SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of taurine as a feed additive for all animal species[1]

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

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Taurine is a beta-amino acid, not incorporated into proteins. Taurine is involved in a number of physiological processes. In cats, dietary taurine at requirement/allowance levels is safe with a margin of safety of between 4 and 20. The few data available for carnivorous fish indicate that levels between 2.0 % and 2.5 % are safe. It is further concluded that up to 0.2 % taurine in feed is tolerated by all animal species. The FEEDAP Panel estimates the observed safe level in humans to be 6 g/person per day (corresponding to 100 mg/kg body weight per day). Exposure resulting from the consumption of foodstuffs and 'energy drinks' together would amount to about one-third of the observed safe level. Population oral exposure data include taurine from foodstuffs of animal origin, such as animal tissue and products, resulting from feed supplementation. However, exposure resulting from this source is estimated to be low since, to the knowledge of the FEEDAP Panel, the use of taurine as a feed additive is mainly restricted to cats and dogs. The use of taurine as a feed additive for all animal species would not raise concerns about consumer safety. In the absence of data, taurine is considered to be a skin and eye irritant and skin sensitiser, and to be hazardous if inhaled. A risk to the environment resulting from the use of taurine in animal nutrition is not foreseen. Synthetic taurine is considered efficacious for use in cat, dog and carnivorous fish diets. In the case of poultry, pigs and ruminants, no studies demonstrating beneficial effects of taurine supplementation on performance, health or product quality have been found. In laying hens, dietary supplementation with 0.25–0.5 % taurine has been shown to have an adverse effect (reduced egg weight).

KEY WORDS

Nutritional additive, vitamins and provitamins, taurine, safety, efficacy

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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 taurine as an additive to feed and water for drinking for all animal species.

Taurine is an essential beta-amino acid for some species. Taurine is not incorporated into proteins and is found in the tissues of most animal species in its free form. Taurine is involved in a number of physiological processes including bile acid conjugation, osmoregulation, neuronal excitability, inflammatory reactions and glucose metabolism. In some animal species low dietary levels of taurine have been associated with retinal degeneration, dilated cardiomyopathy and growth retardation.

Oral administration routes of taurine via feed or water for drinking are considered bioequivalent.

In the cat, dietary taurine at requirement/allowance levels (0.05–0.25 % in complete feed dry matter (DM)) is safe with a margin of safety of between 4 and 20. The few data available for carnivorous fish indicate that levels between 2.0 % and 2.5 % are safe. No data were provided or found which would allow firm conclusions on the safety of certain levels of taurine for other target species. However, the historical use of diets containing up to 20 % feedingstuffs of animal origin led to the conclusion that up to 0.2 % taurine in complete feed is tolerated by all animal species. A margin of safety cannot be given.

The FEEDAP Panel estimates the observed safe level (OSL) in humans to be 6 g/person per day (corresponding to 100 mg/kg body weight (bw) per day). Exposure resulting from the consumption of foodstuffs and 'energy drinks' together would amount to about one-third of the OSL. Population oral exposure data include taurine from foodstuffs of animal origin, such as animal tissue and products, resulting from feed supplementation. However, exposure resulting from this source is estimated to be low since, to the knowledge of the FEEDAP Panel, the use of taurine as a feed additive is mainly restricted to cats and dogs. The use of taurine as an additive for all animal species would not raise concerns about consumer safety.

In the absence of data, taurine is considered to be a skin and eye irritant and skin sensitiser, and to be hazardous if inhaled.

The use of taurine as an additive in animal nutrition is not expected to substantially increase the concentration in the environment. Therefore, a risk to the environment resulting from the use of taurine in animal nutrition is not expected.

Synthetic taurine in the diet of cats, dogs and carnivorous fish is considered efficacious. In the case of poultry, pigs and ruminants, no studies demonstrating beneficial effects of taurine supplementation on performance, health or product quality have been found. In laying hens, dietary supplementation with 0.25–0.5 % taurine has been shown to have an adverse effect (reduced egg weight) .

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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 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, 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 time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from the VITAC EEIG Vitamins Authorisation Consortium[5] for (i) authorisation of a new use (i.e. use in water for drinking), and (ii) re-evaluation of authorisation of the product taurine, when used as a feed additive for all animal species (category: nutritional additive; functional group: vitamins, provitamins and chemically well-defined substances having similar effect) under the conditions mentioned in Table 1.

