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SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of L-cysteine hydrochloride monohydrate as a flavouring additive for pets[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

L-Cysteine is a non-essential amino acid produced by hydrolysis of natural keratin (typically from duck feathers). In the absence of information on bacterial fermentation, the FEEDAP Panel cannot conclude on this way of manufacturing. The addition of L-cysteine to the food of cats and dogs is safe if the balance between cysteine and methionine in the complete diet is maintained. Owing to the unknown total content of free L-cysteine in the final diet, it cannot be assessed whether or not the addition of L-cysteine as a feed flavouring would disrupt this balance. In the absence of data, the FEEDAP Panel considers it prudent to assume that exposure of the skin, eyes and mucous membranes poses a risk to users. As L-cysteine is intended for use in pets, assessment of the safety for the environment is not needed. It is not clear if the use of L-cysteine, applied as described by the applicant, is the same as that for human food and, therefore, efficacy cannot be assumed and has not been demonstrated. The FEEDAP Panel made a recommendation regarding the specification of the additive.

KEY WORDS

sensory additive, flavourings, L-Cysteine, pets, safety, efficacy

[1] On request from the European Commission, Question No EFSA-Q-2010-01284, adopted on 10 October 2013.

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SUMMARY

Following a request from the European Commission, the 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 L-cysteine hydrochloride monohydrate when used as a flavouring additive for pets.

L-Cysteine is a non-essential amino acid produced by hydrolysis of natural keratin (typically from duck feathers).

In the absence of information on bacterial fermentation, the FEEDAP Panel cannot conclude on this way of manufacturing.

The addition of L-cysteine to the food of cats and dogs is safe if the balance between cysteine and methionine in the complete diet is maintained. Owing to the unknown total content of free L-cysteine in the final diet, it cannot be assessed whether or not the addition of L-cysteine as a feed flavouring would disrupt this balance.

In the absence of data, the FEEDAP Panel considers it prudent to assume that exposure of the skin, eyes and mucous membranes poses a risk to users.

As L-cysteine is intended for use in pets, assessment of the safety for the environment is not needed.

It is not clear if the use of L-cysteine, applied as described by the applicant, is the same as that for human food and, therefore, efficacy cannot be assumed and has not been demonstrated.

The FEEDAP Panel made a recommendation regarding the specification of the additive.

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BACKGROUND

Regulation (EC) No 1831/2003[4] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, 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, at the latest one year before the expiry date of the authorisation given pursuant to Directive 70/524/EEC for additives with a limited authorisation period, and within a maximum of seven years after the entry into force of this Regulation for additives authorised without a time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from Mars GmbH [5] for re-evaluation of the product, L -cysteine hydrochloride monohydrate, when used as a feed additive for all pet animals (category: sensory additives; functional group: flavouring compounds) under the conditions mentioned in Table 1. During the assessment, the applicant requested a change in the category of additive from nutritional and sensory to sensory only. Table 1 was modified accordingly.

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 10(2) (re-evaluation of an authorised feed additive).[6] 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 additive complies with the conditions laid down in Article 5. The particulars and documents in support of the application were considered valid by EFSA as of 18 April 2011.

L-Cysteine and L -cysteine hydrochloride are permitted food additives under Directive 95/2/EC[7] and may also be used for nutritional purposes in processed cereal-based foods and foods for infants and young children (Directive 96/5/EC, Annex IV)[8], in infant formulae and follow-on formulae (Directive 91/321/EC, Annex III)[9], and also as a nutritional substance in foods intended for particular nutritional uses (Directive 2001/15/EC).[10] The Scientific Committee on Food (SCF) evaluated the safety of L -cysteine in 1990 and considered that its use as a flour treatment agent was toxicologically acceptable provided its addition to food does not give rise to a nutritional imbalance of amino acids (EC, 1991). The SCF also concluded that the addition of amino acids to foods intended for infants and young children should be permitted solely for the purpose of improving the nutritional value of the foodstuff and only in the proportions necessary for that purpose, without specifying the reason for this recommendation (EC, 1983, 1991). In addition, the Joint FAO/WHO Expert Committee (JECFA) has evaluated L -cysteine as a flavouring agent (WHO, 2004) while EFSA has evaluated the oxidised form of L -cysteine, L -cystine, also as a flavouring agent (EFSA, 2006, 2008a) and for use in foods intended for infants and young children, and for use as feed additive for all animal species (EFSA FEEDAP Panel, 2013).

