SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 2 October 2018

doi: 10.2903/j.efsa.2018.5456

Safety and efficacy of Hostazym® X (endo-1,4-beta-xylanase) as a feed additive for sows in order to have benefit in piglets

EFSA Panel on Additives and Products or Substances used in Animal Feed (EFSA FEEDAP Panel),
Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Maryline Kouba, Mojca Kos Durjava, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Gabriele Aquilina, Paul Brantom, Noël Albert Dierick, Montserrat Anguita and Guido Rychen

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 HOSTAZYM® X as a feed additive for sows in order to have benefit in piglets. The additive HOSTAZYM® X contains endo-1,4-beta-xylanase and is available in liquid and solid formulations. This product is authorised as a feed additive for chickens for fattening, turkeys for fattening, laying hens, minor poultry species for fattening and laying, weaned piglets, pigs for fattening and carps. The applicant has now requested to extend the authorisation to sows in order to have benefit in piglets. The FEEDAP Panel considered that the new use of the additive would not change the previous conclusions regarding the safety for the consumer, user and environment. The FEEDAP Panel concluded that there are no concerns for consumer safety and no risks for the environment are expected. Considering the safety for the user, it was concluded that the additive should be considered a potential skin and eye irritant, and a potential skin and respiratory sensitiser. A tolerance study was submitted to support the safety of the additive in the new target species/category. The results showed that sows tolerated well a 100-fold the recommended enzyme activity level in feed. Consequently, the FEEDAP Panel concluded that the additive is safe for sows at 1,500 EPU/kg feed. A total of four studies were submitted to support the efficacy of the additive, one of which was not considered further in the assessment due to the high mortality registered in piglets. In the other three, a significant and positive effect on a relevant parameter was found in only one trial. Therefore, the Panel concluded that there is insufficient information to conclude on the efficacy of the additive.

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

Keywords: safety, efficacy, zootechnical additives, digestibility enhancer, endo-1, 4-beta-xylanase, sows

Requestor: European Commission

Question number: EFSA-Q-2017-00747

Correspondence: feedap@efsa.europa.eu

Panel members: Giovanna Azimonti, Vasileios Bampidis, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Maryline Kouba, Mojca Kos Durjava, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa and Ruud Woutersen.

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, Matteo Lorenzo Innocenti, Paola Manini, Maria Vittoria Vettori.

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, Kouba M, Kos Durjava M, López-Alonso M, López Puente S, Marcon F, Mayo B, Pechová A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Aquilina G, Brantom P, Dierick NA, Anguita M, Rychen G, 2018. Scientific opinion on the safety and efficacy of Hostazym® X (endo-1,4-beta-xylanase) as a feed additive for sows in order to have benefit in piglets. EFSA Journal 2018;16(10):5456, 8 pp. https://doi.org/10.2903/j.efsa.2018.5456

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 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 4
1.2. Additional information 4
2. Data and methodologies 4
2.1. Data 4
2.2. Methodologies 5
3. Assessment 5
3.1. Characterisation 5
3.2. Safety 5
3.2.1. Safety for sows 5
3.3. Efficacy 6
4. Conclusions 8
Documentation provided to EFSA 8
Chronology 8
References 8
Abbreviations 8

1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] 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 Huvepharma NV[2] for authorisation of the product Hostazym® X (endo-1,4-beta-xylanase), when used as a feed additive for sows in order to have benefit in piglets (category: zootechnical additives; functional group: digestibility enhancers).

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. The particulars and documents in support of the application were considered valid by EFSA as of 12 February 2018.

According to Article 8 of Regulation (EC) No 1831/2003, 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. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the product HOSTAZYM® X (endo-1,4-beta-xylanase), when used under the proposed conditions of use.

1.2. Additional information

The additive HOSTAZYM® X is a preparation of endo-1,4-beta-xylanase available in liquid and solid formulations. This product is authorised as a feed additive for chickens for fattening, turkeys for fattening, laying hens, minor poultry species for fattening and laying, weaned piglets and pigs for fattening,[3] chickens reared for laying and minor poultry species,[4] and carps.[5]

The FEEDAP Panel adopted two opinions on the safety and efficacy of the product as a feed additive for poultry and pigs (EFSA FEEDAP Panel, 2013, 2015), another one for its use as a feed additive in chickens reared for laying and minor poultry species reared for laying (EFSA FEEDAP Panel, 2017a) and one on its use in feed for carps (EFSA FEEDAP Panel, 2017b).

