>7</sup> The full report is available on the EURL website: [https://ec.europa.eu/jrc/sites/jrcsh/files/finrep-fad-2010-0355-cdg\\_cats\\_dogs.pdf](https://ec.europa.eu/jrc/sites/jrcsh/files/finrep-fad-2010-0355-cdg_cats_dogs.pdf)

<sup>8</sup> 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.

CG 02 12-Methyltridecanal [05.169] 	CG 03 Hexa-2( <i>trans</i> ),4( <i>trans</i> )-dienal [05.057] 	CG 03 Tridec-2-enal [05.078] <sup>a</sup> 
CG 13 2-Ethyl-4-hydroxy-5-methyl-3(2H)-furanone [13.084] <sup>b</sup> 	CG 20 Phenylmethanethiol [12.005] 	CG 20 Benzyl methyl sulfide [12.077] 
CG 25 2,5-Dimethylphenol [04.019] 	CG 29 2-Pentyl thiophene [15.096] 	

- (a) sum of *cis*, *trans* isomers  
(b) racemate

**Figure 1:** Molecular structures, chemical groups and (FLAVIS numbers) of the eight flavouring compounds under assessment

**Table 1:** CAS number, FLAVIS number and some physico-chemical characteristics of the eight flavouring compounds under assessment

EU Register name	CAS No	FLAVIS No	Molecular formula	Molecular weight	Physical state	Log $K_{ow}$
12-Methyltridecanal	75853-49-5	05.169	C <sub>14</sub> H <sub>28</sub> O	212.38	Liquid	6.04
Hexa-2( <i>trans</i> ),4( <i>trans</i> )-dienal	142-83-6	05.057	C <sub>6</sub> H <sub>8</sub> O	96.13	Liquid	1.37
Tridec-2-enal	7774-82-5	05.078	C <sub>13</sub> H <sub>24</sub> O	196.33	Liquid	5.30
2-Ethyl-4-hydroxy-5-methyl-3(2H)-furanone	27538-09-6	13.084	C <sub>7</sub> H <sub>10</sub> O <sub>3</sub>	142.15	Liquid	0.87
Phenylmethanethiol	100-53-8	12.005	C <sub>7</sub> H <sub>8</sub> S	124.2	Liquid	2.48
Benzyl methyl sulfide	766-92-7	12.077	C <sub>8</sub> H <sub>10</sub> S	138.23	Liquid	2.63
2,5-Dimethylphenol	95-87-4	04.019	C <sub>8</sub> H <sub>10</sub> O	122.17	Solid	2.33
2-Pentylthiophene	4861-58-9	15.096	C <sub>9</sub> H <sub>14</sub> S	154.27	Liquid	4.48

CAS: Chemical Abstracts Service; FLAVIS: The EU Flavour Information System; log  $K_{ow}$ : logarithm of octanol–water partition coefficient.

All of the compounds under consideration are produced by chemical synthesis and typical routes of synthesis are described for each compound.<sup>9</sup>

Batch-to-batch variation data were provided for five batches of each additive, with the exception of 12-methyltridecanal and tridec-2-enal (two batches) and benzyl methyl sulfide (three batches).<sup>10</sup> The content of the active substance exceeded the specification set by the JECFA for all compounds except for 12-methyltridecanal. This compound is specified to contain 10% 12-methyltridecanal in a medium-chain triglycerides solution (to improve stability) (Table 2).

<sup>9</sup> Technical dossiers/Section II.

<sup>10</sup> Technical dossier/Section II/Annex 2.1 and Supplementary information November 2018.

**Table 2:** Identity of the substances and data on purity

EU Register name	Chemical group	FLAVIS No	JECFA specification minimum %	Assay %	
				Average	Range
12-Methyltridecanal	02	05.169	97	10.84 <sup>(a)</sup>	10.79–10.89
Hexa-2( <i>trans</i> ),4( <i>trans</i> )-dienal	03	05.057	97	98.61	98.00–98.93
Tridec-2-enal	03	05.078	92 <sup>(b)</sup>	92.93	91.17–94.68
2-Ethyl-4-hydroxy-5-methyl-3(2 <i>H</i> )-furanone	13	13.084	96	98.12	97.75–98.53
Phenylmethanethiol	20	12.005	98	99.73	99.4–99.82
Benzyl methyl sulfide	20	12.077	98	99.62	99.53–99.73
2,5-Dimethylphenol	25	04.019	99	99.96	99.8–100
2-Pentylthiophene	29	15.096	95	99.10	98.61–99.27

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

(a): The additive at 10% as a solution in Miglyol (medium-chain triglycerides) as carriers; they represent around 90% of the total composition of 12-Methyltridecanal 10% MIG.

(b): Sum of *cis/trans*-isomers; secondary components: 2-tridecenoic acid.

Potential contaminants are considered as part of the product specification and are monitored as part of the Hazard Analysis and Critical Control Point (HACCP) 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.

### 3.1.1. Shelf-life

The shelf-life for the compounds under assessment is stated to be at least 12 months for all the compounds, except 12-methyltridecanal for which a shelf-life of 6 months is claimed, 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.

