Assessment of the feed additive consisting of *Lactiplantibacillus plantarum* (previously *Lactobacillus plantarum*) DSM 19457 for all animal species for the renewal of its authorisation (Biomin GmbH)

Reference Number RP1359

Risk Assessment Unit
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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

MIC	Minimum inhibitory concentration
OECD	Organisation for Economic Co-operation and Development
QPS	Qualified 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 RP 1359 for the renewal of authorisation of *Lactiplantibacillus plantarum* DSM 19457 (previously *Lactobacillus plantarum*) 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 2022. FSA/FSS have reviewed the information available, including the EFSA renewal opinion[1] and confirmed that *Lactiplantibacillus plantarum* DSM 19457, as described in this application, is unlikely to have any adverse effects 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 RP1359 for the use of *Lactiplantibacillus plantarum* DSM 19457 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: BIOMIN GmbH
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3131 Getzersdorf
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2.2 Genetic modification step

Not applicable.

3. Details of other Regulators opinions

The additive *Lactiplantibacillus plantarum* DSM 19457 has previously been authorised in the EU by Commission implementing regulation (EU) 2023/1443[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 2022, EFSA published a risk assessment opinion[1] on the renewal of application of *Lactiplantibacillus plantarum* DSM 19457 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

The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) assessed the safety and the efficacy of *Lactiplantibacillus plantarum* DSM 19457 in accordance with EFSA FEEDAP Panel guidance documents: Guidance on the characterisation of microorganisms used as feed additives or as production organisms[5], Guidance on the renewal of the authorisation of feed additives[6], Guidance on studies concerning the safety of use of the additive for users/workers[7] and principles in Regulation (EC) No 429/2008[8] .

3.2 Compound

The current authorization for the additive requires a minimum content of the active agent (*L. plantarum* DSM 19457) at 1.0×10^{10} colony forming units (CFU)/g of the additive. An average of 1.7×10^{10} CFU/g additive was shown in analysis of five batches of additive. It was stated by the applicant that the manufacturing process and composition of the additive remains unchanged since the initial authorization. The additive may contain approximately 6% of fermentation medium and 65% of cryoprotectants.

3.3 Specification

Analysis of 6 batches of the additive demonstrated compliance with predefined specifications: *Escherichia coli* (<10 CFU/g), *Salmonella spp.* (not detectable in 25 g), yeasts and filamentous fungi (<1000 CFU/g) and coliforms (<1000CFU/g). In addition, testing for arsenic (< 2mg/kg), mercury (<0.1 mg/kg), lead (< 5mg/kg) and cadmium (0.5 mg/kg) showed compliance with their respective limits. Furthermore, an analysis of three batches showed levels of aflatoxin B1 below the quantification limit of the analytical method and *Enterobacteriaceae* counts below 10 CFU/g. Dusting potential of 3 batches was tested using the Stauber-Heubach method showing a mean value of 3.1 g/m^3.

3.4 Characterisation of the active agent

The strain DSM 19457 underwent taxonomical identification through bioinformatic analysis of the whole genome sequence (WGS). The average nucleotide identity value was 99.16% with the type strain *Lactiplantibacillus plantarum* ATCC 14917^T. The strain has undergone no genetic modifications. It was originally isolated from silage.

The broth microdilution method was used to assess 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 the specified cut-off values in the EFSA FEEDAP Guidance with the exception of kanamycin and erythromycin[5]. Kanamycin and erythromycin exceeded the cut-off values by one dilution, which was considered within experimental error of the method by the EFSA Panel.

The strain's whole genome sequence (WGS) was examined for the presence of antimicrobial resistance (AMR) genes by cross-referencing against two relevant databases. No concerns were identified from the search with set thresholds of 70% similarity and 60% length coverage.

The current authorization allows the use of the additive in all animal species. Incorporation of the additive into the forage can be done directly or sprayed after dissolving in water. No changes to these conditions of use were proposed.

3.5 Toxicological data

No adverse effects on the health of workers 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 the target species, consumers, and the environment in the silage production[9]. 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.

Results from *in vitro* skin irritation testing following OECD guideline 439 showed that the additive (with maltodextrin as carrier) is non-irritant to skin. The eye *in vitro* irritation study following OECD guideline 437 showed the additive (with maltodextrin as carrier) is non-irritant to eyes. 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 respiratory sensitiser due to proteinaceous nature of the active agent. It is recommended to use breathing gloves and breathing protection during handling.

After obtaining authorization for active agent as a silage additive, various formulations can be introduced to the market based on that approval. Several cryoprotectants and carriers were listed by the applicant allowing multiple additive formulations. Nevertheless, the primary focus in evaluating user safety lies in the active agent, as long as other components do not pose safety concerns. In the case of this particular product, the excipients used in the final formulation do not add extra risks.

3.6 Analytical Method Review

FSA/FSS accept the EURL analytical method evaluation report[10]. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Other regulators opinions and conclusions

EFSA (2022) concluded that the *Lactiplantibacillus plantarum* DSM 19457 raises no safety concerns for the target species, consumers and the environment under the authorised conditions of use.

The additive is not a skin or eye irritant. The additive should be considered as a respiratory sensitiser due to the proteinaceous nature of the active agent.
No conclusion was drawn on the skin sensitisation potential of the additive.

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 have reviewed the applicant's renewal application, supporting documentation, and other regulators risk assessments, most notably the EFSA risk assessment opinion (2022) and consider sufficient evidence has been demonstrated to conclude without further questions or risk assessment activities.

The FSA/FSS conclude that the *Lactiplantibacillus plantarum* DSM 19457 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, 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), 2022. Scientific Opinion on the assessment of the feed additive consisting of *Lactiplantibacillus plantarum* DSM 19457 for all animal species for the renewal of its authorisation (Biomin GmbH) EFSA Journal 2022; 20(12):7697.8 pp. https://doi.org/10.2903/j.efsa.2023.7697

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), 2023. Regulation No 2023/1443 of the European Parliament and of the Council on additives for use in animal nutrition. Available at L_2023177EN.01005901.xml (europa.eu)

4. EC (European Commission), 2012. Regulation No 1065/2012 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), 2013. Guidance on the renewal of the authorisation of feed additives. *EFSA Journal* 2013;11(10):3431, 8 pp. https://doi.org/10.2903/j.efsa.2013.3431

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. 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)

9. EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2012b. 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

10. EURL-FA (European Reference Laboratory for Feed Additives), 2011. EURL 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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