

ADOPTED: 17 April 2018

doi: 10.2903/j.efsa.2018.5271

Safety and efficacy of Amylofeed[®] (endo-1,3(4)- β -glucanase and endo-1,4- β -xylanase and α -amylase) as a feed additive for piglets and minor growing porcine species

EFSA Panel on Additives and Products or Substances used in Animal Feed
(EFSA FEEDAP Panel),

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Abstract

Amylofeed[®] is a feed additive that contains glucanase, xylanase and amylase activities, and it is intended to be used as a zootechnical additive for weaned piglets and minor porcine species. In previous assessments, the additive was characterised and the safety for the target species, consumers and environment was established. Considering the safety for the user, the EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that the additive should be considered as a potential skin and eye irritant and a potential skin and respiratory sensitiser. Furthermore, the Panel concluded that the additive has a potential to be efficacious in the target species. However, the efficacy at the recommended enzyme activities could not be established. In order to overcome this limitation, the applicant proposed to modify the specifications of the additive whilst keeping the recommended level of addition of 500 mg additive/kg feed. The Panel evaluated the new specifications and their impact on the relevant aspects of the safety and efficacy of the additive. The newly proposed specifications of the additive were supported by analytical data. The Panel considered that the modification proposed by the applicant on the specifications would not have an impact on the safety aspects related to the consumer, user and environment. Therefore, the conclusions previously drawn would still apply. Moreover, it was considered that the tolerance trial previously evaluated would still support the safety for the target species. The addition of the additive with the new specifications would result in higher enzyme activities than those that were found in the efficacy studies that supported the efficacy of the product. Therefore, the additive has the potential to be efficacious at the newly proposed level of enzyme activities.

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Keywords: zootechnical additive, digestibility enhancer, endo-1, 3(4)- β -glucanase, endo-1, 4- β -xylanase, α -amylase, safety, efficacy

Requestor: European Commission

Question number: EFSA-Q-2018-00001

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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: Jaume Galobart, Orsolya Holczknecht, Gloria López-Gálvez and Jordi Tarrés-Call.

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, Saarela M, Villa RE, Wallace RJ, Wester P, Brantom P, Dierick N and Anguita M, 2018. Scientific Opinion on the safety and efficacy of Amylofeed® (endo-1,3(4)- β -glucanase and endo-1,4- β -xylanase and α -amylase) as a feed additive for piglets and minor growing porcine species. *EFSA Journal* 2018;16(5):5271, 7 pp. <https://doi.org/10.2903/j.efsa.2018.5271>

ISSN: 1831-4732

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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, Andrés Pinaluba S.A., is seeking a Community authorisation of endo-1,3(4)-beta-glucanase EC 3.2.1.6, endo-1,4-beta-xylanase EC 3.2.1.8 & alpha-amylase EC 3.2.1.1 to be used as a zootechnical additive for piglets (weaned) and young minor porcine species (Table 1).

Table 1: Description of the substances

Category of additive	Zootechnical additives
Functional group of additive	Digestibility enhancers
Description	Endo-1,3(4)-beta-glucanase EC 3.2.1.6, endo-1,4-beta-xylanase EC 3.2.1.8 & alpha-amylase EC 3.2.1.1
Target animal category	Piglets (weaned) and young minor porcine species
Applicant	Andrés Pinaluba S.A.
Type of request	New opinion

On 16 May 2017, 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, was not in a position to conclude on the efficacy at the recommended dose in terms of enzyme activity.

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 the EFSA on 31 October 2017.

In view of the above, the Commission asks the Authority to deliver a new opinion for endo-1,3(4)-beta-glucanase EC 3.2.1.6, endo-1,4-beta-xylanase EC 3.2.1.8 & alpha-amylase EC 3.2.1.1 to be used as a zootechnical additives for piglets (weaned) and young minor porcine species based on the additional data submitted by the applicant.

1.2. Additional information

Amylofeed® is a product authorised as a zootechnical additive for weaned piglets that was subject to re-evaluation. EFSA performed the re-evaluation of the additive and released two opinions (EFSA FEEDAP Panel, 2013, 2017). In those opinions the additive was characterised and the safety for the target species, consumers and environment were established. However, the efficacy in terms of recommended enzyme activities could not be established because in three out of four studies glucanase and xylanase activities were higher than the ones resulting from the addition of 500 mg additive/kg feed considering the minimum specifications of enzyme activities.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of Supplementary information¹ following two previous applications on the same product.²

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and efficacy of Amylofeed® (endo-1,3(4)-β-glucanase, endo-1,4-β-xylanase and α-amylase) 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), Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011) and Technical Guidance: Extrapolation of data from major species to minor species regarding the assessment of additives for use in animal nutrition (EFSA, 2008).

