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## Safety and efficacy of 4-phenylbut-3-en-2-one and benzophenone belonging to chemical group 21 when used as flavouring compounds for all animal species

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Mojca Kos Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Paul Brantom, Andrew Chesson, Johannes Westendorf, Lucilla Gregoret, Paola Manini and Birgit Dusemund

### 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 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032] belonging to chemical group 21, when used as feed flavourings for all animal species. They are currently authorised for use as flavours in food. The use of 4-phenyl-3-butene-2-one [07.024] is safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species. Benzophenone [07.032] is safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species except chicken for fattening, laying hens and piglets, for which the calculated safe concentration in feed is 0.5 mg/kg. No safety concern would arise for the consumer from the use of 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032] as feed flavourings. In the absence of studies to assess the safety for the user, the FEEDAP Panel cannot conclude on the safety for users when handling the additives. The use of 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032] in animal feed at the maximum safe use level in feed is also considered safe for the environment. Since 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.

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**Correspondence:** feedap@efsa.europa.eu

**Panel members:** Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Maryline Kouba, Mojca Kos Durjava, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa and Ruud Woutersen.

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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, 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 authorisation of 10 substances (1-phenylethan-1-ol, acetophenone, vanillyl acetone, 4-methylacetophenone, 4-phenylbut-3-en-2-one, 4-(4-methoxyphenyl)-butan-2-one, benzophenone, 4-methoxyacetophenone, 4-(p-hydroxyphenyl)-butan-2-one (hereafter referred as 4-(4-hydroxyphenyl)-butan-2-one) and 1-phenethyl acetate) belonging to chemical group (CG) 21, when used as feed additives for all animal species (category: sensory additives; functional group: flavourings). CG 21 for flavouring substances is defined in Commission Regulation (EC) No 1565/2000<sup>3</sup> as 'aromatic ketones, secondary alcohols and related esters.' During the course of the assessment, this application was split and the present opinion covers only two out of the 10 substances under application (see Section 1.2).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the applications to the European Food Safety Authority (EFSA) as applications 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.<sup>4</sup> EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of this application were considered valid by EFSA as of 20 September 2010.

According to Article 8 of that Regulation, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additives comply 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 4-phenylbut-3-en-2-one (EU Flavour Information System (FLAVIS) number) [07.024] and benzophenone [07.032], when used under the proposed conditions of use (see Section 3.1.3).

### 1.2. Additional information

The initial application on CG 21 concerned 10 compounds, intended to be used as feed flavourings for all animal species. The European Food Safety Authority (EFSA) Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) has already delivered an opinion on eight of the 10 compounds included in CG 21 (EFSA FEEDAP Panel, 2016).

The remaining compounds 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032] were excluded from the previous opinion because at that time the assessment for use in food as flavouring was not complete. For 4-phenylbut-3-en-2-one [07.024], the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) had requested additional toxicity data to complete the assessment (EFSA, 2008a; EFSA CEF Panel 2014). The EFSA Panel on Food Additives and Flavourings (EFSA FAF Panel) has delivered an opinion and concluded that the genotoxicity concerns for 4-phenylbut-3-en-2-one [07.024] could be ruled out (EFSA FAF Panel, 2019). EFSA issued an opinion on the safety of benzophenone [07.032] as food flavour (EFSA, 2008a) and another opinion on the toxicological evaluation of benzophenone as food contact material (EFSA, 2009). Subsequently, 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> 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.

<sup>4</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.

Joint FAO/WHO Expert Committee on Food Additives (JECFA) (WHO, 2011) and IARC (2013) evaluated the same substance based on studies that were not considered in EFSA opinions. Consequently, the European Commission requested that the existing literature on the safety of this flavouring substance should be reviewed. Following this review, the EFSA CEF Panel concluded that there is no safety concern for benzophenone when used as a flavouring substance (EFSA CEF Panel, 2017).

The compounds under assessment 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032] are currently listed in the European Union database of flavouring substances<sup>5</sup> and in the European Union Register of Feed Additives, respectively, 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 technical dossiers<sup>6</sup> in support of the authorisation request for the use of the compounds under assessment 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 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 flavourings from Chemical group 21 – saturated and unsaturated aliphatic secondary alcohol/ketones/esters with esters containing secondary alcohols. No aromatic or heteroaromatic moiety as a component of an ester or ketal – 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 'aromatic ketones, secondary alcohols and related esters' is in line with the principles laid down in Regulation (EC) No 429/2008<sup>8</sup> and the relevant guidance documents<sup>9</sup>: 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 2008b), 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 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, 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032], belong to chemical group 21 – 'aromatic ketones, secondary alcohols and related esters as feed additives' and are intended for use as sensory additives (functional group: flavouring compounds) in feed for all animal species.