TERMS OF REFERENCE

According to Article 8 of Regulation (EC) No 1831/2003, EFSA shall 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, user and the environment and the efficacy of the product L-cysteine hydrochloride monohydrate, when used under the conditions described in Table 1.

[4] 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.
[5] Mars GmbH, Eitzer Strasse, 215 D-27283 Verden (Aller), Germany.
[6] EFSA Dossier reference: FAD-2010-0152.
[7] European Parliament and Council Directive No 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. OJ L 61, 18.3.1995, p. 1.
[8] Commission Directive 96/5/EC, Euratom of 16 February 1996 on processed cereal-based foods and baby foods for infants and young children. OJ L 49, 28.2.1996, p. 17.
[9] Commission Directive 91/321/EEC of 14 May 1991 on infant formulae and follow-on formulae. OJ L 175, 4.7.1991, p. 35.
[10] Commission Directive 2001/15/EC of 15 February 2001 on substances that may be added for specific nutritional purposes in foods for particular nutritional uses. OJ L 52, 22.2.2001, p. 19.

Table 1: Description and conditions of use of the additive as proposed by the applicant

Additive	L-Cysteine Hydrochloride Monohydrate			
Registration number/EC No/No (if appropriate)	CAS Reg No 7048-04-06			
Category(ies) of additive	Sensory			
Functional group(s) of additive	Flavouring Compounds			
Description				
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)	
White crystals or crystalline powder	**$C_3H_7NO_2S.HCl.H_2O$**	**92% (anhydrous basis)**	**Infra-red spectrum vs. known standard**	
Trade name (if appropriate)	None			
Name of the holder of authorisation (if appropriate)	None			
Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		mg/kg of complete feedingstuffs		
All pet animals	None	None	None	N/A
Other provisions and additional requirements for the labelling				
Specific conditions or restrictions for use (if appropriate)	N/A			
Specific conditions or restrictions for handling (if appropriate)	N/A			
Post-market monitoring (if appropriate)	N/A			
Specific conditions for use in complementary feedingstuffs (if appropriate)	N/A			
Maximum Residue Limit (MRL) (if appropriate)				
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues	
N/A	N/A	N/A	N/A	

ASSESSMENT

1. Introduction

The substance subject to this request of authorisation is L-cysteine hydrochloride monohydrate. This is a non-essential amino acid.

L-Cysteine and L-cysteine hydrochloride are permitted food additives under Directive 95/2/EC[11] and may also be used for nutritional purposes in processed cereal-based foods and foods for infants and young children (Directive 96/5/EC, Annex IV),[12] in infant formulae and in follow-on formulae, (Directive 91/321/EC, Annex III)[13] and also as a nutritional substance in foods intended for particular nutritional uses (Directive 2001/15/EC).[14] The Scientific Committee for Food (SCF) evaluated the safety of L-cysteine in 1990 and considered that its use as a flour treatment agent was toxicologically acceptable, provided its addition to food does not give rise to a nutritional imbalance of amino acids (EC, 1991). The SCF also concluded that the addition of amino acids to foods intended for infants and young children should be permitted solely for the purpose of improving the nutritional value of the foodstuff and only in the proportions necessary for that purpose, without specifying the reason for this recommendation (EC, 1983, 1991). In addition, the Joint FAO/WHO Expert Committee (JECFA) has evaluated L-cysteine as a flavouring agent (WHO, 2004) while EFSA has evaluated the oxidised form of L-cysteine, L-cystine, also as a flavouring agent (EFSA, 2006, 2008a) and for use in foods intended for infants and young children and for use as a feed additive for all animal species (EFSA FEEDAP Panel, 2013).

Regulation (EC) No 429/2008[15] allows substances already approved for use in human food to be assessed with a more limited procedure than for other feed additives. However, use of this procedure is always subject to the condition that food safety assessment is relevant to the use in feed.

