SCIENTIFIC OPINION

efsa JOURNAL

ADOPTED: 26 September 2023

doi: 10.2903/j.efsa.2023.8357

Assessment of the feed additive consisting of niacinamide for all animal species for the renewal of its authorisation (Arxada Ltd)

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Mojca Durjava, Birgit Dusemund, Maryline Kouba, Marta López Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Roberto Edoardo Villa, Ruud Woutersen, Paul Brantom, Luca Tosti, Orsolya Holczknecht, Matteo Lorenzo Innocenti, Paola Manini, Maria Vittoria Vettori and Fabiola Pizzo

Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the assessment of the application for renewal of niacinamide as a nutritional additive for use in all animal species. The applicant has provided evidence that the additive currently on the market complies with the existing conditions of authorisation. There is no new evidence that would lead the FEEDAP Panel to reconsider its previous conclusions. Thus, the Panel concludes that the additive remains safe for all animal species, consumers and the environment under the authorised conditions of use. Regarding user safety, the additive is not irritant to skin but irritant to eyes. It is not a dermal sensitiser. Exposure through inhalation is likely. There is no need for assessing the efficacy of the additive in the context of the renewal of the authorisation.

Keywords: nutritional additives, vitamins, renewal, safety, niacinamide

Requestor: European Commission

Question number: EFSA-Q-2022-00512

Correspondence: feedap@efsa.europa.eu

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

Declarations of interest: If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

Acknowledgements: The Panel wishes to thank the following for the support provided to this scientific output (in alphabetical order of the last name): Daniel Pagés Plaza.

Suggested citation: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis, V., Azimonti, G., Bastos, M. L., Christensen, H., Durjava, M., Dusemund, B., Kouba, M., López Alonso, M., López Puente, S., Marcon, F., Mayo, B., Pechová, A., Petkova, M., Ramos, F., Villa, R. E., Woutersen, R., Brantom, P., Tosti, L., … Pizzo, F. (2023). Assessment of the feed additive consisting of niacinamide for all animal species for the renewal of its authorisation (Arxada Ltd). *EFSA Journal*, *21*(10), 1–8. https://doi.org/10.2903/j.efsa.2023.8257

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.

Table of contents

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 1 year before the expiry date of the authorisation.

The European Commission received a request from Arxada Ltd Switzerland (represented in the EU by YOU Solutions Germany GmbH, Germany)[2] for the renewal of the authorisation of the additive consisting of niacinamide, when used as a feed additive for all animal species (category: nutritional additives; functional group: vitamins, pro-vitamins and chemically well-defined substances having similar effect).

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). The dossier was received on 10 August 2022 and the general information and supporting documentation are available at https://open.efsa.europa.eu/questions/EFSA-Q-2022-00512 The particulars and documents in support of the application were considered valid by EFSA as of 17 April 2023.

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, consumers, users and the environment and on the efficacy of the feed additive consisting of niacinamide, when used under the proposed conditions of use (see Section 3.1.4).

1.2. Additional information

The additive niacinamide (synonym of nicotinamide) is currently authorised for use in feed for all animal species (3a315).[3]

EFSA issued four opinions on the safety and efficacy of niacinamide when used as a feed additive in all animal species (EFSA FEEDAP Panel, 2012a,b,c,d). In two of these four opinions (EFSA FEEDAP Panel, 2012c,d), the term 'niacin' was used to identify both nicotinic acid and nicotinamide (niacinamide) with pyridine as the basic structure. The present assessment deals with niacinamide only and the term 'niacinamide' will be used through the opinion.

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 niacinamide as a feed additive.

The confidential version of the technical dossier was subject to a target consultation of the interested Member States from 17 April 2023 to 17 July 2023 for which the received comments were considered for the assessment.

In accordance with Article 38 of the Regulation (EC) No 178/2002[5] and taking into account the protection of confidential information and of personal data in accordance with Articles 39 to 39e of the same Regulation, and of the Decision of EFSA's Executive Director laying down practical arrangements concerning transparency and confidentiality,[6] a non-confidential version of the dossier has been published on Open.EFSA.