### 3.1. Characterisation

#### 3.1.1. Characterisation of the flavouring substance

The molecular structure of the additives under application is shown in Figure 1 and their physicochemical characteristics in Table 1.

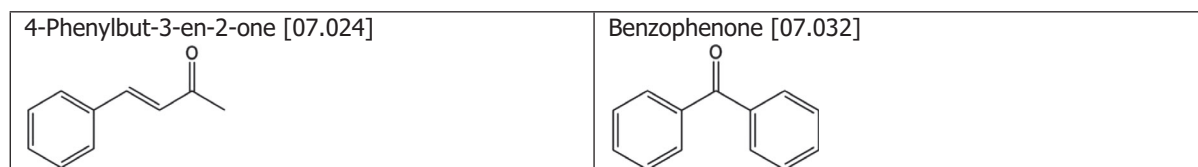
<sup>5</sup> Commission Implementing Regulation (EU) No 872/2012 of 1 October 2012 adopting the list of flavouring substances provided for by Regulation (EC) No 2232/96 of the European Parliament and of the Council, introducing it in Annex I to Regulation (EC) No 1334/2008 of the European Parliament 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.

<sup>6</sup> FEED dossier reference: FAD-2010-0417.

<sup>7</sup> The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/default/files/FinRep-FAD-2010-0074.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.

<sup>9</sup> The Guidance documents in force in 2011–2012 were exceptionally applied to the present assessment to ensure consistency in the assessment of feed flavourings (re-evaluation of authorised feed additives).



**Figure 1:** Molecular structures, EU register names and [FLAVIS numbers] of the 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 $K_{ow}$
4-Phenylbut-3-en-2-one	122-57-6	07.024	C <sub>10</sub> H <sub>10</sub> O	146.19	Solid	2.07
Benzophenone	119-61-9	07.032	C <sub>13</sub> H <sub>10</sub> O	182.22	Solid	3.18

The compounds under consideration are produced by chemical synthesis and the typical routes of synthesis are described for each compound.<sup>10</sup>

Data were provided on the batch to batch variation in five batches of the additives.<sup>11</sup> The content of the active substance for each compound exceeded in all batches the minimum content reported in the JECFA specifications (FAO, 2006).

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

EU register name	Flavis no	JECFA specification minimum % <sup>(a)</sup>	Assay %	
			Average	Range
4-Phenylbut-3-en-2-one	07.024	97	99.6	99.5–99.8
Benzophenone	07.032	98	99.6	99.0–100

(a): FAO (2006).

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.

### 3.1.2. Stability

The minimum shelf-life of 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032] is claimed to be 21 and 24 months, respectively, when stored in closed containers under recommended conditions.<sup>12</sup> This assessment is made on the basis of compliance with the original specification over this storage period.

### 3.1.3. Conditions of use

4-Phenylbut-3-en-2-one [07.024] and benzophenone [07.032] are intended for use in feed for all animal species without withdrawal period. For the compounds under assessment, the applicant proposes a normal use level of 1 mg/kg feed and a high use level of 5 mg/kg 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, 2017; EFSA FAF Panel, 2019), and no safety concerns were identified.

<sup>10</sup> Technical dossiers FAD-2010-0417.

<sup>11</sup> Technical dossier FAD-2010-0417/Section II/Annex 2.1 and Supplementary information May 2011.

<sup>12</sup> Technical dossier FAD-2010-0417/Supplementary information May 2011.

### 3.2.1. Absorption, distribution, metabolism and excretion (ADME) and residue studies

Information on the metabolism of 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032] in laboratory animals has been described in a previous assessment by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, WHO, 2002).

Experiments with [<sup>14</sup>C-ring](E)-4-phenyl-3-buten-2-one given to rats as single oral dose showed a rapid absorption and excretion of the compound mainly via the kidneys. No accumulation of radioactivity occurred in the tissues. The main metabolic pathway was the oxidation of the side chain to result in phenylacetic acid, which was conjugated with glycine and excreted via urine. Less than 10% of the parent compound was also transformed to benzoic acid, which was also excreted in urine as glycine conjugate (hippuric acid). Other metabolites formed in small amounts (5% or less) were the glutathione conjugate of the parent ketone and the secondary alcohol resulting from reduction of the ketone. The parent ketone could not be observed in the excreta (Sauer et al., 1997a, as quoted by WHO, 2002). Similar results were obtained in mice with the difference of the excretion of about 8% of the parent ketone in the urine (Sauer et al., 1997b, as quoted by WHO, 2002).

