

ADOPTED: 21 February 2018

doi: 10.2903/j.efsa.2018.5201

## Efficacy of Cylactin<sup>®</sup> (*Enterococcus faecium* NCIMB 10415) as a feed additive for pigs for fattening

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP),  
Guido Rychen, Gabriele Aquilina, Giovanna Azimonti, Vasileios Bampidis,  
Maria De Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli,  
Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Marta López-Alonso,  
Secundino López Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos,  
Roberto Edoardo Villa, Robert John Wallace, Pieter Wester, Rosella Brozzi and Maria Saarela

### Abstract

Cylactin<sup>®</sup> is the trade name for a feed additive based on dehydrated cells of *Enterococcus faecium*. It is marketed in three forms: Cylactin<sup>®</sup> LBC ME10 and Cylactin<sup>®</sup> LBC ME20 Plus – which contain the microencapsulated bacterium in concentrations of  $1 \times 10^{10}$  CFU/g and  $2 \times 10^{10}$  CFU/g, respectively – and Cylactin<sup>®</sup> LBC G35, a granulated form with a guaranteed content of  $3.5 \times 10^{10}$  CFU/g. In 2012, EFSA was requested by the European Commission to re-evaluate the product when used as a zootechnical additive in feed for weaned piglets, sows and pigs for fattening. In the opinion delivered in 2015, the safety of the additive for consumers, users, the environment and target animals and its efficacy for piglets and sows were established. However, since only two efficacy studies with pigs for fattening could be considered and showed positive results, the Panel could not conclude on the efficacy for this target species due to insufficient data. The applicant has produced three additional feeding trials in pigs for fattening receiving the additive at the proposed inclusion level of  $3.5 \times 10^8$  CFU/kg feedingstuffs, which are the subject of this assessment. None of these studies showed a significant effect on the performance of pigs for fattening. The data on average daily gain and feed to gain ratio of the three new studies and of the two from the previous opinion were pooled. Based on the results of this pooled analysis of five studies, but not supported by four out of the five individual studies, the EFSA Panel on Additives and Products or Substances used in Animal Feed concludes that Cylactin<sup>®</sup> has some potential to improve performance of pigs for fattening at  $3.5 \times 10^8$  CFU/kg feed.

© 2018 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

**Keywords:** Zootechnical additive, gut flora stabilisers, Cylactin<sup>®</sup>, *Enterococcus faecium*, pigs for fattening, efficacy

**Requestor:** European Commission

**Question number:** EFSA-Q-2017-00525

**Correspondence:** feedap@efsa.europa.eu

**Panel members:** Gabriele Aquilina, Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Coconcelli, Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Guido Rychen, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace and Pieter Wester.

**Acknowledgements:** The EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed) wishes to thank the following for the support provided to this scientific output: Montserrat Anguita, Jaume Galobart and Gloria López.

**Suggested citation:** 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, Coconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Villa RE, Wallace RJ, Wester P, Brozzi R and Saarela M, 2018. Scientific Opinion on the efficacy of Cylactin® (*Enterococcus faecium* NCIMB 10415) as a feed additive for pigs for fattening. EFSA Journal 2018;16(3):5201, 6 pp. <https://doi.org/10.2903/j.efsa.2018.5201>

**ISSN:** 1831-4732

© 2018 European Food Safety Authority. *EFSA Journal* published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

This is an open access article under the terms of the [Creative Commons Attribution-NoDerivs](https://creativecommons.org/licenses/by/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.



The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.



## Table of contents

Abstract.....	1
1. Introduction.....	4
1.1. Background and Terms of Reference as provided by the requestor.....	4
1.2. Interpretation of the ToR .....	4
2. Data and methodologies.....	4
2.1. Data.....	4
2.2. Methodologies.....	4
3. Assessment.....	4
3.1. Efficacy for pigs for fattening .....	5
4. Conclusions.....	6
Documentation provided to EFSA .....	6
References.....	6
Abbreviations.....	6

## 1. Introduction

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

Regulation (EC) No 1831/2003 establishes rules governing the Community authorisation of additives for animal nutrition and, in particular, Article 9 defines the terms of the authorisation by the Commission.

The applicant, DSM Nutritional Products Ltd, is seeking a Community authorisation of *Enterococcus faecium* NCIMB 10415 to be used as a zootechnical additive for pigs for fattening, piglets (suckling and weaned piglets) and sows, in order to have benefit in piglets. (Table 1)

**Table 1:** Description of the substance

<b>Category of additive</b>	Zootechnical additive
<b>Functional group of additive</b>	Gut flora stabiliser
<b>Description</b>	<i>Enterococcus faecium</i> NCIMB 10415
<b>Target animal category</b>	pigs for fattening, piglets (suckling and weaned piglets) and sows, in order to have benefit in piglets
<b>Applicant</b>	DSM Nutritional Products Ltd
<b>Type of request</b>	New opinion

On 17 June 2015, the Panel on Additives and Products or Substances used in Animal Feed of the European Food Safety Authority ("Authority"), in its opinion on the safety and efficacy of the product, considered that insufficient data were provided to support the efficacy of Cylactin® when used in pigs for fattening.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and to allow a revision of Authority's opinion. The new data have been sent to the Commission and EFSA on 22 March 2017.