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[6] in support of the authorisation request for the use of Hostazym® X (endo-1,4-beta-xylanase) as a feed additive.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[7]

[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] Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerp, Belgium.
[3] Commission implementing Regulation (EU) 2015/1043 of 30 June 2015 concerning the authorisation of the preparation of endo-1,4-beta-xylanase (EC 3.2.1.8) produced by *Trichoderma citrinoviride* Bisset (IM SD135) as a feed additive for chickens for fattening, turkeys for fattening, laying hens, weaned piglets, pigs for fattening and minor poultry species for fattening and for laying, and amending Regulations (EC) No 2148/2004, (EC) No 828/2007 and (EC) No 322/2009 (holder of authorisation Huvepharma NV). OJ L 167, 1.7.2015, p.63.
[4] Commission implementing Regulation (EU) 2017/1906 of 18 October 2017 concerning the authorisation of a preparation of endo-1,4-b-xylanase (EC 3.2.1.8) produced by *Trichoderma citrinoviride* Bisset (IMI SD135) as a feed additive for chickens reared for laying and minor poultry species reared for laying (holder of authorisation Huvepharma NV). OJ L 269, 19.10.2017, p.33.
[5] Commission implementing Regulation (EU) 2018/327 of 5 March 2018 concerning the authorisation of a preparation of endo-1,4-beta-xylanase (EC 3.2.1.8) produced by *Trichoderma citrinoviride* Bisset (IMI SD135) as a feed additive for carp (holder of authorisation Huvepharma NV). OJ L 63, 6.3.2018, p.7.
[6] FEED dossier reference: FAD-2017-0062.
[7] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0001.pdf

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of HOSTAZYM® X (endo-1,4-β-xylanase) 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 Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011).

3. Assessment

This assessment deals with a request from the applicant to extend the use of HOSTAZYM® X in feed for sows in order to have benefit in piglets.

3.1. Characterisation

The additive HOSTAZYM® X is a preparation of endo-1,4-beta-xylanase (xylanase; Enzyme Commission Number 3.2.1.8) produced by a non-genetically modified strain of *Trichoderma citrinoviride* (IMI SD 135). This additive is available in two solid and two liquid formulations. The solid formulations are HOSTAZYM® X 6000 MicroGranulate and 30000 MicroGranulate, which have a minimum guaranteed enzyme activity of 6,000 and 30,000 EPU[8]/g of product, respectively. The liquid formulations are HOSTAZYM® X 6000 Liquid and 15000 Liquid with a minimum guaranteed enzyme activity of 6,000 and 15,000 EPU mL, respectively. The additive was characterised in full in EFSA's previous assessments (EFSA FEEDAP Panel, 2013, 2017b).

The applicant provided new data on the stability and the capacity to homogeneously distribute of HOSTAZYM® 15000 Liquid when added to feed.[9] Three batches of the formulation where added to a complete feed for pigs at 1,500 EPU/kg feed. The stability was studied in mash and pelleted diets after 3 months storage at 25 or 35°C. After 3 months storage, samples kept at 25°C showed recovery values of the initial enzyme activity of 84% in mash or 91.5% for pelleted feed, while the recovery values at 35°C were 72.5% for mash and 84% for pelleted feed. The capacity to homogeneously distribute was measured by analysing ten sub-samples of each feed and calculating the coefficient of variance. The results showed a range between 5 to 6% for mash samples and a range between 7% and 11% for pelleted samples.

The additive is intended to be used in feed for sows (in order to have benefit in piglets) at a recommended enzyme activity of 1,500 EPU/kg feed.

3.2. Safety

Safety aspects regarding the use of this additive in feed including the safety for the consumers, for the users and for the environment have been previously evaluated (EFSA FEEDAP Panel, 2013, 2015). The FEEDAP Panel concluded that there are no concerns for the consumers of food products obtained from animals receiving the additive and no risks for the environment are expected. Considering the safety for the user, it was concluded that the additive should be considered a potential skin and eye irritant, and a potential skin and respiratory sensitiser. The dossier does not contain any new information that that would lead the FEEDAP Panel to reconsider the conclusions drawn previously. Moreover, the FEEDAP Panel considers that the new use would not introduce hazards/risks not considered in the previous assessments.

Since the application covers the use of the additive in sows, the applicant provided a tolerance study in sows.

3.2.1. Safety for sows

A total of 54 sows ((Landrace x LW) x from 1st to 4th parity) were allocated to three dietary treatments (representing 18 sows per treatment) and were kept under study from day 16 before the expected farrowing day to weaning of the piglets (day 27 of lactation). Until day 107 of gestation, the sows were kept in groups of nine sows and then were moved to the lactation barns where they were housed individually. During the experimental period, sows received a commercial diet based on wheat and barley either not supplemented (control) or supplemented with HOSTAZYM® X to provide 1,500 or

[8] EPU: one EPU is the amount of enzyme which releases 0.0083 μmol of reducing sugars (xylose equivalent) per minute from oat spelt xylan at pH 4.7 and 50°C.
[9] Technical dossier/Section II/Annex II.47.

