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SCIENTIFIC OPINION

Scientific Opinion on the modification of the terms of the authorisation of OPTIPHOS® (6-phytase) as a feed additive for pigs for fattening[1]

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

European Food Safety Authority (EFSA), Parma, Italy

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 modification of the terms of the authorisation of OPTIPHOS® (6-phytase) as a feed additive for pigs for fattening. The phytase present in this additive is produced by a genetically modified strain of *Komagaetella pastoris* (formerly known as *Pichia pastoris*). The additive is presented in solid and liquid forms and is authorised for use in avian species, weaned piglets, pigs for fattening and sows. The Panel issued an opinion on the safety and efficacy of OPTIPHOS® as a feed additive for avian and porcine species. This opinion considered the safety aspects of the additive with regard to the consumer, the user, the environment and the genetic modification of the production strain. The applicant seeks a modification of the terms of the authorisation for pigs for fattening, which consists in lowering the minimum recommended dose from 250 OTU/kg feed to 125 OTU/kg feed. Four trials were provided to support the efficacy of the product at the newly recommended dose. Three of these trials were balance trials and the results showed an increase in the retention of phosphorus in pigs for fattening fed diets supplemented with OPTIPHOS® at 125 OTU/kg. Therefore, the FEEDAP panel concluded that OPTIPHOS® has the potential to be efficacious in pigs for fattening at the new minimum recommended dose.

KEY WORDS

zootechnical additives, 6-phytase, efficacy, pigs for fattening

[1] On request from the European Commission, Question No EFSA-Q-2014-00829, adopted on 9 July 2015.

[2] Panel members: Gabriele Aquilina, Vasileios Bampidis, Maria de Lourdes Bastos, Georges Bories, Andrew Chesson, Pier Sandro Cocconcelli, Maria Luisa Fernández-Cruz, Gerhard Flachowsky, Jürgen Gropp, Boris Kolar, Maryline Kouba, Secundino López Puente, Marta López-Alonso, Alberto Mantovani, Baltasar Mayo, Fernando Ramos, Guido Rychen, Maria Saarela, Roberto Edoardo Villa, Robert John Wallace and Pieter Wester. Correspondence: FEEDAP@efsa.europa.eu

[3] The Panel wishes to thank the members of the Working Group on Enzymes, including Paul Brantom, Noël Dierick and Ingrid Halle, for the preparatory work on this scientific opinion.

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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 modification of the terms of the authorisation of OPTIPHOS® (6-phytase) as a feed additive for pigs for fattening. The phytase present in this additive is produced by a genetically modified strain of *Komagaetella pastoris* (formerly known as *Pichia pastoris*). The additive is presented in solid and liquid forms and is authorised for use in avian species, weaned piglets, pigs for fattening and sows.

The FEEDAP Panel issued an opinion on the safety and efficacy of OPTIPHOS® (6-phytase) as a feed additive for avian and porcine species. This opinion considered the safety aspects of the additive with regard to the consumer, the user, the environment and the genetic modification of the production strain. The applicant seeks a modification of the terms of the authorisation for pigs for fattening, which consists in lowering the minimum recommended dose from 250 OTU/kg feed to 125 OTU/kg feed.

Four trials were provided in order to support the efficacy of the product at the newly recommended dose. Three of these trials were balance trials and the results showed an increase in the retention of phosphorus in pigs for fattening fed diets supplemented with OPTIPHOS® at 125 OTU/kg. Therefore, the FEEDAP panel concluded that OPTIPHOS® has the potential to be efficacious in pigs for fattening at the new minimum recommended dose.

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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 13(3) of that Regulation lays down that if the holder of an authorisation proposes changing the terms of the authorisation by submitting an application to the Commission, accompanied by the relevant data supporting the request for the change, the Authority shall transmit its opinion on the proposal to the Commission and the Member States.

The European Commission received a request from Huvepharma AD[5] for the modification of the terms of the authorisation of the product OPTIPHOS®, 6-phytase, when used as a feed additive for pigs for fattening (category: zootechnical additive; 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 13(3) (modification of the authorisation 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 25 February 2015.

