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Safety and efficacy of Natuphos[®] E (6-phytase) as a feed additive for laying hens, minor poultry and other avian species for laying

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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 Natuphos[®] E (6-phytase) as a feed additive for laying hens, minor poultry and other avian species for laying. The additive Natuphos[®] E consists of 6-phytase (phytase; Enzyme Commission Number 3.1.3.26) and is intended to be used as a feed additive for laying hens, minor poultry and other avian species for laying as a zootechnical additive, functional group of digestibility enhancers. This additive was previously assessed by the FEEDAP Panel in 2017 for avian and porcine species. The production strain of the phytase present in the product is a genetically modified strain of *Aspergillus niger*. Based on the previous opinion, the FEEDAP Panel concluded that the genetic modification of the production strain does not give rise to safety concerns. The production strain and its DNA were not detected in the concentrate used to formulate the products. The FEEDAP Panel previously concluded that the additive was safe for the target species, consumers and the environment when used at 200 FTU/kg feed. The additive Natuphos[®] E is not considered to be toxic by inhalation or irritant for skin or eye; however, it should be regarded as a dermal sensitiser and a potential respiratory sensitiser. The additive has the potential to be efficacious in improving the performance and/or the phosphorus utilisation in laying hens at 200 FTU/kg feed; the conclusions drawn in laying hens can be extrapolated to all minor poultry and other avian species for laying.

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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.....	4
3. Assessment.....	5
3.1. Conditions of use.....	5
3.2. Efficacy.....	5
3.2.1. Conclusions on efficacy.....	6
3.3. Post-market monitoring.....	6
4. Conclusions.....	6
5. Documentation as provided to EFSA/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 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 BASF SE² for authorisation of the Natuphos[®] E (6-phytase), when used as a feed additive for laying hens, minor poultry and other avian species for laying (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 1 March 2019.

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 (see Section 3.1).

1.2. Additional information

Natuphos[®] E is a preparation of 6-phytase produced by *Aspergillus niger* (DSM 25770). This additive was previously assessed by the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) for avian and porcine species (EFSA FEEDAP Panel, 2017b). Following this assessment, the additive was authorised for use in feed for chickens for fattening and chickens reared for laying at 750 FTU, turkeys for fattening, turkeys reared for breeding, all other avian species (excluding laying birds) at 125 FTU, weaned piglets at 125 FTU, pigs for fattening, sows and minor porcine species for fattening or for reproduction at 100 FTU.³

The FEEDAP Panel has recently adopted an opinion for the modification of the terms of authorisation of Natuphos[®] E as a feed additive for chickens for fattening or reared for laying/breeding, to reduce the supplementation of the phytase to 125 FTU/kg feed (EFSA FEEDAP Panel, 2019).

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 (6-phytase) 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

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of Natuphos[®] E (6-phytase) is in line with the principles laid down in Regulation (EC) No 429/2008 and the relevant guidance documents: Technical Guidance for assessing the safety of feed additives for the environment

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, G-ENA/MR - F31, 68623 Lampertheim, Germany.

³ Commission Implementing Regulation (EU) 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).

⁴ FEED dossier reference: FAD-2018-0092.

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

(EFSA, 2008), Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017a), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018), Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012b), Guidance for establishing the safety of additives for the consumer (EFSA FEEDAP Panel, 2012c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018).

3. Assessment

The additive Natuphos[®] E consists of 6-phytase (Enzyme Commission Number 3.1.3.26) and is intended to be used as a feed additive for laying hens, minor poultry and other avian species for laying as a zootechnical additive (digestibility enhancers) at the minimum content of 200 FTU/kg⁶ of complete feed. No maximum dose is specified.

The phytase contained in the additive is produced by a genetically modified strain of *A. niger* deposited at the Deutsche Sammlung von Mikroorganismen und Zellkulturen (DSMZ) under the accession number DSM 25770.⁷ Natuphos[®] E is marketed in five forms: a powder (Natuphos[®] E 5000), two granulated forms (Natuphos[®] E 5000 G and Natuphos[®] E 10000 G) and two liquid forms (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 G and 10000 L ensure a minimum phytase activity of 100,000 FTU/g product. The final formulations of the additive, the method of manufacture and the production strain were fully characterised and described previously (EFSA FEEDAP Panel, 2017b). Thus, the data pertaining to composition, impurities, physical properties, shelf-life, stability and homogeneity still apply.

