SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as a feed additive for pigs for fattening and minor porcine species[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The additive AveMix® XG 10 is an enzyme preparation of endo-1,4-beta-xylanase (xylanase) and endo-1,3(4)-beta-glucanase (glucanase), produced by two strains of *Trichoderma reesei*. This product is currently authorised for use in chickens for fattening, laying hens, minor poultry species and weaned piglets as a zootechnical additive, under the functional group of digestibility enhancers. The applicant is now seeking an extension of the authorisation to pigs for fattening and minor porcine species at a recommended dose of 4 000 XU (xylanase units) and 900 BGU (beta-glucanase units) per kg complete feed. The FEEDAP Panel considers that, since the additive has been demonstrated to be safe for piglets at the recommended dose, this conclusion can be extended to pigs for fattening and extrapolated to minor growing porcine species. Supplementation of diets for pigs for fattening with Avemix® XG 10 at the recommended dose (4 000 XU and 900 BGU/kg) resulted in a significantly higher body weight and daily weight gain in one trial and significantly improved feed to gain ratio in two trials. Therefore, the FEEDAP Panel concludes that AveMix® XG 10 has the potential to be efficacious in pigs for fattening at this dose. Since the mode of action of xylanases and glucanases can reasonably be assumed to be the same in all porcine species, the conclusions on efficacy for weaned piglets and pigs for fattening can be extrapolated to include all minor porcine species for growing at 4 000 XU and 900 BGU/kg complete feed.

KEY WORDS

Zootechnical additive, digestibility enhancers, endo-1,4-beta-xylanase, endo-1,3(4)-beta-glucanase, pigs, safety, efficacy

[1] On request from the European Commission, Question No EFSA-Q-2012-00727, adopted on 12 March 2013.

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SUMMARY

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 AveMix® XG 10 (endo-1,4-beta-xylanase, endo-1,3(4)-beta-glucanase) as a feed additive for pigs for fattening and minor porcine species.

The additive AveMix® XG 10 is an enzyme preparation of endo-1,4-beta-xylanase (xylanase) and endo-1,3(4)-beta-glucanase (glucanase), produced by two strains of *Trichoderma reesei*. This product is currently authorised for use in chickens for fattening, laying hens, minor poultry species and weaned piglets as a zootechnical additive, under the functional group of digestibility enhancers. The applicant is now seeking an extension of the authorisation to pigs for fattening and minor porcine species at a recommended dose of 4 000 XU and 900 BGU/kg complete feed.

A full description of the formulations, manufacturing processes, purity, stability and homogeneity of the product has already been provided in a previous assessment. The FEEDAP Panel considers that the safety aspects other than safety for the new target species have been covered in the previous assessment and would not be affected by the requested extension of use. Therefore, the present opinion focuses only on the safety and efficacy of this enzyme preparation for the new target species.

The applicant provided a tolerance study performed in weaned piglets that was previously evaluated by the FEEDAP Panel. In this study the piglets tolerated well a 100-fold overdose of the recommended dose (4 000 XU and 900 BGU/kg feed) and therefore the Panel concluded that the additive is safe for weaned piglets when used at the recommended dose. The FEEDAP Panel considers that conclusions reached in piglets can be extended to pigs for fattening, provided that the same maximum dose applies. The conclusions on the tolerance in piglets can be extrapolated to include all minor growing porcine species at 4 000 XU and 900 BGU/kg complete feed.

Three efficacy studies performed in pigs for fattening were provided. The supplementation of the diets with Avemix® XG 10 at the recommended dose (4 000 XU and 900 BGU/kg) resulted in a significantly higher body weight and daily weight gain in one trial and in a significantly improved feed to gain ratio in two trials. Therefore, the FEEDAP Panel concludes that AveMix® XG 10 has the potential to be efficacious in pigs for fattening at the dose of 4 000XU and 900 BGU/kg feed. Since the mode of action of xylanases and glucanases can be reasonably assumed to be the same in all porcine species, the conclusions on the efficacy in weaned piglets and pigs for fattening can be extrapolated to include all minor growing porcine species at 4 000 XU and 900 BGU/kg complete feed.

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BACKGROUND

Regulation (EC) No 1831/2003[4] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of a feed additive shall submit an application in accordance with Article 7.

The European Commission received a request from the company AVEVE NV[5] for authorisation of the product AveMix® XG 10, endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase, when used as a feed additive for pigs for fattening and minor porcine species (category: zootechnical additives; functional group: digestibility enhancers) under the conditions mentioned in Table 1.

