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Safety and efficacy of Taminizer D (dimethylglycine sodium salt) as a feed additive for chickens for fattening

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of Taminizer D (dimethylglycine sodium salt) as a feed additive for chickens for fattening, based on a dossier submitted for the modification of the terms of authorisation of the additive. The product is authorised in the European Union for chickens for fattening at the maximum content of 1,000 mg/kg complete feedingstuffs. The applicant proposed the introduction of an additional manufacturing process, which introduces an impurity (dimethylamino-ethanol (DMAE)) in the additive at concentrations up to 0.09%. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) considered that the proposed modification would not substantially affect the previous assessment as related to the safety of the environment and the efficacy of the product. Since the safety of the active substance was established, the current assessment has dealt with the impurity DMAE. Considering the toxicological profile of DMAE, the estimated intake by the target animal and consumers, and making use of the Threshold of Toxicological Concern (TTC) approach, the Panel concluded that Taminizer D, manufactured by the DMAE route, is safe for both chickens for fattening and consumers, up to the maximum level of 1,000 mg/kg feed. The FEEDAP Panel extends its conclusions about Taminizer D produced by the original method to cover also Taminizer D produced by the new DMAE method. There is minimal risk to users from dust produced as a result of normal handling of the additive. Taminizer D is not irritant to skin but may be irritant to eyes; it is regarded as a potential skin sensitiser. The FEEDAP Panel recommended to set a specification for the DMAE content in the additive.

Keywords: zootechnical additive, Taminizer D, dimethylglycine sodium salt, dimethylamino-ethanol (DMAE), chickens for fattening, safety

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 13(3) of that Regulation lays down that if the holder of an authorisation proposes changing the terms of the authorisation by submitting an application to the Commission, accompanied by the relevant data supporting the request for the change, the Authority shall transmit its opinion on the proposal to the Commission and the Member States.

The European Commission received a request from Taminco B.V.B.A (a subsidiary of Eastman Chemical Company)[2] for authorisation of the product Taminizer D (dimethylglycine sodium salt), when used as a feed additive for chickens for fattening (category: zootechnical additive; functional group: other zootechnical additives).

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 13(3) (modification of the authorisation of a feed additive). 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 28 February 2017.

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 the product Taminizer D (dimethylglycine sodium salt), when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

The additive Taminizer D is a preparation of dimethylglycine sodium salt (DMG-Na) produced by chemical synthesis. The additive is intended to increase the performance of chickens for fattening. The safety and efficacy of the additive when used in chickens for fattening was the subject of an opinion published in 2011 (EFSA FEEDAP Panel, 2011a).

The product is authorised in the European Union (EU) for its use in chickens for fattening[3] at the maximum content of 1,000 mg/kg complete feedingstuffs.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[4] in support of the authorisation request for the use of Taminizer D (dimethylglycine sodium salt) as a feed additive. The technical dossier was prepared following the provisions of Article 7 of Regulation (EC) No 1831/2003, Regulation (EC) No 429/2008[5] and the applicable EFSA guidance documents.

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.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[6]

[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] Taminco N.V. (a subsidiary of Eastman Chemical Company), Pantserschipstraat 207, B-9000 Gent, Belgium.
[3] Regulation (EU) No 371/2011 of 15 April 2011 concerning the authorisation of dimethylglycine sodium salt as feed additive for chickens for fattening. OJ L 102, 16.4.2011, p. 6.
[4] FEED dossier reference: FAD-2016-0072.
[5] 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.
[6] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2009-0036.pdf

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Taminizer D (dimethylglycine sodium salt) is in line with the principles laid down in Regulation (EC) No 429/2008 and the relevant guidance documents: Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012a), Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011b), Technical Guidance for assessing the safety of feed additives for the environment (EFSA, 2008), Guidance for establishing the safety of additives for the consumer (EFSA FEEDAP Panel, 2012b) and Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012c).

3. Assessment

The additive Taminizer D is a preparation of DMG-Na produced by chemical synthesis. The product is authorised as a zootechnical additive, under the functional group of other zootechnical additives, intended to increase the performance of chickens for fattening at the recommended dose of 1,000 mg/kg complete feedingstuffs.

