Assessment of the safety and efficacy of an additive of Saccharomyces cerevisiae CNCM I-1079 as a feed additive for calves, all other ruminant species (for rearing and fattening), and camelids (for rearing and fattening)

Reference number RP694

Regulated Products Risk Assessment Unit
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Regulated Product Dossier Assessment
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Abbreviations

Acronym	Definition
ACAF	Advisory Committee on Animal Feedingstuffs
ADG	Average Daily Gain
AFFAJEG	Animal Feed and Feed Additives Joint Expert Group
CFU	Colony forming units
CGYE	Yeast Dextrose Chloramphenicol Agar
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
EURL	European Union Reference Laboratory
FCR	Feed conversion ratio
FSA	Food Standards Agency
FSS	Food Standards Scotland
GRAS	Generally Recognised as Safe
HACCP	Hazard Analysis and Critical Control Points
OECD	Organisation for Economic Cooperation and Development
QPS	Qualified Presumption of Safety

Summary

An application was submitted to the Food Standards Agency in March 2021 from Lallemand Animal Nutrition UK ("the applicant") for the new authorisation of an additive (*Saccharomyces cerevisiae* CNCM I-1079), under the category of 'zootechnical' functional groups 'gut flora stabiliser' and 'physiological condition stabiliser' for its use in calves, and all other ruminants and camelids, for rearing and fattening, at their correspondent developmental stage.

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 ACAF concluded that the additive was correctly identified and characterised. No causes for concern were raised in this section of the application.

The ACAF concluded the additive can be considered safe for the target species, the consumer, and the environment owing to the QPS status of the microorganism *Saccharomyces cerevisiae* CNCM I-1079. The additive should be considered a respiratory sensitiser. In its non-encapsulated form, it may form dust. The additive is not an eye irritant, skin irritant or skin sensitiser.

Based on data from three trials in calves, the ACAF concluded that *Saccharomyces cerevisiae* CNCM I-1079 can be considered efficacious in calves, all other ruminant species at the correspondent developmental stage (for rearing and for fattening), and camelids at the correspondent developmental stage (for rearing and for fattening) at a minimum inclusion rate of $1x10^9$ CFU/kg of complete feed.

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 (*Saccharomyces cerevisiae* CNCM I-1079, Lallemand Animal Nutrition UK, 11-13 Spring Lane North, Malvern WR14 1BU) under retained regulation (EC) No 1831/2003[1] under the category of 'zootechnical' additive, functional groups 'gut flora stabiliser' and 'physiological condition stabiliser'. To support the safety assessment by FSA and FSS, the ACAF provided advice to the FSA and FSS outlined in this document.

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 February 2023 meetings. Further information was provided by the applicant in March 2022 and November 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 *Saccharomyces cerevisiae* CNCM I-1079 as a feed additive.

2. Assessment

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

The additive is a preparation of dried viable cells of *Saccharomyces cerevisiae* CNCM I-1079 available in two forms:

- A non-encapsulated/coated preparation with a minimum $2.0x10^{10}$ CFU of *Saccharomyces cerevisiae* CNCM I-1079 per g of additive.
- A microencapsulated/coated preparation with a minimum of $1.0x10^{10}$ CFU of *Saccharomyces cerevisiae* CNCM I-1079 per g of additive.

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

Table 1: Identity table *Saccharomyces cerevisiae* CNCM I-1079

Composition	
Saccharomyces cerevisiae CNCM I-1079	Minimum: $2.0x10^{10}$ CFU/g (non-coated) Minimum: $1.0x10^{10}$ CFU/g (coated)
Feed materials (coating agents for preparations with micro-encapsulated active substance/agent)	Vegetable oil derivatives (40-50%)
Physico-chemical specifications	
Dusting potential Particle size distribution	0.43 g/m^3 (non-coated) No dust (coated) 0.3% of diameter <45µm; 0.8% of diameter >45µm but <90µm (non-coated)
Purity specifications	
Enterobacteriaceae or coliforms	<1000 CFU/g
Salmonella spp.	Negative in 25g
E. coli	<10 CFU/g

The Committee evaluated the identity and characterisation of the additive, noting that the genomic characterisation of *Saccharomyces cerevisiae* CNCM I-1079 was comprehensive and assured equivalence to the organism listed in the Qualified Presumption of safety (QPS) and FDA GRAS (generally recognised as safe) lists. Both the stability and homogeneity of the additive were deemed acceptable.