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive). EFSA received directly from the applicant the technical dossier in support of this application.[6] According to Article 8 of that Regulation, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. The particulars and documents in support of the application were considered valid by EFSA as of 22 August 2012.

The additive AveMix® XG 10 is a preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754). This product is currently authorised for use as feed additive in feed for chickens for fattening,[7,8] weaned piglets[9] and laying hens and minor poultry species for fattening and laying.[10]

The European Food Safety Authority issued a scientific opinion on the safety and efficacy of AveMix® XG 10 as a feed additive for chickens for fattening (EFSA, 2009) and one on the modification of the terms of the authorisation of the product for this species (EFSA, 2010). Opinions on the safety and efficacy of the product as a feed additive for weaned piglets and laying hens and minor poultry species were published on 2011 and 2012, respectively (EFSA, 2011 and 2012).

TERMS OF REFERENCE

According to Article 8 of Regulation (EC) No 1831/2003, EFSA shall determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and the efficacy of the product

[4] 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.
[5] AVEVE NV, Eugeen Meeusstraat 6, 2170 Merksem, Belgium.
[6] EFSA Dossier reference: FAD-2012-0022.
[7] Commission Regulation (EC) No 1091/2009 of 13 November 2009 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive for chickens for fattening (holder of authorisation Aveve NV) OJ L 299, 14.11.2009, p. 6.
[8] Commission Regulation (EU) No 335/2011 of 7 April 2011 amending Regulation (EC) No 1091/2009 as regards the minimum content of the enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive in feed for chickens for fattening OJ L 94, 08.04.2011, p. 14.
[9] Commission Implementing Regulation (EU) No 1088/2011 of 27 October 2011 concerning the authorisation of an enzyme preparation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive for weaned piglets (holder of authorisation Aveve NV) OJ L 281, 28.10.2011, p. 14.
[10] Commission Implementing Regulation (EU) No 989/2012 of 25 October 2012 concerning the authorisation of endo-1,4-beta-xylanase produced by *Trichoderma reesei* (MUCL 49755) and endo-1,3(4)-beta-glucanase produced by *Trichoderma reesei* (MUCL 49754) as a feed additive for laying hens and minor poultry species for fattening and laying (holder of authorisation Aveve NV). OJ L 297, 26.10.2012, p. 11.

AveMix® XG 10, endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase, when used under the conditions described in Table 1.

Table 1: Description and conditions of use of the additive as proposed by the applicant

Additive	endo-1,4-beta-xylanase EC 3.2.1.8 and endo-1,3(4)-beta-glucanase EC 3.2.1.6 (AveMix® XG 10)
Registration number/EC No/No (if appropriate)	4a9
Category(-ies) of additive	Zootechnical additive
Functional group(s) of additive	Digestibility enhancer

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
Enzyme preparation containing endo-1,4-beta-xylanase (EC 3.2.1.8) produced by Trichoderma reesei and endo-1,3(4)-beta-glucanase (EC 3.2.1.6) produced by Trichoderma reesei. Solid or liquid having a minimum activity of endo-1,4-beta-xylanase: 40000 XU/g endo-1,3-(4)-beta-glucanase: 9000 BGU/g	Not applicable	Complies with JECFA guidelines on microbial quality, heavy metals, toxins and undesirable substances	Assay based on colometric reaction of dinitrosalicylic acid on reducing sugar yield produced by action of endo-1,4-beta-xylanase on a xylan containing substrate or endo-1,3(4)-beta-glucanase on a beta-glucan containing substrate

Trade name (if appropriate)	AveMix® XG 10
Name of the holder of authorisation (if appropriate)	AVEVE NV

Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		U/kg of complete feedingstuffs		
Pigs for fattening and minor porcine species	Until slaughter age	Endo-1,4-beta-xylanase: 4000 XU/kg complete feed endo-1,3-(4)-beta-glucanase: 900 BGU/kg complete feed		Not relevant

Other provisions and additional requirements for the labeling	
Specific conditions or restrictions for use (if appropriate)	In the directions for use of the additive and premixture, indicate the storage temperature, storage life, and stability to pelleting
Specific conditions or restrictions for handling (if appropriate)	-
Post-market monitoring (if appropriate)	-
Specific conditions for use in complementary feedingstuffs (if appropriate)	Recommended dosages per kilogram of complete feedingstuff for pigs for fattening and minor porcine species: endo-1,4-beta-xylanase: 4000 XU, endo-1,3(4)-beta-glucanase: 900 BGU