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive) and under Article 10(2) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application.[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 3 January 2011.

The Scientific Committee on Food expressed an opinion on caffeine, taurine and D-glucurono-γ-lactone as constituents of the so-called 'energy' drinks (EC, 1999) and an opinion on additional information on 'energy' drinks (EC, 2003). The Panel on Food Additives and Nutrient Sources added to food (ANS) issued an opinion on the use of taurine and D-glucurono-γ-lactone as constituents of the so-called 'energy' drinks (EFSA, 2009a). The NDA Panel expressed an opinion on the substantiation of health claims related taurine and protection of DNA, proteins and lipids from oxidative damage (ID 612, 1658, 1959), energy-yielding metabolism (ID 614), and delay in the onset of fatigue and enhancement of physical performance (ID 1660) pursuant to Article 13(1) of Regulation (EC) No 1924/2006 (EFSA, 2009b).

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, consumer, user and the environment and the efficacy of taurine, when used under the conditions described in Table 1.

[4] Regulation (EC) 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] VITAC EEIG Vitamins Authorisation Consortium, Avenue Louise 130A, B-1050 Brussel, Belgium. Companies: ORFFA International Holding BV, The Netherlands.
[6] EFSA Dossier reference: FAD-2010-0215.

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

Additive	Taurine
Registration number/EC No/No (if appropriate)	--
Category(ies) of additive	Nutritional additives
Functional group(s) of additive	Vitamins, provitamins and chemically well defined substances having a similar effect

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
Taurine	$C_2H_7NO_3S$	Min. 98.0 %	Current Japanese Pharmacopoeia method
Loss on drying	NA	Max. 0.2 %	Current Japanese Pharmacopoeia method

Trade name (if appropriate)	--
Name of the holder of authorisation (if appropriate)	--

Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		mg/kg of complete feedingstuffs (select what applicable)		
All animal species and categories	--	--	--	--

Other provisions and additional requirements for the labelling	
Specific conditions or restrictions for use (if appropriate)	Only for manufacture of animal feed. Applicable in premix, feed & water. The additive may be incorporated as such or in the form of an additive preparation containing min. 98 % taurine and max. 0,8 % anti-caking agent.
Specific conditions or restrictions for handling (if appropriate)	--
Post-market monitoring (if appropriate)	No specific requirements other than the traceability and complaint system implemented in compliance with the requirements of Regulation No 183/2005.
Specific conditions for use in complementary feedingstuffs (if appropriate)	Applicable in premix, feed & water. Direct incorporation of the additives necessitates specific equipment in the production site, in order to ensure proper and homogeneous mixing.

Maximum Residue Limit (MRL) (if appropriate)			
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues
--	--	--	--

ASSESSMENT

This opinion is based in part on data provided by a consortium of companies involved in the production/distribution of chemically synthesised taurine. It should be recognised that these data cover only a fraction of existing additives containing taurine. The application is for the active substance and the composition of the additive formulations is not the subject of the application. The Panel has sought to use the data provided together with data from other sources to deliver an opinion.

1. Introduction

Taurine is an essential beta-amino acid for some species. Taurine is not incorporated into proteins and is found in the tissues of most animal species in its free form. Taurine is involved in a number of physiological processes including bile acid conjugation, osmoregulation, neuronal excitability, inflammatory reactions and glucose metabolism. In some animal species, low dietary levels of taurine have been associated with retinal degeneration, dilated cardiomyopathy and growth retardation.

Taurine is included in the European Union Register of Feed Additives pursuant to Regulation (EC) No 1831/2003. It is authorised without a time limit in application of Article 9t (b) of Council Directive 70/524/EEC[7] concerning additives in feedingstuffs (2004/C 50/01) for use in all animal species as a nutritional additive.

The applicant asks for the re-evaluation of the use of taurine as an additive to feed for all animal species and categories without restrictions for age, (withdrawal) time and content in feedingstuff. The applicant is also seeking authorisation for a new use of taurine in water for drinking.

