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Safety and efficacy of 8-mercapto-*p*-menthan-3-one and *p*-menth-1-ene-8-thiol belonging to chemical group 20 when used as flavourings for all animal species

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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 two compounds belonging to chemical group 20 (aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups). 8-Mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085] are currently authorised as flavours in food. The FEEDAP Panel concludes that the two compounds are safe for the target species at the proposed maximum use level (0.05 mg/kg complete feed). No safety concern would arise for the consumer from the use of 8-mercapto-*p*-menthan-3-one and *p*-menth-1-ene-8-thiol up to the highest safe level in feedingstuffs for all animal species. Both compounds should be considered as irritants to skin and eyes, and 8-mercapto-*p*-menthan-3-one [12.038] also as irritant to the respiratory tract. No conclusions can be drawn on skin sensitisation potential. No environmental risk is foreseen for these compounds at the maximum proposed use level in feed. Since the two compounds are used as flavourings in food 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, aliphatic and aromatic mono- and di-thiols and mono-, di-, tri- and polysulfides with or without additional oxygenated functional groups, chemical group 20

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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 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)² for the authorisation of the 34 substances belonging to chemical group 20, when used as a feed additive for all animal species (category: sensory additives; functional group: flavourings). Chemical group (CG) 20 for flavouring substances is defined in Commission Regulation (EC) No 1565/2000³ as 'aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups'. During the course of the assessment, this application was split and the present opinion covers only two out of the 34 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 27 August 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 8-mercapto-*p*-menthan-3-one [The EU Flavour Information System (FLAVIS) Number 12.038] and *p*-menth-1-ene-8-thiol [12.085], when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

The initial application concerned 34 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 32 of the 34 compounds (EFSA FEEDAP Panel, 2013).

The remaining two compounds, 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085], were excluded from the previous assessment because the EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF) had requested additional genotoxicity and toxicity data to complete its assessment (EFSA CEF Panel, 2010, 2011). Based on the new data, the CEF Panel delivered an opinion (2014) in which it concluded that there are no genotoxic concerns for both compounds. The CEF Panel also concluded that for tertiary thiols including the two compounds under assessment, there are no adequate no observed adverse effect levels (NOAELs) for these compounds or structurally related substances and that additional toxicity data are required to finalise the evaluation of these substances. For the two compounds, additional information on the use levels is also needed to estimate dietary exposure (EFSA CEF Panel, 2014).

¹ Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.

² On 19/12/2012, the rights of FFAC EEIG were transferred to FEFANA asbl, Avenue Louise 130A-Box 1, 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.

The two compounds are currently listed in the European Union database of flavouring substances⁵ and in the European Union Register of Feed Additives, respectively, and thus authorised for use in food and feed in the European Union (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 dossier⁶ in support of the authorisation request for the use of aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups 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 European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups in animal feed. The Executive Summary of the EURL report can be found in Annex A.⁷

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of the aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups is consistent with the principles laid down in Regulation (EC) No 429/2008⁸ 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 consumer (EFSA FEEDAP Panel, 2012c) and 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 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085], two tertiary thiols belonging to CG 20, intended for use as sensory additive (functional group: flavouring compounds) in feed for all animal species.

3.1. Characterisation

3.1.1. Characterisation of the flavouring additives

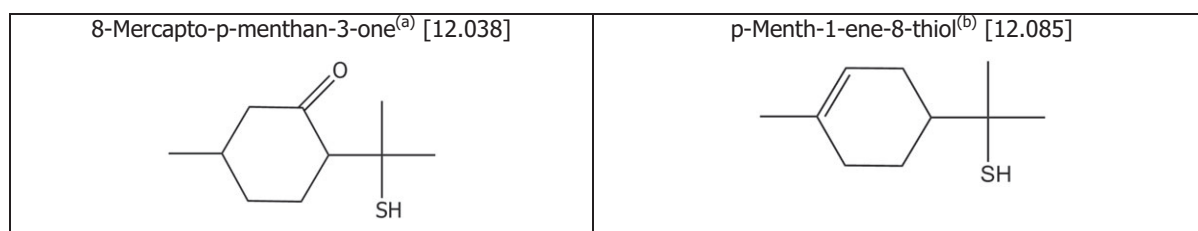
The molecular structures of the two additives under application are shown in Figure 1 and their physico-chemical characteristics are summarised in Table 1. The two compounds are tertiary thiols.

