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SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 27 January 2021

doi: 10.2903/j.efsa.2021.6456

Safety and efficacy of a feed additive consisting of endo-1,4-β-xylanase produced by *Bacillus subtilis* LMG S-15136 (Belfeed B MP/ML) for sows in order to have benefits in piglets and for all porcine species (Beldem, a division of Puratos NV)

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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 safety and efficacy of Belfeed B MP/ML as a feed additive for sows in order to have benefits in piglets. The additive is to be used in to sows in order to have benefits in piglets and to all porcine species at any developmental stage at 10 IU/kg feed. This additive consists of endo-1,4-β-xylanase produced by a genetically modified strain of *Bacillus subtilis* (LMG S-15136). In a previous opinion, the FEEDAP Panel could not conclude on the safety of the additive for the users regarding the potential of the additive as dermal sensitiser and on the efficacy of the additive when added to feed for sows in order to have benefits in piglets. In the absence of new information, the FEEDAP Panel retained its previous conclusion that the additive is not irritant to skin or eyes but should be considered a respiratory sensitiser. No conclusions could be drawn on its potential to be a dermal sensitiser. The applicant provided new efficacy data and complementary information regarding a previous study. Based on the previously assessed data and the newly submitted ones, the Panel concludes that although the additive has a potential to be efficacious as a zootechnical additive in sows during the lactation period at the level of 10 IU/kg feed, the data are considered not sufficient to conclude on a beneficial effect on the performance of the litters.

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Keywords: zootechnical additives, digestibility enhancers, xylanase, safety, efficacy, sows

Requestor: European Commission

Question number: EFSA-Q-2020-00444

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Declarations of interest: The declarations of interest of all scientific experts active in EFSA's work are available at https://ess.efsa.europa.eu/doi/doiweb/doisearch.

Acknowledgments: The Panel wishes to acknowledge the contribution of Rosella Brozzi, Davide Guerra and Angelica Amaduzzi to this opinion.

Suggested citation: EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis V, Azimonti G, Bastos ML, Christensen H, Dusemund B, Durjava MF, Kouba M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Dierick N, Martelli G, Galobart J, Anguita M and Revez J, 2021. Scientific Opinion on the safety and efficacy of a feed additive consisting of endo-1,4-β-xylanase produced by *Bacillus subtilis* LMG S-15136 (Belfeed B MP/ML) for sows in order to have benefits in piglets and for all porcine species (Beldem, a division of Puratos NV). EFSA Journal 2021;19(3):6456, 8 pp. https://doi.org/10.2903/j.efsa.2021.6456

ISSN: 1831-4732

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

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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 and, in particular, Article 9 defines the terms of the authorisation by the Commission.

The applicant, Beldem – a division of Puratos NV[2] is seeking a Community authorisation of endo-1,4-β-xylanase EC 3.2.1.8 produced by *Bacillus subtilis* (LMG S-15136) as a feed additive to be used as a digestibility enhancer for pigs and sows, in order to have benefit in piglets (Table 1).

Table 1: Description of the substances

Category of additive	Zootechnical additives
Functional group of additive	Digestibility enhancers
Description	endo-1,4-β-xylanase EC 3.2.1.8 produced by *Bacillus subtilis* (LMG S-15136)
Target animal category	Pigs and sows, in order to have benefit in piglets
Applicant	Beldem - a division of Puratos NV
Type of request	New opinion

On 29 November 2019, 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, could not conclude on the safety for the users and efficacy for sows of endo-1,4-β-xylanse EC 3.2.1.8 produced by *Bacilllus subtilis* (LMG S-15136). After the discussion with the Member States on the Standing Committee, it was suggested to check for the possibility to demonstrate the safety for users and on the efficacy in sows.

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 received on 29 April 2020 and were already transmitted to the EFSA by the applicant.

In view of the above, the Commission asks the Authority to deliver a new opinion on endo-1,4-β-xylanase EC 3.2.1.8 produced by *Bacillus subtilis* (LMG S-15136) as a feed additive for pigs and sows, in order to have benefit in piglets based on the additional data submitted by the applicant.