The additive aims to supply a minimum of $1x10^9$ CFU/kg of completed feed for growing calves, all other ruminant species (for rearing and for fattening), and camelids (for rearing and fattening). Conditions of use of the additive are summarised in Table 2.

Table 2: Proposed mode of use of *Saccharomyces cerevisiae* CNCM I-1079

Proposed mode of use in animal nutrition				
Additive	*Saccharomyces cerevisiae* CNCM I-1079			
Category(-ies) of additive	Zootechnical feed additive			
Functional group(s) of additive	Gut flora stabilisers Physiological condition enhancers			
Description				
Composition description	**Purity criteria**	**Method of analysis**		
Preparation of *Saccharomyces cerevisiae* CNCM I-1079	Containing a minimum of: $2.0x10^{10}$ CFU/g (non-coated) and $1.0x10^{10}$ CFU/g (coated)	Ring-trial CEN validated methods (1789:2009, 15790:2008,15789:2009)		
Trade name (if appropriate)		-		
Name of holder authorisation (if appropriate)		Danstar Ferment AG (Switzerland) represented by Lallemand SAS (France)		
Conditions of use				
Species or category of animal	**Min-max Age**	**Min. content**	**Max. content**	**Withdrawal period**
		CFU of *Saccharomyces cerevisiae* per kg of complete feed		
Calves, all other ruminant species (for fattening and for rearing), camelids (for rearing and for fattening)	-	$1x10^9$	-	-

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

As the organism *Saccharomyces cerevisiae* CNCM I-1079 has QPS status, no studies are required to demonstrate the safety of the additive for the target species, the consumer, or the environment.

2.2.1. Safety for the user

Three studies were presented to demonstrate the effects on eyes and skin:

- Acute dermal irritation/corrosion study following OECD 404.
- Acute eye irritation/corrosion study following OECD 405.
- Skin sensitisation study: Local Lymph-Node Assay following OECD 429.

Based on the data presented, the ACAF concluded that the additive is not an irritant to skin or eyes, and that it should not be considered a skin sensitiser. The dusting potentials of both forms of the additive were below the threshold of concern that is usually used (1.0 g/m^3). Nevertheless, it was noted that the non-capsulated form of the additive could form some dust when handled. The Committee concluded the additive should be considered a potential respiratory sensitiser.

2.2.2. Conclusions on safety

The ACAF concluded that the additive can be considered safe for the target animal species, the consumer, and the environment, due to the QPS status of the microorganism *Saccharomyces cerevisiae* CNCM I-1790.

The additive should be considered a respiratory sensitiser. The additive is not an eye irritant, skin irritant or skin sensitiser.

2.3. Section IV: Efficacy

The Committee evaluated Section IV of the dossier, containing three efficacy trials in calves, using the non-encapsulated preparation of the additive.

2.3.1. Efficacy studies in calves

- Study 1 was carried out on 31 calves for 60 days, with an inclusion rate of $1.4x10^9$ CFU/kg.
- Study 2 was carried out on 39 calves for 57 days, with an inclusion rate of $0.9x10^9$ CFU/kg.
- Study 3 was carried out on 41 calves for 90 days, with an inclusion rate of $1.2x10^9$ CFU/kg.