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 FEED dossier reference: FAD-2010-0409.

⁷ The full report is available on the EURL website: <http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2010-0043.pdf>

⁸ Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.



(a): Mixture of four diastereoisomers, each about 25 % (EFSA CEF Panel, 2014).

(b): Racemate (EFSA CEF Panel, 2014).

Figure 1: Molecular structures and [FLAVIS numbers] of the two flavouring compounds under assessment

Table 1: Chemical Abstracts Service (CAS) number, FLAVIS number and some physico-chemical characteristics of the two flavouring compounds under assessment

EU Register name	CAS no	FLAVIS no	Molecular formula	Molecular weight	Physical state	Log K_{ow} ^(a)
8-Mercapto- <i>p</i> -menthan-3-one	38462-22-5	12.038	C ₁₀ H ₁₈ OS	186.31	Liquid	2.78*
<i>p</i> -Menth-1-ene-8-thiol	71159-90-5	12.085	C ₁₀ H ₁₈ S	170.31	Liquid	4.74*

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

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

*: Generated from Epi-Suite 4.01.

The two compounds are produced by chemical synthesis. The routes of synthesis are described in the dossier.⁹

Batch-to-batch variation data were provided for five batches of each additive.¹⁰ The content of the active substance 8-mercapto-*p*-menthan-3-one [12.038] exceeded the specification set by the Joint Food and Agriculture Organization of the United Nations (FAO/WHO) Expert Committee on Food Additives (JECFA), whereas the content of *p*-menth-1-ene-8-thiol [12.085] was below the JECFA specifications (Table 2).

Table 2: Identity of the substances and data on purity

EU Register name	FLAVIS no	JECFA specification minimum % ^(a)	Assay %	
			Average	Range
8-Mercapto- <i>p</i> -menthan-3-one	12.038	> 97	97.8	97.0–99.1
<i>p</i> -Menth-1-ene-8-thiol	12.085	> 98	95.7	93.9–98.0

FLAVIS No: EU Flavour Information System number; JECFA: the Joint Food and Agriculture Organization of the United Nations (FAO/WHO) Expert Committee on Food Additives.

(a): FAO (2006).

The applicant states that 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 for the compounds under assessment is at least 24 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.

⁹ Technical dossier/Section II.

¹⁰ Technical dossier/Section II/Annex 2.1 and Supplementary information June 2011.

3.1.3. Conditions of use

The applicant proposes the use of the additives in feed for all animal species without withdrawal. For the two additives, the applicant proposes a normal use level of 0.01 mg/kg complete feed and a high use level of 0.05 mg/kg complete feed.

3.2. Safety

The assessment of safety is based on the highest use level proposed by the applicant (0.05 mg/kg complete feed).

The compounds belonging to CG 20 were evaluated by JECFA (WHO, 2000) and EFSA (EFSA CEF Panel, 2010, 2011, 2014).

3.2.1. Absorption, distribution, metabolism and excretion

8-Mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085] belong to subgroup III, tertiary thiol compounds, and their absorption, distribution, metabolism and excretion (ADME) was reviewed previously by the EFSA CEF Panel (EFSA CEF Panel, 2012). These two compounds have low relative molecular mass and are sufficiently lipophilic to be absorbed from the intestine. They can be metabolised via many different pathways, including S-oxidation, oxidative desulfuration and dealkylation, alkylation and conjugation with glutathione (GSH) and/or glucuronic acid. Metabolism will usually result in increased polarity and a greater likelihood of excretion; these substances not being expected to accumulate in the body.

Studies of metabolism of compounds belonging to CG 20 in animals other than rodents are lacking in the scientific literature.¹¹ However, the enzymes involved in the biotransformation pathways of these compounds are present in all target species (reviewed in EFSA FEEDAP Panel, 2013). Therefore, food-producing animals, including fish and birds, can also be assumed to have the ability to metabolise and excrete the two flavourings under assessment.