Taurine is authorised as an additive for specific nutritional purposes in foods for particular nutritional uses (Regulation (EC) No 953/2009),[8] in infant formulae and in follow-on formulae when reconstituted as instructed by the manufacturer (Directive 2006/141/EC, Annex III).[9] It is also used as an active ingredient in energy drinks (EFSA, 2009a). Taurine is listed as ingredient in cosmetic products as buffering agent (Commission decision 2006/257/EEC).[10]

2. Characterisation

2.1. Characterisation of the active substance

Taurine (IUPAC name: 2-amino-ethanesulfonic acid; synonyms: beta-aminoethylsulfonic acid, tauric acid) is identified by Chemical Abstracts Service (CA) no 107-35-7 and European Inventory of Existing Chemical Substances (EINECS) no 203-483-8. The structural formula of taurine is shown in Figure 1.

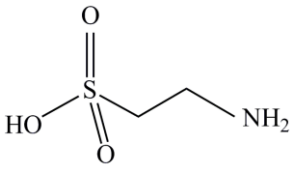

Figure 1: Structural formula of taurine

[7] Commission List of the authorised additives in feedingstuffs published in application of Article 9t (b) of Council Directive 70/524/EEC concerning additives in feedingstuffs (2004/C 50/01). OJ C 50, 25.2.2004, p.1.
[8] Commission Regulation (EC) 953/2009 of 13 October 2009 on substances that may added for specific nutritional purposes in foods for particular nutritional uses. OJ L 269, 14.10.2009, p. 9.
[9] Commission Directive 2006/141 EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC. OJ L 401 30.12.2006, p. 1.
[10] Commission Decision 2006/257/EC of 9 February 2009 amending Decision 96/335/EC establishing an inventory and a common nomenclature of ingredients employed in cosmetic products. OJ L 97 5.04.2006, p. 1.

The molecular formula of taurine is $C_2H_7NO_3S$ and its molecular weight is 125.15. It has a pK_a of 1.5 (at 25 °C) and a melting point of 300 °C (decomposition) and shows a bulk density of 0.65–0.75 g/cm^3 and a density of approximately 1.7 g/cm^3. It is soluble in water (10 g dissolves in 100 mL at 25 °C) and insoluble in ethanol, ethyl ether and acetone. The pH of a 5 % solution in water is 4.1–5.6.

Taurine is a white crystalline powder that is almost odourless but with a slightly acidic taste. It contains by specification at least 98.0 % taurine in dried substance. Analysis of five batches of the active substance showed an average content of 99.5 ± 0.1 % taurine and a loss on drying of 0.07 ± 0.01 %.[11]

The final additive may be formulated by adding a maximum 0.8 % of an anti-caking agent (SiO_2).

Three batches of the additive were analysed for impurities, one batch with six replicate samples and another batch with three replicate samples.[11] In all batches, sulphated ash was < 0.06 % (in one batch residue on ignition 0.06 %), chloride < 0.01 %, sulphate < 0.01 %, ammonium salt < 0.02 %, related substances < 0.2 %, heavy metals (expressed as lead) < 10 mg/kg and arsenic < 1.0 mg/kg (two batches).

Two batches of the additive were analysed for particle size distribution by laser diffraction. The particle fractions below 10, 50 and 100 µm amounted to 0 %, 3 % and 14 %, respectively. The particle shape was needle-like (mass-median aerodynamic diameter not given).[12] One batch of the additive showed a dusting potential of 59.5 mg/50 g (corresponding to 3.0 g/m^3). The active substance content of the dust fraction was 76 % (compared with > 99 % in the additive).

2.2. Manufacturing process

Taurine is synthesised starting from ethylene oxide and sodium bisulphite. Subsequently, liquid ammonia and sulphuric acid are added. The product is then decolourised, purified, crystallised, centrifuged, dried, sieved and blended with the carrier to obtain the additive. The applicant provided a flow chart and detailed description of the synthetic process, and critical control points are identified and monitored.[13]

2.3. Stability and homogeneity

2.3.1. Shelf-life of taurine

Taurine (three batches, stored in polyethylene sealed bags) was demonstrated to have a shelf-life of 36 months at 25 °C. Shelf-life was measured under accelerated conditions at 40 °C and no loss was observed for six months (three batches).[14]

2.3.2. Stability of the additive when added to premixtures, feed and water for drinking

The applicant provided data on the stability of taurine (one batch) when incorporated in a mineral premixture for chickens at 50 g/kg and kept in plastic containers at 25 °C up to four months. No losses of taurine in the premixture were observed during four months' storage.

When incorporated in complete feed for chickens at 1 000 mg/kg and kept in plastic containers at 25 °C, no losses of taurine (one batch) were detected. Information on the stability of taurine during feed processing and in a typical pet food with high moisture content was not provided despite being requested.