In view of the above, the Commission asks the Authority to deliver a new opinion of *Enterococcus faecium* NCIMB 10415 to be used as a zootechnical additive for pigs for fattening, piglets (suckling and weaned piglets) and sows, in order to have benefit in piglets.

### 1.2. Interpretation of the ToR

The safety of Cylactin® for pigs for fattening, piglets, sows, consumers, users, and the environment, and its efficacy for sows and weaned piglets were established in a previous opinion (EFSA FEEDAP Panel, 2015). Since no conclusion could be drawn on the efficacy for pigs for fattening, this opinion will focus only on the efficacy of Cylactin® to improve performance of this target species.

## 2. Data and methodologies

### 2.1. Data

The present assessment is based on data submitted by the applicant in the form of additional information<sup>1</sup> to a previous application on the same product.<sup>2</sup>

### 2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the efficacy of Cylactin® is in line with the principles laid down in Regulation (EC) No 429/2008 and the relevant guidance documents: Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012) and the Technical guidance: tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011).

## 3. Assessment

Cylactin® is a feed additive based on dehydrated cells of *Enterococcus faecium* NCIMB 10415. It is marketed in three forms: Cylactin® LBC ME10 and Cylactin® LBC ME20 Plus (coated forms) which contain the microencapsulated bacterium in concentrations of  $1 \times 10^{10}$  CFU/g and  $2 \times 10^{10}$  CFU/g, respectively, and Cylactin® LBC G35, a granulated non-coated form with a guaranteed content of  $3.5 \times 10^{10}$  CFU/g. The additive was fully characterised in the previous opinion (EFSA FEEDAP Panel, 2015).

<sup>1</sup> FEED dossier reference: FAD-2017-0020.

<sup>2</sup> FEED dossier reference: FAD-2010-0269.

Cylactin® is intended for use in feeds for pigs for fattening at the minimum concentration of  $3.5 \times 10^8$  CFU/kg complete feed and the maximum of  $1 \times 10^9$  CFU/kg complete feed.

The scope of this opinion is to assess the efficacy of Cylactin® when used as a zootechnical additive (gut flora stabiliser) in feed for pigs for fattening at the minimum concentration of  $3.5 \times 10^8$  CFU/kg complete feed.

### 3.1. Efficacy for pigs for fattening

The dossier submitted in 2012 included six efficacy studies with pigs for fattening aiming to demonstrate the potential of Cylactin® to improve zootechnical performance of animals (EFSA FEEDAP Panel, 2015). However, four of them were rejected due to limitations in the design or reporting and only two could be considered. In these two studies, feed to gain ratio was significantly improved in Cylactin® treated-animals, in one case when the additive was used at the minimum recommended dose and the other at the maximum recommended dose (studies 4<sup>3</sup> and 5,<sup>4</sup> respectively).

The applicant has submitted three new studies conducted in two Member States, in two different locations aiming to investigate the effects of the additive on the growth of pigs for fattening. The design of the studies is presented in Table 2. The new studies are identified as 1<sup>5</sup>, 2<sup>6</sup> and 3,<sup>7</sup> while the two studies already presented in the previous opinion (EFSA FEEDAP Panel, 2015) are studies 4<sup>3</sup> and 5.<sup>4</sup> The results are presented in Table 3.

In the three new studies animals were individually housed and allocated, based on body weights and gender, to two experimental groups: a control group receiving the basal diets and a second group receiving the basal diets supplemented with Cylactin® LBC ME20 Plus in order to provide  $3.5 \times 10^8$  CFU/kg feed. Intended cell counts were confirmed by analysis of feed. The FEEDAP Panel considers that the three available formulations are equivalent when used to deliver the same dose. The diets were offered to the animals *ad libitum*. Health status was monitored throughout the experimental periods. Individual feed intake and body weight of the animals were measured and the average daily gain (ADG) and feed to gain ratio were calculated. Morbidity and mortality of animals were also monitored. In these three studies, data were analysed using an analysis of variance (ANOVA) and considering the animal as the experimental unit. Significance was established at  $p < 0.05$ .

No significant differences in any of the studied parameters were observed in the new studies submitted (Table 3).

