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# Assessment of the feed additive consisting of dimethylglycine sodium salt (Taminizer D) for chickens for fattening for the renewal of its authorisation (Taminco N.V.)

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Rosella Brozzi, Jaume Galobart, Lucilla Gregoretti, Matteo L Innocenti, Maria Vittoria Vettori and Gloria López-Gálvez

## Abstract

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 assessment of the application for renewal of authorisation of the feed additive consisting of dimethylglycine sodium salt (trade name: Taminizer D) as a zootechnical additive for chickens for fattening. In 2011, the FEEDAP Panel delivered an opinion on the safety and efficacy of the additive, and subsequently, the additive was authorised in the EU. In 2018, a second scientific assessment was made based on a dossier submitted for the modification of the terms of authorisation of the additive. The additive is authorised as 'dimethylglycine sodium salt with a purity of at least 97%' for chickens for fattening under the category 'zootechnical additives' and functional group 'other zootechnical additives (improvement of zootechnical parameters)'. The evidence provided by the applicant indicated that the additive currently in the market, produced by the two manufacturing routes, complies with the conditions of authorisation. No new evidence was found that would make the FEEDAP Panel reconsidering its previous conclusions in the safety for target species, consumers and environment. The FEEDAP Panel concludes that Taminizer D is not a skin irritant but may be an eye irritant and a skin sensitiser; although uncertainty remains on the presence of formaldehyde, exposure is considered extremely low. There is no need to assess the efficacy of the additive in the context of the renewal of the authorisation.



**Keywords:** zootechnical additive, other zootechnical additives, dimethylglycine sodium salt, Taminizer D, chickens for fattening, safety, renewal

**Requestor:** European Commission

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**Correspondence:** feedap@efsa.europa.eu

**Panel members:** Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa and Ruud Woutersen.

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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 14(1) of that Regulation lays down that an application for renewal shall be sent to the Commission at the latest one year before the expiry date of the authorisation.

The European Commission received a request from Taminco B.V. (a subsidiary of Eastman Chemical Company)[2] for the renewal of the authorisation of the additive consisting of dimethylglycine sodium salt (Taminizer D), 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 14(1) (renewal of the authorisation). 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 13 November 2020.

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 additive consisting of dimethylglycine sodium salt (Taminizer D), when used under the proposed conditions of use (see Section 3.1.4).

## 1.2. Additional information

The safety and efficacy of the additive Taminizer D were the subject of an opinion of the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) published in 2011 (EFSA FEEDAP Panel, 2011). In 2018, a second opinion was delivered following a request of modification of the terms of the authorisation, in which the applicant introduced a new manufacturing process (EFSA FEEDAP Panel, 2018).

Dimethylglycine sodium salt was first authorised in 2011 in the European Union (EU) as a zootechnical additive for its use in chickens for fattening at the maximum content of 1,000 mg/kg complete feedingstuffs (4d4).[3] The Regulation was further amended in 2013 for an administrative matter[4] and later on in 2018 following the introduction of a modification in the manufacturing process.[5]

# 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[6] in support of the authorisation request for the use of the product consisting of dimethylglycine sodium salt (Taminizer D) as a feed additive for chickens for fattening.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers and other scientific reports, to deliver the present output.

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.[7]

[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] Commission Implementing Regulation (EU) No 371/2011 of 15 April 2011 concerning the authorisation of dimethylglycine sodium salt as feed additive for chickens for fattening (holder of the authorisation Taminco N.V.). OJ L 102, 16.4.2011, p. 6.
[4] Commission Implementing Regulation (EU) No 105/2013 of 4 February 2013 amending Implementing Regulation (EU) No 371/2011 as regards the name of the holder of the authorisation of dimethylglycine sodium salt. OJ L 34, 5.2.2013, p. 15.
[5] Commission Implementing Regulation (EU) 2018/1936 of 10 December 2018 amending Implementing Regulation (EU) No 371/2011 as regards the maximum limit of dimethylaminoethanol (DMAE).
[6] FAD-2020-0028.
[7] 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 the additive consisting of dimethylglycine sodium salt (Taminizer D) is in line with the principles laid down in Regulation (EC) No 429/2008[8] and the relevant guidance documents: Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013) and Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017).

