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Safety of methanethiol [12.003] when used as a feed additive 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 of methanethiol [12.003] 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). Methanethiol [12.003] is currently authorised as a flavour in food. The additive under assessment is safe for all animal species up to the maximum proposed use level of 0.05 mg/kg complete feed. No concerns for the consumer and the environment were identified following the use of the additive at the proposed conditions of use in feed. Methanethiol [12.003] should be considered as irritant to skin and eyes and to the respiratory tract. No conclusions can be drawn on skin sensitisation.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1831/2003¹ establishes the rules governing the Community authorisation of additives for use in animal nutrition and, in particular, Article 9 defined the term of the authorisation by the Commission.

The applicant, FEFANA ASBL,² is seeking a Community authorisation of methanethiol [12.003] as a feed additive to be used as a flavouring compound for all animal species (Table 1).

Table 1: Description of the substances

Category of additive	Sensory additives
Functional group of additive	Flavouring compounds
Description	Methanethiol [12.003]
Target animal category	All animal species
Applicant	FEFANA ASBL
Type of request	New opinion

On 17 April 2013, the Panel on Additives and Products or Substances used in Animal Feed of the European Food Safety Authority ("Authority"), in its opinion on the safety and efficacy of this additive could not conclude on the safety of methanethiol [12.003] because of issues related to the purity of the compound.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and to allow a revision of Authority's opinion. The new data have been received on 04 May 2020.

In view of the above, the Commission asks the Authority to deliver a new opinion on the safety of methanethiol [12.003] as a feed additive for all animal species based on the additional data submitted by the applicant.

1.2. Additional information

Methanethiol [The EU Flavour Information System (FLAVIS) Number 12.003] has been previously assessed for use as a flavouring agent in food by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). No safety concern was identified for methanethiol at the current levels of intake when used as a flavouring agent (WHO, 2000). According to Regulation (EC) No 1565/2000³, 'Substances classified by JECFA as to present no safety concern at the current levels of intake with the exception of substances which have been accepted on the sole basis that their estimated intake is lower than the threshold of concern of 1.5 µg/person per day, as laid down in the reports of the 46th, 49th, 51st and 53rd JECFA meetings, do not need to be re-evaluated'.

Methanethiol belongs to chemical group (CG) 20 for flavouring substances, which 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.' The FEEDAP Panel issued an opinion on the safety and efficacy of 34 compounds belonging to CG 20. For six compounds, including methanethiol, the Panel was unable to perform a safety assessment because of issues related to the purity of the compounds, which did not allow conclusions on the safety of the additive (EFSA FEEDAP Panel, 2013).

Methanethiol [12.003] is listed in the European Union database of flavouring substances with a purity of at least 95%⁴ and in the European Union Register of Feed Additives, respectively, and thus authorised for use in food and feed in the European Union (EU).

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 FEFANA asbl, Avenue Louise 130 A, 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. No longer in force, Date of end of validity: 21/04/2013. Repealed by Commission Implementing Regulation (EU) No 872/2012 of 1 October 2012.

⁴ 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.

The applicant has now provided new data to address the issues previously identified regarding the characterisation of the additive.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁵ in support to a previous application on the same product.⁶

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment regarding 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 are valid and applicable for the current application.⁷

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety of methanethiol [12.003] is in line 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), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012b), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017c) and Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

3. Assessment

The additive under assessment is methanethiol [12.003] and is intended for use as a sensory additive (functional group: flavouring compounds) in feed for all animal species.

The additive was previously described as an aqueous solution containing a minimum of 1% of the compound. This description did not allow for setting a specification or for the extrapolation of consumer safety assessments of methanethiol to this product. Consequently, the additive was excluded from further consideration (EFSA FEEDAP Panel, 2013). The applicant has changed the specification of the additive and provided new data.

3.1. Characterisation

3.1.1. Characterisation of the additive

Methanethiol (synonyms: mercaptomethane, methyl sulfhydrylate, thiomethyl alcohol) is a clear liquid (at temperatures below 6°C) or a colourless gas with odour of rotten cabbage or garlic (above 6°C). Methanethiol is identified by the Chemical Abstract Service (CAS) number 74-93-1. It has a molecular formula CH₄S and a molecular weight of 48.1 g/mol. Methanethiol has a pK_a of 10.33 and a logarithm of octanol-water partition coefficient (logK_{ow}) of 0.78. Its solubility in water is of 24 g/L.⁹

Methanethiol is produced by chemical synthesis. The routes of synthesis are described in the dossier.¹⁰

The additive methanethiol [12.003] is authorised for use in food with a purity of at least 95%, as specified by JECFA.

⁵ FEED dossier reference: FAD-2020-0046.

⁶ FEED dossier reference: FAD-2010-0043.

