Assessment of a feed additive consisting of all-rac-alpha-tocopheryl acetate (vitamin E) for all animal species for the renewal of its authorisation (DSM)

Reference Number RP1249

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Regulated Product Dossier Assessment
Assessment finalised: 15/03/2024

Contents

Abbreviations

CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
FSA	Food Standards Agency
FSS	Food Standards Scotland
GB	Great Britain
OECD	Organisation for Economic Co-operation and Development
RP	Regulated Product
UL	Upper limit
UK	United Kingdom

1. Executive summary

The Food Standards Agency and Food Standards Scotland (FSA/FSS) have reviewed an assessment of application RP1249 for the renewal of authorisation of all-rac-alpha-tocopheryl acetate (vitamin E) for its use as a nutritional additive in all animal species.

This feed additive application has been made to renew the authorisation in Great Britain (GB) as it is 10 years since the product was authorised and placed on the market in the EU. The same product and uses have been authorised in multiple other countries as the information and data demonstrate the regulatory criteria are met. This feed additive had its application for renewal of authorisation assessed by the European Food Safety Authority (EFSA) which was published in 2021. FSA/FSS have reviewed the information available, including the EFSA renewal opinion[1] and confirmed that all-rac-alpha-tocopheryl acetate (vitamin E), as described in this application, is unlikely to have any adverse effect on human or animal health or the environment in the context of its intended uses in GB.

2. Background and purpose of review

In accordance with Assimilated EU Regulation 1831/2003[2] on feed additives, the application RP1249 for the use of all-rac-alpha-tocopheryl acetate (vitamin E) as a feed additive for all animal species has been submitted for authorisation in each nation of Great Britain (GB).

Whilst it was a Member State of the EU, the UK accepted the risk assessments of the European Food Safety Authority (EFSA) in respect of authorisations for regulated food and feed products. When GB left the EU, it retained the same regulations for food and feed regulated products; FSA/FSS also adopted equivalent technical guidance and quality assurance processes to be able to undertake GB risk assessments for regulated product applications.

To ensure our regulatory systems are risk proportionate and resources are used effectively, FSA/FSS have used the evidence submitted by the applicant and other information in the public domain, including the EFSA risk assessment opinion, to provide a summary assessment of the evidence of safety presented in this report.

Specifically, in reviewing the risk assessment that EFSA have recently completed, the reviewers have verified that the standard approach taken, when compared to the relevant guidance applied in GB, has been followed and the conclusions made are consistent with the data summarised in the opinion. Consideration has been given to the processes undertaken to ensure the EFSA opinion is robust and whether there are any aspects that would require further review, such as specific issues for the countries of GB. The result of the assessment is that there is sufficient evidence of safety to conclude without requiring further risk assessment at this time.

2.1 Applicant

Name: DSM Nutritional Products Ltd.
Address: Heanor Gate Ind. Est.,
Heanor,
Derbyshire,
DE75 7SG

2.2 Genetic modification step

Not applicable.

3. Details of other Regulators opinions

The additive Vitamin E has previously been authorised in the EU by Commission implementing regulation (EU) 2023/341[3] and Commission Regulation (EU) No 26/11[4]. The additive is also a Generally Recognised As Safe (GRAS) substance by the FDA[5]. Vitamin E does not require registration in Australia as it is marketed to maintain normal physiology and not to modify it[6]. In 2021, EFSA published a risk assessment opinion[1] on the renewal of application of all-rac-alpha tocopherol for

its use as a feed additive. This opinion has been reviewed by FSA/FSS risk assessors.

3.1 Methodology applied in the EFSA opinion

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) guidance: Guidance on the assessment of the safety of feed additives for the consumer[7], Guidance on the renewal of the authorisation of feed additives[8] and principles in Regulation (EC) No 429/2008[9] on detailed rules for the implementation of Regulation (EC) No 1831/2003.

3.2 Compound

The additive's active substance is all-rac-alpha-tocopheryl acetate (CAS number 7695-91-2) at an average concentration across 5 batches of 95.08% in oil form, meeting the additive's specification of >93% all-rac-alpha tocopheryl acetate. The all-rac-alpha-tocopheryl acetate is produced through chemical synthesis.