3.2.2. Toxicological studies

Subchronic studies or other repeated-dose studies with multiple doses tested could not be found for the two compounds under assessment.¹²

3.2.3. Safety for the target species

As adequate tolerance studies in the target species or sub-chronic, repeated-dose studies in laboratory animals performed with the additives under assessment were not available, the threshold of toxicological concern (TTC) approach was followed to derive the maximum safe feed concentration (EFSA FEEDAP Panel, 2012a). The two compounds belong to Cramer Class II. The calculated safe use level for these compounds is 0.5 mg/kg complete feed for cattle, salmonids and non-food producing animals and 0.3 mg/kg complete feed for pigs and poultry.

The content of *p*-menth-1-ene-8-thiol [12.085] was below the specifications set by JECFA for use as a food flavouring (Section 3.1.1). However, a purity of 96% (on average) was not considered to be of concern as it would lead to about 1 µg/kg feed of unidentified material at the maximum proposed use level of 0.05 mg/kg. This level is below the TTC for compounds belonging to Cramer class III, the lowest threshold applicable to compounds without genotoxic potential.

3.2.3.1. Conclusions on safety for the target species

The FEEDAP Panel concludes that the two compounds under assessment, 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085], are safe at the proposed maximum use level (0.05 mg/kg complete feed) for all animal species.

3.2.4. Safety for the consumer

Although JECFA concluded that the compounds were of no safety concern when used at the current levels of estimated intake (WHO, 2000), the EFSA CEF Panel indicated the need of additional toxicity data to identify a NOAEL as well as of information on the use levels to finalise the evaluation

¹¹ Technical dossier/Section III.

¹² Technical dossier/Supplementary information May 2012.

(EFSA CEF Panel, 2014). The two compounds are presently authorised as food flavourings without limitations, pending the evaluation of the CEF Panel to be finalised.⁵

The levels applied in feed (0.05 mg/kg complete feed) are 10-fold lower than those considered safe for the target animals applying the TTC approach (0.3–0.5 mg/kg complete feed).

Although EFSA has yet to complete the risk assessment of 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085] as a food flavour, the FEEDAP Panel considers that the possible residues in food derived from animals fed with these flavourings would not appreciably increase the human intake levels of these compounds. This is based on the very low use levels to be applied in feed and the expected metabolism and excretion in target animals (see Section 3.2.1). Consequently, no safety concern would arise for the consumer from the use of 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085] up to the highest use level in feeds (0.05 mg/kg complete feed).

3.2.5. Safety for the user

No specific data on the safety for the user were provided. In the safety data sheets,¹³ hazard for skin and eye contact are recognised for both compounds. Hazard for respiratory exposure is recognised for 8-mercapto-*p*-menthan-3-one [12.038].

Based on this, both compounds should be considered as irritants to skin and eyes, and 8-mercapto-*p*-menthan-3-one also as irritant to the respiratory tract. No conclusions can be drawn on skin sensitisation potential.

3.2.6. Safety for the environment

The addition of naturally occurring substances that will not result in a substantial increase of the concentration in the environment are exempt from further assessment. Examination of the published literature shows that the two compounds under assessment, 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085], could not be shown to occur in the environment at levels above the application rate of 0.05 mg/kg complete feed.¹⁴

Considering the very low use level and also that these compounds are expected to be extensively metabolised by the target species (see Section 3.2.1), no environmental risk is foreseen for these compounds at the maximum proposed use level in feed (0.05 mg/kg complete feed).

3.3. Efficacy

Since 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085] 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 FEEDAP Panel concludes that 8-mercapto-*p*-menthan-3-one [12.038] and *p*-menth-1-ene-8-thiol [12.085] are safe at the proposed maximum use level (0.05 mg/kg complete feed) for all animal species.

No safety concern would arise for the consumer from the use of the two compounds up to the highest proposed level in feeds.

Both compounds should be considered as irritants to skin and eyes, and 8-mercapto-*p*-menthan-3-one [12.038] also as irritant to the respiratory tract. No conclusions can be drawn on skin sensitisation potential.