[11] Technical dossier/Section II/Annex 2.1 and Annex 2.2.
[12] Technical dossier/Section II/Annex 2.6.
[13] Technical dossier/Section II/Annex 2.5.
[14] Technical dossier/Section II/Annex 2.14.

Taurine (three batches) was stable in a 1 % and a 2 % solution (tap water) when stored at room temperature in a dark place for one week.[15]

2.3.3. Homogeneity

Based on a statistical method (Jansen, 1992), the coefficient of variation (CV) for homogeneity of taurine in dry cat feed containing 400 mg supplemental taurine/kg feed was calculated to be 2.3 % for a daily ration of 63 g. Similar calculations for Japanese quails, broilers and piglets resulted in CVs of 5.2 %, 7.3 % and 0.14 %, respectively. However, this method has been developed to test the working accuracy of mixing equipment.

Taurine is highly soluble in water and, therefore, homogeneity in water for drinking need not be demonstrated.

2.4. Physico-chemical incompatibilities in feed

No physico-chemical incompatibilities or interactions have been reported between taurine and feed materials, carriers, other approved additives or medicinal products when the additive was added to premixtures and feed. No such incompatibilities or interactions are expected.

2.5. Conditions of use

Taurine is intended for use in all animal species and categories via feed and water for drinking without a maximum content or a withdrawal period.

The applicant stated that the active substance can be used as supplied or in the form of the additive for direct incorporation into complete feed or via premixtures.

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

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

3. Safety

According to Regulation (EC) No 429/2008, tolerance, metabolism and residue, and toxicological (concerning consumer safety) studies are not required for vitamins, pro-vitamins and chemically defined substances having similar effects which are already authorised as feed additives under Directive 70/524/EEC and which do not have the potential to accumulate, which the FEEDAP Panel considers is the case for taurine.

3.1. Absorption, distribution, metabolism and excretion of taurine

There are two sources of taurine in the body: dietary and endogenous. In mammals, taurine is synthesised in many tissues; the main sites are liver, brain (Huxtable, 1992) and pancreas, predominantly in α-islets (Bustamante et al., 2001). Taurine is synthesised from cysteine and methionine in a few steps, one of which requires pyridoxal-5′-phosphate (vitamin B_6) as coenzyme of cysteine sulphinate decarboxylase. In species other than mammals, the biosynthesis of taurine has been poorly studied. The extent of synthesis varies widely between species. An adult rat consuming standard laboratory food produces about 80 % of its total body taurine and obtains the remainder from the diet. However, if required, rats can obtain all body taurine from biosynthesis, since rats fed taurine-free diets for extended periods do not exhibit any decrease in tissue taurine concentrations (Sturman, 1973). Cats have low levels of activity of cysteine sulphinate decarboxylase, the rate-limiting enzyme for taurine biosynthesis, and are, therefore, dependent on a dietary source to maintain their body pool of this amino acid. Thus, taurine is an essential nutrient in cats.

[15] Technical dossier/Section II/Annex 2.16.

Taurine is a highly polar and lipophobic compound; hence passive diffusion of taurine through the cell wall is limited. The predominant route of absorption into enterocytes is via transporters. However, taurine uptake across the intestinal brush-border membrane of the adult cat seems not to be mediated by a specific transport mechanism (Wolffram et al., 1991). Therefore, taurine absorption from the gastrointestinal tract may be another limiting factor in the maintenance of taurine homeostasis in the cat.