Cysteine hydrochloride monohydrate is described in the European Pharmacopoeia as Monograph (MG) 0895 (PhEur, 2010).

2. Characterisation

2.1. Characterisation of the active substance

The additive L-cysteine hydrochloride monohydrate is identified by the Chemical Abstracts Service (CAS) number 7048-4-6.[16] The molecular formula is $C_3H_7NO_2S.HCl{\cdot}H_2O$ and its molecular weight is 175.64. The structural formula of L-cysteine hydrochloride monohydrate is shown in Figure 1.

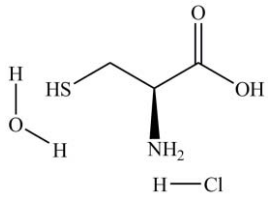

Figure 1: Structural formula of L-cysteine hydrochloride monohydrate

[11] OJ L 61, 18.3.1995, p. 1.
[12] OJ L 49, 28.2.1996, p. 17.
[13] OJ L 175, 4.7.1991, p. 35.
[14] OJ L 52, 22.2.2001, p. 19.
[15] 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.
[16] Technical Dossier/ Supplementary Information September 2013/04_Cys HCL - Reply to EFSA (ex June 2012).doc.

L-Cysteine hydrochloride monohydrate is a white or almost white crystalline powder or colourless crystals, freely soluble in water. Cysteine hydrochloride monohydrate is described in the European Pharmacopoeia (PhEur, 2010) as having a purity of 98.5–101.0 % (calculated with reference to the dried substance), loss on drying of 8–12 %, optical rotation + 5.5 to + 7.0, < 300 mg/kg sulphates, < 200 mg/kg ammonium, < 20 mg/kg iron, < 10 mg/kg heavy metals and < 0.1 % sulphated ash.

By specification, the proportion by weight in the final product is not less than 92 % (anhydrous basis). Five batches of the additive showed levels of the active substance in the range 99.5–99.8 % (loss on drying 10.6–10.7 %).[17] In the same batches, the optical rotation ranged between + 5.93 and + 6.08, the percentage of chloride ranged between 20.0 and 20.7 %, sulphate and ammonium were < 200 mg/kg, iron and lead were < 10 mg/kg and arsenic was < 1 mg/kg. In another batch, cadmium was < 0.01 mg/kg, mercury was < 0.005 mg/kg, lead was < 0.05 mg/kg and arsenic was < 0.1 mg/kg.[18] All parameters comply with the specifications of PhEur (2010). Aflatoxins B1, B2, G1 and G2 analyses in three batches were all below the quantification level of 0.1 µg/kg.[19] No data on pesticides, dioxin and dioxin-like products were provided, even upon request. The applicant stated that the materials used for the manufacturing of L-cysteine hydrochloride monohydrate do not contain pesticides, dioxins or dioxin-like products.[20] The dossier does not contain data on the microbial contamination.

Three batches of the additive were analysed for particle size distribution by laser diffraction. The fraction of particles below 50 µm was < 1 % (v/v).[21] The dusting potential, measured in the same batches using the Stauber–Heubach method, ranged from 0.96 to 1.23 mg dust per 50 g of product,[22] corresponding to 48–61 mg/m^3.

L-Cysteine is produced by electrolytic reduction and filtration of L-cystine obtained by hydrolysis at 110 °C of natural keratin (typically from duck feathers). An alternative way of manufacturing that is also envisaged is via fermentation of substrate with *Escherichia coli* strains. However, the applicant did not provide information on the producing strain and the FEEDAP Panel cannot conclude on this way of manufacturing.

2.2. Stability

The applicant claimed that the two batches of the product were stable for 11 months[23] when stored in a dry, clean, well-ventilated place, protected from moisture and light (in polyethylene bags) at 15 °C.[24] Two additional batches were shown to be stable for 12 months under the same conditions.[25] The applicant did not provide studies on the stability of the additive in premixtures or feedingstuffs. There were also no data on the stability of the additive to processing. The absence of these data was justified by the applicant on the basis that it is not possible to assess the stability of the additive in feedingstuffs with any degree of accuracy, because it is consumed in Maillard reactions. Furthermore, the applicant points out that it is difficult to separate the cysteine that is added from what is naturally present in feed materials.[26]

2.3. Conditions of use

The additive is intended to be used in pet foods as a flavouring substance. The applicant does not specify a maximum level; however, it envisages an inclusion level of 0.4 % L-cysteine hydrochloride monohydrate in feed at 75–80 % moisture.