In the previous opinion (EFSA FEEDAP Panel, 2017b), the Panel established the safety of the additive for the target species (including laying hens, minor poultry and other avian species for laying), consumers and the environment. As regards the safety for the user, Natuphos[®] E is not considered to be toxic by inhalation or irritant for skin or eyes. However, it should be regarded as a dermal sensitiser and a potential respiratory sensitiser. The FEEDAP Panel is not aware of any new information that would lead to reconsider the conclusions drawn previously.

In the same opinion, the Panel could not conclude on the efficacy of the additive for laying hens, minor poultry and other avian species for laying due to insufficient data.

3.1. Conditions of use

Natuphos[®] E is intended to be included in feed for laying hens, minor poultry and other avian species for laying during the whole production stage at the minimum content of 200 FTU/kg⁶ of complete feed. No maximum dose is specified.

3.2. Efficacy

In the previous opinion (EFSA FEEDAP Panel, 2017a), the applicant submitted three short-term and three long-term studies in laying hens; from these, positive results we seen only in two studies:

plus an additional short-term trial which is described below.

⁶ 1 FTU = 1 unit of phytase activity. This is the amount of enzyme which liberates 1 micromole of inorganic phosphate per minute from sodium phytate at pH 5.5 and 37°C (Technical dossier/Section II/2.5.1).

⁷ Technical dossiers/Section II/Annex II_52b_DSMZ_CoD.



Results are provided in Table 1.

Table 1: Effect of Natuphos[®] E on the utilisation of calcium and phosphorus and egg content of phosphorus measured during the collection period

Natuphos [®] E (FTU/kg feed)	Retention		Egg
	Ca (%)	P (%)	P (g/kg DM)
0 ⁽¹⁾	54.92	50.82 ^b	15.10 ^{ab}
100 ⁽²⁾	55.02	54.61 ^{ab}	15.50 ^{ab}
200 ⁽³⁾	56.65	57.07 ^a	15.60 ^a
Positive control ⁽⁴⁾	55.06	43.70 ^c	14.93 ^b

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

(1): Negative control (NC), no phytase supplemented.

(2): Negative control (NC) + 100 FTU Natuphos[®] E /kg of feed.

(3): Negative control (NC) + 200 FTU Natuphos[®] E /kg of feed.

(4): Positive control (PC), no phytase supplemented (with adequate phosphorous and calcium content: 0.52% and 3.8%, respectively).

Phosphorous utilisation was significantly improved with Natuphos[®] E at 200 FTU/kg feed, compared to the control group.

3.2.1. Conclusions on efficacy

Based on two short-term studies in which the additive showed improvements in phosphorous utilisation (one at 100 FTU/kg feed and another one at 200 FTU/kg feed) and one long-term study in which performance parameters were enhanced in laying hens at 200 FTU/kg feed, the FEEDAP Panel concludes that Natuphos[®] E has the potential to be efficacious at a minimum dose of 200 FTU/kg feed. The conclusions of the efficacy of the additive can be extrapolated to minor poultry and other avian species for laying.

3.3. 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 use of the product as a feed additive Natuphos[®] E is safe for laying hens, minor poultry and other avian species for laying, for the consumers and for the environment when used at 200 FTU/kg feed. The additive Natuphos[®] E is not considered to be toxic by inhalation or irritant for skin or eyes; however, it should be regarded as a dermal sensitiser and a potential respiratory sensitiser.

The additive has the potential to be efficacious in improving the performance and/or the phosphorous utilisation in laying hens at 200 FTU/kg feed. The conclusions drawn in laying hens can be extrapolated to all minor poultry and other avian species for laying.

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.

5. Documentation as provided to EFSA/Chronology

Date	Event
20/12/2018	Dossier received by EFSA. Natuphos [®] E laying hens, minor poultry and other avian species for laying. Submitted by BASF SE
18/01/2019	Reception mandate from the European Commission
01/03/2019	Application validated by EFSA – Start of the scientific assessment
03/04/2019	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>
10/04/2019	Reception of supplementary information from the applicant – Scientific assessment re-started
01/06/2019	Comments received from Member States
03/07/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

DM	dry matter
DSMZ	Deutsche Sammlung von Mikroorganismen und Zellkulturen
EURL	European Union Reference Laboratory
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed