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Modification of the terms of the authorisation of Natuphos[®] E as a feed additive for chickens for fattening or reared for laying/breeding

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Abstract

The additive Natuphos[®] E presents 6-phytase produced by a genetically modified strain of *Aspergillus niger*. The additive is currently authorised in the EU for use as a feed additive for chickens for fattening, chickens reared for laying, pigs for fattening, sows, minor porcine species for fattening or for reproduction, turkeys for fattening, turkeys reared for breeding, all other avian species (excluding laying birds) and weaned piglets. The authorisation for chickens for fattening or reared for laying is at a minimum content of 750 FTU/kg feed. The applicant has requested to lower this dose to 125 FTU/kg feed. The Panel considered a total of three short-term trials and five long-term trials. In two short-term trials, the birds that received 125 FTU/kg feed showed a significantly better retention of phosphorus from the diets. Similarly, in two long-term trials, the birds that received 125 FTU/kg feed showed a significantly better performance. Consequently, the Panel concluded that the additive has a potential to improve the performance/phosphorus retention of the birds at the dose of 125 FTU/kg feed.

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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
3.3. Efficacy for chickens for fattening.....	5
3.4. Post-market monitoring.....	6
4. Conclusions.....	6
Documentation provided to EFSA.....	7
Chronology.....	7
References.....	7
Abbreviations.....	7

1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003¹ 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 BASF SE² for a modification of the terms of the authorisation of the product Natuphos® E (6-phytase) when used as a feed additive for chickens for fattening or in chickens reared for laying/breeding (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 13(3) (modification of the authorisation of a feed additive). The particulars and documents in support of the application were considered valid by EFSA as of 19 September 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 Natuphos® E (6-phytase), when used under the proposed conditions of use.

1.2. Additional information

The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) has adopted an opinion on the additive under assessment regarding the safety and efficacy of its use as a feed additive for avian and porcine species (EFSA FEEDAP Panel, 2017).

The additive is currently authorised in the European Union for use as a feed additive for chickens for fattening, chickens reared for laying, pigs for fattening, sows, minor porcine species for fattening or for reproduction, turkeys for fattening, turkeys reared for breeding, all other avian species (excluding laying birds) and weaned piglets. The authorisation for chickens for fattening or reared for laying is at a minimum level of 750 FTU/kg feed.³ The applicant is now requesting to lower this minimum level to 125 FTU/kg feed.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁴ in support of the authorisation request for the use of Natuphos® E 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.⁵

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 BASF SE, F-ENA/MR, F31 68623 Lampertheim, Germany.

³ COMMISSION IMPLEMENTING REGULATION (EU) No 2018/338 of 7 March 2018 concerning the authorisation of a preparation of 6-phytase, produced by *Aspergillus niger* (DSM 25770) as feed additive for chickens for fattening, chickens reared for laying, pigs for fattening, sows, minor porcine species for fattening or for reproduction, turkeys for fattening, turkeys reared for breeding, all other avian species (excluding laying birds) and weaned piglets (holder of the authorisation BASF SE). OJ L 65, 8.3.2018, p. 17.

⁴ FEED dossier reference: FAD-2018-0053.

⁵ The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/finirep-fad-2015-0040-natuphose_g.pdf

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Natuphos® E is in line with the principles laid down in Regulation (EC) No 429/2008⁶ 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

Natuphos® E contains a 6-phytase (phytase; Enzyme Commission Number 3.1.3.26) is currently authorised as a zootechnical additive, functional group of digestibility enhancers. This assessment deals with the request from the applicant to reduce the authorised minimum recommended level in chickens for fattening or reared for laying/breeding from 750 FTU⁷ /kg feed to 125 FTU/kg feed.