The application is for the modification of the current authorisation to introduce an additional manufacturing process.

3.1. Characterisation

3.1.1. Manufacturing process

The manufacturing process is described in the dossier.[7] [redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

3.1.2. Characterisation of the additive

The additive is a 'white microgranular' product containing at least 97% of DMG-Na and not more than 3% of impurities, including water.

The analysis of five batches of Taminizer D obtained with the alternative manufacturing process showed a mean content of DMG-Na of 97.5% (range 97.1–97.9%).[8] Residual DMAE was also analysed in the five batches of the additive.[9] The results for DMAE were in the range of < 0.07%[10] to 0.09%.

The content of undesirable substances, including heavy metals, arsenic, nitrites and dioxins, were analysed in three batches of the additive.[11,12,13,14] The highest results reported were: arsenic < 0.25 mg/kg, cadmium < 0.13 mg/kg, lead < 0.15 mg/kg, mercury < 0.1 mg/kg, fluorine 0.06 mg/kg, nitrites < 5, dioxins 0.048 ng WHO-PCDD/F-TEQ per kg and sum of dioxins plus dioxin-like PCBs 0.10 ng WHO-PCDD/F-PCBTEQ per kg.[15]

[7] Technical dossier/Section II/Identity.
[8] Technical dossier/Section II/4.Annex II_2.
[9] Technical dossier/Section II/5.Annex II_2.
[10] Corresponding to the Limit of Quantification of the analytical method: 0.07%. Technical dossier/Section II/Annex II_9.
[11] Technical dossier/Section II/6.Annex II_3.
[12] Technical dossier/Section II/7.Annex II_4.
[13] Technical dossier/Supplementary Information/October 17/Annex 7, 8a, 8b, 8c, 9a, 9b, 9c.
[14] Technical dossier/Supplementary Information/January 18.
[15] Values preceded with the sign '<' indicates that correspond to the limit of quantification (LOQ). The analysis was done by two different laboratories reporting different LOQs for each analyte.

Particle size distribution was assessed by sieve screening: particles below 100 μm, 53 μm and 45 μm were reported, being less than 0.1% in the two latter cases.[16]

The dusting potential was analysed in two samples of the additive, following a procedure compatible with the Collaborative International Pesticides Analytical Council (CIPAC) method MT171.[17] The highest value obtained was 0.2 mg/30 g[16]; according to the categories proposed by the CIPAC, this value corresponds to a 'nearly dust free' product.

3.1.3. Stability and homogeneity

Based on the physicochemical properties, there are no relevant differences regarding the feed additive produced by either manufacturing routes. Therefore, in the view of the FEEDAP Panel the data reported in the first dossier and evaluated by the Panel (EFSA FEEDAP Panel, 2011a) regarding stability and homogeneity are still valid.

3.1.4. Conditions of use

The additive is intended to be used to increase the performance of chickens for fattening at the maximum dose of 1,000 mg/kg complete feedingstuffs.

3.2. Safety

The FEEDAP Panel assessed the safety and efficacy of Taminizer D in a previous opinion (EFSA FEEDAP Panel, 2011a). From the safety standpoint, the principal change, as compared to the previous opinion, is the presence of DMAE as an impurity previously not assessed and the potential toxicological significance of the amount of DMAE present. Accordingly, the current assessment by the FEEDAP Panel pivots on whether the presence of DMAE in the additive can be considered safe for the target species, the consumer, the user and the environment.