# 3. Assessment

The subject of the assessment is the additive consisting of dimethylglycine sodium salt, with trade name Taminizer D. The additive is currently authorised for use in feed for chickens for fattening as a zootechnical additive (functional group: other zootechnical additives (improvement of zootechnical parameters)) and is intended to increase the performance of chickens for fattening. The applicant is requesting the renewal of the authorisation. From here onwards the additive will be referred to as Taminizer D.

## 3.1. Characterisation

The applicant stated that no changes in the manufacturing processes, composition, purity or activity of the additive have been introduced since the last amendment of the authorisation in 2018.

### 3.1.1. Manufacturing process

The additive consists on dimethylglycine sodium salt (DMG-Na) produced by chemical synthesis by two different manufacturing processes (two routes), [redacted]

### 3.1.2. Characterisation of the additive/active substance

The additive is currently authorised as a minimum of 97% dimethylglycine sodium salt, with a maximum of 0.1% DMAE in the active substance.

The active substance is dimethylglycine sodium salt (sodium N,N-dimethylglycine). It is identified by Chemical Abstracts Service (CAS) Number: 18319–88–5, and the European Inventory of Existing Commercial Chemical Substances (EINECS) number: 242–206–5. The molecular formula of sodium N, N-dimethylglycine is $C_4H_8NO_2Na$, its molecular weight: 125.1 g/mol. The structural formula is given in Figure 1.

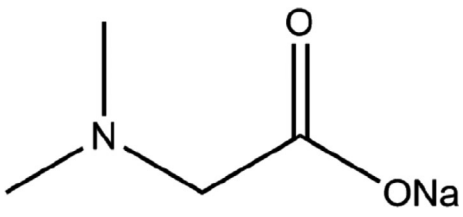


**Figure 1:** Structural formula of sodium N,N-dimethylglycine

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

[9] Technical dossier/Section II/Identity.

The additive is a white micro-granular product containing by specification at least 97% of DMG-Na and not more than 3% of crystal bound water.

Separated analytical data sets on the composition of the additive, including batch to batch variation, heavy metals, fluorine, nitrite, dioxins and other impurities of the additive obtained following the two manufacturing routes were provided. These data are described below.

#### 3.1.2.1. Additive obtained following the manufacturing Route 1

The analysis of five recent batches of Taminizer D obtained with the manufacturing Route 1 showed a mean content of DMG-Na of 99.7% (range 99.2–99.9%).[10] The concentration of residual cyanide analysed in the same batches resulted in < 3 mg/kg (the reported limit of quantification (LOQ) of the analytical method). The typical composition of the final additive produced by Route 1 was reported by the applicant and indicates the presence of formaldehyde (0.007 mg/kg); however, this statement was not supported by analytical data. In the absence of data, uncertainty remains on the presence of formaldehyde in the final additive obtained by Route 1.

Levels of fluorine and nitrite, analysed in five separate batches, resulted in < 5 mg/kg in both cases,[11] corresponding to the LOQ of the analytical method.[12] Levels of heavy metals, arsenic and dioxins were analysed in other three batches.[13] The results reported were: arsenic < 0.10 mg/kg, cadmium < 0.05 mg/kg, lead < 0.05 mg/kg, mercury < 0.05 mg/kg additive.[14] The sum of polychlorinated dibenzo-p-dioxin and dibenzofuran (PCDD/F) resulted in 0.069 ng WHO-PCDD/F-TEQ/kg (0.066–0.071), dioxin-like polychlorinated biphenyls (PCBs) in 0.050 WHO-PCB-TEQ/kg (0.049–0.051) and the sum of dioxins and dioxin-like PCBs in 0.12 ng WHO-PCDD/F-PCB-TEQ/kg.

#### 3.1.2.2. Additive obtained following the manufacturing Route 2

The analysis of five recent batches of Taminizer D obtained with the manufacturing Route 2 showed a mean content of DMG-Na of 99.3% (range 99.2–99.4%).[15] The concentration of residual DMAE analysed in the same batches, resulted in < 0.07% (the reported LOQ of the analytical method).