3.1. Characterisation

The phytase in Natuphos® E is produced by a genetically modified strain of *Aspergillus niger* (DSM 25770) and is available in one powder formulation (Natuphos® E 5000), two granulated formulations (Natuphos® E 5000 G and 10000 G) and two liquid formulations (Natuphos® E 5000 L and Natuphos® E 10000 L). Natuphos® E 5000, 5000 G and 5000 L ensure a minimum phytase activity of 5,000 FTU/g of product and the formulations Natuphos® E 10000, 10000 G and 10000 L ensure a minimum phytase activity of 10,000 FTU/g product. The production strain and the final formulations of the additive were fully characterised and described previously (EFSA FEEDAP Panel, 2017).

3.2. Safety

The safety aspects regarding the use of this additive in feed including the safety of the genetic modification of the production strain, the safety for the target species, the safety for the consumers, for the user and for the environment have been previously assessed (EFSA FEEDAP Panel, 2017). The Panel concluded that the use of the product as a feed additive raises no concerns for the target species, for consumer safety or for the environment. Regarding the safety for the user the Panel concluded that the additive in any formulation is not irritant to skin or eyes but it is a dermal sensitiser and should be considered a potential respiratory sensitiser. The FEEDAP Panel is not aware of any new information that would lead it to reconsider the conclusions drawn previously. The reduction in the recommended use level in chickens for fattening would not have an impact on the safety aspects already considered.

3.3. Efficacy for chickens for fattening

In the previous opinion, the Panel evaluated a total of five trials (EFSA FEEDAP Panel, 2017). From the results of the studies the Panel concluded that the product has a potential to be efficacious at 750 FTU/kg feed. A significant and positive effect on the performance of the birds when the additive was added at 125 FTU/kg was found only in one trial. The applicant has now provided two new short-term trials and a long-term trial in order to support the efficacy at 125 FTU/kg feed.

The short-term trials were done in the same place and followed the same experimental design. A total of 120 (Trial 1) or 96 (Trial 2) seven-day-old male chickens for fattening (Ross 308) were caged in groups of two birds and allocated to five/four dietary treatments (representing 12 replicates per treatment).⁸ A basal diet based on maize and soybean meal (total phosphorus content of 0.40–0.43%; calcium content 0.58%) was either not supplemented (control) or supplemented with Natuphos® E (10000 G in trial 1 and 5000 G in trial 2) to provide 125, 250, or 500 FTU/kg feed in trial 1 and 125 or 250 FTU/kg in trial 2. Enzyme activities were confirmed by analysis. A positive control, including higher levels of phosphorus (total phosphorus content of 0.68%; calcium content 0.98%), was also considered in every study. Feed was offered *ad libitum* in pelleted form from day 7 to day 25 in trial 1 and up to day 22 in trial 2. Total excreta was collected during 3–4 consecutive days starting on day 21

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 FTU, one FTU is the amount of enzyme which releases one micromole of inorganic phosphate from sodium phytate per minute at pH 5.5 and 37°C.

⁸ Technical dossier/Section IV/Annex IV.1 and IV.2.

(trial 1) or day 18 (trial 2), pooled per cage and analysed to study phosphorus retention. In trial 1, on day 25 one bird per cage was killed and tibia bones were collected to study bone ash content. An ANOVA was done with the data from each study.

In the first trial, the phosphorus retention was 52%, 62%, 63%, 69% and 38% for the control, 125, 250, 500 and positive control, respectively. The corresponding values for the ash content in tibia bone were 39%, 42%, 42%, 44% and 48% (dry tibia). The phosphorus retention and tibia ash content were significantly higher in the groups that received the phytase compared to control from 125 FTU/kg and onwards.

In the second, two animals died during the study. The phosphorus retention was 58%, 65%, 65% and 45% for control, 125, 250 and positive control, respectively. The groups receiving the phytase from 125 FTU/kg feed and onwards showed significantly higher values than the control.