No environmental risk is foreseen for these compounds at the maximum proposed use level in feed.

Because the two 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

- 1) Chemically defined flavourings from Flavouring Group 20 – Aliphatic and aromatic mono- and di- thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated

¹³ Technical dossier/Section II/Annex II.3.

¹⁴ Technical dossier/Supplementary information June 2011. Data taken from the Netherlands Organisation for Applied Scientific Research (TNO) database Volatile Compounds in Food ver. 14.1; Burdock, 2003.

- functional groups (CDG 20). June 2010. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
- 2) Chemically defined flavourings from Flavouring Group 20 – Aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups (CDG 20). Supplementary information. June 2011. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
 - 3) Chemically defined flavourings from Flavouring Group 20 – Aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups (CDG 20). Supplementary information. May 2012. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
 - 4) Chemically defined flavourings from Flavouring Group 20 – Aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups (CDG 20). Supplementary information. July 2012. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
 - 5) Chemically defined flavourings from Flavouring Group 20 – Aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups (CDG 20). Supplementary information. January 2013. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
 - 6) Chemically defined flavourings from Flavouring Group 20 – Aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups (CDG 20). Supplementary information. October 2014. Submitted by Feed Flavourings Authorisation Consortium European Economic Interest Grouping (FFAC EEIG).
 - 7) Evaluation report of the European Union Reference Laboratory for Feed Additives on the Methods(s) of Analysis for Chemically Defined Flavourings – Group 20 (CDG 20 – Aliphatic and aromatic mono- and di- thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups).
 - 8) Comments from Member States.

Chronology

Date	Event
22/6/2010	Dossier received by EFSA
19/7/2010	Reception mandate from the European Commission
27/8/2010	Application validated by EFSA – Start of the scientific assessment
28/9/2010	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, and efficacy</i>
30/11/2010	Comments received from Member States
22/11/2010	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
7/7/2011	Request of supplementary 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</i>
22/6/2012	Request of supplementary 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</i>
20/7/2012	Reception of supplementary information from the applicant - Scientific assessment re-started
6/12/2012	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: safety</i>
12/4/2013	The applicant was informed that the application was split into two separate questions with two different EFSA-Q-numbers. The initial EFSA-Q-2010-00998 was assigned to the 32 compounds for which EFSA has completed the evaluation as food flavours, whereas the new EFSA-Q-2013-00325 was assigned to the two compounds, for which the assessment was pending
10/3/2016	Reception of the partial withdrawal of the application under Article 4 (use in water)
1/10/2018	Reception of supplementary information from the applicant - Scientific assessment restarted
27/11/2018	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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- EFSA CEF Panel (EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids), 2012. Scientific Opinion on Flavouring Group Evaluation 08, Revision 5 (FGE.08Rev5): aliphatic and alicyclic mono-, di-, tri-, and polysulphides with or without additional oxygenated functional groups from chemical groups 20 and 30. *EFSA Journal* 2012;10(7):2837, 154 pp. <https://doi.org/10.2903/j.efsa.2012.2837>
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Abbreviations

ADME	absorption, distribution, metabolism and excretion
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
FFAC	Feed Flavourings authorisation Consortium of FEFANA (EU Association of Specialty Feed Ingredients and their Mixtures)

FLAVIS	The EU Flavour Information System
FL-no	FLAVIS number
GSH	glutathione
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
log K_{ow}	logarithm of octanol-water partition coefficient
NOAEL	no observed adverse effect level
RTL	Retention Time Locking
TTC	threshold of toxicological concern
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 20 (CDG20, Aliphatic and aromatic mono- and di- thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups)

The Chemically Defined Flavourings – Group 20 (aliphatic and aromatic mono- and di- thiols and mono-, di-, tri-, and polysulfides with or without additional oxygenated functional groups), in this application comprises 34 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 90% 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 *CDG20* 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 *CDG20* 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 twenty chemically defined flavourings belonging to twenty 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 *CDG20* 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 *CDG20* 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 listed in Table 1 (*) 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 listed in Table 1 (*) 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.