Levels of fluorine and nitrite, analysed in five separate batches, resulted in < 5 mg/kg in both cases,[16] corresponding to the LOQ of the analytical method.[12] Levels of heavy metals, arsenic and dioxins were analysed in other three batches.[17] Results for arsenic and heavy metals were: arsenic < 0.10 mg/kg, cadmium < 0.05 mg/kg, mercury < 0.05 mg/kg and lead < 0.05 mg/kg additive.[14] Dioxins resulted in 0.073 ng WHO-PCDD/F-TEQ TEQ/kg (0.071–0.075), dioxins like-PCBs in 0.042 ng WHO-PCB-TEQ/kg (0.026–0.051) and the sum of dioxins and dioxin-like PCBs in 0.12 ng WHO-PCDD/F-PCB-TEQ/kg (0.12–0.13).

### 3.1.3. Physico-chemical properties, stability and homogeneity of the additive

The data submitted supporting the physico-chemical properties of the additive (including particle size and dusting potential), stability and the capacity for homogeneous distribution of the additive in feedingstuff are the same as those provided in the previous dossiers and were evaluated by the FEEDAP Panel (EFSA FEEDAP Panel 2011, 2018). Since no changes in the manufacturing processes have been introduced, those data are still considered valid in the context of the renewal application.

### 3.1.4. Conditions of use

The additive is currently authorised for use in feed for chickens for fattening at the maximum use level of 1,000 mg/kg complete feedingstuff.

The current authorisation includes the following *other provisions*:

1) For safety: glasses and gloves shall be used during handling.
2) Minimum recommended dose: 1,000 mg/kg of complete feedingstuff with a moisture content of 12%.

The applicant proposed to keep the same conditions of use as authorised.

[10] Technical dossier/Section II/Annex_II_1_CoA_TamD_batch to batch (manuf. Route 1).
[11] Technical dossier/Section II/Annex_II_3_CoA_Tam D_nitrite_fluor (manuf. Route 1).
[12] Technical Dossier/Supplementary information/January 2021.
[13] Technical dossier/Section II/Annex_II_4_Heavy metals (manuf. Route 1), Annex_II_5_dioxin (manuf. Route 1).
[14] Values preceded with the sign '<' correspond to the limit of detection (LOD).
[15] Technical dossier/Section II/Annex_II_2_CoA_TamD_ batch to batch (manuf. Route 2).
[16] Technical dossier/Section II/Annex_II_3_CoA_Tam D_nitrite_fluor (manuf. Route 2).
[17] Technical dossier/Section II/Annex_II_5_ Heavy metals (manuf. Route 2).

## 3.2. Safety

The applicant stated that the additive has not been changed or altered in composition, purity or activity from the original authorisation, and also that the use levels and target species have also remained unchanged.

The applicant has provided a statement to certify that, in the context of the requirements of the EU Feed Hygiene Regulation,[18] no reports of adverse effects events on target animals or on humans have been received since the additive's initial authorisation on 2011.[19]

Following the requirements of the Guidance for renewal of feed additives (EFSA FEEDAP Panel, 2013), the applicant provided a literature search on the safety of Taminizer D. The search focused on the safety for target animals, consumers and users/workers, and on the components of the additive of safety concerns, i.e. DMG-Na and DMAE.[20] The following databases were used: Cab Abstracts and Global Health, and FSTA (the food science resource) on the Web of Science interface and PubMed (in NCBI webpage). The search covered the period January 2011 to February 2020.[12] The search was performed using the review questions in which the effect of intervention or exposure (PICO[21] or PECO[22]) criteria was chosen. The search terms used were related to DMG-Na, DMAE, poultry, residues, user/worker and consumer safety. The search protocol described the inclusion and exclusion criteria applied for the screening process. In total, 97 publications were considered for the screening and after applying the inclusion/exclusion criteria described in the protocol, a total of 19 scientific papers were considered eligible: seven related to DMG-Na safety and 10 related to DMAE safety, and two were opinions of the FEEDAP Panel (EFSA FEEDAP Panel, 2011, 2018).

