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Assessment of the application for renewal of the authorisation of Natuphos (3-phytase) as a feed additive for poultry and pigs

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Abstract

Natuphos® is a feed additive that contains 3-phytase which is produced [redacted] The product is currently authorised for use as a feed additive in chickens for fattening, piglets (weaned) and pigs for fattening, laying hens and turkeys for fattening, ducks, sows, all minor avian species other than ducks and ornamental birds. This scientific opinion concerns the renewal of the authorisation of this additive for those species. The application also included chickens reared for laying/breeding, turkeys reared for breeding and breeding hens. The applicant provided evidence that the additive in the market complies with the conditions of authorisation. According to the information provided by the applicant, no new evidence has been identified that would make the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) reconsider the previous conclusions regarding the safety for the target species, consumer and environment under the authorised conditions of use. The additive is a respiratory sensitiser and a potential skin sensitiser. The present application for renewal of the authorisation does not include a proposal for amending or supplementing the conditions of the original authorisation that would have an impact on the efficacy of the additive. Therefore, there was no need for assessing the efficacy of the additive in for those species for which an authorisation exists. The Panel also considered that the additive is safe and has a potential to be efficacious in chickens reared for laying/breeding, turkeys reared for breeding, breeding hens and suckling piglets at the corresponding recommended doses.

Keywords: zootechnical additives, digestibility enhancers, phytase, safety, efficacy, poultry, pigs

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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 14(1) of that Regulation lays down that an application for renewal shall be sent to the Commission at the latest 1 year before the expiry date of the authorisation.

The European Commission received a request from BASF SE[2] for renewal of the authorisation of the product Natuphos® (3-phytase), when used as a feed additive for chickens for fattening, chickens reared for laying and breeding, laying hens and breeding hens, ducks for fattening, ducks for breeding and laying, turkeys reared for breeding, turkeys for fattening, ornamental birds, minor avian species, all other poultry for laying and breeding (except ducks) piglets (suckling and weaned piglets), pigs for fattening, sows for reproduction (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 14(1) (renewal of the authorisation). The particulars and documents in support of the application were considered valid by EFSA as of 14 September 2016.

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® (3-phytase), when used under the proposed conditions of use (see Section 3.1.2).

1.2. Additional information

Natuphos® is a preparation of 3-phytase obtained [redacted] The Scientific Committee on Animal Nutrition (SCAN) issued two opinions on the efficacy and safety of this enzyme preparation: one for piglets, pigs for fattening, sows, chickens for fattening and laying hens (SCAN, 2000), and the other for the same target species and the consumer, user and environment (SCAN, 2002). These SCAN opinions [redacted] The opinion also included considerations on the use of new liquid and solid formulations with a double concentration compared to that of the preparation previously authorised, the assessment of the safety for the target species (poultry and pigs) the consumer, the user and the environment as well as the safety aspects of the genetic modification. As a follow-up opinion, other opinions were adopted on the safety of the enzyme preparation for target species/categories: laying hens and turkeys for fattening (EFSA, 2007a), sows (EFSA, 2007c) and ducks (EFSA, 2007b). Later on, EFSA adopted an opinion on the modification of the conditions of use in pigs for fattening (EFSA, 2009) and another one on the use as a feed additive for minor avian species (quails, pheasants, partridges, guinea fowl, geese, pigeons, ostriches, peacocks, flamingos) and ornamental birds (EFSA FEEDAP Panel, 2010).

This product is authorised for use as a feed additive in chickens for fattening, piglets (weaned) and pigs for fattening,[3] laying hens and turkeys for fattening,[4] ducks,[5] sows,[6] all minor avian species other than ducks and ornamental birds.[7] The applicant requested for the renewal of the authorisation of the additive. In the application and in the mandate chickens reared for laying/breeding, turkeys reared for

[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, ENS/LR 67056 Ludwigshafen, Germany.
[3] Commission Regulation (EC) No 243/2007 of 6 March 2007 concerning the authorisation of 3-phytase (Natuphos) as a feed additive. OJ L 73, 13.3.2007, p. 4 and amending Commission Regulation (EU) No 1269/2009 of 21 December 2009 amending Regulation (EC) No 243/2007 as regards the minimum content of the feed additive in feed for pigs for fattening. OJ L 339, 22.12.2009, p. 27.
[4] Commission Regulation (EC) No 1142/2007 of 1 October 2007 concerning the authorisation of a new use of 3-phytase (Natuphos) as a feed additive. OJ L 256, 2.10.2007, p. 20.
[5] Commission Regulation (EC) No 165/2008 of 22 February 2008 concerning the authorisation of a new use of 3-phytase (Natuphos) as a feed additive. OJ L 50, 23.2.2008, p. 8.
[6] Commission Regulation (EC) No 505/2008 of 6 June 2008 concerning the authorisation of a new use of 3-phytase (Natuphos) as a feed additive. OJ L 149, 7.6.2008, p.33.
[7] Commission Regulation (EU) No 327/2010 of 21 April 2010 concerning the authorisation of a new use of 3-phytase as a feed additive for all minor avian species, other than ducks, and for ornamental birds (holder of authorisation BASF SE). OJ L 100, 22.4.2010, p. 3.

breeding, breeding hens and suckling piglets are mentioned. EFSA considers that no formal assessment has been done in the past for these species/categories, and therefore, the opinion will take them into account.

