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# Assessment of the feed additive consisting of *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) DSM 12836 for all animal species for the renewal of its authorisation (Lactosan GmbH & Co KG)

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## Abstract

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the assessment of the application for renewal of authorisation of *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) DSM 12836, as a technological additive for all animal species. The applicant has provided evidence that the additive currently in the market complies with the existing conditions of authorisation. There was no new evidence that would lead the FEEDAP Panel to reconsider its previous conclusions. Thus, the Panel concluded that the additive remains safe for all animal species, consumer and the environment under the authorised conditions of use. The additive was not irritant to skin and eyes but is considered a skin and respiratory sensitiser. The present application for renewal of the authorisation did 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 was no need for assessing the efficacy of the additive in the context of the renewal of the authorisation.

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# 1. Introduction

## 1.1. Background and Terms of Reference as provided by the requestor

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 Lactosan GmbH & Co KG[2] for the renewal of the authorisation of the product consisting of *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) DSM 12836, when used as a feed additive for all animal species (category: technological additives; functional group: silage additives).

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 particulars and documents in support of the application were considered valid by EFSA as of 20 November 2020.

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 product consisting of *Lactiplantibacillus plantarum* DSM 12836, when used under the proposed conditions of use (see Section 3.1.3).

## 1.2. Additional information

The additive is a preparation containing viable cells of *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) DSM 12836. It is currently authorised as a feed additive in the European Union (1k2078).[3]

EFSA has adopted an opinion on the safety and efficacy of *Lactobacillus plantarum* DSM 12836 for all animal species (EFSA FEEDAP Panel, 2011).

# 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 *Lactiplantibacillus plantarum* DSM 12836 as a feed additive.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[5]

## 2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of *L. plantarum* DSM 12836 is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance on the characterisation of microorganisms used as feed additives or as

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] Lactosan GmbH & Co KG, Industriestraße West 5, A-8605, Kapfenberg, Austria.
[3] Commission Implementing Regulation (EU) No 1263/2011 of 5 December 2011 concerning the authorisation *of Lactobacillus buchneri* (DSM 16774), *Lactobacillus buchneri (*DSM 12856), *Lactobacillus paracasei* (DSM 16245), *Lactobacillus paracasei* (DSM 16773), *Lactobacillus plantarum* (DSM 12836), *Lactobacillus plantarum* (DSM 12837), *Lactobacillus brevis* (DSM 12835), *Lactobacillus rhamnosus* (NCIMB 30121), *Lactococcus lactis* (DSM 11037), *Lactococcus lactis* (NCIMB 30160), *Pediococcus acidilactici* (DSM 16243) and *Pediococcus pentosaceus* (DSM 12834) as feed additives for all animal species. OJ L, 322, 6.12.2011, p. 3.
[4] FEED dossier reference: FAD-2020-0060.
[5] The full report is available on the EURL website: https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports
[6] 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.

production organisms (EFSA FEEDAP Panel, 2018) and Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013).

# 3. Assessment

The additive is a preparation of viable cells of a single strain of *Lactiplantibacillus plantarum* (formerly *Lactobacillus plantarum*) currently authorised as a technological additive (functional group: silage additives) for use in forages for all animal species. This assessment regards the renewal of the authorisation of *L. plantarum* DSM 12836 for the above-mentioned species.

## 3.1. Characterisation

### 3.1.1. Characterisation of the additive

The product currently authorised consists of ~ 35–50% bacterial cells and 50–65% carriers ([redacted]) and cryoprotectants ([redacted]). The minimum concentration of active agent (*L. plantarum* DSM 12836) is $5 \times 10^{11}$ CFU per gram of additive.

The information submitted regarding the manufacturing process lists some modifications applied to the fermentation process and composition of the additive which have been developed since the first authorisation was granted. The modifications regard the composition of the fermentation medium (e.g. [redacted]). Regarding the composition of the additive, [redacted] are also used as cryoprotectants, and [redacted] is used in replacement of [redacted].

Analysis of three recent batches for viable lactic acid bacterial cells showed compliance with the specifications of the authorisation with a mean value of $5.7 \times 10^{11}$ CFU/g additive (range $5.5 - 5.9 \times 10^{11}$ CFU/g additive).[7]

Limits are set for Enterobacteriaceae ($10^2$ CFU/g), yeasts and filamentous fungi ($10^2$ CFU/g) and *Salmonella* spp. (not detected in 25 g). Analysis of the above-referred batches of the additive showed compliance with these limits.[8] These recent batches were also tested for aflatoxins (B1, B2, G1 and G2), deoxynivalenol, zearalenone,[9] lead, mercury, cadmium and arsenic concentration.[10] Results showed levels below the respective limits of quantification,[11] except for two batches that showed levels of cadmium of 0.03 and 0.04 mg/kg which do not give rise to concerns.

No new data have been provided regarding the physico-chemical properties or stability of the additive. Since the changes introduced in the additive and its manufacturing process are not expected to have a significant effect on these characteristics, the data described in the previous opinion still apply.

### 3.1.2. Characterisation of the active agent

The active agent was isolated from silage. It is deposited in the Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ) with the accession number DSM 12836.[12] It has not been genetically modified.

The taxonomical identification was achieved by [redacted] using the whole genome sequence (WGS). The results of the analyses using the [redacted][13] Moreover, the results of [redacted].