### 3.2.1. Safety for the target species

In its opinion of 2011, the FEEDAP Panel concluded that Taminizer D was safe for chickens for fattening at the proposed use level of 1,000 mg/kg feed; a margin of safety of 10 was identified (EFSA FEEDAP Panel, 2011). In the FEEDAP Panel's second assessment of the additive, in which an additional manufacturing process that introduced the impurity DMAE in the additive at concentrations up to 0.1% was evaluated, the safety of the additive for chickens for fattening up to 1,000 mg/kg feed was also established making use of the Threshold of Toxicological Concern (TTC) approach (EFSA FEEDAP Panel, 2018); in this opinion it was reported that '*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).*'

From the literature review performed, it was identified that some of the potentially relevant papers had been already assessed in full (Kalmar et al., 2011a, 2014) or in part (Kalmar, 2011) in the first EFSA Opinion (EFSA FEEDAP Panel, 2011). Two of the retrieved papers described studies investigating the efficacy of the additive (Prola et al., 2013; Kou et al., 2015), but were not designed as tolerance studies; these studies did not report any adverse effects of the additive for the target species. The two remaining studies that could be related with safety for target animals are described below.

Kalmar (2011) evaluated in a challenge study (cold stress conditions and high energy diets) the effect of dietary DMG-Na (167 mg/kg feed) on nutrient digestibility and development of pulmonary hypertension syndrome in broilers; the results did not advocate any adverse effects of the additive at the tested level.

Kalmar et al. (2011b) studied the effects of the addition of Taminizer D to feed of chickens for fattening at four supplementation levels (from 0 to 1 g/kg feed), in diets containing animal fat or vegetable fat as the main fat source. No adverse or undesirable effects were reported.

Based on the assessment above, including the new data provided, the FEEDAP Panel concludes that Taminizer D remains safe for chickens for fattening up to the maximum level of 1,000 mg/kg feed.

[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.
[19] Technical dossier/Supplementary information/January 2021/Annex_III_36b_Quality statement.
[20] Technical dossier/Section III/Annex_III_35_Literature search_final_Na-DMG_LR_2500309.
[21] Population, Intervention, Comparison, Outcomes.
[22] Population, Exposure, Comparison, Outcomes.

### 3.2.2. Safety for the consumer

In its opinions of 2011 and 2018, the FEEDAP Panel concluded that the use of Taminizer D in feed for chickens for fattening at 1,000 mg/kg would not raise concerns for the safety of consumers (EFSA FEEDAP Panel, 2011, 2018). In the second assessment, the risk for consumers of the impurity DMAE in the additive at concentrations up to 0.1% was also evaluated, making use of the TTC approach (EFSA FEEDAP Panel, 2018); in this opinion, it was reported that '*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.*'

#### 3.2.2.1. Results from the literature review

From the literature review, 10 scientific papers (one related to DMG-Na and nine to DMAE) were reported to be potentially relevant for the assessment. From those only three, all concerning DMAE, were selected as directly relevant to support the safety for consumers and are described below.

Shipkowskia et al. (2019) investigated the disposition of radiolabelled DMAE in rats and mice (single gavage or intravenous administration) and the effect on choline disposition following pre-treatment with DMAE. [$^{14}$C]DMAE was administered at 10, 100 or 500 mg/kg body weight (bw). At 24 and 72 h after a single oral administration of DMAE to rats, about 60% was recovered in urine for all the three doses; tissue distribution ranged from 14% to 40% dose; the total recovery was almost 100%. In mice, DMAE was excreted in urine and expired air; tissue distribution ranged from 20% to 60%, depending on the dose. The total recovery of [$^{14}$C]DMAE after 500 mg/kg bw oral administration was 97% either after 24 h or 72 h. In urine, the DMAE metabolites identified by liquid chromatography-mass spectrometry (LC-MS) were DMAE N-oxide and N,N-dimethylglycine; N-N-dimethylnitrosamine was not detected (limit of detection, (LOD) not given). A single oral administration of 100 or 500 mg/kg bw of [$^{14}$C]DMAE or three oral doses of 100 mg/kg in a 48 h period to male rats did not significantly increase serum and tissue choline levels, as well as its excretion. This study showed that DMAE is well absorbed after oral administration, both in rats and in mice, broadly distributed in tissues (up to 40% 24 h after administration and 14% after 72 h in rats), partly metabolised and almost all excreted in urine. Additionally, it was proved that DMAE administration does not alter the tissue levels and excretion of choline.

Malanga et al. (2012) investigated the role of DMAE as antioxidant through the analysis of the capacity of DMAE to inhibit rat liver microsomal NADPH-dependent lipid peroxidation as well as the generation of hydroxyl radical and ascorbyl radical by Electron Spectroscopic Resonance (EPR). DMAE significantly reduced the formation of the radical intermediates of lipid peroxidation and hydrophilic radicals in comparison to the control samples without DMAE addition in a dose dependent manner.