In the long-term trial, a total of 960 one-day-old male chickens (Ross 308) were distributed to pens (30 birds per pen) and allocated to four dietary treatments (representing 8 replicates per treatment).⁹ Three basal diets, starter, grower and finisher, based on maize and soybean meal (total phosphorus content 0.46/0.43/0.40%; calcium content 0.64/0.61/0.56%) were either not supplemented (control) or supplemented with Natuphos® E 5000 to provide 125 or 250 FTU/kg feed. Enzyme activities were analysed and found to be higher than the intended 211 FTU/kg feed for the 125 and 310 FTU/kg feed for the 250.¹⁰ A positive control (total phosphorus content 0.64/0.60/0.57%; calcium 0.90/0.85/0.80%) was also considered. Diets were offered *ad libitum* in mash form for 39 days. Health status of the birds was monitored throughout the study. Birds were weighed and feed intake was measured. Feed to gain ratio was calculated. An ANOVA was done with the data and the group means were compared with the Tukey test. The results are presented in Table 1.

Table 1: Effects of Natuphos® E on the performance of chickens for fattening

FTU/kg feed	Daily feed intake (g)	Final body weight (g)	Feed to gain ratio	Mortality (%)
Control	89.1 ^c	2,155 ^c	1.61 ^b	4.46
125	97.2 ^b	2,372 ^b	1.60 ^b	1.62
250	97.1 ^b	2,426 ^b	1.56 ^a	1.21
Positive control	106.0 ^a	2,692 ^a	1.54 ^a	2.02

^{a,b,c}: Values within one column with different superscript are significantly different ($p < 0.05$).

For the assessment of the efficacy in chickens for fattening, data from three short-term trials and five long-term trials were available. In two short-term trials, the birds that received 125 FTU/kg feed showed a significantly better retention of phosphorus from the diets. Similarly, in two long-term trials, the birds that received 125 FTU/kg feed showed a significantly better performance. However, the dosage in one of the long-term trials showed the animals received a higher enzyme activity (211 FTU/kg feed) than the intended (125 FTU/kg feed).

Considering the studies previously assessed and the newly submitted studies the FEEDAP Panel concludes that the additive has the potential to be efficacious as a zootechnical additive in chickens for fattening at 125 FTU/kg feed. This conclusion is extended to chickens reared for laying/breeding.

3.4 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 Regulation¹¹ and Good Manufacturing Practice.

4. Conclusions

The proposed modification to the conditions of the authorisation does not have an impact on the safety conclusions previously established. The additive is safe for chickens for fattening or reared for laying/breeding and raises no concerns for the consumer of products obtained from animals receiving

⁹ Technical dossier/Section IV/Annex IV.3.

¹⁰ Technical dossier/Supplementary information January 2019.

¹¹ Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

it or for the environment. The additive in any formulation is not irritant to skin or eyes but it is a dermal sensitiser and should be considered a potential respiratory sensitiser.

Natuphos® E has the potential to be efficacious at 125 FTU/kg feed in chickens for fattening and the conclusion is extended to chickens reared for laying/breeding.

Documentation provided to EFSA

- 1) Natuphos® E for chickens for fattening or reared for laying breeding. July 2018. Submitted by BASF SE.
- 2) Natuphos® E for chickens for fattening or reared for laying breeding. Supplementary information. January 2019. Submitted by BASF SE.

Chronology

Date	Event
31/7/2018	Dossier received by EFSA
7/8/2018	Reception mandate from the European Commission
19/9/2018	Application validated by EFSA – Start of the scientific assessment
20/12/2018	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. <i>Issues: efficacy</i>
3/1/2019	Reception of supplementary information from the applicant – Scientific assessment re-started
23/1/2019	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), 2017. Scientific opinion on the safety and efficacy of Natuphos® E (6-phytase) as a feed additive for avian and porcine species. EFSA Journal 2017;15(11):5024, 35 pp. <https://doi.org/10.2903/j.efsa.2017.5024>

Abbreviations

- EURL European Union Reference Laboratory
 FEEDAP EFSA Panel on Additives and Products or Substances used in Animal Feed