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] Arxada Ltd Switzerland, represented in the EU by YOU Solutions Germany GmbH, Freundallee 9A, 30173 Hannover Germany.
[3] COMMISSION IMPLEMENTING REGULATION (EU) No 642/2013 of 4 July 2013 concerning the authorisation of niacin and niacinamide as feed additives for all animal species (Text with EEA relevance).
[4] Dossier reference: FEED-2022-7753
[5] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–48.
[6] Decision available online: https://www.efsa.europa.eu/en/corporate-pubs/transparency-regulation-practical-arrangements

According to Article 32c(2) of Regulation (EC) No 178/2002 and to the Decision of EFSA's Executive Director laying down the practical arrangements on pre-submission phase and public consultations, EFSA carried out a public consultation on the non-confidential version of the technical dossier from 20 July to 10 August 2023 for which no comments were received.

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, other scientific reports and experts' (elicitation) knowledge, to deliver the present output.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment regarding the methods used for the control of the active substance in animal feed are valid and applicable for the current application.[7]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of niacinamide is in line with the principles laid down in Regulation (EC) No 429/2008[9] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012a), Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2021).

3. Assessment

The product consisting of niacinamide is authorised as a nutritional additive (functional group: Vitamins, pro-vitamins and chemically well-defined substances having similar effect) for use in feed for all animal species. This assessment regards the renewal of the authorisation of niacinamide for all animal species.

3.1. Characterisation

3.1.1. Characterisation of the additive

The additive consists of niacinamide (CAS No 98–92-0, molecular formula $C_6H_6N_2O$, the molecular weight 122.13 g/mol) and is authorised with a purity of at least 99%.[3] The additive and the active substance are identical.

Analytical data to confirm the existing specifications were provided for five batches of the additive showing an average value of 99.92% (range: 99.7–100%).[8]

According to the applicant, the additive under assessment is identical to that previously evaluated and the manufacturing has not been changed since the authorisation (EFSA FEEDAP Panel, 2012c).

Three batches of the additive were analysed for impurities.[9] The following impurities were measured: cadmium (< 0.005–< 0.03 mg/kg), lead (< 0.02–< 0.05 mg/kg), mercury (< 0.03–< 0.05 mg/kg), arsenic (< 0.05–< 0.15 mg/kg), sulfur dioxide (< 0.9–< 10 mg/kg), aluminium (< 0.03–0.5 mg/kg), sodium (10–28 mg/kg), hydrogen cyanide (< 1–< 1.5 mg/kg), activity in caesium 134 (< 5–< 10 Bq/kg), activity in caesium 137 (<5–< 10 Bq/kg).

Polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar dioxin-like polychlorinated biphenyls (Co-planar PCBs) were analysed in three batches and found below the corresponding limit of quantification (LOQ). The calculated (upper bound) levels of dioxins and the sum of dioxins and dioxin-like-PCBs were 0.07 ng WHO-PCDD/F-TEQ/kg and 0.13 ng WHO-PCDD/F-PCB-TEQ/kg, respectively (in all batches).

The same batches were also screened for possible presence of pesticides. All the values were below the respective limit of detection (LOD).

The analysis of mycotoxins, included aflatoxins M_1 (< 0.01–0.026 μg/kg), B1, G1, B2, G2 (< 0.02–0.1 μg/kg), ochratoxin A (< 0.03–0.5 μg/kg), deoxynivalenol (< 2 μg/kg), zearalenone (< 0.5–< 10 μg/kg), patulin (0.15–< 20 μg/kg), fumonisin B1 (< 3–< 20 μg/kg), fumonisin B2 (< 20 μg/kg), ergot alkaloids (< 3 μg/kg).