Ait-Ghezala et al. (2016) investigated the effects of several natural compounds (including dimethylaminoethanol L-bitartrate on telomerase activity) in an established cell model of telomere shortening (i.e. IMR90 cells). The results showed that DMAE did not induce significant changes in the levels of activity of the enzyme, measured at early- and late-passage cultures. Cytotoxicity and cell proliferation were also analysed; telomere length was not evaluated. It has to be pointed out that recently non-canonical functions of telomerase have emerged in addition to the canonical telomere-dependent effects, and that among the telomere-independent effects are promotion of cell proliferation and mitochondrial integrity maintenance; thus, telomerase may have also extra-telomere effects not directly related to the integrity of chromosomes.

Overall, the studies by Malanga et al. (2012) and Ait-Ghezala et al. (2016) provide further details on the mechanism of action of DMAE, yet reporting no evidence of genotoxic potential.

In its opinion of 2018, the FEEDAP Panel reported that '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' (EFSA FEEDAP Panel, 2018). There is no new evidence that would lead to change the previous FEEDAP conclusion in relation to toxicological studies of DMAE or the safety of the additive manufactured by the Route 2 for consumers.

#### 3.2.2.2. Updated DMAE intake estimate

The FEEDAP Panel opted to update the estimate of the consumer exposure to DMAE, making use of the Feed Additive Consumer Exposure (FACE) calculator (FEEDAP Guidance for consumer; EFSA FEEDAP Panel, 2017) (Appendix A). The data of a study in chickens for fattening already assessed by

the FEEDAP Panel in a previous opinion (EFSA FEEDAP Panel, 2018) were used as input for the calculation (Table 1). In this study, the birds were fed the additive containing a supplementary concentration of DMAE leading to a concentration of 7.9 mg DMAE/kg feed, representing an eightfold overdose of the highest DMAE concentration in the additive. This diet 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 (8.3 mg/kg DM). The results of the chronic exposure to DMAE are reported in Table 2.

**Table 1:** Residue data of DMAE (mg/kg tissue) from chickens for fattening of a residue study evaluated by the FEEDAP Panel,(1) used as input data for the exposure calculation

| | Liver | Kidney | Muscle + Abdominal fat |
|---|---|---|---|
| **Residue Concentration** | 5.4 | 4.2 | 3.4(2) |

(1): Data taken from a study in which the chickens were fed the additive with a DMAE concentration of eightfold higher (0.79%) than that expected (EFSA FEEDAP Panel, 2018).
(2): Calculated from the LOD of 8.3 mg/kg DM (EFSA FEEDAP Panel, 2018).

**Table 2:** Chronic dietary exposure of consumers to DMAE based on residue data in chicken tissues – Summary statistics across European dietary surveys

| Population class | Number of surveys | Highest exposure estimate (mg/kg bw per day) |
|---|---|---|
| Infants | 6 | 0.0231 |
| Toddlers | 10 | 0.0262 |
| Other children | 18 | 0.0219 |
| Adolescents | 17 | 0.0151 |
| Adults | 17 | 0.0084 |
| Elderly | 14 | 0.0080 |
| Very elderly | 12 | 0.0071 |

The highest maximum highest reliable percentile (HRP) is estimated as 0.0262 mg/kg bw per day for toddlers. This exposure is still below the TTC value of 0.030 mg/kg bw per day. Therefore, the updated estimate showed that Taminizer D manufactured by Route 2 (containing maximum of 0.1% DMAE) is safe for consumers at the proposed supplementation level in chicken's feed (1,000 mg/kg feed).

#### 3.2.2.3. Conclusions on safety for the consumer

The additional data provided, including the recalculation on the consumer exposure, do not report any evidence that would lead to modify the previous conclusion on the safety of the additive for consumers. Therefore, the FEEDAP Panel concludes that Taminizer D remains safe for the consumers under the authorised conditions of use.

### 3.2.3. Safety for user

In its opinion of 2011, the FEEDAP Panel concluded that due to the low dusting potential of the additive, a significant exposure via inhalation is not expected, and that Taminizer D is not a skin irritant but may be an eye irritant and a skin sensitiser (EFSA FEEDAP Panel, 2011). In 2018, the FEEDAP Panel extended those conclusions about Taminizer D produced by Route 1 to cover also the additive manufactured by the Route 2.