The additive is formulated in two forms, an adsorbate powder and a spray-dried powder, both containing ≥ 50% all-rac-alpha-tocopheryl acetate which was demonstrated across 5 batches

3.3 Specification

Information provided on the identity, composition and specifications of the production species does not raise safety concerns.

Five batches of the active substance were tested for impurities, including: all-rac-trans-2,3,4,6,7-pentamethyl-2-(4,8,12-trimethyltridecyl)-2,3-dihydrobenzofuran-5-yl acetate, all-rac-cis-2,3,4,6,7-pentamethyl-2(4,8,12-trimethyltridecyl)-2,3-dihydrobenzofuran-5-yl acetate, all-rac-alpha-tocopherol, 4-methoxy-2,3,6-trimethyl-5-[(all-RS,E)-3,7,11,15-tetramethylhexadec-2 enyl] phenylacetate, (all-RS, all-E)-2,6,10,14,19,23,27,31-octamethyldotriaconta-12,14,18- triene, pyridine,

toluene, heavy metals, dioxins and sum of dioxins and dioxin-like polychlorinated biphenyls. These were either not detected, or below recommended limits.

Physicochemical properties and stability data were evaluated in a previous assessment by EFSA[10], concluding that the additive is stable in both formulations for 48 months at 25°C and 60% relative humidity. In premixtures and feed, stability was measured at 80-100% after storage for 6 months (premixtures) or 3 months (feed) at 25°C. During pelleting at 75°C, the additive was deemed as stable, with a 40% loss of the active substance reported. The additive is stable in water.

The additive was tested for dusting potential and particle size distribution. Results for both formulations are summarised in Table 1:

Table 1: Dusting potential and particle size distribution of vitamin E.

Vitamin E	Adsorbate powder	Spray-dried powder
Dusting potential (Stauber-Heubach method)	1.9 – 2.1 g/m^3	4.6 – 6.8 g/m^3
Particle size distribution (Laser diffraction)	< 33 µm – 10 % < 101 µm – 50% < 236 µm – 90%	-

This application included the request for use for all species. The additive is presently authorised without a specified maximum content, for its use in feed and water. No changes to these conditions of use were proposed.

3.4 Exposure assessment

EFSA undertook a dietary exposure assessment as part of their opinion. Relevant residue data for vitamin E in the edible tissues of birds, fish and mammals, as well as milk, seafood and eggs, were extracted from published papers, some of which were previously also used by EFSA in its previous opinion published in 2010 and some of which were newly identified from the applicant's literature review. Although no maximum use level is specified in the authorisation, EFSA used residues data corresponding to realistic feed supplementation levels (i.e. 100 mg/kg feed). Consumption data from the EFSA Comprehensive European Food

Consumption Database, incorporated in EFSA's Feed Additives Consumer Assessment (FACE) tool, were used to estimate exposures at the highest reliable percentiles, usually the 95th percentile, for different age groups from different EU Member State's dietary surveys. The exposure estimates were on a per kg bodyweight basis, and these were adjusted to a per person basis using default values for body weights from EFSA guidance[11] in order to compare with tolerable upper levels (ULs) for vitamin E. The ULs were established by the former Scientific Committee on Food in 2003[12] and the ULs used were 300 mg/day for adults, 260 mg/day for ages 15-17 years, 120 mg/day for ages 4-6 years and 100 mg/day for ages 1-3 years. The exposure giving the highest percent of the UL at the highest reliable percentile was for "other children," which was 15.3% of the UL for children aged 4-6 years of 120 mg/day. EFSA concluded that there are no safety concerns for consumers from the intake of food from all animal species fed with vitamin E in the form of all-rac-alpha-tocopheryl acetate under the conditions of the existing authorisation.

The consumption data used included historic UK data submitted to EFSA when the UK was an EU Member State, and the highest estimated exposure compared to its respective UL was for Spanish consumers. Therefore, the risk assessment addresses the exposures of UK consumers, including GB.

3.5 Toxicological data

Vitamin E is currently authorised as a food additive, as a food for nutritional purposes, as an antioxidant in cosmetics and as a veterinary medicinal product. It is also currently authorised as a feed additive for all animal species as a nutritional and a technological additive.

The opinion under review refers to previous conclusions from the prior 2010 EFSA evaluation[10] to derive conclusions on the safety for the target species, consumers, users and the environment, raising no safety concerns for any of these categories (excluding certain uncertainties for user safety, described below).

