Assessment of the feed additive consisting of *Lactiplantibacillus plantarum* DSM 23375 for all animal species for the renewal of its authorisation (Agri-King, Inc.)

Reference Number RP1367

Risk Assessment Unit
Science, Evidence and Research Division, FSA

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

Contents

Abbreviations

AMR	Antimicrobial resistance
CAS	Chemical Abstracts Service
CFU	Colony forming units
EC	European Commission
EU	European Union
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
LOQ	Limits of quantification

MIC	Minimum inhibitory concentration
OECD	Organisation for Economic Co-operation and Development
QPS	Quality Presumption of Safety
RP	Regulated Product
UK	United Kingdom
WGS	Whole genome sequence

1. Executive summary

The Food Standards Agency and Food Standards Scotland (FSA/FSS) have reviewed an assessment of application RP1367 for the renewal of authorisation of *Lactiplantibacillus plantarum* DSM 23375 for its use as a technological additive, functional group of silage 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 2023. FSA/FSS have reviewed the information available, including the EFSA renewal opinion[1] and confirmed that *Lactiplantibacillus plantarum* DSM 23375, 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 RP1367 for the use of *Lactiplantibacillus plantarum* DSM 23375 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: Agri-King, Inc.
Address: 18246 Waller Road
Fulton, Illinois
61252
USA

2.2 Genetic modification step

Not applicable.

3. Details of other Regulators opinions

The additive *Lactiplantibacillus plantarum* DSM 23375 has previously been authorised in the EU by Commission implementing regulation (EU) 2024/252[3] and Regulation (EU) No 1065/2012[4]. In Australia silage additives are exempt from registration under Schedule 3 of the Agvet Code Regulations. In 2023, EFSA published a risk assessment opinion[1] on the renewal of application of *Lactiplantibacillus plantarum* DSM 23375 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) assess the safety and the efficacy of *Lactiplantibacillus plantarum* DSM 23375 in accordance with guidance documents: Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018)[5], Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2021)[6], Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012b)[7], EFSA statement on the requirements for whole genome sequence analysis of microorganisms intentionally used in the food chain (EFSA, 2021)[8] and principles in Regulation (EC) No 429/2008[9].

3.2 Compound

The current authorization for the additive requires a minimum content of the active agent (*L. plantarum* DSM 23375) at 2.0×10^{10} colony forming units (CFU)/g of the additive. An average of 1.19×10^{11} CFU/g additive was shown in analysis of five batches of the additive. It was stated by the applicant that the manufacturing process remains unchanged since the initial authorization. The applicant stated that no antimicrobials are employed in the manufacturing of the product.

3.3 Specification

Analysis of three batches of the additive demonstrated compliance with predefined specifications: *Escherichia coli* (<10 CFU/g), *Salmonella spp.* (not detectable in 25 g), yeasts and moulds (<10 CFU/g) and coliforms (<10 CFU/g). In addition, testing for arsenic (As), mercury (Hg), lead (Pb), cadmium (Cd) and aflatoxins (B1, B2, G1, and G2) showed concentrations below their respective limits of quantification (LOQ) for these batches. Furthermore, an analysis of three batches was conducted for polychlorinated dibenzofurans (PCDFs), polychlorinated dibenzodioxins (PCDDs), and coplanar dioxin-like polychlorinated biphenyls (Co-planar PCBs), showing levels below the corresponding LOQ. In all three batches, the calculated (upper bound) concentrations of dioxins ranged from 0.0623 to 0.119 ng WHO-PCDD/F-TEQ/kg and the calculated (upper bound) concentrations of the summed total of dioxins and dioxin-like PCBs ranged from 0.0956 to 0.182 ng WHO-PCDD/F-PCB-TEQ/kg.

It was concluded by the EFSA FEEDAP Panel that the microbial contamination and the levels of identified impurities do not give rise to safety concerns. The description of physico-chemical properties of the additive in the previous EFSA 2012 opinion[10] are still applicable as no new data was provided.

3.4 Characterisation of the active agent

The strain DSM 23375, originally isolated from natural forage, underwent species-level identification as *L. plantarum* through bioinformatic analysis of the whole genome sequence (WGS). The strain has undergone no genetic modifications.

The broth microdilution method following CLSI standards was used to assess in triplicate the strain's susceptibility to antimicrobials. The strain is considered susceptible to all relevant antibiotics because all the minimum inhibitory concentration (MIC) values were below or equal to the specified cut-off values in the EFSA FEEDAP Guidance[5].

The strain's WGS was examined for the presence of antimicrobial resistance (AMR) genes by cross-referencing against three databases, but only results from ResFinder and AMRFinderPlus were considered by the EFSA Panel. No concerns were identified from the search.