The literature search did not retrieve any study concerning safety of the additive for the users. Concerning impurities of the additive, uncertainty remains on the presence of formaldehyde in the additive produced by Route 1; however, exposure of users to formaldehyde is considered extremely low.

The FEEDAP Panel concludes that Taminizer D is not a skin irritant but may be an eye irritant and a skin sensitiser. Although uncertainty remains on the presence of formaldehyde, exposure is considered extremely low.

### 3.2.4. Safety for the environment

In its first assessment of the additive, 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 (EFSA FEEDAP Panel, 2011). In the further opinion of 2018, which evaluated a new manufacturing method, the amount of DMAE potentially present in the additive was considered and the FEEDAP Panel retained that the conclusions on the safety for the environment reached in the previous opinion applied to the product manufactured with the additional process.

The FEEDAP Panel reiterates its previous conclusions on the safety for the environment.

## 3.3. Efficacy

The present application for renewal of the authorisation does not include a proposal for amending or supplementing the conditions of the original authorisation that would have an impact on the efficacy of the additive. Therefore, there is no need for assessing the efficacy of the additive in the context of the renewal of the authorisation.

## 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[18] and Good Manufacturing Practice.

# 4. Conclusions

The applicant has provided evidence demonstrating that the additive currently in the market, produced by the two manufacturing routes, complies with the conditions of authorisation.

The FEEDAP Panel concludes that the use of Taminizer D under the current authorised conditions of use remains safe for chickens for fattening, the consumers and the environment.

The FEEDAP Panel concludes that Taminizer D is not a skin irritant but may be an eye irritant and a skin sensitiser; although uncertainty remains on the presence of formaldehyde, exposure is considered extremely low.

There is no need for assessing the efficacy of the additive in the context of the renewal of the authorisation.

# 5. Documentation as provided to EFSA/Chronology

| Date | Event |
|---|---|
| 09/07/2020 | Dossier received by EFSA. Taminizer D (Dimethylglycine sodium salt) for chickens for fattening. Submitted by Taminco B.V.BA. |
| 06/05/2019 | Reception mandate from the European Commission |
| 13/11/2020 | Application validated by EFSA – Start of the scientific assessment |
| 18/12/2020 | Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterization, safety* |
| 18/01/2021 | Reception of supplementary information from the applicant - Scientific assessment re-started |
| 13/02/2021 | Comments received from Member States |
| 22/02/2021 | Request of supplementary information to the applicant by email. *Issue: characterization* |
| 03/03/2021 | Reply to the email posted on 22nd February |
| 05/05/2021 | Opinion adopted by the FEEDAP Panel. End of the Scientific assessment |

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## Abbreviations

| | |
|---|---|
| bw | body weight |
| DMG-Na | dimethylglycine sodium salt |
| EPR | Electron Spectroscopic Resonance |
| EURL | European Union Reference Laboratory |
| FEEDAP | Panel on Additives and Products or Substances used in Animal Feed |
| HRP | highest reliable percentile |
| LC-MS | liquid chromatography-mass spectrometry |
| LOD | limit of detection |
| LOQ | limit of quantification |
| PCDD/F | polychlorinated dibenzo-p-dioxin and dibenzofuran |
| PCBs | polychlorinated biphenyls |
| RAC | raw agricultural commodities |
| TTC | Threshold of Toxicological Concern |

# Appendix A – Calculation of consumer exposure with FACE model

## Methodology

As described in the Guidance on the safety of feed additives for consumers (EFSA FEEDAP Panel, 2017), consumption data of edible tissues and products as derived from the EFSA Comprehensive European Food Consumption Database (Comprehensive Database) will be used to assess exposure to residues from the use of feed additives in different EU countries, age classes[23] and special population groups. For each EU country and age class, only the latest survey available in the Comprehensive Database will be used.

While the residue data reported for feed additives refer to organs and tissues (raw agricultural commodities (RAC)), the Comprehensive Database includes consumption data for foods as consumed. In order to match those consumption data with the available residue data for feed additives, the consumption data reported in the Comprehensive Database have been converted into RAC equivalents. For assessing the exposure to DMAE from Taminizer D from their use in chickens for fattening, the following list of commodities is considered: meat, liver and other offals (kidney). In the case of the additive under assessment, the FEEDAP Panel considered that only the chronic exposure assessment would be appropriate.