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[8] in support of the authorisation request for the use of Natuphos® as a feed additive. The technical dossier was prepared following the provisions of Article 14 of Regulation (EC) No 1831/2003, Regulation (EC) No 429/2008 and the applicable EFSA guidance documents.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessments are valid and applicable for the current application.[9]

2.2. Methodologies

The approach followed by the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) to assess the safety and the efficacy of Natuphos® 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), Guidance on the renewal of the authorisation of feed additives (EFSA FEEDAP Panel, 2013), Guidance on the risk assessment of genetically modified microorganisms and their products intended for food and feed use (EFSA GMO Panel, 2011), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017a,b), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018).

3. Assessment

Natuphos® (3-phytase) is currently authorised as a zootechnical feed additive (functional group of digestibility enhancers) for chickens for fattening, piglets (weaned) and pigs for fattening, laying hens and turkeys for fattening, ducks, sows, all minor avian species other than ducks and ornamental birds. This opinion deals with the request for the renewal of the authorisation for those species and for the assessment of the safety and efficacy for chickens reared for laying/breeding, turkeys for breeding, breeding hens and suckling piglets.

3.1. Characterisation

3.1.1. Characterisation of the additive

Natuphos® is a preparation of the phytase that is authorised in solid and liquid formulations. There are three solid formulations, Natuphos® 5000 (powder), Natuphos® 5000 G (granular) and Natuphos® 10000 G (granular), and two liquid formulations, Natuphos® 5000 L and Natuphos® 10000 L.

The information submitted regarding the manufacturing process confirms that it is the same as the one described in the first assessment of the product [redacted] (EFSA, 2006). The applicant stated that no antimicrobial substances are used during the process.

[redacted]

[8] FEED dossier reference: FAD-2016-0025.

[9] The full reports are available on the EURL website: https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports/fad-2005-0008 and https://ec.europa.eu/jrc/en/eurl/feed-additives/evaluation-reports/fad-2008-0043

[redacted]

The production strain was assessed by EFSA in 2006 and it was concluded that the genetic modification does not raise safety concerns.

No recent data has been submitted by the applicant.

The production organism was incubated and used as a control. The production strain was not detected in any of the batches analysed.

3.1.2. Conditions of use

The additive is authorised at the following minimum enzyme activities per kg feed: at 100 FTU/kg feed in pigs for fattening (recommended level 400–500 FTU/kg feed), at 250 FTU/kg feed in turkeys for fattening (recommended level 500 FTU/kg feed), laying hens (recommended level 300–400 FTU/kg feed), minor avian species (except in ducks) and ornamental birds (recommended level 300–500 FTU/kg feed), at 300 FTU/kg feed in ducks (recommended level 300–750 FTU/kg feed), at 375 FTU/kg feed in chickens for fattening (recommended level 500–700 FTU/kg feed) and at 500 FTU/kg in piglets and sows. The applicant proposes to keep the current conditions of use for these species/categories.

For those species/categories for which no formal assessment/authorisation is currently available, the conditions would be as follows: chickens reared for laying/breeding 375 FTU/kg feed (recommended level 500–700 FTU/kg feed), turkeys reared for breeding 250 FTU/kg feed (recommended level 500 FTU/kg feed), for breeding hens 250 FTU/kg feed (recommended level 300–400 FTU/kg feed) and for suckling piglets 500 FTU/kg feed.

Under the other provisions of the authorisation it is stated in the directions for use of the additive and premixture, it should be indicated the storage temperature, storage life and stability to pelleting. It is also stated that the additive is for use in feed containing more than 0.23% phytin-bound phosphorus.

3.2. Safety

3.2.1. Previous assessments

The FEEDAP Panel evaluated, in 2006, the safety of the genetic modification of the production strain, for the consumer, users and environment and concluded that the genetic modification is of no concern and that the use of the product as a feed additive would be of no concern for the consumers of products derived from animals fed with the additive or for the environment. The safety concerns for the user were limited to its potential to be a skin and respiratory sensitiser.

The FEEDAP Panel has assessed previously the safety of the additive for the target species for which an authorisation exists and concluded that the additive is safe for piglets, pigs for fattening and chickens for fattening (EFSA, 2006), laying hens and turkeys for fattening (EFSA, 2007a), ducks (EFSA, 2007b), sows (EFSA, 2007c), minor avian species and ornamental birds (EFSA FEEDAP Panel, 2010) under the corresponding conditions of use. The Panel also considers that the safety of the additive established in chickens and turkeys for fattening (EFSA, 2006, 2007a), laying hens (EFSA, 2007a) and weaned piglets (EFSA, 2006) can be extended to chickens reared for laying/breeding, turkeys reared for breeding, breeding hens and suckling piglets at the corresponding recommended levels.