Microbiological contamination was analysed by determination of total aerobic count (< 10 colony forming unit (CFU)/g), total yeast and mould count (< 10 CFU/g), *Pseudomonas aeruginosa* (absent in

[7] Evaluation report received on DD/MM/YYYY and available on the EU Science Hub https://joint-research-centre.ec.europa.eu/eurl-fa-eurl-feed-additives/eurl-fa-authorisation/eurl-fa-evaluation-reports_en

[8] Annex_II_06_CoA.

[9] Annex_II_07 Impurities-a.

10 g), *Enterobacteriaceae* (absent in 100 g), *Escherichia coli* (absent in 10 g) and *Salmonella* spp. (absent in 125 g), *Staphylococcus aureus* (absent in 10 g), spore forming sulfite reducing Clostridia (< 10 CFU/g), presumptive *Bacillus cereus* (< 100 CFU/g), *Cronobacter sakazakii* (absent in 100 g).

Three batches of the additive were also analysed for toluene residues and all the batches were below the LOQ (0.01 mg/kg).[10]

The FEEDAP Panel considers that the microbial contamination and the amounts of the detected impurities do not raise safety concerns.

3.1.2. Physical properties of the additive

The additive appears as white, odourless and crystalline granules. It is freely soluble[11] in water (619 g/L at 20°C).[12]

The dusting potential of three batches of the additive was determined using the Stauber–Heubach method and showed values on average of 137 mg/m^3 (range 110–155 mg/m^3) (mg airborne dust per m^3 of air).[13]

The particle size of the additive was analysed on three batches by laser-diffraction method; the results showed that 16.33% of the particles were < 100 μm, 4.85% < 50 μm, 1.68% < 10 μm and 0.23% < 1 μm.[13]

3.1.3. Stability and homogeneity

No new data on stability and homogeneity have been provided by the applicant in the current dossier. Considering that the manufacturing process has not been changed since the previous authorisation, the data available in the first assessment (EFSA FEEDAP Panel, 2012c) still apply.

3.1.4. Conditions of use

The additive is currently authorised for use in feed for all animal species without a specified maximum or minimum level. Under other provisions of the authorisation, it is specified that:

1) In the directions for use of the additive and premixture, indicate the storage conditions.
2) Niacinamide may be used also via water for drinking.
3) For safety: breathing, eye and skin protection shall be used during handling

The applicant has requested to maintain the same conditions of use.

3.2. Safety

The safety of niacin (nicotinic acid and nicotinamide) was evaluated in a previous opinion (EFSA FEEDAP Panel, 2012c) and the FEEDAP Panel concluded that the additive is safe for the target animals with a margin of safety that is at least 10 times the requirements and use levels. The additive was considered also safe for the consumers and the environment. The FEEDAP Panel considered niacin not irritant to skin, irritant to eyes and mucous membranes, but unlikely to cause skin sensitisation. Nicotinamide did not produce any measurable dust during Stauber–Heubach test and was therefore considered to be of no concern for inhalation exposure.

The applicant provided a statement declaring that no adverse effects related to the use of the additive during the years since authorisation were recorded.

The applicant sent results from a comprehensive automatic literature search[14] conducted to identify new data related to the safety of the additive which were made available since the previous authorisation.

Four cumulative databases (LIVIVO, NCBI, Ovid and Toxinfo), 13 single databases and 12 publisher databases were used. The search covered the period from the previous assessment (January 2012) to June 2022. No other limits were set. The keywords used cover different aspects of safety and the inclusion and exclusion criteria were provided by the applicants.

[10] Annex_II_07 Impurities-b.
[11] The solubility is above the threshold set in Section 2.3.1 of the Guidance on Particle – TR (EFSA Scientific Committee, 2021); therefore, the additive is expected to be fully solubilised either in the feed matrix or in the gastrointestinal tract of the target species.
[12] Identification_and_characterisation_Niacinamide.
[13] Annex_II_08_DP_PSD_Report.
[14] Annex_III_01 and Annex_III_02.

In addition to the automatic literature search, a manual search was conducted using Google Scholar restricting the period from January 2012 to June 2022.

