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Assessment of the feed additive consisting of *Lacticaseibacillus paracasei* (formerly *Lactobacillus paracasei*) DSM 16245 for all animal species for the renewal of its authorisation (Lactosan GmbH & Co KG)

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Maria Saarela, Jaime Galobart, Lucilla Gregoretti, Joana Revez, Maria Vittoria Vettori and Rosella Brozzi

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 *Lacticaseibacillus paracasei* (formerly *Lactobacillus paracasei*) DSM 16245 as a technological additive for all animal species. The additive aims to improve the production of silage and is currently authorised at a proposed application rate of 1×10^8 colony forming units (CFU)/kg fresh material. The applicant has provided evidence that the additive currently on the market complies with the existing conditions of authorisation. There was no new evidence to lead the FEEDAP Panel to reconsider its previous conclusions. Thus, the Panel concluded that the additive remains safe for all animal species, consumers and the environment under the authorised conditions of use. Regarding user safety *L. paracasei* DSM 16245 is not irritant to skin and eyes but is considered a skin and respiratory sensitiser.

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Correspondence: feedap@efsa.europa.eu

Panel members: Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Fašmon Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa and Ruud Woutersen.

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003¹ 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.KG² for the renewal of the authorisation of the additive consisting of *Lacticaseibacillus paracasei* (formerly *Lactobacillus paracasei*) DSM 16245 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). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as of 14 January 2021.

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 *Lacticaseibacillus paracasei* DSM 16245, when used under the proposed conditions of use (see Section 3.1.3).

1.2. Additional information

The additive consists of viable cells of *Lacticaseibacillus paracasei* (formerly *Lactobacillus paracasei*) DSM 16245. It is currently authorised as a feed additive in the European Union (1k2076).³

EFSA has adopted one opinion on the safety and efficacy of this product 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 dossier⁴ in support of the authorisation request for the use of *L. paracasei* DSM 16245 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. paracasei* DSM 16245 is in line with the principles laid down in Regulation (EC) No 429/2008⁶ 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 the 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-2020-0081.

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 product consisting of viable cells of *L. paracasei* DSM 16245 is currently authorised for use as a technological additive (functional group: silage additives) in forages for all animal species. This assessment regards the renewal of the authorisation of *L. paracasei* DSM 16245 for all animal species.

3.1. Characterisation

3.1.1. Characterisation of the additive

The product currently authorised consists of ~ 35–50% bacterial cells and 50–65% of carriers ([REDACTED]) and cryoprotectants ([REDACTED] ascorbic acid, [REDACTED]). The minimum concentration of the active agent (*L. paracasei* DSM 16245) is 5.0×10^{11} colony forming units (CFU) per gram of additive.

The information submitted regarding the manufacturing process lists a series of modifications applied to the fermentation process and the 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 instead of [REDACTED].

Analysis of three batches showed a mean value of 5.7×10^{11} CFU/g additive (range $5.3\text{--}5.9 \times 10^{11}$ CFU/g additive).⁷

Specifications are set for Enterobacteriaceae (< 1,000 CFU/g), yeasts and filamentous fungi (< 1,000 CFU/g) and *Salmonella* spp. (no detection in 25 g). Analysis of three recent batches of the additive showed compliance with these limits.⁸ Three other recent batches⁹ were also analysed for aflatoxins (B1, B2, G1 and G2), deoxynivalenol, zearalenone¹⁰ and three others for lead, mercury, cadmium and arsenic concentration. Results showed levels below the respective limits of quantification.¹¹

No new data have been provided regarding the physico-chemical properties 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 was deposited in the Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ) with the accession number DSM 16245.¹² It has not been genetically modified.

The taxonomic identification of the strain as *L. paracasei* was confirmed by [REDACTED]¹³

The susceptibility of the strain to the antimicrobials recommended by the FEEDAP Panel (EFSA FEEDAP Panel, 2018) was tested by broth microdilution following the methodology of the Clinical and Laboratory Standards Institute (CLSI).¹⁴ [REDACTED]

The WGS of the strain, [REDACTED] was interrogated for the presence of acquired antimicrobial resistance genes [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 Limits of quantification: aflatoxins B1, B2, G1 and G2: 0.03 µg/kg, deoxynivalenol: 10 µg/kg, zearalenone: 5 µg/kg, Pb: 0.1 mg/kg, Hg: 0.1 mg/kg, Cd: 0.03 mg/kg and As: 0.1 mg/kg.

¹² Technical dossier/Supplementary information May 2021/Annex 16245.

¹³ Technical dossier/Section II/Annexes II_2_4_WGS and II_4a.gbk.

¹⁴ Technical dossier/Section II/Annex II_2_5_Antibio.

as thresholds.¹⁵ No hits were identified.

3.1.3. Conditions of use

The additive is currently authorised for use in forages for all animal species. Under other provisions of the authorisation, the following is specified:

- '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: 1×10^8 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 Panel concluded that following the qualified presumption of safety (QPS) approach, the use of *L. paracasei* DSM 16245 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. paracasei* DSM 16245 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.

In the previous assessment (EFSA FEEDAP Panel, 2011), the Panel concluded regarding user safety: '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. paracasei* DSM 16245. 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'.

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 November 2020 without time restrictions. The search term used was '*Lactobacillus paracasei* DSM 16245', no further restrictions were made. The applicant searched in a total of seven relevant databases Agricola, Agris, Google scholar, Ingenta, PubMed, Science Direct and World Cat Library. Fifteen hits were retrieved after removing duplicates. However, none was considered relevant because they referred either to the previous EFSA opinion (1), to the authorisation of the additive (1) or to efficacy (13).¹⁷

Therefore, the FEEDAP Panel concludes that there is no new evidence that would lead it to reconsider the previous conclusions that *L. paracasei* DSM 16245 is safe for the target species, consumers and the environment under the authorised conditions of use.

Regarding user safety *L. paracasei* DSM 16245 is not irritant to skin and eyes but is considered a skin and respiratory sensitiser.

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.

¹⁵ Technical dossier/Section II/Annex_II_2_6_AMR.

¹⁶ Technical dossier/Section III.

¹⁷ Technical dossier/Section III/Annex_III_3_Literature.

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 *Lacticaseibacillus paracasei* DSM 16245 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 provided to EFSA/Chronology

Date	Event
15/10/2020	Dossier received by EFSA. <i>Lactobacillus paracasei</i> DSM 16245. Submitted by Lactosan GmbH & Co.KG
16/10/2020	Reception mandate from the European Commission
14/01/2021	Application validated by EFSA – Start of the scientific assessment
21/05/2021	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: characterisation</i>
27/05/2021	Reception of supplementary information from the applicant - Scientific assessment re-started
15/04/2021	Comments received from Member States
29/09/2021	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 paracasei* (DSM 16245) as a silage additive for all species. EFSA Journal 2011;9(9):2363, 11 pp. <https://doi.org/10.2903/j.efsa.2011.2363>
- 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
CLSI	Clinical and laboratory standards institute
dDDH	digital DNA–DNA hybridization
DSMZ	German Collection of Microorganisms and Cell Cultures
EURL	European Union Reference Laboratory
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
QPS	Qualified presumption of safety
MIC	minimum inhibitory concentration
TYGS	DSMZ Type strain Genome Server
WGS	whole genome sequence