In all vertebrates except mammals, taurine is the sole amino acid conjugated to form bile salts. Among the mammals, carnivores also tend to be conjugators of taurine only, whereas other species tend to conjugate both taurine and glycine. High concentrations of taurine are present in retina, liver, pancreas, central nervous system and white blood cells. The largest pools of taurine are found in skeletal and cardiac muscles, where it regulates intracellular Ca^{2+} concentration (Szymanska and Winiarska, 2008). The cells have specific Na^{+}/Cl^{-}-dependent carriers (TauT), which allow maintenance of a high intracellular to extracellular taurine ratio. The concentration of taurine in tissues is independent of dietary supplementation. Sved et al. (2007) found that the concentrations in the different tissues did not differ greatly between controls (30 mg/kg) and treated rats (300 mg/kg), and were not influenced to any large extent by dose level or duration of treatment. The rate of elimination of intracellular taurine will depend on the rate of turnover of the intracellular pool for that particular tissue; brain has the lowest rate of taurine turnover (Sved et al., 2007). Taurine synthesis in the brain is physiologically very important, even in species lacking the overall ability to synthesise sufficient taurine for their needs (Reichert and Urban, 1986). In brain, taurine is involved in osmoregulation and also acts as a neuromediator and neuromodulator (e.g. it is an agonist of $GABA_A$ receptors). In cartilaginous fish, taurine serves a prime osmoregulatory function, i.e. the variations in taurine content of a tissue are sufficient to account for a significant proportion of the osmotic adjustment of that tissue. In little skate (*Raja erinacea*), taurine is neither synthesised nor metabolised (King et al., 1980 1988). In overdose in rats, taurine was rapidly absorbed and then rapidly excreted in urine (Sved et al., 2007).

Considering the body's pools of taurine, feedingstuffs of animal origin except milk products are rich in taurine, e.g. fish DM 1 000–9 000 mg/kg; poultry meat DM 1 000–8 000 mg/kg, beef DM 200–2 000 mg/kg; and meat and bone meal 90–1 100 mg/kg (Spitze et al., 2003).

3.2. Safety for the target species

3.2.1. Obligate carnivorous species

3.2.1.1. Cats

The taurine requirement of cats depends on diet composition, primarily the type, quantity and digestibility of protein (as a source of taurine precursors methionine/cysteine) and of fibre. The minimum requirement (MR) at all stages of life of cats fed purified diets containing little fibre, highly digestible protein and 16.7 MJ metabolisable energy (ME)/kg is about 425 mg/kg. Because of the variability of fibre type and concentrations used and of protein concentrations and digestibility, no MR can be determined for commercial diets (NRC, 2006).

Allowances for adult cats are 400–500 mg/kg complete feed (AWT, 2002), for kittens 400 mg/kg and for reproduction 500 mg/kg. Morris and Rogers (1994) recommended up to 1 000 mg taurine/kg commercial dry feed and up to 2 500 mg taurine/kg DM commercial wet feed. Heat-processing of diets reduces the availability of taurine (Hickman et al., 1992).

Sturman and Messing (1992) fed weanling kittens 10 g taurine/kg diet containing about 18.8 MJ ME/kg for up to 3 years and found no adverse effects; thus the safe upper level for kittens is > 8.9 g/kg diet containing 16.7 MJ ME/kg.

3.2.1.2. Fish

Taurine can also be considered essential for salmonids and some marine fish species although requirement data are not well established. Values up to 2.5 % are reported by Takeuchi (2001) and Matsunari et al. (2008). Taurine supplementation up to 20 g taurine/kg diet had no adverse effects in predominantly carnivorous fish species (rainbow trout, *Oncorhynchus mykiss*, and red sea bream *Pagrus major*) fed diets marginally deficient in taurine (Gaylord et al., 2007; Matsunari et al., 2008).

3.2.2. Non-obligate carnivores and herbivores

3.2.2.1. Dogs

In dogs fed commercial (Kramer et al., 1995) or purified amino acid diets (Delaney et al., 2003), plasma taurine levels were normal even if there was no taurine in the diet, and dogs fed these types of diets did not develop signs of taurine deficiency. Thus, the minimum requirement for taurine in dogs fed normal diets is zero (NRC, 2006). Although beneficial effects of additional taurine on dilated cardiomyopathy have been observed in dogs (Kittleson et al., 1997; Tôrres et al., 2003), particularly large breeds (Backus et al., 2006), no recommendations were suggested. The dose was mostly chosen to normalise plasma taurine. No reports could be found investigating acute or chronic toxicity related to feeding large quantities of taurine to dogs, so no safe upper level can be established (NRC, 2006).

3.2.2.2. Poultry

Broilers with stress-induced pulmonary hypertension syndrome had depleted taurine reserves, which were thought to have contributed to cardiac weakness (Ruiz-Feria et al., 1999; Ruiz-Feria and Wideman, 2001). Yamazaki and Takemasa (1998) showed that the supplementation of maize soybean layer diet with 0.25 % and 0.5 % taurine reduced egg weight independent of methionine addition. Lower doses (up to 0.05 %) were better tolerated by growing Japanese quails; however, feed intake was depressed for the 6-week feeding period (Wang et al., 2009).