3.2.1. Toxicological profile of DMAE

A literature search concerning the toxicological profile of DMAE has been provided[18] and is summarised below.[19]

- DMAE did not show genotoxicity in an appropriate set of tests (two bacterial reverse mutation assays, one hypoxanthine-guanine-phosphoribosyltransferase (HGPRT) forward mutagenicity assay *in vitro* on CHO cells, one *in vitro* sister chromatid exchange assay on CHO cells, one unscheduled DNA synthesis assay performed *in vitro* on rat hepatocytes, two *in vivo* micronucleus assays on mice by the intraperitoneal route using dose levels up to 860 mg/kg bw).
- Subchronic oral toxicity assays were not available. One inhalation subchronic study on rats showed no effects indicating toxicity other that adverse changes in the upper respiratory tract and corneal opacity. Thus, the results of this study indicate site-of-contact toxicity with a no-observed adverse-effect concentration (NOAEC) of 87.5 mg/m^3. There was no indication of any systemic toxicity.
- A carcinogenicity assay was performed with single low dose levels of DMAE administered for at least 2 years via drinking water to female mice belonging to two strains prone to the development of mammary tumours; 0.9 mg/L or 1.3 mg/L to C3H/HeN and C3H/He J+ mice, respectively, corresponding to 0.08 or 0.12 mg/kg bw per day. No treatment-related effects were observed.
- No multigeneration or one-generation reproduction toxicity studies are available. No effects on reproductive tissues were observed in the subchronic inhalation toxicity study in rats or in the carcinogenicity assay in female mice.
- In mouse embryos *in vitro*, 375 μM DMAE caused death and morphological abnormalities related to the inhibition of choline uptake and metabolism. DMAE was given orally to rat dams from gestation day 6 until post-natal day 3 at the dose levels of 300 and 600 mg/kg bw per day. The results showed maternal toxicity (stomach erosion/ulceration, with increased liver weight at the top dose level) and pre/perinatal toxicity (increased post-implantation loss and reduced viability of newborn pups) at both doses levels. No oral no-observed-adverse-effect

[16] Technical dossier/Supplementary Information/October 17/Annex 10.
[17] CIPAC MT 171.1 Dustiness of Granular Products.
[18] Technical dossier/Supplementary Information/October 17/Annex 11.
[19] Technical dossier/Supplementary Information/October 17/Annex 12, Annex 13.

level (NOAEL) can be derived for either maternal or developmental toxicity. No adverse effects were observed in litters from pregnant rat dams exposed by inhalation to up to 365 mg/m^3 on pregnancy days 6–15; conversely, the treatment induced maternal toxicity (reduced weight gain, ocular changes) with a NOAEC of 36.5 mg/m^3. Overall, DMAE showed developmental toxicity *in vivo* at dose levels causing maternal toxicity.

The FEEDAP Panel additionally considered a review of the available toxicological literature of DMAE published in the US National Institute of Environmental Health Sciences (NIEHS, 2002). According to the US NIEHS review, most of the DMAE given orally enters the metabolic route for the synthesis of phospholipids; up to 33% is excreted unchanged in humans. The document also confirms the information on DMAE toxicology provided in the literature review submitted, including the evidence for the absence of genotoxicity potential.

In addition, the US NIEHS review reports that DMAE tartrate may induce pharmacological effects in humans (increase in muscle tone and perhaps an increased frequency of convulsions in susceptible individuals) at dose levels equal to or greater than 20 mg/day (0.3 mg/kg bw per day in a 60-kg individual). A pharmacological no-observed-effect level (NOEL) is not identified; the FEEDAP Panel notes that a possible relationship between pharmacological effects with an inhibitory effect on choline may not be ruled out.

Overall, DMAE can elicit serious adverse effects on respiratory tract and eyes upon inhalation exposure and can cause damage to the stomach when given orally. These effects were probably due to the corrosive nature of DMAE. The increased liver weight seen only in pregnant rats in the top dose group (600 mg DMAE/kg bw per day) of the developmental toxicity study was not confirmed by a finding of liver pathology. The available data do not indicate concerns for mutagenicity/genotoxicity, carcinogenicity or organ toxicity resulting from the presence of the contaminant DMAE in Taminizer D. Pre/perinatal toxicity was seen in an oral rat developmental toxicity study in the presence of maternal toxicity. DMAE may induce pharmacological effects in humans and by implication possibly also in animals. Since oral toxicity was not fully investigated (there were no available oral subchronic toxicity studies or multigeneration/extended one-generation reproduction studies; the carcinogenicity/chronic toxicity study was inadequate as it used only single dosages given to each strain of mouse), an oral NOAEL for DMAE toxicity cannot be reliably derived.

