Assessment of the safety and efficacy of Lactococcus lactis DSM 11037 as a feed additive for all animal species

Reference number RP686

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Regulated Product Dossier Assessment
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Abbreviations

Acronym	Definition
ACAF	Advisory Committee on Animal Feedingstuffs
ADI	Acceptable daily intake
ADME	Absorption, distribution, metabolism and excretion
CFU	Colony forming units
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
EURL	European Union Reference Laboratory
FSA	Food Standards Agency
FSS	Food Standards Scotland
ISO	International Organisation for Standardisation
LOD	Limit of detection
MRS	Man, Rogosa and Sharpe agar
NP-HPLC	Normal Phase High-Performance Liquid Chromatography
PFGE	Pulsed Field Gel Electrophoresis
ppm	Parts-per million
QPS	Qualified presumption of safety

Summary

An application was submitted to the Food Standards Agency in March 2021 from Chr. Hansen A/S ("the applicant") for the renewal of authorisation of an additive (*Lactococcus lactis* DSM 11037), under the category of 'technological – silage additives'. The additive is proposed to be included in silage at a rate of 10^8 CFU/kg of fresh plant material. The additive aims to improve silage quality in easy, moderately difficult and difficult to ensilage crops.

To support the Food Standards Agency (FSA) and Food Standards Scotland (FSS) in evaluating the dossier, the Advisory Committee on Animal Feedingstuffs (ACAF) were asked to review the dossier and the supplementary information from the applicant.

The additive was fully characterised in the application and no causes for concern were identified by the ACAF in the identity and characterisation.

The ACAF concluded that the additive can be considered safe for the target species, consumers and the environment, based on the QPS status of *Lactococcus lactis* DSM 11037 and the evidence presented through a literature review. The additive should be considered an eye and skin irritant, and a skin and respiratory sensitiser. As the additive is dusty and contains a large proportion of small particles, measures should be taken to reduce the inhalation exposure of workers.

No efficacy evaluation was required for the renewal of authorisation.

The views of ACAF have been taken into account in the safety assessment which represents the opinion of the FSA and FSS.

1. Introduction

The FSA and FSS have undertaken a risk assessment for a feed additive (*Lactococcus lactis* DSM 11037, Chr. Hansen A/S, 10-12 Boege Allé, P.O. Box 407, DK-2970 Hoersholm, Denmark) requesting a renewal of authorisation under retained regulation No 1831/2003[1] under the category of 'technological' additives, functional group 'silage additives'.

The dossier was evaluated on behalf of the FSA and FSS by the ACAF. In line with Article 8 of 1831/2003, the assessment has considered whether the feed additive complies with the conditions laid down in Article 5, including: safety considerations for human, animal and environmental health; efficacy of the additive for its intended effect; potential impairment of the distinctive features of animal products. This, and the guidance put in place by EFSA for the evaluation of feed additive applications, has formed the basis and structure for the assessment.

With thanks to the members of the ACAF during the course of the assessment, who were: Professor Nicholas Jonsson, Martin Briggs, Professor Katrina Campbell, Susan MacDonald, Professor Matthew Fisher, Christine McAlinden, Dr. Donald Morrison, Derek Renshaw, Dr. Michael Salter, Dr. Adam Smith, Dr. Helen Warren and Dr. Nick Wheelhouse.

The dossier was evaluated by the ACAF at their October 2022 and December 2022. Further information was provided by the applicant in October 2022, responding to queries by the FSA.

This document outlines the discussion and conclusions of the ACAF's assessment on the safety and efficacy of *L. lactis* DSM 11037 as a feed additive.

2. Assessment

2.1. Section II: Identity, characterisation and conditions of use

The additive is a dry powder formulation containing a minimum 5 x 10^{10} *Lactococcus lactis* per gram of additive, silica as an anti-caking agent and maltodextrin as a carrier.

The applicant provided data from several batches supporting the specification values outlined below (Table 1):

Table 1: Identity table *Lactococcus lactis DSM 11037*

Composition	**CFU/g**	**w/w%**
Lactococcus lactis DSM 11037 (active substance)	Minimum 5 x 10^{10}	~30%
Silica	-	8%
Maltodextrin	-	~70%
Physico-chemical specifications		
Dusting potential	1180 mg/m^3	
Particle size distribution	55.9% of 200 µm or less; 40.8% of 100 µm or less; 27.3% of 50 µm or less; 6.6% of 10 µm 1.7% of 4 µm or less	
Purity specifications		
Coliform bacteria	<10^3/g	
Yeasts and moulds	<10^3/g	
Salmonella spp.	Negative in 25 g	
E. coli	<10/g	
Aflatoxin B1	<0.005 mg/kg	

The Committee evaluated the physico-chemical and technological properties of the additive, concluding that the products used for purity and composition testing were representative of the characteristics that the product under assessment would show. The applicant provided further data upon the Committee's request demonstrating absence of *Salmonella* on 5g of dried product, equivalent to 25g of fresh product.