The additive OPTIPHOS® is a preparation of 6-phytase produced by a genetically modified strain of *Komagaetella pastoris* (DSM 23036; formerly known as *Pichia pastoris*). This additive is authorised for use in avian species, weaned piglets, pigs for fattening and sows.[7]

The Panel on Additives and Products or Substances in Animal Feed issued an opinion on the safety and efficacy of OPTIPHOS® (6-phytase) as a feed additive for avian and porcine species (EFSA FEEDAP Panel 2011). This opinion considered the safety aspects of the additive regarding the consumer, the user, the environment and the genetic modification of the production strain.

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 OPTIPHOS®, 6-phytase, when used under the conditions described in Table 1.

[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] Huvepharma AD, James Boucher Blvd 33, 1407 Sofia, Bulgaria.
[6] EFSA Dossier reference: FAD-2014-0023.
[7] Commission Implementing Regulation (EU) No 98/2012 of 7 February 2012 concerning the authorisation of 6-phytase (EC 3.1.3.26) produced by *Pichia pastoris* (DSM 23036) as a feed additive for chickens and turkeys for fattening, chickens reared for laying, turkeys reared for breeding, laying hens, other avian species for fattening and laying, weaned piglets, pigs for fattening and sows (holder of authorisation Huvepharma AD). OJ L 35, 8.2.2012, p. 6.

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

Additive	6-phytase
Registration number/EC No/No (if appropriate)	98/2012
Category(-ies) of additive	Zootechnical additives
Functional group(s) of additive	Digestibility enhancers

Description			
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)
Preparation 6-phytase (EC 3.1.3.26) produced by *Pichia pastoris* (DSM 23036) with a minimum activity of: 4 000 OTU/g in solid form 8 000 OTU/mL in liquid form	NA	-	Colorimetric method based on the quantification of the inorganic phosphate released by the enzyme from the sodium phytate

Trade name (if appropriate)	OPTIPHOS
Name of the holder of authorisation (if appropriate)	Huvepharma AD

Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		Units/kg of complete feedingstuffs		
Pigs for fattening	NA	125 OTU	NA	NA

Other provisions and additional requirements for the labelling	
Specific conditions or restrictions for use (if appropriate)	NA
Specific conditions or restrictions for handling (if appropriate)	NA
Post-market monitoring (if appropriate)	NA
Specific conditions for use in complementary feedingstuffs (if appropriate)	NA

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

ASSESSMENT

1. Introduction

The additive OPTIPHOS® is a preparation of 6-phytase produced by a genetically modified strain of *Komagaetella pastoris* (DSM 23036; formerly known as *Pichia pastoris*). It is presented in solid (G/CT) and liquid (L) forms ensuring 4 000 OTU[8]/g and 8 000 OTU/mL, respectively. This additive is authorised for use in avian species, weaned piglets, pigs for fattening and sows.

The Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) issued an opinion on the safety and efficacy of OPTIPHOS® (6-phytase) as a feed additive for avian and porcine species (EFSA FEEDAP Panel, 2011). This opinion considered the safety aspects of the additive with regard to the consumer, the user, the environment and the genetic modification of the production strain. The applicant seeks a modification of the terms of the authorisation for pigs for fattening, which consists in lowering the minimum recommended dose from 250 OTU/kg feed to 125 OTU/kg feed.

Safety aspects of the product have been addressed in the previous opinion. The Panel is not aware of any new information that would lead it to reconsider the conclusions drawn in this previous assessment. Therefore, the present assessment will address only the efficacy for pigs for fattening at the new recommended dose.

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.[9]

3. Efficacy for pigs for fattening

Four digestibility/balance trials carried out at four different locations were presented in the dossier. In one of these trials,[10] only faecal phosphorus digestibility was studied and, therefore, it was not further considered in the assessment.

3.1. Trial 1

A total of 48 hybrid barrows (initial weight of 37 kg) were individually housed in digestibility cages and allocated to six dietary treatments (representing eight replicates per treatment).[11] A basal diet based on maize and soya bean meal (total phosphorus content of 3.1 g/kg) was supplemented with OPTIPHOS® to provide 0 (low phosphorus control), 125, 250, 500 or 1 000 OTU/kg (confirmed by analysis). A high phosphorus control diet (total phosphorus content of 5.6 g/kg) was also considered. The feed was offered as pellets and feeding was restricted. After an adaptation period of nine days, faeces and urine (preserved with acid) were quantitatively collected over five days and analysed for phosphorus content. An analysis of variance (ANOVA) was performed with the data and the mean of the groups were compared with a Tukey test.