¹ FAD-2017-0063.

² FAD-2010-0353 and FAD-2014-0019.

3. Assessment

Amylofeed® is a feed additive that contains, endo-1,3(4)- β -glucanase (glucanase; Enzyme commission number (EC) 3.2.1.6), endo-1,4- β -xylanase (xylanase; EC 3.2.1.8) and α -amylase (amylase; EC 3.2.1.1). The additive is to be used as a zootechnical additive (functional group: digestibility enhancers) for weaned piglets and minor porcine species.

In previous assessments (EFSA FEEDAP Panel, 2013, 2017), the additive was characterised and the safety for the target species, consumers and environment was established. Considering the safety for the user, the Panel concluded that the additive should be considered as a potential skin and eye irritant and a potential skin and respiratory sensitiser. In 2017, the Panel also concluded that the additive has a potential to be efficacious in weaned piglets and minor young porcine species at a nominal level of inclusion (500 mg additive/kg feed). However, the efficacy at the recommended enzyme activities could not be established.

For enzymes, the efficacious level of the additive in feed should be established according to the enzyme activity administered to the animals. The additive characterised in previous opinions (EFSA FEEDAP Panel, 2013, 2017) contained per gram of product a minimum activity of 275 Units (U)³ of endo-1,3(4)- β -glucanase (glucanase), 400 U⁴ of endo-1,4- β -xylanase (xylanase) and 3,100 U⁵ of α -amylase (amylase). In the conditions of use, the applicant proposed to add this additive in feed at the level of 500 mg/kg feed. Considering the minimum specifications of the additive, 500 mg additive/kg feed would deliver an enzyme activity (in U/kg feed) of 138 for glucanase, 200 for xylanase and 1,550 for amylase. In the four efficacy studies assessed, the additive was added at the level of 500 mg additive/kg feed. The analytical data of the feed used in those studies showed overages in glucanase and xylanase enzyme activities in three of the trials (trials 2–4, see Table 2). For glucanase, the overage ranged from 2.5 to 4.5 times the intended enzyme activity, for xylanase from 2.5 to 3.6. This was the result of overages in glucanase and xylanase activities in the batches of the additive used to prepare the feed offered to the animals.

Table 2: Intended and analysed enzyme activities (U/kg feed) in the feeds used in the four efficacy trials in weaned piglets

Trial	Glucanase		Xylanase		Amylase	
	Intended	Analysed	Intended	Analysed	Intended	Analysed
1 ^(a)	138	281	200	160	1,550	1,091
2 ^(b)	138	620	200	562	1,550	1,872
3 ^(c)	138	378	200	507	1,550	1,056
4 ^(d)	138	338	200	719	1,550	1,542
Average		404		487		1,390

(a): Technical dossier FAD-2014-0019/Annex IV.3.1.

(b): Technical dossier FAD-2014-0019/Supplementary information December 2015/Annex IV.3.7.

(c): Technical dossier FAD-2014-0019/Supplementary information November 2016/Annex IV.3.8.

(d): Technical dossier FAD-2014-0019/Supplementary information January 2017/Annex IV.3.9.

The applicant has proposed to modify the specifications of the additive in terms of minimum enzyme activity. The applicant wishes to increase the minimum glucanase and xylanase activities while keeping the same level of addition in feed of 500 mg additive/kg feed. This modification would permit to achieve higher glucanase and xylanase activities in feed; activities that would be more in line with the ones found in the feeds used in the efficacy trials.

The Panel evaluated this modification and the impact on the relevant aspects of the safety and efficacy of the additive.

³ 1 U is the amount of enzyme that liberates 1 micromole of reducing sugars (glucose equivalents) from oat β -glucan per minute at pH 4.0 and 30°C.

⁴ 1 U is the amount of enzyme that liberates 1 micromole of reducing sugars (glucose equivalents) from rye arabinoxylan per minute at pH 4.0 and 30°C.

⁵ 1 U is the amount of enzyme that liberates 1 micromole of reducing sugars (glucose equivalents) from wheat starch per minute at pH 5.0 and 30°C.