[17] Technical dossier/Section II/Annex II_Cys HCl_Batch data 1 to Annex II_Cys HCl_Batch data 5.
[18] Technical Dossier/Supplementary information September 2013/10_Annex_II_Cys HCl - heavy metals.pdf.
[19] Technical Dossier/Supplementary information September 2013/14_Annex_ II_Dust&Mtox (1).pdf to 16_Annex_ II_Dust&Mtox (3).pdf.
[20] Technical dossier/Supplementary information September 2013/17_Annex _II_CysHCl - Dioxin&Pest.pdf.
[21] Technical dossier/Supplementary information September 2013/12_Annex _II_CysHCl - Particle.pdf.
[22] Technical Dossier/Supplementary information September 2013/13_Annex_II_Cys HCl - Dust potl.pdf.
[23] Technical Dossier/Supplementary information September 2013/08_Annex_II_Cys HCl - stability 3.pdf.
[24] Technical Dossier/Supplementary information September 2013/18_Annex_II_Cys HCl - Temp&RH.pdf.
[25] Technical Dossier/Supplementary information September 2013/07_Annex_II_Cys HCl - stability x2.pdf.
[26] Technical Dossier/Supplementary information September 2013/03_Cys HCl—Reply to EFSA (ex July 2012)-2.doc.

The FEEDAP Panel notes that the inclusion level exceeds the minimum requirement for cysteine of cats and dogs by approximately 460 %, which would be considered unusual for feed flavourings (NRC, 2006). The applicant claims that much of the added cysteine is consumed during feed production owing to the Maillard reaction.[21]

2.4. Evaluation of the analytical methods by the European Union Reference Laboratory (EURL)

EFSA has verified the EURL report as it relates to the methods used for the control of L-cysteine hydrochloride monohydrate in animal feed. The Executive Summary of the EURL report can be found in the Appendix.

3. Safety

3.1. Safety for the target species

Excessive doses of amino acids lead to nutritional imbalances, which may provoke interactions and can eventually result in adverse effects (growth reduction, reduced food consumption, changes in plasma amino acid pattern, mortality). Although nutritionally equivalent to L-cystine, L-cysteine is more toxic than L-cystine (Harper et al., 1970; Anderson and Raiten, 1992; Baker, 2006).

L-Cysteine, which is also the first metabolic intermediate of L-cystine after a reduction step, can act as a precursor of glutathione, can be further decarboxylated to cysteamine (a precursor of coenzyme A) or can be used for pyruvate synthesis. The pyruvate formation can occur via two alternative routes: either by desulphydration followed by deamination, or mainly via cysteinesulphinic acid, which is also a precursor of alanine, taurine and 3′-phosphoadenosine 5′-phosphosulphate (PAPS). The metabolic pathways to pyruvate are associated with the release of hydrogen sulphide, ammonia and sulphate ions.

In dogs and other omnivores, cysteine is primarily converted to taurine, homocysteine and S-adenosylmethionine, which is a precursor of glutathione. Cats have a higher requirement for cysteine, which serves as a precursor for gluconeogenesis and thus for energy production (NRC, 2006). This metabolism reflects the fact that cats have very little carbohydrate in their natural diet. Another reason for the high requirement of cysteine in cats is its role in the formation of hair and felinine, a sulphur-containing amino acid found in the urine of cats (Hendriks et al., 1995).