The results showed that the phosphorus retention was 29.6, 50.5, 55.4, 61.5, 63.2 and 53.9 % for 0, 125, 250, 500 and 1 000 OTU/kg feed and the high phosphorus diet, respectively. The addition of OPTIPHOS® (at doses of 125 OTU/kg feed and above) significantly increased ($P < 0.05$) the retention of phosphorus compared with the non-supplemented low phosphorus diet.

[8] One unit of phytase activity (OTU) is defined as the amount of enzyme that catalyses the release of 1.0 micromole of inorganic phosphate per minute from 5.1 mM sodium phytate in pH 5.5 citrate buffer at 37 ºC, measured as the blue P-molybdate complex colour at 820 nm.
[9] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/default/files/FinRep-FAD-2010-0008.pdf
[10] Technical dossier/Section IV/Annex IV.1.
[11] Technical dossier/Section IV/Annex IV.2.

3.2. Trial 2

A total of 24 hybrid barrows (initial weight of 53 kg) were individually housed in digestibility cages and allocated to four dietary treatments (representing six replicates per treatment).[12] A basal diet based on maize and soya bean meal (total phosphorus content of 3.6 g/kg) was supplemented with OPTIPHOS® to provide 0 (low phosphorus control), 125 or 250 OTU/kg (confirmed by analysis). A high phosphorus control diet (total phosphorus content of 5.1 g/kg) was also considered. The feed was offered as pellets and feeding was restricted. After an adaptation period of 10 days, faeces and urine (preserved with acid) were quantitatively collected for five days. An ANOVA was performed with the data and the means of the groups were compared using a Duncan's test.

The results showed that the phosphorus retention was 19.0, 27.6, 33.5 and 20.8 % for 0, 125 and 250 OTU/kg feed and the high phosphorus diet, respectively. The addition of OPTIPHOS® (at doses of 125 OTU/kg feed and above) significantly increased ($P < 0.001$) the retention of phosphorus compared with the non-supplemented low phosphorus diet.

3.3. Trial 3

Trial 3 was performed with 20 commercial cross-bred pigs (10 males, 10 females), with an initial body weight of 56 kg, which were individually housed in digestibility cages and allocated to two dietary treatments (representing 10 replicates per treatment).[13] A basal diet based on maize and soya bean meal (total phosphorus content of 4.5 g/kg) was supplemented with OPTIPHOS® to provide 0 or 125 OTU/kg feed (confirmed by analysis). The feed was offered on an *ad libitum* basis in mash form. After an adaptation period of 10 days, faeces and urine were quantitatively collected for three days and were analysed for phosphorus content. An ANOVA was performed with the data.

Phosphorus retention was significantly increased ($P < 0.01$) by the addition of OPTIPHOS® at 125 OTU/kg feed (57 % vs. 66 %).

3.4. Conclusions on the efficacy

The three trials considered showed a significant increase in the retention of phosphorus in pigs for fattening fed diets supplemented with OPTIPHOS® at 125 OTU/kg. Consequently, the FEEDAP panel concludes that OPTIPHOS® has the potential to be efficacious in pigs for fattening at the new minimum recommended dose.

4. 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[14] and Good Manufacturing Practice.

CONCLUSIONS

The FEEDAP Panel concludes that the additive has the potential to be efficacious in pigs for fattening at the dose of 125 OTU/kg feed.

DOCUMENTATION PROVIDED TO EFSA

1. OPTIPHOS® for pigs for fattening. November 2014. Submitted by Huvepharma AD.
2. Comments from Member States received through the ScienceNet.

[12] Technical dossier/Section IV/Annex IV.3.
[13] Technical dossier/Section IV/Annex IV.4.
[14] 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.

REFERENCES

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), 2011. Scientific Opinion on the safety and efficacy of Optiphos® (6-phytase) as a feed additive for chickens and turkeys for fattening, chickens reared for laying, turkeys reared for breeding, laying hens, other birds for fattening and laying, weaned piglets, pigs for fattening and sows. EFSA Journal 2011;9(11):2414, 29 pp. doi:10.2903/j.efsa.2011.2414