1.2. Additional information

The additive consists of endo-1,4-β-xylanase produced by a genetically modified strain of *Bacillus subtilis* (LMG-S 15136), available in solid (Belfeed B MP) and liquid (Belfeed B ML) formulations. The additive (4a1606i) is authorised in the European Union for poultry, weaned piglets and pigs for fattening.[3]

The FEEDAP Panel adopted two opinions on the safety and efficacy of the additive, the first one regarding the use in poultry, piglets and pigs for fattening (EFSA FEEDAP Panel, 2016) and the second one regarding the use in sows, in order to have benefits in piglets, and in all porcine species (EFSA FEEDAP Panel, 2019). In the latter, the FEEDAP Panel could not conclude on the safety for the users regarding the potential of the additive as dermal sensitiser and on the efficacy of the additive when added to feed for sows in order to have benefits in piglets.

[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] Beldem - a division of Puratos NV, rue Bourrie 12, 5300 Andenne, Belgium.
[3] Commission implementing Regulation (EU) 2017/211 of 7 February 2017 concerning the authorisation of a preparation of endo-1,4-beta-xylanase (EC 3.2.1.8) produced by *Bacillus subtilis* (LMG-S 15136) as a feed additive for poultry, weaned piglets and pigs for fattening, and amending Regulations (EC) No 1259/2004, (EC) No 1206/2005, and (EC) No 322/2009 and repealing Regulation (EC) No 516/2007 (holder of authorisation Beldem, a division of Puratos NV).

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of supplementary information[4] to a previous application of the additive Belfeed B MP/ML (endo-1,4-β-xylanase).[5]

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA.

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Belfeed B MP/ML (endo-1,4-β-xylanase) is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018).

3. Assessment

The product Belfeed B MP/ML is a feed additive consisting of endo-1,4-β-xylanase (Enzyme Commission number 3.2.1.8; xylanase), produced by a genetically modified strain of *Bacillus subtilis* (LMG S-15136). The additive is available in two formulations, solid (Belfeed B MP) and liquid (Belfeed B ML). The two formulations of the additive have a guaranteed minimum xylanase activity of 400 IU[7]/g. The additive was characterised in full in EFSA's previous assessments (EFSA FEEDAP Panel, 2016, 2019).

The additive is intended to be used in sows in order to have benefits in piglets, as a zootechnical additive (functional group: digestibility enhancers), at 10 IU/kg feed. In a previous opinion on the safety and efficacy of the product as a feed additive for sows in order to have benefits in piglets, and for all porcine species (EFSA FEEDAP Panel, 2019), the FEEDAP Panel could not conclude, owing to the lack of data, on the safety for the users regarding the potential of the additive as dermal sensitiser. Moreover, the Panel could not conclude on the efficacy of the additive for sows in order to have benefits in piglets. The applicant has provided new data to support the efficacy of the product in sows in order to have a benefit in piglets.

3.1. Safety for the user

The safety aspects regarding the use of this additive in feed have been previously assessed (EFSA FEEDAP Panel, 2016, 2019). However, owing to the lack of data, the Panel could not conclude on the potential as dermal sensitiser of the additive for the user.

In the current application, no additional data have been provided, thus the conclusion from the Panel remains that the additive is not irritant for skin or eyes, but is a respiratory sensitiser, and no conclusion can be drawn on its dermal sensitiser potential.

3.2. Efficacy

In the previous assessment, the FEEDAP Panel evaluated four trials in sows conducted during the lactation period, two presented as digestibility trials and two as long-term trials (EFSA FEEDAP Panel, 2019). The results of the digestibility trials showed that compared to the control group, the sows receiving the additive at the recommended level had a better utilisation of the energy of the diets in only one trial. Similarly, the results of one of the long-term trials showed a better performance of the piglets from sows that received the additive at the recommended level (10 UI/kg) compared to the control. In the other long-term trial, significant effects were seen in different parameters but due to limitations identified in the reporting of the study and on the results, the Panel considered that the effects seen could not only be ascribed to the addition of the additive. In that trial, the Panel noted the following limitations: (i) initial number of the piglets per sow after cross-fostering was different