For chronic exposure assessments, the total relevant residues will be combined for each individual with the average daily consumptions of the corresponding food commodities, and the resulting exposures per food will be summed in order to obtain total chronic exposure at individual level (standardised by using the individual body weight). The mean and the higher percentile (usually the 95th percentile) of the individual exposures will be subsequently calculated for each dietary survey (country) and each age class separately.

## Detailed results on chronic exposure calculation

**Table A.1:** Chronic dietary exposure per population class, country and survey (mg/kg body weight per day) to DMAE residues based on residue data in chickens for fattening

| Population class | Survey's country | Number of subjects | HRP(1) | HRP description |
|---|---|---|---|---|
| Infants | Bulgaria | 523 | 0.0231131072 | 95th |
| Infants | Germany | 142 | 0.0040934775 | 95th |
| Infants | Denmark | 799 | 0.0050411626 | 95th |
| Infants | Finland | 427 | 0.0075368922 | 95th |
| Infants | United Kingdom | 1,251 | 0.0099414515 | 95th |
| Infants | Italy | 9 | 0.0000000000 | 50th |
| Toddlers | Belgium | 36 | 0.0111169695 | 90th |
| Toddlers | Bulgaria | 428 | 0.0262147269 | 95th |
| Toddlers | Germany | 348 | 0.0072305989 | 95th |
| Toddlers | Denmark | 917 | 0.0055934255 | 95th |
| Toddlers | Spain | 17 | 0.0108974359 | 75th |
| Toddlers | Finland | 500 | 0.0120395052 | 95th |
| Toddlers | United Kingdom | 1,314 | 0.0114638690 | 95th |
| Toddlers | United Kingdom | 185 | 0.0117226264 | 95th |
| Toddlers | Italy | 36 | 0.0099295455 | 90th |
| Toddlers | Netherlands | 322 | 0.0121975556 | 95th |
| Other children | Austria | 128 | 0.0096299830 | 95th |
| Other children | Belgium | 625 | 0.0132986952 | 95th |
| Other children | Bulgaria | 433 | 0.0219182226 | 95th |
| Other children | Czech Republic | 389 | 0.0205314010 | 95th |
| Other children | Germany | 293 | 0.0075075309 | 95th |

[23] Infants: < 12 months old, toddlers: ≥ 12 months to < 36 months old, other children: ≥ 36 months to < 10 years old, adolescents: ≥ 10 years to < 18 years old, adults: ≥ 18 years to < 65 years old, elderly: ≥ 65 years to < 75 years old and very elderly: ≥ 75 years old.