3.2.2. Safety for chickens for fattening

The previous opinion (EFSA FEEDAP Panel, 2011a) showed that a 10-fold overdose of DMG-Na was well tolerated by chickens for fattening during the 39-day tolerance study.

The alternative manufacturing process changing the synthesis route of the DMG-Na and starting from different raw materials introduced residual DMAE in the final product. A tolerance trial was performed to study the effect of an overdosing of residual DMAE on the safety of chickens for fattening and the possible deposition of DMAE in the edible parts.[20]

A total of 30 one-day-old male Ross 308 chickens were allotted to two treatments, each with one pen of 15 birds. The animals were fed a basal maize-soybean meal diet supplemented with Taminizer D at either 0 or 1,000 mg/kg. Supplementary DMAE was added to the Taminizer D and therefore the concentration of DMAE in the batch of the additive used was 0.79% (7.9 mg/kg feed), which corresponded to a 8× overdosing compared to the highest DMAE concentration of 0.09% measured in the additive.[21] Birds were fed a starter diet from day 1 until day 14, a grower diet from day 15 until day 28 and a finisher diet from day 29 until day 43. Feed was provided *ad libitum*. The confirmed Taminizer D concentration was 1,164 mg/kg in the starter diet, 980 mg/kg in the grower diet and 733 mg/kg in the finisher diet[22]; therefore, the corresponding actual DMAE concentrations were 9.2, 7.7 and 5.8 mg/kg feed, respectively.

Animals were monitored for health status and mortality. At the end of the trial (day 43), all chickens were killed and blood was taken for measurement of haematological[23] and serum biochemistry parameters.[24] From all chickens, samples of liver, kidney, abdominal fat and breast meat

[20] Technical dossier/Section III/2.Annex III_1.
[21] Technical dossier/Section III/3.Annex III_2.
[22] Technical dossier/Section III/3.Annex III_4.
[23] Haemoglobin, erythrocytes, total leucocytes, heterophils, lymphocytes, monocytes, basophils, eosinophils.
[24] Uric acid, total protein, albumin, cholesterol, triglycerides, alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST).

were taken to determine the deposition of DMAE. No report on gross pathology was provided and no histopathology was performed.

No treatment-related clinical signs were observed and no deaths were recorded. Haematological and biochemical parameters were similar in the unsupplemented and the treated groups, although no statistical analysis was performed. Content of DMAE (8× dose) was below the limit of detection (LOD) (8.3 mg/kg dry matter (DM)) in muscle and fat. For liver and kidney, DMAE content was 19 and 17.5 mg/kg (DM), respectively (corresponding to 5.4 and 4.2 mg/kg fresh tissue); seven samples of liver tissue and two samples of kidney tissue, out of 15 in each case, were above the limit of quantification of the method (15.1 mg/kg DM) and were used for calculations.[25]

The FEEDAP Panel considers that the study presents several limitations (e.g. no experimental replicates, no tolerance doses of the additive, no statistical analysis was performed); therefore, the study can only provide information for potential tissue deposition of DMAE.

The FEEDAP Panel applied the Threshold of Toxicological Concern (TTC) approach (EFSA and WHO, 2016) to DMAE. The compound DMAE belongs to Cramer structural Class I. According to this classification, the maximum acceptable concentration of DMAE in poultry feed is 1 mg/kg feed (EFSA FEEDAP Panel, 2012d); this amount is above the maximum measured concentration of DMAE in feeds (0.9 mg/kg feed).