### 3.1.2. Conditions of use

The applicant proposes the use of the additives in feed for cats and dogs. The proposed use levels are shown in Table 3.

**Table 3:** Conditions of use of the eight flavourings under application

EU Register name	FLAVIS No	Use level (mg/kg complete feed)
12-Methyltridecanal	05.169	0.5
Hexa-2( <i>trans</i> ),4( <i>trans</i> )-dienal	05.057	1.5
Tridec-2-enal	05.078	0.5
2-Ethyl-4-hydroxy-5-methyl-3(2 <i>H</i> )-furanone	13.084	2.25
Phenylmethanethiol	12.005	0.05
Benzyl methyl sulfide	12.077	0.05
2,5-Dimethylphenol	04.019	1
2-Pentylthiophene	15.096	0.1

FLAVIS: The EU Flavour Information System.

## 3.2. Safety

Following the provisions of the Regulation (EC) No 429/2008, there is no requirement for the assessment of the safety of an additive when used in pets, for the consumers and the environment.

The assessment of target animal safety is based on the highest use level proposed by the applicant.

### 3.2.1. Toxicological studies

Subchronic studies or other repeated-dose toxicity studies with multiple doses tested were submitted for one out of the eight compounds under assessment.

In a subchronic study in rats (males/females, 10 animals/sex and group), hexa-2(*trans*),4(*trans*)-dienal [05.057] was administered in corn oil by gavage at doses of 0, 7.5, 15, 30, 60 and 120 mg/kg body weight (bw) per day, 5 days/week, for 14 weeks (NTP, 2003). The study examined survival, body weight, haematology (on days 4 and 19), gross pathology and histopathological changes. No mortality was observed. A decrease in the mean body weight was observed in males treated with 30, 60, and 120 mg/kg bw compared to vehicle controls. Hypersalivation was the only clinical finding attributed to hexa-2(*trans*),4(*trans*)-dienal administration and was observed in males treated with 30 mg/kg bw and in females treated with 120 mg/kg bw. A significant increase in the incidences of forestomach hyperplasia and nasal olfactory atrophy or necrosis was observed at the dose of 120 mg/kg bw in both sexes. Nasal lesions occurred in most 120 mg/kg male rats. A no observed adverse effect level (NOAEL) of 15 mg/kg was determined by the authors of the study for hexa-2(*trans*),4(*trans*)-dienal [05.057]. The FEEDAP Panel agrees with this conclusion.

In the assessment of 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084] as food flavour, the EFSA CEF Panel applied a NOAEL of 200 mg/kg bw per day derived from a structurally related compound 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone [FL-no 13.010] (EFSA CEF Panel, 2015b). This NOAEL was identified from a 2-year carcinogenicity study in rats (Kelly and Bolte, 2003 as referenced in EFSA CEF Panel, 2015b), based on decreases in mean body weight and body weight gains of males and females observed at higher doses, in the absence of neoplastic lesions attributable to the test item. The FEEDAP Panel agrees on the same approach.

### 3.2.2. 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 if suitable data are available (EFSA FEEDAP Panel, 2012a).

Toxicological data derived from a subchronic study was available for hexa-2(*trans*),4(*trans*)-dienal [05.057] resulting in a NOAEL of 15 mg/kg bw per day. For 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084], a NOAEL of 200 mg/kg bw was derived by extrapolation from a 2 year carcinogenicity study performed with the structural related compound 4-hydroxy-2,5-dimethylfuran-3(2*H*)-one. Applying an uncertainty factor (UF) of 100 to the NOAEL the maximum safe intake for cats and dogs was derived following the EFSA Guidance on the assessment of the safety of feed additives for the target species for (EFSA FEEDAP Panel, 2012a), and thus the maximum safe feed concentration was calculated.

The calculated maximum safe concentrations of hexa-2(*trans*),4(*trans*)-dienal [05.057] in feed for cats and dogs are 7 and 8 mg/kg complete feed, respectively. The corresponding values for 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084] are 88 and 106 mg/kg complete feed.

As adequate tolerance studies in the target species or subchronic, repeated-dose studies in laboratory animals performed with the additives under assessment were not available for the remaining six compounds, the threshold of toxicological concern (TTC) approach was followed to derive the maximum safe feed concentration (EFSA FEEDAP Panel, 2012a) (Table 4).

**Table 4:** Maximum safe concentration in feed for cats and dogs for six compounds under assessment

EU Register name	FLAVIS No	Cramer Class	Maximum safe concentration in feed
12-Methyltridecanal	05.169	I	1.5
Tridec-2-enal	05.078	I	1.5
Phenylmethanethiol	12.005	II	0.5
Benzyl methyl sulfide	12.077	II	0.5
2,5-Dimethylphenol	04.019	I	1.5
2-Pentylthiophene	15.096	II	0.5

FLAVIS: The EU Flavour Information System.