3.2.2.3. Pigs

Two piglet litters weaned at 11 days of age were fed a casein-based milk replacer with or without 0.4 % taurine supplementation for three weeks. No differences in growth rate or feed consumption were noted between the groups (Stephen et al., 1991). Plasma taurine, which responded in the second week to the dietary supply, returned to initial values in both groups at the end of the study, indicating increasing endogenous synthesis.

3.2.2.4. Ruminants

Thorstensen et al. (2012) showed that plasma taurine in sheep responded to the nutrition levels (feeding according to standard compared with 10–15 % body weight reduction) for a period of about 105 days including 97 days of pregnancy.

3.2.3. Conclusions on the safety for target species

In cats, dietary taurine at requirement/allowance levels (0.05–0.25 % in complete feed DM) is safe with a margin of safety of between 4 and 20. The few data available for carnivorous fish indicate that levels between 2.0 % and 2.5 % are safe.

No data were provided or found which would allow firm conclusions on the safety of certain levels of taurine for other target species. However, the historical use of diets containing up to 20 % feedingstuffs of animal origin led to the conclusion that up to 0.2 % taurine in complete feed is tolerated by all animal species. A margin of safety cannot be given.

3.3. Safety for the consumer

Taurine is not genotoxic, teratogenic or carcinogenic (EC, 1999). However, a tolerable upper intake level (UL) could not be derived from the available NOAELs (no observed adverse effects levels) by

the SCF (EC, 2003) or the ANS Panel (EFSA, 2009a) because the studies did not investigate all the relevant toxicological endpoints (e.g. some aspects of reproductive toxicity). Shao and Hathcock (2008) performed OSL[16] risk assessments for taurine based on the available published human clinical trial data. Since the evidence for the absence of adverse effects is strong for taurine at supplemental intakes up to 3 g/day, this level was identified as the OSL for normal healthy adults. Although much higher levels of taurine have been tested without adverse effects and may be safe, the data for intakes above these levels are not sufficient to draw any confident conclusions about long-term safety. It was noted by the ANS Panel in 2009 (EFSA, 2009a) that the results of a large number of studies in adults, children and infants indicated that daily ingestion of taurine doses of up to 6 g/person per day for periods up to one year (including supplements) did not produce adverse health effects. On the basis of this information, an OSL of 6 000 mg/person per day (equal to 100 mg/kg bw per day for a 60-kg person) can be identified. This value is taken as a reference for comparison with population exposure. The possibility of an increased susceptibility during pregnancy and/or nursing was not taken into consideration in the OSL.

3.3.1. Consumer exposure

Exposure to taurine is unavoidable as it is a natural constituent of the body and is present in foods of animal origin. Spitze et al. (2003) determined the taurine content of a variety of foodstuffs. Animal muscle tissue, particularly fish flesh, contained high concentrations of taurine. Plant products contained either low or undetectable amounts of taurine. Cooking in water, such as in boiling or basting, induced some loss of taurine, whereas food preparation methods that minimised water loss, such as baking or frying, resulted in higher rates of taurine retention.

The mean daily exposure to taurine from omnivore diets has been estimated to range from 9–40 (lowest range values) to up to 200–400 mg/person per day (top range values) (Rana and Sanders, 1986; Laidlaw et al., 1990; Hayes and Trautwein, 1994). Taurine intake was negligibly low in subjects following a strict vegetarian diet (Rana and Sanders, 1986). The highest, as well as the most recent, of the top range estimates is 400 mg/person per day (Hayes and Trautwein, 1994), equal to 6.7 mg/kg bw per day for a 60-kg person. This value is 150 times lower than the NOAEL of 1 000 mg/kg bw per day in laboratory animals and 15 times lower than the human OSL (100 mg/kg bw per day).

Consumers of 'energy drinks' can ingest quite high levels of taurine (for example, the 50th and 95th percentiles are 8.3 and 23.3 mg/kg bw, respectively; EFSA, 2009a). Thus, regular consumption of energy drinks would lead to a taurine intake (mean 500 mg/person per day, 95th percentile 1 400 mg/person per day) higher than the upper range of daily intake from omnivore diets (EFSA, 2009a).