A literature review presented by the applicant was evaluated. One hundred and twenty-two relevant papers were selected as relevant for the evaluation of the additive's safety. None of the papers identified a safety concern for the target species, consumers, users or the environment. EFSA confirmed their previous conclusion of 2010 of not being able to conclude on maximum dosage levels of vitamin E with respect to safety for target species, due to inconsistencies in the available literature data. However, no concerns were identified for the safety of the target species, the consumer or the environment at what were considered to be current use levels in practice.

No new data to evaluate the safety for the user was provided since the 2010 evaluation. For that previous opinion, results from skin irritation and eye irritation studies in rabbits showed that the additive is not a skin or eye irritant. No skin sensitisation studies were provided, in light of which no conclusion was drawn on the sensitisation potential of the additive, yet EFSA states that 'no concern for user safety is expected'.

3.6 Analytical Method Review

FSA/FSS accept the EURL analytical method evaluation report[13]. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Other regulators opinions and conclusions

EFSA (2021) found that this product, herein denoted as Vitamin E, in the form of all-rac-alpha-tocopheryl acetate raises no safety concerns for the target species.

It is noted that the additive raises no safety concerns for the consumer. Estimated intakes of vitamin E from animal derived food products were well within the ULs established for vitamin E.

Vitamin E is a naturally-occurring compound, and no significant increase of concentration in the environment is expected.

The additive is not a skin or eye irritant. There are no expected causes for concern from a user safety standpoint although a conclusion on its potential to be a skin sensitiser could not be reached

No relevant impurities were detected above acceptable levels in five batches of the active substance and final product.

5. Caveats and uncertainties

No maximum dosage level of the additive can be established based on safety for the target species given the lack of consistency in the scientific data on hypervitaminosis E.

No conclusion can be drawn on the skin sensitisation potential of the additive.

6. FSA - FSS conclusion for GB risk analysis

The application has been assessed in line with the applicable guidance and is partially based on considerations of detailed proprietary information available to the Panel, whilst this is only briefly summarised this description is consistent with the conclusions. The conclusions of the EFSA opinion have been reviewed in detail by FSA/FSS and are considered appropriate and consistent within the identified caveats and uncertainties identified in the opinion and would be applicable to GB.

7. Outcome of assessment

FSA/FSS has reviewed the applicant's renewal application, supporting documentation, and other regulators risk assessments, most notably the EFSA risk

assessment opinion (2021) and consider sufficient evidence has been demonstrated to conclude without further questions or risk assessment.

The FSA/FSS conclude that the all-rac-alpha-tocopheryl acetate (vitamin E) feed additive, as described in this application, is safe and is not liable to have an adverse effect on the target species, worker safety, environmental safety and human health at the intended concentrations of use. In the absence of data for assessment, the additive should be regarded as a potential skin sensitiser.

In making this assessment, the following principles have been applied:

1) There is not a legal duty to perform a separate risk assessment for GB, there was sufficient scientific evidence to make a conclusion on safety with no further questions to the applicant, and therefore no further risk assessment activities are necessary.

2) The application is for a renewal or authorisation where the UK/GB already has accepted the established risk of the products on the market.

3) Sufficient evidence was available in the literature, for example, where other National food safety authorities had positively assessed the application using the same risk assessment guidance in principle and legal requirements in GB with the exception to changes in the General Food Law.

4) Applicants provided sufficient relevant information as requested by FSA/FSS.

5) The FSA/FSS review did not find any issues of divergence from guidance or mutual approaches or new scientific issues for consideration.

6) There were no other specific issues that would require an assessment for the UK or the nations of the UK.

8. References

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5. FDA (U.S. Food & Drug Administration), 2020. SCOGS (Select Committee on GRAS Substances) Database. Available at: SCOGS (Select Committee on GRAS Substances) (fda.gov)

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10. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2010. Scientific Opinion on the safety and efficacy of vitamin E as a feed additive for all animal species. EFSA Journal 2010;8(6):1635. https://doi.org/10.2903/j.efsa.2010.1635

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12. EFSA NDA PANEL (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2006. Tolerable upper intake levels for vitamins and minerals. Available at: complet_chapitres.indd (europa.eu)

13. EURL-FA (European Reference Laboratory for Feed Additives), 2010. CRL Evaluation Report on the Analytical Methods submitted in connection with the

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