The current authorization allows the use of the additive in fresh material for all animal species without any specified maximum content. No changes to these conditions of use were proposed.

3.5 Toxicological data

No adverse effects for target animals, consumers, users and/or the environment have been reported since the approval of the additive according to the applicant. It was concluded in the previous EFSA 2012 opinion that following the Qualified Presumption of Safety (QPS) approach to safety assessment, the strain was deemed safe for target species, consumers, and the environment in the silage production[10]. Based on the provided evidence showing the absence of acquired antimicrobial determinants for antibiotics of human and veterinary significance and confirming the identity of the strain, the previously drawn conclusions remain valid in that the additive is considered safe for the target species, consumers and the environment

Regarding safety for the user, no new data to evaluate the safety of the respiratory system was provided since the 2012 evaluation. Results from skin irritation testing following OECD guideline 404 showed that the additive is not a skin irritant. The eye irritation study following OECD guideline 405 showed the additive is not an eye irritant. No skin sensitisation studies were provided, in light of which no conclusion was drawn on the sensitisation potential of the additive. The additive should be considered as a respiratory sensitiser due to the proteinaceous nature of the active agent. It is recommended to use gloves and breathing protection during handling.

3.6 Analytical Method Review

FSA/FSS accept the EURL analytical method evaluation report[11]. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Other regulators opinions and conclusions

EFSA (2023) concluded that the microbial contamination and the levels of identified impurities do not give rise to safety concerns. *Lactiplantibacillus plantarum* DSM 23375 raises no safety concerns for the target species, consumers and the environment.

The additive is not a skin or eye irritant. The additive should be considered as a respiratory sensitiser due to proteinaceous nature of the active agent. Conclusions could not be drawn on the potential to cause skin sensitisation. There are no expected causes for concern from a user safety standpoint.

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

5. Caveats and uncertainties

The current authorization allows the use of the additive without any specified maximum content.

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 (2023) and consider sufficient evidence has been demonstrated to conclude without further questions or risk assessment.

The FSA/FSS conclude that the *Lactiplantibacillus plantarum* DSM 23375 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 making this assessment, the following principles have been applied:

1) There is not a legal duty to perform a separate risk assessment for GB and therefore, 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

1. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2021. Scientific Opinion on the assessment of the feed additive consisting of Lactiplantibacillus plantarum DSM 23375 for all animal species for the renewal of its authorisation (Agri-King, Inc.). EFSA Journal 2023; 21(6):8054. 8 pp. https://doi.org/10.2903/j.efsa.2023.8054

2. EC (European Commission), 2003. Regulation No 1831/2003 of the European Parliament and of the Council on additives for use in animal nutrition. Available at Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition (Text with EEA relevance) (legislation.gov.uk)

3. EC (European Commission), 2024. Regulation No 2024/252 of the European Parliament and of the Council on additives for use in animal nutrition. Available at Implementing regulation - EU - 2024/252 - EN - EUR-Lex (europa.eu)

4. EC (European Commission), 2012. Regulation No 1065/212 of the European Parliament and of the Council on additives for use in animal nutrition. Available at Implementing regulation - 1065/2012 - EN - EUR-Lex (europa.eu)

5. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2018. Guidance on the characterisation of microorganisms used as feed additives or as production organisms. *EFSA Journal* 2018;16(3):5206, 24 pp. https://doi.org/10.2903/j.efsa.2018.5206

6. EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 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

7. 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

8. EFSA (European Food Safety Authority), 2021. EFSA statement on the requirements for whole genome sequence analysis of microorganisms intentionally used in the food chain. *EFSA Journal* 2021;19(7):6506, 14 pp. https://doi.org/10.2903/j.efsa.2021.6506

9. EC (European Commission), 2008. Regulation No 429/2008 of the European Parliament and of the Council on additives for use in animal nutrition. Available at 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 (Text with EEA relevance) (legislation.gov.uk)

10. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2012a. Scientific Opinion on the safety and efficacy of 18 strains of Lactobacillus plantarum (DSM 23375, CNCM I-3235, DSM 19457, DSM 16568, LMG 21295, DSM 16565, VTT E-78076, CNCM MA 18/5U, NCIMB 30238, ATTC PTA-6139, DSM 18112, ATCC 55058, DSM 18113, DSM 18114, ATCC 55942, ATCC 55943, ATCC 55944 and NCIMB 30094) as silage additives for all species. EFSA Journal 2012;10(6):2732,36 pp. https://doi.org/10.2903/j.efsa.2012.2732

11. EURL-FA (European Reference Laboratory for Feed Additives), 2011. CRL Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of new Feed Additive according to Regulation (EC) No 1831/2003. Forty five “micro-organisms used as silage agents”. Available at FAD-2010-0048

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