The results of study carried out in laboratory rodents (Sved et al., 2007) suggest that dietary taurine does not affect taurine levels in tissues except liver. No data are available as regards the influence of taurine intake on its content in milk or eggs, or in bird tissues. In fish, equilibrium between oral intake and excretion is reached at rather high taurine dietary concentrations (2.5 %) (Takeuchi, 2001; Matsunari et al., 2008).

3.3.2. Conclusions on consumer safety

Taurine is not genotoxic, teratogenic or carcinogenic. An upper limit (UL) is not established.

The FEEDAP Panel estimates the OSL in humans to be 6 g/person per day (corresponding to 100 mg/kg bw per day). Exposure resulting from the consumption of foodstuffs and "energy drinks"' together would amount to about one-third of the OSL.

[16] 'Observed safe level (OSL)' is a model based on observations of exposed humans, in which 'the highest intake with convincing evidence of safety, even if there are no established adverse effects at any level' is taken without applying additional safety factors (Hathcock and Shao, 2008). A FAO/WHO report (2006) gave a similar definition for the highest observed intake.

Population oral exposure data include taurine from foodstuffs of animal origin, such as animal tissue and products, resulting from feed supplementation. However, exposure due to this source is estimated to be low since, to the knowledge of the FEEDAP Panel, the use of taurine as a feed additive is mainly restricted to cats and dogs.

The use of taurine as an additive for all animal species would not raise concerns to consumer safety.

3.4. Safety for the user

Three per cent of particles are below 50 µm and, since the additive shows a considerable dusting potential (3 g/m^3), a potential for inhalation exposure cannot be ruled out. In the absence of inhalation toxicity data, it would be prudent to consider taurine as potentially hazardous if inhaled.

No studies were performed on irritation or sensitisation.

In the absence of any data, taurine is considered to be a skin and eye irritant and skin sensitiser, and to be hazardous if inhaled.

3.5. Safety for the environment

Taurine occurs widely in feedingstuffs of animal origin (seafood and mammalian and poultry tissues). Most plant feedingstuffs contain very low amounts of taurine. Excess doses of taurine to food-producing animals would increase taurine excretion.

Several species of bacteria and fungi are known to degrade taurine (e.g. to sulphate/sulphide, ammonia, acetate and carbon dioxide) (MetaCyc database, 2004).[17] The use of taurine as an additive in animal nutrition is not expected to substantially increase the concentration in the environment. Therefore, a risk to the environment resulting from the use of taurine in animal nutrition is not expected.

4. Efficacy

According to Regulation (EC) No 429/2008, efficacy studies are not required for vitamins, pro-vitamins and chemically well-defined substances having similar effects which are already authorised as feed additives.

Synthetic taurine can serve as a source of taurine in the metabolism of animals. The efficacy of taurine in cats is widely demonstrated in the literature, and consequently requirement data exist. The situation in dogs is different as no requirement exists and dose–effect relationships in the case of dilated cardiomyopathy, for which beneficial effects of taurine have been described for certain breeds, are not available. Although its use in dog nutrition is primarily driven by a medical indication, the FEEDAP Panel suggests that taurine might be effective in preventing dilated cardiomyopathy in dogs.

Limited data indicate taurine requirements of predominantly carnivorous fish (e.g. salmonids) of up to 2.5 % in the diet. When natural sources (e.g. fish meal) are in short supply, synthetic taurine may contribute in meeting the requirement.

In the case of poultry, pigs and ruminants, no studies were found to demonstrate beneficial effects of taurine supplementation on performance, health or product quality of these animal species. In laying hens, dietary supplementation with 0.25–0.5 % taurine was shown to have an adverse effect (reduced egg weight).

[17] MetaCyc database, 2004: http://www.biocyc.org/META/NEW-IMAGE?type=PATHWAY&object=PWY-1263

5. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[18] and Good Manufacturing Practice.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Oral administration routes of taurine via feed or water for drinking are considered bioequivalent.

In cats, dietary taurine at requirement/allowance levels (0.05–0.25 % in complete feed DM) is safe with a margin of safety of between 4 and 20. The few data available for carnivorous fish indicate that levels between 2.0 % and 2.5 % are safe. No data were provided or found which would allow firm conclusions on the safety of certain levels of taurine for other target species. However, the historical use of diets containing up to 20 % feedingstuffs of animal origin led to the conclusion that up to 0.2 % taurine in complete feed is tolerated by all animal species. A margin of safety cannot be given.