[4] FEED dossier reference: FAD-2020-0039.
[5] FEED dossier reference: FAD-2018-0007.
[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.
[7] One International Unit (IU) is defined as the amount of enzyme which liberates one micromole of reducing sugars (xylose equivalents) from birchwood xylan per minute at pH 4.5 and 30°C.

between the groups (control: 13 vs Belfeed B: 12), (ii) duration of the lactation not reported and it probably differed between litters, (iii) final number of piglets not reported, and (iv) no indication on the use of creep feeding during the lactation. Regarding the results, the Panel considered that the higher average daily weight gain (ADG) in the piglets from sows that received Belfeed B, would be in contrast with the total body weight gain of the piglets during the lactation. This could only be explained by an error in the reporting or by a different period of lactation between treatments. Furthermore, a numerically greater number of piglets after cross-fostering could also influence the ADG. In a similar way, the results showed a significantly lower body weight loss and back-fat loss in sows receiving Belfeed B. However, these results could have been due to the lower total weight gain of the litter in the sows receiving Belfeed B, yet no data were provided at this regard.

The applicant has provided supplementary information regarding the long-term trial for which limitations were identified (referred to as Trial A below)[8] and a new long-term trial (herein referred as Trial B) has been reported.[9]

The new data on Trial A provided by the applicant indicated that the piglets did not receive creep-feeding during the study. Further data were provided including (i) the statistical analysis of the initial (after-cross fostering) and final number of piglets, (ii) duration of the lactation and (iii) litter body weight gain.

The data showed (Table 2) that the lactation duration was significantly shorter in the Belfeed B group (average of 20 days, range 14–26 days) compared to the control (average of 23 days, range 15–29 days). The Panel notes that the piglets were weaned with a different duration of the lactation which may preclude certain comparisons of the effects in this kind of study. Moreover, in the Belfeed B group, a total of seven litters were weaned earlier than day 21, which would not be in line with Directive 2008/120/EC[10].

Table 2: Effects of Belfeed B on the sow's body condition and feed intake and on the litter performance during the lactation

	Trial A[(a),(b)]		Trial B[(c)]	
	Control	**Belfeed B**	**Control**	**Belfeed B**
Sow parameters				
Lactation, days	**23**[a]	**20.2**[b]	25.0	24.8
Feed intake, kg/d	4.85	4.94	4.83	4.83
Body weight (BW) loss, kg	**32**[a]	**23**[b]	33.6	28.1
Back fat loss, %	**21.5**[a]	**7.8**[b]	–	–
Back fat loss, mm	–	–	3	1.1
Digestibility[(1)] dry matter, %	77.5	77.6	**81.4**[a]	**82.4**[b]
Digestibility[(1)] gross energy, %	78.9	79.5	**82.6**[a]	**83.5**[b]
Litter parameters				
Number of piglets after cross-fostering	13.1	12.3	11.3	11.7
Number of piglets weaned	11.9	11.0	10.0	9.5
BW after cross-fostering, kg	1.49	1.48	1.66	1.48
BW weaning, kg	6.20	6.11	7.21	7.04
Litter weight gain, kg/day	2.43	2.46	2.15	2.01
Average weight gain, g/day	**211**[a]	**235**[b]	222	224
Mortality (%)	8.4	9.3	11.5	18.4

1: Apparent faecal digestibility.
a,b: Values within a row and study with different superscript are significantly different ($p < 0.05$).
(a): Technical dossier FAD-2018-0007/Section IV/Supplementary information February 2019/Annex 3.
(b): Technical dossier FAD-2020-0039/Annex Ia and Ib and supplementary information November 2020/Annex I.01 and Annex I.02.
(c): Technical dossier FAD-2020-0039/Annex IIa and supplementary information November 2020/Annex IIb.

[8] Technical dossier FAD-2020-0039/Annex Ia and Ib and supplementary information November 2020/Annex I.01 and Annex I.02.
[9] Technical dossier FAD-2020-0039/Annex IIa and supplementary information November 2020/Annex IIb.
[10] Council Directive 2008/120/EC of 18 December 2008 laying down minimum standards for the protection of pigs (Codified version). OJ L 047, 18.2.2009, p. 5.