### 3.2.2.1. Conclusions on safety for the target species

The FEEDAP Panel concludes that all eight additives are safe for cats and dogs at the proposed use levels:

- phenylmethanethiol [12.005] and benzyl methyl sulfide [12.077] at 0.05 mg/kg complete feed
- 2-pentylthiophene [15.096] at 0.1 mg/kg complete feed
- tridec-2-enal [05.078] and 12-methyltridecanal [05.169] at 0.5 mg/kg complete feed
- 2,5-dimethylphenol [04.019] at 1 mg/kg complete feed
- hexa-2(*trans*),4(*trans*)-dienal [05.057] at 1.5 mg/kg complete feed
- 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084] at 2.25 mg/kg complete feed.

### 3.2.3. Safety for the user

The applicant as required produced a safety data sheet<sup>11</sup> 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 additives.

## 3.3. Efficacy

Since all eight 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.

## 4. Conclusions

The eight additives are safe for cats and dogs at the proposed use levels: phenylmethanethiol [12.005] and benzyl methyl sulfide [12.077] at 0.05 mg/kg complete feed; 2-pentylthiophene [15.096] at 0.1 mg/kg complete feed; tridec-2-enal [05.078] and 12-methyltridecanal [05.169] at 0.5 mg/kg complete feed; 2,5-dimethylphenol [04.019] at the 1 mg/kg complete feed; hexa-2(*trans*),4(*trans*)-dienal [05.057] at 1.5 mg/kg complete feed; 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084] at 2.25 mg/kg complete 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.

Since all eight 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.

## Documentation provided to EFSA

- 1) Chemically defined flavourings for use in cats and dogs from different Chemical Groups. November 2011. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 2) Chemically defined flavourings for use in cats and dogs from different Chemical Groups. November 2018. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 3) Evaluation report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Chemically defined flavourings for use in cats and dogs from different chemical groups.
- 4) Comments from Member States.

## Chronology

Date	Event
8/11/2011	Dossier received by EFSA
16/2/2018	Reception mandate from the European Commission
9/3/2018	Application validated by EFSA – Start of the scientific assessment

<sup>11</sup> Technical dossier/Section II/Annex II.3. Hazard for skin and eye contact are recognised for 2,5-dimethylphenol [04.019], 12-methyltridecanal [05.169], hexa-2(*trans*),4(*trans*)-dienal [05.057], phenylmethanethiol [12.005], benzyl methyl sulfide [12.077], 2-ethyl-4-hydroxy-5-methyl-3(2*H*)-furanone [13.084] and 2-pentylthiophene [15.096]. Hazard for respiratory exposure is recognised for 12-methyltridecanal [05.169], benzyl methyl sulfide [12.077] and 2-pentylthiophene [15.096].

Date	Event
3/5/2018	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 user and efficacy</i>
6/6/2018	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
20/6/2018	Comments received from Member States
30/11/2018	Reception of supplementary information from the applicant – Scientific assessment restarted
30/11/2018	Partial withdrawal from EC: use in water (Art. (4)) and 15 compounds
27/2/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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## 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
EURL	European Union Reference Laboratory
FAO	Food Agricultural Organization
FEEDAP	EFSA 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)
FGE	food group evaluation
FLAVIS	The EU Flavour Information System
FL-no	FLAVIS number
GC-MS	gas chromatography–mass spectrometry
HACCP	Hazard Analysis and Critical Control Point

JECFA	The Joint FAO/WHO Expert Committee on Food Additives
Log $K_{ow}$	logarithm of octanol–water partition coefficient
MSDI	Maximised Survey-derived Daily Intake
MW	molecular weight
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 for use in cats and dogs from different chemical groups

In the current application authorisation is sought under Article 10(2) of Regulation (EC) No 1831/2003 for '*Chemically defined flavourings for use in cats and dogs from different chemical group*' (*CDFs cats & dogs*). The authorisation as *feed additive* 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. This group application includes twenty-three flavouring compounds belonging to twelve chemical groups included in Annex I of Commission Regulation (EC) No 1565/2000. The flavouring compounds of interest have a purity ranging from 92 to 99%. *Mixtures of flavouring compounds* are intended to be incorporated only into *feedingstuffs*. The Applicant suggested no minimum or maximum levels of the additive in *feedingstuffs*. The authorisation is sought for cats & dogs.

For the identification of volatile CDFs in the *feed additive*, the Applicant submitted a qualitative multi-analyte Gas Chromatography–Mass Spectrometry (GC–MS) method, using Retention Time Locking (RTL). 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 databases/libraries (FLAVOR2 – for retention times and for MS spectra) containing data for more than 409 flavouring compounds. These libraries, that include the typical chromatogram for the *CDFs* of interest, were provided to the EURL.

In order to demonstrate the transferability of the proposed analytical method, the Applicant prepared, in the frame of a previous dossier, 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 *CDFs cats & dogs* 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 *CDFs cats & dogs* in the *mixture of flavouring compounds*.

Based on the satisfactory experimental evidence provided for the qualitative identification in the *feed additive* of the individual (or mixture of) *flavouring compounds* of interest, the EURL recommends for official control the GC–MS–RTL method submitted by the Applicant (\*).

As no experimental data were provided by the Applicant for the identification of the *active substance* (s) in *feedingstuffs*, 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* (\*).