The FEEDAP Panel estimates the OSL in humans to be 6 g/person per day (corresponding to 100 mg/kg bw per day). Exposure by consumption of foodstuffs and 'energy drinks' together would amount to about one-third of the OSL. Population oral exposure data include taurine from foodstuffs of animal origin, such as animal tissue and products, resulting from feed supplementation. However, exposure due to this source is estimated to be low since, to the knowledge of the FEEDAP Panel, the use of taurine as a feed additive is mainly restricted to cats and dogs. The use of taurine as an additive for all animal species would not raise concerns to consumer safety.

In the absence of any data, taurine is considered as a skin and eye irritant and skin sensitiser, and as hazardous if inhaled.

A risk for the environment resulting from the use of taurine in animal nutrition is not expected.

For use in diet for cats, dogs and carnivorous fish, synthetic taurine is considered efficacious. In the case of poultry, pigs and ruminants, no studies demonstrating beneficial effects of taurine supplementation on performance, health or product quality were found. In laying hens, supplementation of the diet with 0.25–0.5 % taurine has been shown to have an adverse effect (reduced egg weight).

RECOMMENDATIONS

Since synthetic taurine is not effective in poultry, pigs or ruminants, and has an adverse effect on egg production, the FEEDAP Panel recommends that taurine should no longer be authorised for use in these animal species.

DOCUMENTATION PROVIDED TO EFSA

1. Taurine as a feed additive for all animal species. November 2010. Submitted by VITAC EEIG Vitamins Authorisation Consortium.

2. Taurine as a feed additive for all animal species. Supplementary information. November 2011. VITAC EEIG Vitamins Authorisation Consortium.

3. Evaluation report of the European Union Reference Laboratory for Feed Additives on the methods(s) of analysis for taurine.

[18] Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

4. Comments from Member States received through the ScienceNet.

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APPENDIX

Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for taurine[19]

In the current application authorisation is sought under articles 4(1) and 10(2) for *Taurine* under the category/functional group 3(a) 'nutritional additives'/'vitamins, pro-vitamins and chemically well defined substances having similar effect' according to Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of *Taurine* for all animal species and categories. *Taurine* is a white crystalline powder with a minimum purity of 98 %. It is intended to be incorporated directly in *feedingstuffs* or through *premixtures* or directly in *water*. However, the Applicant did not specify any minimum or maximum concentrations of the *feed additive* in *feedingstuffs* or *water*.

For the determination of *Taurine* in the *feed additive* the Applicant proposed the Japanese Pharmacopoeia method, based on infrared absorption and potentiometric titration with sodium hydroxide. The EURL identified instead the European Pharmacopoeia method (01/2010:20256) for the determination of amino acids, based on ion-exchange chromatography with post column ninhydrin derivatisation and spectrophotometric detection at 570 nm. The Applicant provided experimental evidence of the applicability of the European Pharmacopoeia method for the determination of *Taurine* in *feed additive* in the frame of the CDG 34 dossier (FAD-2010–0107). Based on the experimental evidence presented, the EURL recommends for official control the European Pharmacopoeia method for the determination of *Taurine* in *feed additive*.

The Applicant proposed the dedicated ring-trial validated AOAC method (AOAC 999.12) for the determination of *Taurine* in pet food and the ring-trial validated Community method (Commission Regulation (EC) No 152/2009 – Annex III, F) for determination of *amino acids* in *premixtures* and *feedingstuffs*, based on ion-exchange chromatography with post column ninhydrin derivatisation and photometric detection at 570 nm. *Taurine* is a derivative of cysteine, an amino acid which contains a sulfhydryl group. Structurally related to amino acids, *Taurine* could be analysed by analytical methods developed for the determination of amino acids. Therefore, the Applicant applied the Community method, slightly modified, and proved that the method is suitable for the determination of *Taurine* in *premixtures* and *feedingstuffs*. Based on the performance characteristics presented, the EURL recommends for official control, the AOAC and the modified Community method for the determination of *Taurine* in *premixtures* and *feedingstuffs.*

For the determination of *Taurine* in *water* the Applicant proposed the ring-trial validated AOAC method (AOAC 997.05) for determination of *Taurine* in powdered milk and powdered infant formula, based on liquid chromatography. Based on the performance characteristics presented and rationale that water is simpler matrix than milk, the EURL recommends for official control, the AOAC method for the determination of *Taurine* in *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.

[19] The full report is available on the EURL website. http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2010-0215.pdf