Studies in rats and rabbits showed a complete absorption of benzophenone and a rapid excretion of its metabolites via the kidneys. The absorption rate of the compound in mice after oral application was only half of that observed in rats. The main metabolic pathway was the reduction of the ketone to the secondary alcohol (benzhydrol), which was conjugated with glucuronic acid and excreted via urine (Dix et al., 1997a,b as quoted by WHO, 2002). About 1% of the compound was p-hydroxylated at one aromatic ring and excreted as glucuronide.<sup>13</sup>

Studies of metabolism of compounds belonging to CG 21 in animals other than rodents are lacking in the scientific literature.<sup>14</sup> However, the enzymes involved in the biotransformation pathways of these 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 flavourings under assessment.

### 3.2.2. Toxicological studies

Subchronic studies or other repeated-dose studies were not made available by the applicant for 4-phenylbut-3-en-2-one [07.024].

The toxicological profile of benzophenone [07.032] has been recently reviewed by the EFSA CEF Panel, which confirmed the conservative approach taken by EFSA in 2009 to derive a tolerable daily intake (TDI) of 0.03 mg/kg body weight (bw) per day when used as a food contact material (EFSA, 2009; EFSA CEF Panel, 2017). This was based on the lower 95% confidence limits of the benchmark dose for a 10% effect (BMDL<sub>10</sub>) of 3.1 mg/kg bw pw day derived for non-neoplastic kidney effects in male rats in a 2-year study (NTP, 2006). The FEEDAP Panel agrees with the assessment of the EFSA CEF Panel and considers this BMDL<sub>10</sub> as a suitable point of departure to derive safe concentrations in feed.

### 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 No Observed Adverse Effect Level (NOAEL) or BMDL<sub>10</sub> identified, if suitable data are available (EFSA FEEDAP Panel, 2012a).

Toxicological data derived from a chronic study were available for benzophenone [07.032] (see Section 3.2.2) for which a BMDL<sub>10</sub> of 3.1 mg/kg bw per day was derived. Applying an uncertainty factor (UF) of 100 to the BMDL<sub>10</sub>, the maximum safe intake for the target species was derived for the compounds following the EFSA Guidance for sensory additives (EFSA FEEDAP Panel, 2012a), and thus, the maximum safe feed concentration was calculated (Table 3).

<sup>13</sup> FAD-2010-0417/Section III/Annex 3.18 HDBS 2010.

<sup>14</sup> Technical dossiers FAD-2010-0417/Section III.

**Table 3:** Maximum safe concentration in feed for different target animals for benzophenone [07.032]

	Body weight (kg)	Feed intake (g/day) <sup>(a)</sup>	Maximum safe intake (mg/day)	Maximum safe concentration (mg/kg feed) <sup>(b)</sup>
Salmonids	2	40	0.06	1.6
Veal calves (milk replacer)	100	2,000	3.10	1.6
Cattle for fattening	400	8,000	12.4	1.4
Dairy cows	650	20,000	20.2	0.9
Piglets	20	1,000	0.62	0.6
Pigs for fattening	100	3,000	3.10	1.0
Sows	200	6,000	6.20	1.0
Chickens for fattening	2	120	0.06	0.5
Laying hens	2	120	0.06	0.5
Turkeys for fattening	12	400	0.37	0.9
Dogs	15	250	0.47	1.6
Cats	3	60	0.09	1.3

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

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

Since an individual reliable NOAEL could not be found for 4-phenylbut-3-en-2-one [07.024], the threshold of toxicological concern (TTC) approach was followed to derive the maximum safe feed concentration as described in the guidance on sensory additives (EFSA FEEDAP Panel, 2012a).<sup>15</sup> For this Cramer class I compound, 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.

### Conclusions on safety for the target species

The FEEDAP Panel concludes that

- 4-phenylbut-3-en-2-one [07.024] is safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species,
- benzophenone [07.032] is safe at the proposed normal use levels of 1 mg/kg complete feed for all animal species except chicken for fattening, laying hens and piglets, for which the calculated safe concentration in feed is 0.5 mg/kg complete feed.