3.2.2.1. Conclusions on safety for the target species

Since the safety of the active substance, DMG-Na, has been established, the current assessment has dealt with the issue of tolerance of the impurity DMAE, which is present in the additive at concentrations up to 0.09%. Taking into account the toxicological profile of DMAE, the estimated intake by the target animal and making use of the TTC approach, the FEEDAP Panel concludes that the presence of this impurity in Taminizer D up to the highest level detected in the additive is unlikely to cause adverse effects in chickens for fattening. Therefore, Taminizer D, manufactured by the DMAE route and containing ≤ 0.1% DMAE, is safe for chickens for fattening up to the maximum level of 1,000 mg/kg feed.

3.2.3. Safety for the consumer

The safety of the active substance was already established. The FEEDAP Panel is not aware of any new information that could modify the previous assessment of the active substance; in addition, conditions of use of the additive are the same, thus the consumer exposure to the active substance remains unchanged.

However DMAE is an impurity whose relevance to consumer safety has not been evaluated by EFSA. The FEEDAP Panel notes that with regard to oral exposure, DMAE is found in fish (e.g. salmon roe) and in pig and human brain; Honegger and Honegger (1959) reported a total DMAE (bound to phospholipids and unbound) of 1,922 μg/kg salmon roe, and of 247 μg/kg pig brain. DMAE appears to be used in the USA as an ingredient of commercial food dietary supplements.[26] In the EU, DMAE is not included in Annex II (Vitamin and mineral substances which may be used in the manufacture of food supplements) of the Directive 2002/46/EC. In general, the available data are too limited to allow any conclusion on consumer exposure from other potential dietary sources of DMAE.

In the tolerance study in chickens (see Section 3.2.2), a concentration of 7.9 mg DMAE/kg feed was reported to lead to DMAE residues in liver (5.4 mg/kg fresh tissue) and kidney (4.2 mg/kg fresh tissue), while in abdominal fat and breast muscle the DMAE found was below the LOD of 8.3 mg/kg DM.[27] Notwithstanding the uncertainties in the quantification of DMAE residues, the FEEDAP Panel considers that the deposition data can be used in the safety assessment of DMAE. In the study, the concentration of DMAE was about eightfold the maximum expected level of 0.9 mg DMAE/kg feed, when Taminizer D is used at the maximum dose proposed. The deposition rate of DMAE that would result from feeding birds with the additive containing DMAE at the maximum measured concentration in the additive was not investigated; however, it can reasonably be expected that feeding the additive to the birds would result in lower levels of residues than those observed in the study with the overdose evaluated. In addition, the FEEDAP Panel recognises that poultry offal is a food commodity of

[25] Information sent by the applicant (e-mail received on 27.3.2018). The FEEDAP Panel notes that, according to the information provided in the dossier, the analytical method was verified in another laboratory and the limits of detection and quantification reported were 2 and 1 mg/kg DM, respectively.
[26] Being advertised for intake at doses of 300–2,000 mg DMAE/day.
[27] Technical dossier/Section II/2.Annex II_6.

minor importance in most food consumption scenarios throughout the EU. Using the figures of the Food Basket described in Commission Regulation (EC) No 429/2008 for poultry offal consumption (100 g/day and 10 g/day for liver and kidney, respectively), the deposition resulting from an eightfold overdosing of DMAE in poultry feed would result in a daily intake of 0.59 mg/day (0.45 mg plus 0.042 mg from liver and kidney, respectively) or 0.007 mg/kg bw per day. Considering the uncertainties, the DMAE content in muscle and fat plus skin is set at the LOD, resulting in 3.4 mg/kg fresh tissue. Considering the food basket figures, this will lead to an additional intake of 1.33 mg/kg (1.02 mg plus 0.31 mg from meat and skin plus fat, respectively). The resulting consumer intake from tissues of poultry fed Taminizer with a DMAE concentration at least eightfold higher than expected would be 1.92 mg/day, or 0.032 mg/kg bw day in a 60-kg individual. This highly conservative estimate is considered to account for the uncertainty concerning the possible background content in foods.

The limited available toxicological data are inadequate to derive a safe level upon oral route; however, they do not indicate that DMAE has a potential for genotoxicity.