Maximum Residue Limit (MRL) (if appropriate)			
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues
-	-	-	-

ASSESSMENT

1. Introduction

The additive AveMix® XG 10 is an enzyme preparation of endo-1,4-beta-xylanase (xylanase; EC 3.2.1.8) and endo-1,3(4)-beta-glucanase (glucanase; EC 3.2.1.6), produced by two strains of *Trichoderma reesei* (MUCL 49755 and 49754, respectively). The product is produced in two forms, solid and liquid, with an activity of xylanase of 40 000 XU/g and of glucanase of 9 000 BGU/g. This product is currently authorised for its use in feed for chickens for fattening, laying hens and minor poultry species and weaned piglets as a zootechnical additive, under the functional group of digestibility enhancers. The applicant is now seeking the authorisation of the product as feed additive for pigs for fattening and minor porcine species at a recommended dose of 4 000 XU (xylanase units) and 900 BGU (beta-glucanase units) per kg complete feed (delivered by 100 mg additive/kg feed).

The European Food Safety Authority issued two scientific opinions on the safety and efficacy of AveMix® XG 10 as a feed additive for chickens for fattening (EFSA, 2009, 2010), another one for its use in weaned piglets (EFSA, 2011) and a fourth for its use in laying hens and minor poultry species (EFSA, 2012). A full description of the formulations, manufacturing processes, purity, stability and homogeneity of the product has already been provided in a previous assessment (EFSA, 2009). The FEEDAP Panel considers that the safety aspects other than safety for the new target species have been covered in a previous assessment (EFSA, 2009) and would not be affected by the requested extension of use. Therefore, the present opinion focuses only on the safety and efficacy of this enzyme preparation for the new target species.

2. Evaluation of the analytical methods by the European Union Reference Laboratory (EURL)

The EURL considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[11]

3. Safety for pigs for fattening and minor porcine species

The applicant provided a tolerance study performed with weaned piglets that was previously evaluated by the FEEDAP Panel (EFSA, 2011). In this study the piglets tolerated well a 100-fold overdose of the recommended dose (4 000 XU and 900 BGU/kg feed) and therefore the Panel concluded that the additive is safe for weaned piglets when used at the recommended dose.

The FEEDAP Panel considers that conclusions reached in piglets can be extended to pigs for fattening, provided that the same maximum dose applies. The conclusions on the tolerance in piglets can be extrapolated to include all minor growing porcine species at the dose of 4 000 XU and 900 BGU/kg complete feed.

4. Efficacy

4.1. Efficacy for pigs for fattening

Three performance trials carried out in two different countries were provided and the design of the trials can be found in Table 2 and a summary of the results in Table 3.

The initial mean body weight of the pigs for fattening ranged from 27 to 32 kg. The animals were penned individually in trial 1 (72 males, 36 replicates per group) and in groups of 12 pigs in trials 2 and 3 (blocking according to sex, body weight and litter origin, 12 replicates per treatment). The dietary treatments resulted from the supplementation of grower and finisher diets with AveMix® XG

[11] The full report is available on the EURL website: http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2009-0062.pdf

10 (solid formulation) to provide 0 or 4 000 XU and 900 BGU per kg feed (confirmed by analyses). Diets were offered in pelleted form for at least 91 days (Table 2). In trial 3 the animals had a 10-day adaptation period before the start of the trial. Trials 2 and 3 finished when animals reached slaughter body weight (112 and 119 kg, respectively). General health status and mortality were monitored and performance was measured. In the third trial, carcass parameters at slaughter were also measured (data not shown). For each experiment, the statistical approach involved an analysis of variance (ANOVA) (randomised block design using the pen as experimental unit).

Table 2: Summary of the design of the three performance trials in pigs for fattening considered for the assessment

Trial	AveMix® XG 10 (U/kg)[1]		Diet composition	Animal breed[2] (sex)	Total no of animals *(animals/replicate)* replicates/treatment	Duration (days)
	Intended	Analysed				
1[12]	0/0 4 000/900	62/290 4 427/1 252	Wheat, barley, soya bean meal	Cross-breed (♂)	72 *(1)* 36	91
2[13]	0/0 4 000/900	829/594 5 195/1 546	Wheat, barley, soya bean meal	Cross-breed (♂,♀)	288 *(12)* 12	96
3[14]	0/0 4 000/900	1 226/555 5 631/1 544	Wheat, barley, soya bean meal	Cross-breed (♂,♀)	288 *(12)* 12	99

[1] Values for xylanase (XU)/glucanase (BGU), the analysed values are mean values for grower and finisher diets.
[2] Cross-breed: Duroc × Landrace in trial 1, Tempo × (Dutch Landrace × Great Yorkshire) in trial 2 and Tempo × Great Yorkshire breed in trial 3.