| Population class | Survey's country | Number of subjects | HRP(1) | HRP description |
|---|---|---|---|---|
| Other children | Germany | 835 | 0.0075787047 | 95th |
| Other children | Denmark | 298 | 0.0062525662 | 95th |
| Other children | Spain | 399 | 0.0141584040 | 95th |
| Other children | Spain | 156 | 0.0198154260 | 95th |
| Other children | Finland | 750 | 0.0102650187 | 95th |
| Other children | France | 482 | 0.0085969551 | 95th |
| Other children | United Kingdom | 651 | 0.0103496346 | 95th |
| Other children | Greece | 838 | 0.0101288402 | 95th |
| Other children | Italy | 193 | 0.0106727259 | 95th |
| Other children | Latvia | 187 | 0.0115008000 | 95th |
| Other children | Netherlands | 957 | 0.0088980701 | 95th |
| Other children | Netherlands | 447 | 0.0112045597 | 95th |
| Other children | Sweden | 1,473 | 0.0083949108 | 95th |
| Adolescents | Austria | 237 | 0.0066540970 | 95th |
| Adolescents | Belgium | 576 | 0.0060747876 | 95th |
| Adolescents | Cyprus | 303 | 0.0064346667 | 95th |
| Adolescents | Czech Republic | 298 | 0.0150532884 | 95th |
| Adolescents | Germany | 393 | 0.0058195079 | 95th |
| Adolescents | Germany | 1,011 | 0.0047653300 | 95th |
| Adolescents | Denmark | 377 | 0.0048898457 | 95th |
| Adolescents | Spain | 651 | 0.0082229656 | 95th |
| Adolescents | Spain | 209 | 0.0110351828 | 95th |
| Adolescents | Spain | 86 | 0.0090139268 | 95th |
| Adolescents | Finland | 306 | 0.0061683704 | 95th |
| Adolescents | France | 973 | 0.0055301947 | 95th |
| Adolescents | United Kingdom | 666 | 0.0075854202 | 95th |
| Adolescents | Italy | 247 | 0.0047429675 | 95th |
| Adolescents | Latvia | 453 | 0.0070087762 | 95th |
| Adolescents | Netherlands | 1,142 | 0.0083995675 | 95th |
| Adolescents | Sweden | 1,018 | 0.0063208715 | 95th |
| Adults | Austria | 308 | 0.0076200836 | 95th |
| Adults | Belgium | 1,292 | 0.0057380541 | 95th |
| Adults | Czech Republic | 1,666 | 0.0075036442 | 95th |
| Adults | Germany | 10,419 | 0.0046825103 | 95th |
| Adults | Denmark | 1,739 | 0.0031876307 | 95th |
| Adults | Spain | 981 | 0.0076619718 | 95th |
| Adults | Spain | 410 | 0.0076605329 | 95th |
| Adults | Finland | 1,295 | 0.0060360796 | 95th |
| Adults | France | 2,276 | 0.0046399403 | 95th |
| Adults | United Kingdom | 1,265 | 0.0055987806 | 95th |
| Adults | Hungary | 1,074 | 0.0070223864 | 95th |
| Adults | Ireland | 1,274 | 0.0075048461 | 95th |
| Adults | Italy | 2,313 | 0.0040390505 | 95th |
| Adults | Latvia | 1,271 | 0.0062630064 | 95th |
| Adults | Netherlands | 2,055 | 0.0068854044 | 95th |
| Adults | Romania | 1,254 | 0.0083549283 | 95th |
| Adults | Sweden | 1,430 | 0.0064513972 | 95th |
| Elderly | Austria | 67 | 0.0064073820 | 95th |
| Elderly | Belgium | 511 | 0.0046613537 | 95th |
| Elderly | Germany | 2,006 | 0.0036304785 | 95th |

| Population class | Survey's country | Number of subjects | HRP(1) | HRP description |
|---|---|---|---|---|
| Elderly | Denmark | 274 | 0.0025780179 | 95th |
| Elderly | Finland | 413 | 0.0048788351 | 95th |
| Elderly | France | 264 | 0.0038406804 | 95th |
| Elderly | United Kingdom | 166 | 0.0044946891 | 95th |
| Elderly | Hungary | 206 | 0.0051283333 | 95th |
| Elderly | Ireland | 149 | 0.0061350464 | 95th |
| Elderly | Italy | 289 | 0.0039516799 | 95th |
| Elderly | Netherlands | 173 | 0.0052533171 | 95th |
| Elderly | Netherlands | 289 | 0.0044641167 | 95th |
| Elderly | Romania | 83 | 0.0079643403 | 95th |
| Elderly | Sweden | 295 | 0.0060074632 | 95th |
| Very elderly | Austria | 25 | 0.0016016078 | 75th |
| Very elderly | Belgium | 704 | 0.0053499390 | 95th |
| Very elderly | Germany | 490 | 0.0038906079 | 95th |
| Very elderly | Denmark | 12 | 0.0013461269 | 75th |
| Very elderly | France | 84 | 0.0044701787 | 95th |
| Very elderly | United Kingdom | 139 | 0.0034584543 | 95th |
| Very elderly | Hungary | 80 | 0.0050218569 | 95th |
| Very elderly | Ireland | 77 | 0.0062520018 | 95th |
| Very elderly | Italy | 228 | 0.0040374663 | 95th |
| Very elderly | Netherlands | 450 | 0.0042901993 | 95th |
| Very elderly | Romania | 45 | 0.0070574531 | 90th |
| Very elderly | Sweden | 72 | 0.0045873558 | 95th |

(1): HRP: highest reliable percentile, i.e. the highest percentile that is considered statistically robust for combinations of dietary survey, age class and possibly raw primary commodity, considering that a minimum of 5, 12, 30 and 61 observations are, respectively, required to derive 50th, 75th and 90th and 95th percentile estimates. Estimates with less than five observations were not included in this table.

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