150,000 EPU/kg feed. Enzyme activities were confirmed by analysis. The diet was offered in pelleted form. During the gestation period, sows received 2.7 kg feed/day. When sows were transferred to the farrowing barns the amount of feed was increased until farrowing from 2.7 to 4.0 kg/day, and after farrowing the amount was increased progressively and individually until weaning. Sows' body weight and back-fat thickness were measured at farrowing and at weaning and the difference between the two time points was calculated. Feed consumption was measured daily throughout the study period. Farrowing performance was measured and included number of piglets born (alive, still born) and body weight. Cross-fostering of piglets was performed among sows of the same group and during the first 48 h of life in order to equalise number of piglets between litters and body weight within litter. Growth of the piglets during the lactation was also measured; piglets were weighed at birth, after cross-fostering (when relevant) and at weaning. Piglets did not receive creep-feed during the lactation. An analysis of variance (ANOVA) was performed with the data, considering the sow as the experimental unit. Significance level was set at $p < 0.05$.

No statistical differences were observed in any of the parameters measured. The mean number of piglets born alive per sow was 16 and body weight at birth was 1.3 kg. The mean number of piglets per sow after cross-fostering was 13 and the body weight of the piglets was 1.4 kg. Average feed intake of sows during the lactation was 6.6 kg/day, the body weight loss during lactation per sow was 13 kg and the mean back-fat thickness lost during lactation was 2.4 mm. At the end of the lactation (day 28 of life), the number of piglets per sow was 11.8 and the body weight was 7 kg (average body weight gain 214 g/day). Mortality of piglets during lactation was 10%.

Feeding sows with the xylanase up to 100 times the recommended dose did not have any negative effect on the performance of sows and their litters. The FEEDAP Panel concludes that the additive is safe for sows at the recommended inclusion level of 1,500 EPU/kg feed.

3.3. Efficacy

The applicant submitted a total of four trials in lactating sows, which shared a similar study design, and the results were pooled to be statistically analysed. In all four trials, performance of the sows and their litters as well as sows' apparent faecal digestibility (including energy) were measured. In one study,[10] the piglets showed a poor health status, as denoted by the fact that two-thirds had to receive medication, and a high mortality in piglets was registered (above 20%). The high mortality of the piglets would not allow to draw conclusions on the parameters measured. Therefore, the FEEDAP Panel did not consider it further in the assessment. This fact invalidates also the pooling of the data.[11]

The design of the other three trials is presented in Table 1. A basal diet was either not supplemented (control) or supplemented with HOSTAZYM® X to provide 1,500 EPU/kg feed (confirmed by analysis). The sows were allocated to the experimental groups (control or supplemented) 7 days before farrowing. The lactation period differed between studies (Table 1). Feed was offered restrictively prior to farrowing and then a curve with increasing amounts was followed. Sows' feed intake was measured throughout the study. Sow's body weight and back-fat thickness were measured prior farrowing and at weaning. Farrowing performance and litter performance during lactation (including number of piglets, weight gain and mortality) were measured. Cross-fostering was applied to the litters after farrowing, within 24 h in trial 2 and 48 h in trial 3; in trial 1, details on cross-fostering were not reported. The faecal apparent digestibility of the diets was determined on the last week of lactation. At this scope, the feed administered contained an inert marker and collection of faecal samples was done for three to four consecutive days. The data was statistically analysed, the sow was taken as the experimental unit. In trial 1 and 2, the data were analysed as completely randomised design and in trial 3, an ANOVA was done (room and block used as random factor and diet as fixed effect). The results of the parameters measured in the sows are presented in Table 2; the performance of the litters is presented in Table 3.

[10] Technical dossier/Supplementary information August 2018/Annex IV.05.
[11] Technical dossier/Supplementary information August 2018/Annex IV.06.

Table 1: Design of the efficacy trials performed in lactating sows

Trial	N per treatment	Breed (parity number)	Basal diet composition	Duration of the study[(d)]	
				Start	End
1[(a)]	16	Landrace × Large White (1 to 8)	Barley, corn, wheat, wheat middlings and soybean	7 days before farrowing	Day 21 of lactation
2[(b)]	16	Landrace × Large White (1 to 8)	Barley, corn, wheat, wheat middlings and soybean	7 days before farrowing	Day 21 of lactation
3[(c)]	15	Dutch Landrace × Dutch Large White (1 to 6)	Barley, wheat, wheat middlings and soybean meal	7 days before farrowing	Day 27 of l actation

(a): Technical dossier/Supplementary information August 2018/Annex IV.01.
(b): Technical dossier/Supplementary information August 2018/Annex IV.02.
(c): Technical dossier/Supplementary information August 2018/Annex IV.03 and IV.04.
(d): In trial 1, there were discrepancies on the reported start and end of the study, in a figure the start was 10 days prior to farrowing and the end on day 19 of lactation.