Excessive doses of sulphur-containing amino acids lead, in addition to nutritional imbalances, to species-dependent adverse effects, as shown for sulphur amino acids and in particular for L-cysteine and L-cystine in a series of experiments with broiler chicks, rats and weaned pigs. Overdoses (2.5-, 5-, 7.5- and 10-fold the dietary requirements, corresponding to 10, 20, 30 and 40 g/kg) of either compound caused a general growth retardation in all species. However, an L-cysteine dose of 30 g/kg feed (7.5 times the dietary requirement) caused a 50 % mortality in broiler chicks in only five days, whereas no mortality at similar or higher doses was observed in other species. L-Cystine did not cause mortality even at the highest tested dose (40 g/kg feed) in broilers or in pigs (receiving 6.5- and 13-fold, corresponding to 20 and 40 g/kg cyst(e)ine), whereas some deaths occurred in rats receiving a dose of 72 g/kg feed (corresponding to a 24-fold increase with respect to dietary requirements). It should be noted that the experiments were of a relatively short duration (9–17 days with broilers, 14 days with other species) (Dilger et al., 2007).

Although no definite causes for the toxicities of L-cysteine and L-cystine or for the species differences have been identified, the strong reducing power of L-cysteine, as well as the accumulation of toxic metabolites (ammonia, hydrogen sulphide), have been proposed to play a role.

The FEEDAP Panel has recently concluded that L-cystine is safe for all animal species if the requirements for sulphur-containing amino acids are respected (EFSA FEEDAP Panel, 2013). This conclusion may be extended to L-cysteine, as the two forms can be converted to one another through

redox cycling. However, it is also of nutritional importance that the balance between cysteine and methionine is maintained (NRC, 2006).

According to the NRC (2006), the minimum 'cyst(e)ine' requirements for growing cats and dogs are 3.5 and 3.0 g/kg feed (dry matter (DM)), respectively. At the proposed inclusion level of 2.8 g L-cysteine/kg wet pet food (11–14 g/kg DM), the requirement for cysteine would be grossly exceeded by the addition of L-cysteine as a flavouring if all of the cysteine remained throughout the production process. However, as the applicant claims that most of the L-cysteine is converted in the Maillard process, it is not possible to calculate target animal exposure. It may also be difficult to formulate a diet with an appropriate balance of sulphur-containing amino acids.

The addition of L-cysteine to the food of pets is safe if the balance between cysteine and methionine in the complete diet is maintained. Owing to the unknown total content of free L-cysteine in the final diet, it cannot be assessed whether or not the addition of L-cysteine as a feed flavouring would disrupt this balance.

3.2. Safety for the user/owner

This product is moderately dusty. However, less than 1 % of the particles are < 50 µm in diameter, in which case the possibility of exposure of the lower respiratory tract is considered to be low.[27]

Since no studies on the irritant or sensitising effects were provided, this product has to be considered as potentially irritating to the skin, eyes and mucous membranes and as a potential dermal sensitiser. Therefore, it would be prudent to assume that exposure poses a risk to the user.

3.3. Safety for the environment

Following the provision of the guidance on environmental risk assessment (EFSA, 2008b), there is no requirement for the assessment of the environmental impact of the use of a feed additive when used in pets. This is the case for L-cysteine hydrochloride monohydrate.

4. Efficacy

This compound is used in food as a flavouring. When the function in feed is essentially the same as that in food, no further demonstration of efficacy is necessary. However, the applicant did not provide information on the concentration used for food and no quantification of the final concentration in feed. Given the high level of use of L-cysteine described by the applicant, it is not clear that this additive is used as a flavouring in pet food in the same way as it is used in food and, therefore, efficacy cannot be assumed and has not been demonstrated.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

In the absence of information on bacterial fermentation, the FEEDAP Panel cannot conclude on this way of manufacturing.

The addition of L-cysteine to the food of cats and dogs is safe if the balance between cysteine and methionine in the complete diet is maintained. Owing to the unknown total content of free L-cysteine in the final diet, it cannot be assessed whether or not the addition of L-cysteine as a feed flavouring would disrupt this balance.

In the absence of data, the FEEDAP Panel considers it prudent to assume that exposure of the skin, eyes and mucous membranes poses a risk to users.

[27] Technical Dossier/Supplementary information September 2013/12_Annex_II_Cys HCl - Particle.pdf.

As L-cysteine is intended for use in pets, assessment of the safety for the environment is not needed.