The FEEDAP Panel applied the TTC approach, considering that this procedure can be applied to impurities for which no health guidance value can be derived. DMAE is a compound of Cramer Class I and the TTC is therefore 30 μg (or 0.030 mg)/kg bw per day (EFSA Scientific Committee, 2012); this value corresponds to the estimated DMAE intake resulting from the use of Taminizer D with DMAE level as high as eightfold that expected.

Therefore, the FEEDAP Panel considers that the evidence is sufficient to conclude that the presence of DMAE in feed of chickens for fattening as impurity of Taminizer D at levels up to 0.9 mg/kg feed is unlikely to pose concerns for consumers' safety.

3.2.3.1. Conclusions on safety for the consumer

The presence of DMAE in animal feed as an impurity of Taminizer D at levels up to 0.9 mg/kg feed is unlikely to be of concern for consumer safety. Therefore, the FEEDAP Panel concludes that Taminizer D, manufactured by the DMAE route, is safe for consumers when used in feed for chickens for fattening up to the maximum level of 1,000 mg/kg feed, and with a maximum DMAE content in the additive of 0.1%.

3.2.4. Safety for the user

In a subchronic inhalation study on rats of DMAE, lesions of the upper respiratory tract and corneal opacity were observed, with a NOAEC of 87.5 mg/m^3. A lower NOAEC (36.5 mg/m^3) was observed for maternal toxicity (reduced body weight gain and ocular changes) in a developmental toxicity study on rat dams by inhalation.

The new manufacturing process has not increased the dusting potential or the fraction of inhalable particles: particles below 50 μm are on average 0.68% and < 0.1% in Taminizer D produced with the current method or with the new proposed method, respectively, and dusting potential classified as nearly dust free (see also EFSA FEEDAP Panel, 2011a and Section 3.1.2. above); therefore, the inhalation exposure to DMAE present as an impurity in Taminizer D is expected to be very low (lower than the NOAECs reported in the toxicity studies). Consequently, the FEEDAP Panel considers that the health risk to users by the inhalation route is also very low.

According to the information provided in the literature search, DMAE is not a skin sensitiser; however, it can causes severe skin burns and serious eye damage. The FEEDAP Panel considers that the damage to tissues upon direct contact with DMAE is a result of the corrosive nature of DMAE. Conversely, low concentrations of DMAE are not expected to cause corrosion of tissues; the compound is safely used in cosmetics[28] in concentrations of about 3% (Grossman, 2005). It is noted that DMAE is not genotoxic, and the concentrations of DMAE in Taminizer D (≤ 0.1%) are sufficiently low that skin exposure to the product is unlikely to cause any local or systemic toxicity.

When assessed previously by the FEEDAP Panel, Taminizer D was considered as a skin sensitiser, not irritant to skin, but possibly irritant to eyes. The DMAE impurities in Taminizer D produced by the new method of manufacture, if present at concentrations ≤ 0.1% in the additive, is not expected to increase or change the risk to users resulting from exposure of skin and eyes to the product during normal handling in the workplace.

[28] '2-Dimethylaminoethanol; *N*,*N*-Dimethyl-2-aminoethanol' is listed as a cosmetic ingredient (dimethyl MEA) in the EU Cosmetic ingredient database. Available online: https://ec.europa.eu/growth/sectors/cosmetics/cosing_en

3.2.4.1. Conclusions on safety for the user

The FEEDAP Panel extends its conclusions about Taminizer D produced by the original method to cover also Taminizer D produced by the new method (containing DMAE as impurity at concentrations ≤ 0.1% in the additive). There is minimal risk to users from dust produced as a result of normal handling of the additive. Taminizer D is not irritant to skin but may be irritant to eyes. It is regarded as a potential skin sensitiser.

3.2.5. Safety for the environment

In its previous assessment (EFSA FEEDAP Panel, 2011a), the FEEDAP Panel considered that the use of the product as a feed additive for chickens for fattening would not pose a risk to the environment. Taking into account the amount of DMAE potentially present in the additive, the FEEDAP Panel considers that the conclusions on the safety for the environment do apply to the product currently under assessment.