Table 2: Effect of HOSTAZYM® X on the daily feed intake, body weight and body weight loss of the sows from farrowing to weaning

Trial	Group (EPU/kg feed)	Daily feed intake (kg)	Body weight (kg)			Back-fat loss (mm)	Faecal apparent digestibility of Gross Energy (%)
			Farrowing	Weaning	Loss		
1	0	4.91	265	244	21	2.6	73.7[b]
	1,500	4.85	269	247	22	2.6	75.8[a]
2	0	5.32	252	216	36	2.4	74.5
	1,500	5.32	251	216	35	2.3	76.4
3	0	5.66	269	227	42	4.6	77.8
	1,500	5.66	270	225	45	5.0	78.0

[a,b]Within one trial and within a column mean values with different superscript are different ($p < 0.05$).

The results of the parameters measured on the sows showed no modifications with the exception of the faecal apparent digestibility of the Gross Energy of the diets which in one trial (trial 1) was higher in the sows receiving the additive compared to the controls (with equal performance of the litters).

The results regarding the performance of the litters showed no modifications in any of the parameters measured (Table 3).

Only in one trial a significant and positive effect of the additive on the apparent faecal digestibility of the gross energy of the diets was found. Overall, there is insufficient evidence to conclude on the efficacy of the additive for sows in order to have benefit in piglets.

Table 3: Effect of HOSTAZYM® X on litter size, piglets' weight and mortality during lactation

Trial	Group (EPU/kg feed)	Litter Size (n)		Piglets' weight (kg)		Average daily weight gain (g)	Mortality/ culls (%/n)
		Initial[(1)]	Final	Initial[(2)]	Final		
1	0	11.7	8.8	1.54	5.70	219	9.7
	1,500	11.8	9.5	1.51	5.66	218	5.2
2	0	12.4	10.8	1.76[a]	5.70	202	12.9
	1,500	12.8	10.9	1.51[b]	5.67	212	14.4
3	0	13.6	12.7	1.21	7.31	231	10.8
	1,500	13.4	12.9	1.32	7.84	239	9.8

[a,b]Within one trial and within a column mean values with different superscript are different ($p < 0.05$).
(1): Initial is after cross-fostering.
(2): In trial 3 is birth weight (as reported) and weight after cross-fostering in trials 1 and 2.

4. Conclusions

The FEEDAP Panel concludes that HOSTAZYM® X is safe for sows at the recommended use level (1,500 EPU/kg feed). Owing to the limited data submitted, the FEEDAP Panel cannot conclude on the efficacy of HOSTAZYM® X as a feed additive for sows in order to have benefits in piglets.

Documentation provided to EFSA

1) HOSTAZYM® X for sows. November 2017. Submitted by Huvepharma N.V.
2) HOSTAZYM® X for sows. Supplementary information. August 2018. Submitted by Huvepharma N.V.
3) Comments from Member States.

Chronology

Date	Event
06/11/2017	Dossier received by EFSA
16/11/2017	Reception mandate from the European Commission
12/02/2018	Application validated by EFSA – Start of the scientific assessment
03/04/2018	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: safety and efficacy for the target species*
12/05/2018	Comments received from Member States
13/08/2018	Reception of supplementary information from the applicant - Scientific assessment re-started
02/10/2018	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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), 2013. Scientific Opinion on the safety and efficacy of HOSTAZYM X (endo-1,4-beta-xylanase) as a feed additive for poultry, piglets and pigs for fattening. EFSA Journal 2013;11(2):3105, 23 pp. https://doi.org/10.2903/j.efsa.2013.3105

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2015. Scientific Opinion on the safety of HOSTAZYM X as a feed additive for poultry and pigs. EFSA Journal 2015;13(1):3969, 10 pp. https://doi.org/10.2903/j.efsa.2015.3969

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017a. Safety and efficacy of HOSTAZYM® X (endo-1,4-β-xylanase) as a feed additive for chickens reared for laying and minor poultry species reared for laying. EFSA Journal 2017;15(2):4708, 6 pp. https://doi.org/10.2903/j.efsa.20178.4708

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017b. Scientific Opinion on the safety and efficacy of HOSTAZYM® X (endo-1,4-β-xylanase) as a feed additive for carps. EFSA Journal 2017;15(7):4942, 9 pp. https://doi.org/10.2903/j.efsa.2017.4942

Abbreviations

ANOVA analysis of variance
EURL European Union Reference Laboratory
FEEDAP EFSA Panel on Additives and Products or Substances used in Animal Feed