[7] Technical dossier/Section II/Annex II_1-2 Batch.
[8] Technical dossier/Section II/Annex II_1_3 Purity.
[9] Technical dossier/Section II/Annex II_1_4 Mykotox.
[10] Technical dossier/Section II/Annex II_1_5 heavy met.
[11] Limit of quantification: aflatoxins (B1, B2, G1, and G2): 0.03 μg/kg, deoxynivalenol 10 μg/kg, zearalenone (5 μg/kg), Pb (0.10 mg/kg), Hg (0.10 mg/kg), Cd (0.03 mg/kg) and As (0.10 mg/kg).
[12] Technical dossier/Supplementary information April 2021/Annex_12836.
[13] Technical dossier/Section II/Annex_II_2_4_WGS.

The bacterial strain was tested for antibiotic susceptibility using a broth microdilution method.[14] The battery of antibiotics used included those recommended by EFSA (EFSA FEEDAP Panel, 2018). All the minimum inhibitory concentration values were equal or below the corresponding EFSA cut-off values. Therefore, the strain is considered to be susceptible to all the relevant antibiotics.

The whole genome sequence of the strain [redacted] was searched for acquired antibiotic resistance genes in the databases [redacted].[15] No hits were identified.

### 3.1.3. Conditions of use

The additive is currently authorised for use in forages for all animal species without a minimum inclusion level.

Under other provisions of the authorisation, it is specified that:

- In the directions for use of the additive and premixture, indicate the storage temperature and storage life.
- Minimum dose of the additive when used without combination with other micro-organisms as silage additives: $1 \times 10^8$ CFU/kg fresh material.
- For safety: it is recommended to use breathing protection and gloves during handling.

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

## 3.2. Safety

In the previous opinion the FEEDAP Panel concluded that following the qualified presumption of safety (QPS) approach to safety assessment, the use of this strain in the production of silage was considered safe for target species, consumers and the environment (EFSA FEEDAP Panel, 2011). In the context of this application, the identity of the strain as *L. plantarum* was confirmed and evidence that the strain does not show acquired antimicrobial determinants for antibiotics of human and veterinary importance was provided. Consequently, the conclusions already reached are still valid and *L. plantarum* DSM 12836 is considered safe for the target species, consumers and the environment.

The safety for the user was evaluated by the FEEDAP Panel in a previous assessment (EFSA FEEDAP Panel, 2011). The Panel concluded: 'evidence of a lack of irritancy was provided for one formulation of the additive. It is unlikely that considering the nature of the alternative food grade excipients, different results would be obtained for other formulations containing *L. plantarum* DSM 12836. Given the lack of specific information and its proteinaceous nature, the active agent should be considered to have the potential to be a skin/respiratory sensitiser'. No additional data were provided in the current application.

The applicant declares that no adverse effects on the health of workers have been observed in the production plant or during usage of the additive.[16]

The applicant performed a literature search in order to provide evidence that in the light of the current knowledge the additive remains safe under the approved conditions for target species, consumers, users and the environment. The literature search was conducted in June 2020 without time restrictions.[17] The search term used was '*Lactobacillus plantarum* DSM 12836' and the strategy followed was reported. The applicant searched in a total of seven relevant databases: Agricola, Agris, Google Scholar, Ingenta, PubMed, Science Direct and World Cat Library. The literature search retrieved eight publications. However, none was considered relevant because they regarded the assessment of the efficacy of the product (six publications) or referred to the previous EFSA FEEDAP scientific opinion (EFSA FEEDAP Panel, 2011) or to the authorisation of the additive.

Therefore, the FEEDAP Panel concludes that there is no new evidence that would lead it to reconsider the previous conclusions that *L. plantarum* DSM 12836 is safe for the target species, consumers and the environment under the authorised conditions of use. Regarding user safety *L. plantarum* DSM 12836 is not irritant to skin and eyes but is considered a skin and respiratory sensitiser.

[14] Technical dossier/Section II/Annex_II_2_5_Antibio.
[15] Technical dossier/Section II/Annex_II_2_6_AMR.
[16] Technical dossier/Section III.
[17] Technical dossier/Section III/Annex III_3.

### 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.

## 4. Conclusions

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, consumer and the environment under the authorised conditions of use. Regarding user safety *L. plantarum* DSM 12836 is not irritant to skin and eyes but is considered a skin and respiratory sensitiser.

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

## 5. Documentation as provided to EFSA/Chronology

| Date | Event |
|---|---|
| 23/09/2020 | Dossier received by EFSA. *L. plantarum* DSM 12836. Submitted by Lactosan GmbH & Co KG |
| 06/05/2020 | Reception mandate from the European Commission |
| 16/11/2020 | Application validated by EFSA – Start of the scientific assessment |
| 10/06/2020 | Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives |
| 22/02/2021 | Comments received from Member States |
| 29/03/2021 | Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation* |
| 09/04/2021 | Reception of supplementary information from the applicant - Scientific assessment re-started |
| 05/05/2021 | Opinion adopted by the FEEDAP Panel. End of the Scientific assessment |

## References

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011. Scientific Opinion on the safety and efficacy of *Lactobacillus plantarum* (DSM 12836) as a silage additive for all species. EFSA Journal 2011;9(9):2367, 11 pp. https://doi.org/10.2903/j.efsa.2011.2367

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

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Glandorf B, Herman L, Kärenlampi S, Aguilera J, Anguita M, Brozzi R and Galobart J, 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

## Abbreviations

| | |
|---|---|
| CFU | colony forming unit |
| dDDH | DNA–DNA hybridisation |
| DSMZ | Deutsche Sammlung von Mikroorganismen und Zellkulturen |
| EURL | European Union Reference Laboratory |
| FEEDAP | EFSA Panel on Additives and Products or Substances used in Animal Feed |
| QPS | qualified presumption of safety |
| WGS | whole genome sequence |