3.1. Characterisation

The new specifications of the additive in terms of minimum enzyme activities (U/g additive) are as follows: 900 U glucanase, 1,000 U xylanase and 3,000 U of amylase. The applicant provided data of five batches of the additive supporting the new specifications.⁶ Mean glucanase activity was 1,177 U/g (range 1,001–1,404 U/g, coefficient of variation (CV) 15%), mean xylanase activity was 1,306 U/g (range 1,161–1,450, CV 10%) and mean amylase activity was 5,438 U/g (range 4,314–6,513 U/g, CV of 17%). According to the applicant, this higher enzyme activities could be reached without modifying the manufacturing of the enzymes/additive.

The additive is intended to be used at the level of 500 mg additive/kg feed. Considering the new specifications the addition of 500 mg additive/kg feed would result in 450 U of glucanase, 500 U of xylanase and 1,500 U of amylase per kg feed.

3.2. Safety

In previous assessments, the FEEDAP Panel concluded that the additive is safe for the target species, for the consumers and environment. The Panel also concluded that the additive is a potential skin and eye irritant and a potential skin and respiratory sensitiser.

The Panel considers that the modification proposed by the applicant on the specifications of the additive would not have an impact on the safety aspects related to the consumer, user and environment. Therefore, the conclusions previously drawn would still apply to the additive compliant with the new specifications. However, the new specifications of the additive will result in a higher enzyme activity in the feed and therefore the safety for the target species requires consideration.

In 2013, the FEEDAP Panel evaluated a tolerance study in weaned piglets. The Panel concluded that the additive is safe for weaned piglets and the conclusions were extrapolated to minor porcine species (except breeding animals). In that study, three groups were considered: no additive, additive supplemented at the proposed dose and 100-fold the proposed dose. The comparison of the enzyme activities measured in the feeds offered to the piglets and those that would result from the use of the new additive showed that the feeds prepared as a 100-fold would represent 73-fold the new glucanase activity level (450 U/kg feed), 75-fold the new xylanase activity level (500 U/kg feed) and 115-fold the new amylase activity (1,500 U/kg feed). The parameters measured during the study included the zootechnical data, blood biochemistry and haematology. Consequently, the results obtained in that study can support the safety of the additive with the new specifications in weaned piglets and minor porcine species (except reproductive animals).

3.3. Efficacy

Based on the results obtained in a pooling analysis of four efficacy studies, the FEEDAP Panel concluded, in 2017, that the additive has a potential to be efficacious in weaned piglets (EFSA FEEDAP Panel, 2017). The conclusions were extrapolated to minor porcine species (excluding reproductive animals). The average enzyme activities (in U/kg feed) in those studies were 400 for glucanase, 490 for xylanase and 1,400 for amylase (see Table 2).

The level of 500 mg/kg feed of the additive compliant with the new specifications would result in the following enzyme activities in feed (U/kg feed): 450 U glucanase, 500 U xylanase and 1,500 U amylase per kg feed.

The efficacy of the additive had been demonstrated using feeds containing enzyme activities lower than the ones that would be delivered by 500 mg Amylofeed®/kg feed compliant with the new specifications. Therefore, the Panel concludes that the additive has a potential to be efficacious in weaned piglets and minor porcine species (excluding reproductive animals) at the level of 450 U glucanase, 500 U xylanase and 1,500 U amylase per kg feed.

4. Conclusions

Amylofeed® compliant with the new specifications proposed by the applicant, 900 U glucanase/g product, 1,000 U xylanase/g and 3,000 U amylase/g, is safe for the target species at the recommended dose, safe for the consumers of food products derived from animals receiving the

⁶ Technical dossier FAD-2017-0063/Annex II.1.3.1.

additive and for the environment. The additive is a potential skin and eye irritant and a potential skin and respiratory sensitiser.

Amylofeed® has a potential to be efficacious as a zootechnical additive in weaned piglets and minor porcine species (excluding reproductive animals) at a level of 450 U glucanase, 500 U xylanase and 1,500 U amylase per kg feed.

Documentation provided to EFSA

- 1) Amylofeed® porcine species. October 2017. Submitted by Pinaluba S.A.

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Abbreviations

CV	coefficient of variation
EC	Enzyme Commission
FEEDAP	EFSA Panel on Additives and Products or Substances used in Animal Feed