The Committee evaluated the reports presented and noted an improvement in feed conversion ratio (FCR) in all three studies. The results of the studies are summarised in Table 3. The ACAF determined that the additive has the potential to be efficacious in calves, all other ruminant species at the corresponding developmental stage (for rearing and for fattening), and camelids at the corresponding developmental stage (for rearing and fattening) when included at a minimum concentration of $1x10^9$ CFU/kg in complete feed.

Table 3: Effect of *Saccharomyces cerevisiae* CNCM I-1079 on calves

Study	Additive[1] (actual dose)	N	Study duration	Weight (kg)		Feed intake (g DM/day)		ADG (g/day)	FCR
				Initial	Final	Total[2]	Solid feed		
1	Control	15	60 days	44.4	82.1[a]	1.37	0.408	0.623[a]	2.21
	$1.4x10^9$	16		44.9	85.1[b]	1.38	0.411	0.674[b]	2.06
2	Control	20	57 days	41.1	61.3[a]	1.19	0.417	0.357[a]	3.49
	$0.9x10^9$	19		41.1	65.0[b]	1.22	0.452	0.409[b]	3.21
3	Control	21	90 days	40.2	95.7[a]	1.38	0.532	0.617[a]	2.18[a]
	$1.2x10^9$	20		40.1	102.2[b]	1.46	0.599	0.689[b]	2.01[b]

[a,b]: in given study: means within a column with different superscript letters are significantly different at P<0.10.
[1]in CFU per kg complete feed (at 12% moisture). [2]Total feed intake = solid feed + milk replacer.
AGD: Average daily gain; FCR: Feed conversion ratio.

2.3.2. Conclusions on efficacy

Based on the information presented in three efficacy trials, the ACAF concluded that the additive *Saccharomyces cerevisiae* CNCM I-1079 can be considered to be efficacious in calves, all other ruminant species at the correspondent developmental stage (for rearing and for fattening), and camelids at the correspondent developmental stage (for rearing and fattening).

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 Methods(s) of the Analysis of *Saccharomyces cerevisiae* CNCM I-1079[2]:

“For the identification of *Saccharomyces cerevisiae* CNCM I-1079 the Applicant submitted the polymerase chain reaction (PCR) amplification method. This method was ring trial validated to become the CEN technical standard (CEN/TS 15790:2008).

For the enumeration of *Saccharomyces cerevisiae* CNCM I-1079 in feed additive, premixtures and feedingstuffs the Applicant submitted the ring-trial validated CEN pour plate method for the enumeration of yeast probiotic strains (EN 15789:2009), using yeast dextrose chloramphenicol agar (CGYE). The performance characteristics of the EN 15789 method reported after logarithmic transformation (CFU) are:

- a repeatability standard deviation (sr) ranging from 0.17 to 0.36 log10 CFU/g.

- a reproducibility standard deviation (sR) ranging from 0.55 to 0.60 log10 CFU/g.

- a limit of quantification (LOQ) of $1x10^5$ CFU/kg, well below the minimum dose proposed by the applicant.

Based on these performance characteristics the EURL recommends for official control, the CEN method EN 15789 for the enumeration of *Saccharomyces cerevisiae* CNCM I-1079 in feed additive, premixtures and feedingstuffs.”

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 ACAF concluded that the additive was correctly identified and characterised.

As a QPS organism, studies for safety for the target species, the consumer and the environment were not required for assessment.

The additive is not an irritant to the skin and eyes and should not be considered a skin sensitiser. The additive should be considered a potential respiratory sensitiser.

The ACAF concluded that the additive *Saccharomyces cerevisiae* CNCM I-1079 can be considered to be efficacious in calves, all other ruminant species at the correspondent developmental stage (for rearing and for fattening), and camelids at the correspondent developmental stage (for rearing and fattening).

FSA/FSS accepts 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), 2015. 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. Saccharomyces cerevisiae CNCM I-1079. Available at: finrep-fad-2010-0121-levucell.pdf (europa.eu)

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