⁷ The full report is available on the EURL website: <https://ec.europa.eu/jrc/sites/jrcsh/files/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.

⁹ Technical dossier/FAD-2020-0046/2020-06-18 Annex 3.

¹⁰ Technical dossier FAD-2010-0043/Section II.

The applicant has now updated the specification of the product under assessment to contain at least 98% methanethiol. Analytical data on four batches of the additive showed compliance with the proposed specification ($\geq 98\%$). The content of the active substance exceeds the JECFA specification ($\geq 95\%$).

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 compound under assessment is at least 6 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 methanethiol in feed for all animal species without a withdrawal period at 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

In the previous opinion, in the absence of data on the purity of the compound under assessment, the FEEDAP Panel could not conclude on the safety of methanethiol [12.003] at the proposed use levels for all animal species or for the consumer.

The additional analytical data provided in response to the previous opinion show that the purity of the feed additive complies with the JECFA specifications.

3.2.1. Safety for the target species

In the absence of data of tolerance studies and/or subchronic or other repeated dose studies with multiple doses tested, the threshold of toxicological concern (TTC) approach was applied to derive the maximum safe feed concentration. For methanethiol [12.003], a Cramer class I compound, the calculated safe use level in feed ranges from 0.3 mg/kg feed for poultry to 1.5 mg/kg feed for salmonids and dogs (EFSA FEEDAP Panel, 2017b). These values are between 6 and 30-fold higher than the proposed use levels in feed.

Therefore, the FEEDAP Panel concludes that methanethiol [12.003] is safe at the maximum proposed use level (0.05 mg/kg complete feed) for all animal species.

3.2.2. Safety for the consumer

Methanethiol is currently authorised as a food flavouring without limitations. Considering that the levels applied in feed (0.05 mg/kg complete feed) are between 6- and 30-fold lower than those considered safe for the target animals applying the TTC approach (0.3–1.5 mg/kg complete feed) and considering the expected metabolism and excretion in target animals (EFSA FEEDAP Panel, 2013), the FEEDAP Panel concludes that the possible residues in food derived from animals fed with the additive would not appreciably increase the human intake levels of methanethiol.

Consequently, no safety concern would arise for the consumer from the use of methanethiol at the proposed conditions of use.

3.2.3. Safety for the user

No specific data on the safety for the user were provided. In the safety data sheets,¹¹ hazard for skin and eye contact and for respiratory exposure are recognised for methanethiol [12.003].

The compound should be considered as irritant to skin and eyes and to the respiratory tract. No conclusions can be drawn on skin sensitisation potential.

¹¹ Technical dossier FAD-2010-0043/Section II/Annex_II_3.

3.2.4. 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 methanethiol [12.003] occurs in the environment at levels well above the application rate of 0.05 mg/kg complete feed (e.g. up to 316 ppm in allium species).¹²

Therefore, no environmental risk is foreseen for this compound at the maximum proposed use level in feed (0.05 mg/kg complete feed).

4. Conclusions

The use of methanethiol [12.003] in feed up to the maximum proposed use level of 0.05 mg/kg is considered safe for all animal species.

No concerns for the consumer and the environment were identified following the use of the additive at the proposed conditions of use.

Methanethiol [12.003] should be considered as irritant to skin and eyes and to the respiratory tract. No conclusions can be drawn on skin sensitisation.

5. Documentation as provided to EFSA/Chronology

Date	Event
19/06/2020	Dossier received by EFSA. Chemically defined flavourings from Chemical Group 20 - aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulphides with or without additional oxygenated functional groups when used as flavourings: methanethiol [12.003] for all animal species and categories. Submitted by FEFANA asbl
05/05/2020	Reception mandate from the European Commission
09/07/2020	Application validated by EFSA – Start of the scientific assessment
30/09/2020	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012b. 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), 2013. Scientific Opinion on the safety and efficacy of aliphatic and aromatic mono- and di-thiols and mono-, di-, tri-, and polysulphides with or without additional oxygenated functional groups (chemical group 20) when used as flavourings for all animal species. EFSA Journal 2013;11(5):3208, 34 pp. <https://doi.org/doi:10.2903/j.efsa.2013.3208>
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¹² Technical dossier FAD-2010-0043/ 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.

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WHO (World Health Organization), 2000. Evaluation of certain food additives and contaminants. Fifty-third report of the Joint FAO/WHO Expert Committee on Food Additives. Rome, 1–10 June 1999. WHO Technical Report Series, No 896. WHO, Geneva, Switzerland.

Abbreviations

CAS	Chemical Abstract Service
CG	chemical group
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
FLAVIS	EU Flavour Information System
JECFA	Joint FAO/WHO Expert Committee on Food Additives
log _{K_{ow}}	logarithm of octanol-water partition coefficient
TTC	threshold of toxicological concern