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

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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 niacin (nicotinic acid) 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 is 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: nutrition additives, vitamins, renewal, safety, efficacy, nicotinic acid, niacin

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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 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 niacin, 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). EFSA received directly from the applicant the technical dossier in support of this application. The dossier was received on 27 July 2022 and the general information and supporting documentation are available at https://open.efsa.europa.eu/questions/EFSA-Q-2022-00477. The particulars and documents in support of the application were considered valid by EFSA as of 24 January 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, consumer, user and the environment and on the efficacy of the feed additive consisting of niacin, when used under the proposed conditions of use (see Section 3.1).

1.2. Additional information

The additive niacin (nicotinic acid) is currently authorised for use in feed for all animal species (3a314).[3]

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

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 niacin (nicotinic acid) as a feed additive. The dossier was received on 27 July 2022 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2022-00477.

The confidential version of the technical dossier was subject to a target consultation of the interested Member States from 24 January 2023 to 24 April 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 at https://open.efsa.europa.eu/questions/FEED-2022-7751.

[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, OJ L 186, 5.7.2013, p. 4.
[4] Dossier reference: FEED-2022-7751.
[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,[6] EFSA carried out a public consultation on the non-confidential version of the technical dossier from 26 June to 17 July 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 niacin 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 niacin is in line with the principles laid down in Regulation (EC) No 429/2008[8] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012a) and Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2021).

3. Assessment

The product consisting of niacin (nicotinic acid) 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 nicotinic acid for all animal species.

3.1. Characterisation

3.1.1. Characterisation of the additive

The additive is niacin (nicotinic acid) (CAS No 59-67-6, molecular formula $C_6H_5NO_2$, the molecular weight 123.11 g/mol) and is authorised with a purity of at least 99%.[3] The additive and the active substance are identical.

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

Analytical data to confirm the existing specifications were provided for five batches of the additive, showing the following average value: 99.9% (range: 99.8–100%).[9]

The applicant has sent two sets of analysis on impurities.[10]

The first set was analysed on four batches of the additive, between 2019 and 2022 and reported the following values: arsenic < 0.06–0.5 mg/kg, cadmium < 0.03–0.1 mg/kg, mercury < 0.005–0.1 mg/kg, lead ≤ 0.03–0.1 mg/kg, copper < 0.03–0.5 mg/kg, palladium < 002–0.1 mg/kg, chloride 0.02% (tested on three batches only), sulfate < 0.02% (tested on two batches only), hydrogen cyanide < 0.1–1.5 mg/kg.

Possible presence of benzo(a)anthracene, benzo(a)pyrene, benzo(b)fluoranthene and crysene were tested on four batches and showed values below the limit of quantification ([LOQ] 0.5 μg/kg). Organochlorine and pyrethroids were tested on two batches and showed values below the respective LOQ (0.01 mg/kg). Dioxins and the sum of dioxins plus dioxin like PCBs concentrations were 0.063 pg/g WHO-PCDD/F-TEQ (upper bound) and 0.101 pg/g WHO-PCDD/F-PCB-TEQ/kg; non-dioxin like PCBs (total 6 ndl-PCB upper bound) ranged from 0.356 to 0.383 ng/g additive.

The second set was analysed on two batches of the additive, between 2021 and 2022 and reported the following values: arsenic < 0.5 mg/kg, cadmium < 0.2 mg/kg, mercury < 1.5 mg/kg, lead ≤ 0.2 mg/kg, copper < 2.3 mg/kg (tested on 1 batch), vanadium < 4.5 mg/kg (tested on 1 batch),

[7] Evaluation report 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] 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] Annex_II_05.

[10] Annex_II_06.

chloride < 200 mg/kg, sulfate < 200 mg/kg. The analysis of mycotoxins (aflatoxins B1, G1, B2, G2) performed on four batches showed values below the LOQ (0.1 μg/kg).

The same batches were tested for microbiological contamination by determination of aerobic plate count (< 10 colony forming unit (CFU)/g), moulds (< 10 CFU/g), yeast CFU/g, Enterobacteriaceae (absent in 10 g), *E. coli* (< 1–< 10 CFU/g), *Listeria monocytogenes* (absent in 25 g) and *Salmonella* spp. (absent in 25 g).

Three additional batches were tested for possible presence of nickel. The analysis reported levels below the LOQ (0.1 mg/kg).[11]

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

Niacin (nicotinic acid) is white, odourless, crystalline granules, freely soluble in ethanol and propylene glycol and sparingly soluble[12] in water (15 g/L at 20°C).[13] The bulk density is ~ 650–750 kg/m^3.

For three batches of the additive the particle size distribution was determined by means of laser diffraction.[14] The results showed that on average 0.42% of the particles were below 1 μm, 3.24% below 10 μm, 5.58% below 50 μm and 7.36 < 100 μm.[14]

When considering the difference between the water solubility (15 g/L) and the expected use levels of nicotinic acid (up to 100 mg/kg complete feed, see Section 3.1.4), the Panel concluded that any potential nicotinic acid nanoparticles present in the additive would be fully solubilised in the gastrointestinal tract and, therefore, a conventional risk assessment should be sufficient.

The dusting potential of three batches of the additive was determined using the Stauber–Heubach method and showed values on average of 1,579 mg/m^3 (range 1,206–1,850 mg/m^3) (mg airborne dust per m^3 of air).[14]

3.1.3. Stability and homogeneity

3.1.3.1. Shelf life

The shelf life of the additive (three batches) was studied when stored at 30°C (relative humidity 65%) for 36 months. More than 99% retention was determined.[15]

The stability of the product, when added to premixtures, feed and water for drinking was already reported in the previous assessment (EFSA FEEDAP Panel, 2012c). No additional data were submitted by the applicant.

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) Niacin 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. However, in the dossier the applicant reported typical use levels below 100 mg/kg complete feed.

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 (nicotinic acid) not irritant to skin, irritant to eyes and mucous membranes, but unlikely to cause skin

[11] RFI_Additional_Nickel-test_CONF.pdf.
[12] The solubility is below the threshold set in Section 2.3.1 of the Guidance on Particle – TR (EFSA Scientific Committee, 2021).
[13] Identification_and_characterisation_Niacin.
[14] Annex_II_07.
[15] Annex_II_09.

sensitisation. Workers might be exposed to a respirable dust when handling nicotinic acid, which should be regarded as being potentially harmful to their health.

The applicant provided the monitoring report of the adverse effects related to the use of the additive during the years since authorisation. No adverse effect notifications were received as concerns the safety for the target species, consumers, users/workers and the environment.[16]

The applicant sent results from a comprehensive automatic literature search[17] conducted to identify new data related to the safety of nicotinic acid and nicotinamide 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 applicant.

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

A total of 121 publications were identified as relevant by the applicant for the safety of the additive: 75 for the safety for the target species, 31 for the safety for the consumer 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 nicotinic acid is safe for the target species, consumers and the environment under the authorised conditions of use.

Regarding user safety, the FEEDAP Panel considered nicotinic acid not irritant to skin but irritant to eyes. It is not a dermal sensitiser. Updated data on dusting potential (up to 1,850 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[18] 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 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.

5. Recommendations

The term 'niacin' is the generic name for nicotinic acid, nicotinamide and related derivatives, therefore, the FEEDAP Panel recommends using the term 'nicotinic acid' instead of 'niacin' in the description of the additive in the authorising Regulation.

[16] Annex_III_123.
[17] Annex_III_01 and Annex_III_02.
[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.

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), 2012b. 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 2012;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), 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
LOQ	limit of quantification