The Committee noted that the dusting potential tests show the active substance is a dusty product, with a large proportion of particles (average of 27.3%) being of a diameter of 50 µm or smaller, therefore, showing potential to penetrate deep into the lungs if inhaled. The Committee also concluded that the final formulation of the additive, including a carrier and anti-caking agent, is expected to reduce its dusting potential. No scientific evidence of this potential reduction was provided by the applicant.

The applicant proposes the inclusion of the additive at a rate of 10^8 CFU/kg of fresh plant material (Table 2):

Table 2: Proposed mode of use of *Lactococcus lactis* DSM 11037

Proposed mode of use in animal nutrition			
Additive		*Lactococcus lactis*, DSM 11037	
Registration number		1k2081	
Category(-ies) of additive		Technological feed additive	
Functional group(s) of additive		Silage additive	
Description			
Composition, description		**Formula**	**Method of analysis**
Preparation of *Lactococcus lactis* DSM 11037		Containing a minimum of: $5x10^{10}$ CFU/g	ISO 15214
Conditions of use			
Species or category of animal	**Maximum Age**	**Min. content** CFU/kg fresh plant material	**Withdrawal period**
All animal species	-	10^8	--

2.1.1. Conclusions on Section II

The ACAF concluded that the additive was correctly identified and characterised.

No further concerns were raised for Section II of the dossier.

2.2. Section III: Safety

The applicant presented a literature review, in which they identified three articles of potential safety concern. The Committee evaluated the information presented, and noted that one of the scientific papers identified strains of *L. lactis* having encoding genes for the production of the biogenic amine putrescine. Upon evaluation of the whole genome sequence analysis of the additive's strain, the ACAF concluded that it does not have the capacity to produce biogenic amines. The Committee concluded that no causes for concern had been identified in the review. The additive's active substance is a qualified presumption of safety (QPS) microorganism seeking renewal of authorisation, therefore, no further toxicological tests were required to evaluate the safety for the target species, consumers or the environment.

2.2.1. Safety for the user/worker

The additive is proteinaceous in nature and is, therefore, regarded as a respiratory sensitiser by default. The applicant did not provide testing evidence for effects on skin

and eyes, to which the Committee concluded that the additive would be considered a potential irritant to skin and eyes, as well as a skin sensitiser. As the additive is dusty and contains a large proportion of small particles that could deposit in the lungs of exposed workers, measures should be taken to minimise their exposure by inhalation.

2.2.2. Conclusions on safety

The ACAF concluded that the additive can be considered safe for the target species, consumers and the environment.

The additive should be considered an eye and skin irritant, a skin sensitiser and a respiratory sensitiser. Workers handling the additive may be exposed to an inhalable dust.

2.3. Section IV: Efficacy

The additive is a renewal of authorisation, therefore, no efficacy evaluation was required.

3. Analytical methods evaluation

Conclusions on the analytical methods are presented here as an extract from the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of the Analysis for *Lactococcus lactis* DSM 11037[2]:

"For the enumeration of *L. lactis* DSM 11037, in feed additive, the Applicant proposes a pour plate method based on ISO 15214, using the Man, Rogosa and Sharpe agar (MRS) at pH 5.7. A limit of detection (LOD) of 10^5 CFU/kg is reported in the ISO 7218 standard.

The applicant did not provide any experimental method or data for the determination of L. *lactis* DSM 11037 IN SILAGE. Furthermore, the unambiguous determination of the content of *L. lactis* DSM 11037 added to silage is not achievable by analysis. Therefore, the EURL cannot evaluate nor recommend any method for official control to determine *L. lactis DSM* 11037 in silage.

Molecular methods were used by the applicant for identification of the active agent in the feed additive. The EURL recommends for official control Pulsed Field Gel

Electrophoresis (PFGE), a generally recognised standards methodology for microbial identification."

FSA/FSS accepts the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

4. Conclusions

The additive was fully characterised in the application and no causes for concern were identified by the ACAF in the identity and characterisation.

The ACAF concluded that the additive can be considered safe for the target species, consumers and the environment, based on the QPS status of *Lactococcus lactis* DSM 11037 and the evidence presented through a literature review. The additive should be considered an eye and skin irritant, and a skin and respiratory sensitiser. Workers handling the additive may be exposed to an inhalable dust.

No efficacy evaluation was required for the renewal of authorisation.

FSA/FSS accept the EURL analytical method evaluation reports. FSA/FSS determined the analytical method as appropriate for official controls for this feed additive.

5. References

1. EC (European Commission), 2003. Regulation No 1831/2003 of the European Parliament and of the Council on additives for use in animal nutrition.

2. EURL-FA (European Reference Laboratory for Feed Additives), 2011. Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003. Lactococcus lactis DSM 11037. Available at: Final report FAD-2010-0032 (europa.eu)

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