In total, 121 publications were identified by the applicant as relevant for the safety of the additive: 75 for the safety for the target species, 29 for the safety for the consumers and 15 for the safety for the users. No relevant papers were identified in support of the safety for the environment. All the papers were screened by the FEEDAP Panel that concluded that there is no new evidence to lead it to reconsider the previous conclusions that niacinamide is safe for the target species, consumers and the environment under the authorised conditions of use.

Regarding user safety, the FEEDAP Panel considered niacinamide not irritant to skin but irritant to eyes. It is not a dermal sensitiser. Updated data on dusting potential (up to 155 mg/m^3, see Section 3.1.2) demonstrated that the exposure through inhalation is likely.

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[15] and Good Manufacturing Practice.

4. Conclusions

The applicant has provided evidence that the additive currently on the market complies with the existing terms of the authorisation.

There is no new evidence that would lead the FEEDAP Panel to reconsider its previous conclusions.

Thus, the Panel concludes that the additive remains safe for all animal species, consumers and the environment under the authorised conditions of use.

The additive is not irritant to skin, but it is irritant to eyes. It is not a dermal sensitiser and the exposure through inhalation is likely.

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

References

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012a. Guidance on studies concerning the safety of use of the additive for users/workers. EFSA Journal 2012;10(1):2539, 5 pp. https://doi.org/10.2903/j.efsa.2012.2539

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Scientific Opinion on the safety and efficacy of niacin (nicotinic acid and nicotinamide) for all animal species based on a dossier submitted by VITAC EEIG. EFSA Journal 2012b;10(10):2885, 20 pp. https://doi.org/10.2903/j.efsa.2012.2885

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012c. Scientific Opinion on the safety and efficacy of niacin (nicotinic acid and nicotinamide) for all animal species based on a dossier submitted by Lonza Benelux BV. EFSA Journal 2012;10(7):2788, 19 pp. https://doi.org/10.2903/j.efsa.2012.2788

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012d. Scientific Opinion on the safety and efficacy of niacin (nicotinamide) as feed additive for all animal species based on a dossier submitted by Agrinutrition BV. EFSA Journal 2012;10(6):2731. 18 pp. https://doi.org/10.2903/j.efsa.2012.2731

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012e. Scientific Opinion on the safety and efficacy of niacin (nicotinamide) as a feed additive for all animal species based on a dossier submitted by EUROPE-ASIA Import Export GmbH. EFSA Journal 2012;10(7):2789, 18 pp. https://doi.org/10.2903/j.efsa.2012.2789

[15] 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.

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis V, Azimonti G, Bastos ML, Christensen H, Dusemund B, Fašmon Durjava M, Kouba M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Anguita M, Galobart J, Muñoz Guajardo I and Innocenti ML, 2021. Guidance on the renewal of the authorisation of feed additives. EFSA Journal 2021;19(1):6340, 14 pp. https://doi.org/10.2903/j.efsa.2021.6340

EFSA Scientific Committee, More S, Bampidis V, Benford D, Bragard C, Halldorsson T, Hernandez-Jerez A, Bennekou SH, Koutsoumanis K, Lambre C, Machera K, Naegeli H, Nielsen S, Schlatter J, Schrenk D, Silano (deceased) V, Turck D, Younes M, Castenmiller J, Chaudhry Q, Cubadda F, Franz R, Gott D, Mast J, Mortensen A, Oomen AG, Weigel S, Barthelemy E, Rincon A, Tarazona J and Schoonjans R, 2021. Guidance on technical requirements for regulated food and feedproduct applications to establish the presence of small particles including nanoparticles. EFSA Journal 2021;19(8):6769, 48 pp. https://doi.org/10.2903/j.efsa.2021.6769

Abbreviations

CAS	Chemical Abstracts Service
CFU	colony forming unit
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
LOD	limit of detection
LOQ	limit of quantification
PCDDs	polychlorinated dibenzodioxins
PCDFs	polychlorinated dibenzofurans