3.3. Efficacy

In its previous assessment (EFSA FEEDAP Panel, 2011a), the FEEDAP Panel considered that the use of the additive at the recommended dose has the potential to improve the performance of chickens for fattening. The FEEDAP Panel considers that the presence of DMAE impurities (≤ 0.1%) does not affect the previous conclusions on efficacy.

3.4. 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[29] and Good Manufacturing Practice.

4. Conclusions

Since the safety of the active substance, DMG-Na, has been established, the current assessment has dealt with the impurity DMAE, which is introduced in the additive at concentrations up to 0.09% as a result of a modified manufacturing process.

Taking into account the toxicological profile of DMAE, the estimated intake by the target animal and making use of the TTC approach, the FEEDAP Panel concludes that the presence of DMAE in Taminizer D up to the highest level detected in the additive is unlikely to cause adverse effects in chickens for fattening. Therefore, Taminizer D, manufactured by the DMAE route, is safe for chickens for fattening up to the maximum level of 1,000 mg/kg feed (DMAE content ≤ 0.1% in the additive).

The presence of DMAE in animal feed as an impurity of Taminizer D at levels up to 0.9 mg/kg feed is unlikely to be of concern for consumer safety. Therefore, the FEEDAP Panel concludes that Taminizer D, manufactured by the DMAE route, is safe for consumers when used in feed for chickens for fattening up to the maximum level of 1,000 mg/kg feed (DMAE content ≤ 0.1% in the additive).

As regards user safety, the FEEDAP Panel extends its conclusions about Taminizer D produced by the original method to cover also Taminizer D produced by the new method (containing DMAE as impurity at concentrations ≤ 0.1% in the additive). There is minimal risk to users from dust produced as a result of normal handling of the additive. Taminizer D is not irritant to skin but may be irritant to eyes. It is regarded as a potential skin sensitiser.

The FEEDAP Panel considers that the conclusions of the previous assessment of Taminizer D on the safety for the environment do apply to the product currently under assessment, and thus, the additive would not pose a risk to the environment.

In its previous assessment of Taminizer D, the FEEDAP Panel considered that the use of the additive at the recommended dose has the potential to improve the performance of chickens for fattening. The FEEDAP Panel considers that the presence of DMAE impurities (≤ 0.1%) does not affect the previous conclusions on efficacy.

[29] 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.

5. Recommendations

The FEEDAP Panel recommends that a specification for DMAE content in the additive should be set. A level of ≤ 0.1% is proposed on the basis of data on characterisation of the additive and on safety aspects of the impurity.

Documentation provided to EFSA

1) Taminizer D (dimethylglycine sodium salt) for chickens for fattening. December 2016. Submitted by Taminco BVBA, a subsidiary of Eastman Chemical Company.
2) Taminizer D (dimethylglycine sodium salt) for chickens for fattening. Supplementary information. October 2017. Submitted by Taminco BVBA, a subsidiary of Eastman Chemical Company.
3) Taminizer D (dimethylglycine sodium salt) for chickens for fattening. Supplementary information (provided by e-mail). January 2018. Submitted by Taminco BVBA, a subsidiary of Eastman Chemical Company.
4) Comments from Member States.

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Abbreviations

ALP	alkaline phosphatase
AST	aspartate aminotransferase
bw	body weight
CHO	Chinese hamster ovary
CIPAC	Collaborative International Pesticides Analytical Council
DM	dry matter

DMAE	dimethylamino-ethanol
DMG-Na	dimethylglycine sodium salt
EURL	European Union Reference Laboratory
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
GGT	gamma-glutamyl transferase
HGPRT	hypoxanthine-guanine-phosphoribosyltransferase
LOD	limit of detection
LOQ	limit of quantification
NIEHS	US National Institute of Environmental Health Sciences
NOAEC	no-observed adverse-effect concentration
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
PCB	polychlorinated biphenyl
PCDD/-F	polychlorinated dibenzo-*p*-dioxin/dibenzofuran
TEQ	toxic equivalent
TTC	Threshold of Toxicological Concern
WHO	World Health Organization