### 3.2.4. Safety for the consumer

The safety for the consumer of the compounds used as food flavour has been already assessed by JECFA (WHO, 2001, 2002) and EFSA (EFSA CEF Panel, 2014, EFSA FAF Panel, 2019). The compound is currently authorised in the EU as food flavourings without limitations.<sup>5</sup>

Although deposition and residue studies of the compound in farm animals are not available, the FEEDAP Panel considers that the use of 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032] 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 the compounds up to the highest levels considered safe for target animals.

### 3.2.5. Safety for the user

No specific data to assess the safety for the user were submitted. Therefore, the FEEDAP Panel cannot conclude on the safety for users when handling the additive. The applicant produced a safety data sheet<sup>16</sup> for 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032] where hazards for users have been identified.

<sup>15</sup> When the TTC approach is applied, target species are divided into two groups, one including poultry and pigs and another one including cattle, salmonids and non-food producing animals. For these two groups and for a Cramer class I compound, the calculated safe use levels were rounded to 1.0 and 1.5 mg/kg complete feed, respectively.

<sup>16</sup> Technical dossier FAD-2010-0417/Section II/Annex II.3. Hazards for skin and eye contact and for respiratory exposure are recognised for 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032]. 4-Phenyl-3-butene-2-one [07.024] is also reported to be a skin sensitiser.



### 3.2.6. Safety for the environment

The compounds under assessment are naturally occurring in the environment<sup>17</sup> or expected to be extensively metabolised 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 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.

## 4. Conclusions

The use of 4-phenyl-3-butene-2-one [07.024] is safe at the proposed normal use level of 1 mg/kg complete feed for all animal species. Benzophenone [07.032] is safe at the proposed normal use level of 1 mg/kg complete feed for all animal species except chickens for fattening, laying hens and piglets, for which the calculated safe concentration in feed is 0.5 mg/kg feed.

No safety concern would arise for the consumer from the use of 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032] as feed flavourings.

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

The use of 4-phenyl-3-butene-2-one [07.024] and benzophenone [07.032] in animal feed at the maximum safe use level in feed is also considered safe for the environment.

Since 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.

## Documentation provided to EFSA/Chronology

Date	Event
27/07/2010	Dossier received by EFSA. Chemically defined flavourings from Chemical Group 21 - Aromatic ketones, secondary alcohols and related esters: 4-phenylbut-3-en-2-one [07.024] and benzophenone [07.032] (CDG 21). Submitted by FEFANA Asbl/Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG)
09/08/2010	Reception mandate from the European Commission
20/07/2010	Application validated by EFSA – Start of the scientific assessment
30/09/2010	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>
28/01/2011	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
21/12/2010	Comments received from Member States
11/01/2012	Reception of supplementary information from the applicant - Scientific assessment re-started
04/06/2012	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>
11/03/2013	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 environment</i>
10/03/2016	Partial withdrawal from EC: use in water (Art. (4))
02/03/2016	The applicant was informed that the application was split into two separate questions with two different EFSA-Q-numbers. The initial EFSA-Q-2010-01041 was assigned to the 8 compounds for which EFSA has completed the evaluation as food flavours, whereas the new EFSA-Q-2016-00453 was assigned to the 2 compounds, for which the assessment was pending
26/01/2020	Reception of supplementary information from the applicant - Scientific assessment re-started
28/01/2020	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

<sup>17</sup> Technical dossier FAD-2010-0412/Supplementary information June 2011. Data taken from the TNO database Volatile Compounds in Food ver. 14.1; Burdock (2009).

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## Abbreviations

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 Organisation
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)
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 points
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
Log Kow	logarithm of octanol-water partition coefficient
NOAEL	no observed adverse effect level
RTL	Retention Time Locking
TTC	threshold of toxicological concern
UF	uncertainty factor
WHO	World Health Organisation

## Annex A – Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Aromatic ketones, secondary alcohols and related esters

The *Chemically Defined Flavourings – Group 21 (Aromatic ketones, secondary alcohols and related esters)*, in this application comprises ten 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 95% to 99%.

*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 *CDG21* in the *feed additive*, the Applicant submitted a qualitative multi-analyte 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 EURL. The Applicant provided the typical chromatogram for the *CDG21* 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 *CDG21* 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 *CDG21* 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.

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*.