It is not clear if the use of L-cysteine, applied as described by the applicant, is the same as that for human food and, therefore, efficacy cannot be assumed and has not been demonstrated.

RECOMMENDATIONS

The FEEDAP Panel proposes to adjust L-cysteine hydrochloride monohydrate specifications according to PhEur (purity is 98.5–101.0 % with reference to the dried substances, loss on drying 8–12 %). As long as PhEur MG 0895 is considered mandatory for the applicant, further detailed specifications are not necessary.

GENERAL REMARK

The FEEDAP Panel has reservations regarding the classification of nutrients at levels high enough to cover nutritional requirements as sensory additives and functional group flavourings.

DOCUMENTATION PROVIDED TO EFSA

1. L-Cysteine Hydrochloride Monohydrate. October 2010. Submitted by Mars GmbH.
2. L-Cysteine Hydrochloride Monohydrate. Supplementary information. February 2012. Submitted by Mars GmbH.
3. L-Cysteine Hydrochloride Monohydrate. Supplementary information. May 2012. Submitted by Mars GmbH.
4. L-Cysteine Hydrochloride Monohydrate. Supplementary information. July 2012. Submitted by Mars GmbH.
5. L-Cysteine Hydrochloride Monohydrate. Supplementary information. September 2013. Submitted by Mars GmbH.
6. Evaluation report of the European Union Reference Laboratory for Feed Additives on the Methods(s) of Analysis for L-Cysteine Hydrochloride Monohydrate.
7. Comments from Member States received through the ScienceNet.

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WHO (World Health Organization), 2004. 63rd report Evaluation of certain food additives. WHO Technical Report Series. Available online: http://whqlibdoc.who.int/trs/WHO_TRs_928.pdf

APPENDIX

Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for L-cysteine hydrochloride monohydrate[28]

In the current application authorisation is sought for L-Cysteine Hydrochloride Monohydrate under Articles 4(1) and 10(2), under categories 'sensory additives' and 'nutritional additives', functional groups 2(b) 'flavouring compounds' and 3(c) 'amino acids, their salts and analogues' respectively, according to Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of L -Cysteine Hydrochloride Monohydrate for all pet animals. The *feed additive* is intended to be mixed in *premixtures* or added directly to complete *feedingstuffs*. The Applicant suggested no minimum or maximum *L-Cysteine Hydrochloride Monohydrate* concentrations in *feedingstuffs*.

For the determination of the active substance in the feed additive the EURL recommends the internationally recognised European Pharmacopoeia titrimetric method. Even though no performance characteristics of this method are provided, the EURL considers this method suitable to determine L -Cysteine Hydrochloride Monohydrate in the feed additive within the frame of official control.

For the quantification of L -Cysteine Hydrochloride Monohydrate in premixtures and feedingstuffs the EURL recommends the ring-trial validated Community method (Commission Regulation (EC) No 152/2009). The method applies to the determination of free (synthetic and natural) and total (peptide-bound and free) amino acids, using an amino acid analyzer or High Performance Liquid Chromatography (HPLC) equipment. However, the method is not able to distinguish between Cysteine, Cystine, the correspondent salts and the amino acid enantiomers. All these substances are indicated hereafter as Cyst(e)ine. The performance characteristics for the determination of total Cyst(e)ine are reported:

- a relative standard deviation for *repeatability* (RSDr) ranging from 1.7 to 4.6%;
- a relative standard deviation for *reproducibility* (RSDR) ranging from 8.8 to 19%.

Based on the performance characteristics presented, the EURL recommends for official control, the ring-trial validated Community method based on ion exchange chromatography coupled with post-column derivatisation and photometric detection to determine *Cyst(e)ine* (including *L-Cysteine Hydrochloride Monohydrate*) in *premixtures* and *feedingstuffs*.

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.

[28] The full report is available on the EURL website: http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2010-0152.pdf

GLOSSARY AND ABBREVIATIONS

CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
EURL	European Union Reference Laboratory
FAO	Food and Agriculture Organization
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MRL	Maximum residue limit
SCF	Scientific Committee for Food
WHO	World Health Organization