**Table 2:** Details on the study design for the studies performed in pigs for fattening

Study	Total animals Replicates/ treatment	Breed (sex)	Duration of the study (days)	Basal diets (main ingredients) Form
1	200 100	Line 990 (♀, castrated ♂)	111	(triticale/wheat/rapeseed meal/soybean meal) Pelleted
2	184 92	Pietrain × Danbreed (♀, ♂)	117	(wheat/barley/rye/triticale/soybean meal) mash and pelleted
3	240 120	Pietrain × Topigs (♀, castrated ♂) <sup>(b)</sup>	101	(wheat/rye/triticale/barley/soybean meal) Pelleted
4	60 30	cross-bred (♀, ♂)	121–126 (until slaughter)	(Wheat/barley/cassava/rapeseed/soybean meal) Pelleted
5	216 <sup>(a)</sup> 14	Large White × Landrace (♀, ♂)	84–112 (until slaughter at 105–110 kg)	(commercial diet <sup>(c)</sup> ) pelleted

(a): 112 in the control group and 104 in the treated group, 7/8 animals per replicate.

(b): 119 females and 121 barrows.

(c): In this case the administration of the additive started with the sows.

<sup>3</sup> Technical dossier/Annex 5.

<sup>4</sup> Technical dossier/Annex 6.

<sup>5</sup> Technical dossier/Annex 2.

<sup>6</sup> Technical dossier/Annex 3.

<sup>7</sup> Technical dossier/Annex 4.

**Table 3:** Overview of results of efficacy studies with Cylactin® in pigs for fattening

Study	Cylactin® (CFU/kg feed)	Initial weight (kg)	Final weight (kg)	Average daily feed intake (kg)	Average daily gain (g/day)	Feed to gain ratio	Mortality and removal (n/total)
1	0	27.5	114.7	2.66	869	2.77	2/100
	$3.5 \times 10^8$	27.3	115.9	2.58	886	2.73	2/100
2	0	27.7	122.0	2.41	989	2.45	1/92
	$3.5 \times 10^8$	27.7	122.2	2.41	1,000	2.41	1/92
3	0	29.7	116.2	2.21	852	2.60	10/120*
	$3.5 \times 10^8$	29.6	116.4	2.22	859	2.59	3/120
4	0	24.6	111.6	2.19	861	2.55	2/30
	$3.5 \times 10^8$	24.7	112.2	2.21	867	2.55	1/30
5	0	21.3	107.3	2.28	858	2.69 <sup>a</sup>	0/112
	$3.5 \times 10^8$	22.8	108.8	2.27	882	2.60 <sup>b</sup>	1/104

CFU: colony forming unit.

\*: Six out of 10 animals were removed from the study due to tail biting.

a,b: Means in a column within a given trial with different superscript letters are significantly different  $p < 0.05$ .

The data on ADG and feed to gain ratio of the five studies were pooled.<sup>8</sup> The studies included in the analysis were homogeneous with regards to weight range and study duration, genders involved (1:1 sex ratio), inclusion level of the additive and control diets. The only identifiable source of heterogeneity is related to the different study design of study 5. In this case, piglets entered the study at birth and the administration of the additive started with the sows; however, the data included in the analysis considered only the fattening period. The estimated effects in each study were combined using an inverse-variance-weighting approach. The (random effects) analysis estimate of the true underlying effect of Cylactin® vs the control group on ADG was 11.6 g/day ( $p < 0.05$ ) and on feed to gain ratio it was  $-0.03$  ( $p < 0.05$ ).

## 4. Conclusions

Based on the results of the pooled analysis of five efficacy studies, but not supported by four out of the five individual studies, the FEEDAP Panel concludes that Cylactin® has some potential to improve performance of pigs for fattening at  $3.5 \times 10^8$  CFU/kg feed.

## Documentation provided to EFSA

- 1) Additional data on use of Cylactin® for pigs for fattening. Technical dossier- Efficacy according to Regulation (EC) No 1831/2003 for authorisation. March 2017. Submitted by DSM Nutritional Products Ltd.

## References

- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011. Technical guidance: tolerance and efficacy studies in target animals. EFSA Journal 2011;9(5):2175, 15 pp. <https://doi.org/10.2903/j.efsa.2011.2175>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012. Guidance for the preparation of dossiers for zootechnical additives. EFSA Journal 2012;10(1):2536, 19 pp. <https://doi.org/10.2903/j.efsa.2012.2536>
- EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2015. Scientific Opinion on the safety and efficacy of Cylactin® (*Enterococcus faecium* NCIMB 10415) as a feed additive for pigs for fattening, piglets and sows. EFSA Journal 2015;13(7):4158, 18 pp. <https://doi.org/10.2903/j.efsa.2015.4158>

## Abbreviations

ADG	average daily gain
ANOVA	analysis of variance
CFU	colony forming unit
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed

<sup>8</sup> Technical dossier/Annex 7.