The results showed that Avemix® XG 10 at 4 000 XU/900 BGU significantly increased final weight and daily weight gain in one trial (trial 1), while feed to gain ratio was significantly decreased in two other trials (trials 2 and 3; Table 3). Mortality and culling rate were within the normal range and not related to the dietary treatments. In trials 2 and 3 a total of 21 and 16 pigs, respectively, required medical treatment during the study for different reasons (pneumonia, arthritis, diarrhoea), but were distributed in proportion between the dietary groups. Therefore, the Panel concludes that the additive has the potential to improve the performance of pigs for fattening at the recommended dose.

Table 3: Effect of AveMix® XG 10 on the performance of pigs for fattening

Trial	AveMix® XG 10 (U/kg)[1]	Body weight (kg)		Daily weight gain (g)	Feed to gain ratio	Mortality/culled[2] (*n*)
		Initial	Final			
1	0/0	28.9	102.8[a]	812[a]	2.58	0/0
	4 000/900	28.9	108.5[b]	875[b]	2.51	0/1
2	0/0	27.0	112.1	886	2.59[a]	0/0
	4 000/900	27.0	112.4	890	2.56[b]	3/0
3	0/0	32.3	118.9	880	2.69[a]	0/0
	4 000/900	32.2	118.9	874	2.62[b]	3/3

[1] Intended dose for xylanase (XU)/glucanase (BGU).
[2] In trial 3, three piglets had to be culled at the beginning of the study; the difference in number of piglets per pen was considered in the statistical analysis of the study.
[a,b] Values within one column and within a given trial with different superscripts are significantly different ($P < 0.05$).

[12] Technical dossier/Section IV/Annex IV.2.11.
[13] Technical dossier/Section IV/Annex IV.2.12.
[14] Technical dossier/Section IV/Annex IV.2.13.

4.2. Efficacy for minor porcine species

The additive has the potential to improve the performance of piglets (EFSA, 2011) and of pigs for fattening at the dose of 4 000 XU and 900 BGU per kg feed. Since the mode of action of xylanases and glucanases can reasonably be assumed to be the same in all pig species, the conclusions on efficacy for weaned piglets and pigs for fattening can be extrapolated to include all minor growing pig species at the dose of 4 000 XU and 900 BGU/kg complete feed.

5. 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[15] and Good Manufacturing Practice.

CONCLUSIONS

The two formulations (liquid and solid) of the additive are considered to be equivalent regarding the safety and efficacy for the target species when used at the same level.

The FEEDAP Panel considers that, since the additive has been demonstrated to be safe for piglets at the recommended dose, this conclusion can be extended to pigs for fattening and extrapolated to all minor growing porcine species provided that the same dose applies.

Supplementation of the feed for pigs for fattening with Avemix® XG 10 at the proposed dose (4 000 XU and 900 BGU/kg) resulted in a better performance of the pigs for fattening in three trials. Therefore, the FEEDAP Panel concludes that AveMix® XG 10 has the potential to be efficacious in pigs for fattening at this supplementation level. Since the mode of action of xylanases and glucanases can be reasonably assumed to be the same in all porcine species, the conclusions on efficacy for weaned piglets and pigs for fattening can be extrapolated to include all minor growing porcine species at the dose of 4 000 XU and 900 BGU/kg complete feed.

DOCUMENTATION PROVIDED TO EFSA

1. AveMix® XG 10 pigs for fattening and minor porcine species. June 2012. Submitted by AVEVE NV.

2. AveMix® XG 10 pigs for fattening and minor porcine species. December 2012. Submitted by AVEVE NV.

3. Comments from Member States received through the ScienceNet.

REFERENCES

EFSA (European Food Safety Authority), 2009. Safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) for use as feed additive for chickens for fattening. The EFSA Journal, 1094, 1–17.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2010. Modification of the terms of the authorisation of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as a feed additive for chickens for fattening. EFSA Journal, 8(12):1919, 10 pp.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2011. Safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as feed additive for weaned piglets. EFSA Journal, 9(6):2278, 11 pp.

[15] 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.

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2012. Safety and efficacy of AveMix® XG 10 (endo-1,4-beta-xylanase and endo-1,3(4)-beta-glucanase) as feed additive for laying hens and minor poultry species. EFSA Journal, 10(6): 2728, 10 pp.