No statistically significant differences were observed in the initial number of piglets, nor in the final (although the final number showed a tendency $p = 0.06$ to a lower number in the Belfeed B group) or the daily litter weight gain. The latter results on the daily litter weight gain lead the Panel to consider that the significant difference observed for the ADG may be due to the variation in the number of piglets per litter. Consequently, the Panel considers that this effect should not be retained to support the efficacy of the additive.

The newly submitted trial (Trial B) was conducted with 24 sows (Large White x Landrace, from three batches) allocated to two treatments (12 replicates per treatment).[11] Sows were under study for 37 days, starting from around 12 days prior to farrowing. Basal diets based on wheat, barley and soybean meal were either not supplemented (control) or supplemented with Belfeed B to provide 10 IU/kg feed (analyses confirmed the enzymatic activity, 10.9 IU/kg). The feed contained titanium dioxide as an external marker and was offered in pelleted form for 37 days. Body weight and back fat thickness of the sows were evaluated at seven days prior farrowing and at weaning. Feed intake of the sows was registered daily and at individual level throughout the study. Farrowing performance including litter size, number of piglets born alive, number of stillborn and body weight of the piglets were registered. No creep feed was given to the piglets during the lactation period. Cross-fostering of piglets was done and was not significantly different between control and treatment groups. The performance of the litters was also measured, and the parameters included litter size and body weight of the piglets and mortality. On the last four days before weaning, faeces were collected from the sows to determine the total apparent faecal digestibility of dry matter as well as the energy. An analysis of variance (ANOVA) was done with the data obtained considering the treatment as a main effect and the batch of the sows as a fixed effect. Significance was established at $p < 0.05$.

Significant differences were observed on the apparent faecal digestibility parameters, with increased dry matter (81.4% vs 82.4%) and gross energy digestibility (82.6% vs 83.5%, with calculated digestibility energy content of the diets 3,252 kcal/kg vs 3,290 kcal/kg) in the control sows compared to sows that received the additive. No differences were observed in any other parameter measured.

3.2.1. Conclusions on the efficacy

The results of five efficacy trials showed that the sows that received the additive at the recommended inclusion level showed, compared to the control group, an improvement in the faecal apparent digestibility of the gross energy of the diets in two trials (first short-term trial in the previous opinion and trial B in the current opinion) and an improvement on the performance of the litters in another trial (first long-term trial in the previous opinion). Although the additive has a potential to be efficacious as a zootechnical additive in sows during the lactation period at the level of 10 IU/kg feed, the data are considered not sufficient to conclude on a beneficial effect on the performance of the litters.

3.3. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[12] and Good Manufacturing Practice.

4. Conclusions

In the absence of new information, the FEEDAP Panel retains its previous conclusion that the additive is not irritant to skin or eyes but should be considered a respiratory sensitiser. No conclusions can be drawn on its potential to be a dermal sensitiser.

The FEEDAP Panel concludes that, although the additive has a potential to be efficacious as a zootechnical additive in sows during the lactation period at the level of 10 IU/kg feed, the data are considered not sufficient to conclude on a beneficial effect on the performance of the litters.

[11] Technical dossier FAD-2020-0039/Annex IIa and Supplementary Information November 2020 – Annex IIb.

[12] Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

5. Documentation as provided to EFSA/Chronology

Date	Event
15/05/2020	Reception mandate from the European Commission
05/06/2020	Reception of additional data from Beldem - a division of Puratos NV
19/06/2020	Application validated by EFSA – Start of the scientific assessment
22/09/2020	Request of supplementary information to the applicant in line with Article 7(3) of Regulation (EC) No 1304/2003 – Scientific assessment suspended. *Issues: efficacy*
04/11/2020	Reception of supplementary information from the applicant - Scientific assessment re-started
27/01/2021	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ADG	average daily gain
ANOVA	analysis of variance
BW	body weight
DM	dry matter
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed
IU	International Unit