3.2.2. Further evidence

In line with the requirements established in the EFSA guidance on the renewal (EFSA FEEDAP Panel, 2013), the applicant performed a literature search to support the safety of the additive under the approved conditions of use. [redacted] The main search term was 'phytase', and the searches included terms relevant for toxicological and ecotoxicological aspects.

The searches done revealed a total of 92 hits (see Appendix A), 74 excluding repetitions. Some publications on human respiratory sensitisation effects were identified as relevant to evaluate the safety aspects of the additive. These included case studies, reviews and epidemiological data on respiratory sensitisation at the workplace. Among them, the FEEDAP Panel considers relevant the study made in workers of factory-producing premixes who were responsible for the addition of Natuphos phytase powder or sprayed the Natuphos liquid preparation in feed (Doekes et al., 1999). The authors concluded that phytase is an occupational allergen causing specific IgE immune responses among exposed workers, being responsible for their respiratory symptoms, namely wheezing and shortness of breath. The conclusion is also supported by the findings reported by Baur et al. (2002). The studies confirm that the additive is a respiratory sensitiser.

The applicant claims that no adverse effects, including accidents, for target animals, consumers or environment have been reported in the framework of its quality management system.

[redacted]

3.2.3. Conclusions on the safety

Based on the above, the fact that the additive has not been modified and the conditions of use for the species/categories for which the additive is authorised have not been modified, the FEEDAP Panel confirms its previous conclusion that Natuphos® is safe for the target species/categories, consumers of products from animals fed the additive and the environment. The additive is a respiratory sensitiser and should be considered as a potential skin sensitiser.

3.3. Efficacy

The present application for renewal of the authorisation does not include a proposal for amending or supplementing the conditions of the original authorisation that would have an impact on the efficacy of the additive. Therefore, there is no need for assessing the efficacy of the additive in the context of the renewal of the authorisation.

The efficacy has been previously established in chickens and turkeys for fattening, laying hens and piglets. Considering that the mode of action of the phytase is similar among the poultry species/categories, the FEEDAP Panel extends the conclusions to chickens reared for laying/breeding at 375 FTU/kg feed, to turkeys reared for breeding purposes and breeding hens at the 250 FTU/kg feed and to suckling piglets at 500 FTU/kg feed.

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 Regulation[20] and Good Manufacturing Practice.

4. Conclusions

The Panel concludes that the additive currently in the market complies with the existing conditions of authorisation.

The FEEDAP Panel confirms its previous conclusion that Natuphos® is safe for the target species/categories for which it is authorised; consumers of products from animals fed the additive and the environment. The additive is a respiratory sensitiser and is considered a potential dermal sensitiser.

There is no need for assessing the efficacy of the additive for those species for which an authorisation exists. The Panel concludes that the additive is safe and has a potential to be efficacious as a zootechnical additive in chickens reared for laying/breeding at 375 FTU/kg feed (recommended levels 500–700 FTU/kg feed), turkeys reared for breeding at 250 FTU/kg feed (recommended levels 500 FTU/kg feed), for breeding hens at 250 FTU/kg feed (recommended levels 300–400 FTU/kg feed) and for suckling piglets 500 FTU/kg feed.

Documentation provided to EFSA

1) Natuphos® 5000, Natuphos® 5000 G, Natuphos® 5000 L, Natuphos® 10000 G, Natuphos® 10000 L (3-phytase) Renewal dossier. April 2016. Submitted by BASF SE.
2) Natuphos® 5000, Natuphos® 5000 G, Natuphos® 5000 L, Natuphos® 10000 G, Natuphos® 10000 L (3-phytase) Renewal dossier. Supplementary information. March 2018. Submitted by BASF SE.
3) Comments from Member States.

Chronology

Date	Event
5/4/2016	Dossier received by EFSA
14/4/2016	Reception mandate from the European Commission
14/9/2016	Application validated by EFSA – Start of the scientific assessment

[20] 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.

Date	Event
10/5/2017	Request of supplementary information to the applicant in line with Article 8(1)(2) of Regulation (EC) No 1831/2003 – Scientific assessment suspended. *Issues: characterisation and safety*
14/12/2016	Comments received from Member States
4/7/2017	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
26/2/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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EFSA (European Food Safety Authority), 2009. Opinion of the Scientific Panel on Additives and Products or Substances on the efficacy of the enzyme preparation Natuphos (3-phytase) as feed additive for growing pigs. EFSA Journal, 1184, 6–11. Available online: http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2009.1184/epdf

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2010. Scientific Opinion on the safety and efficacy of Natuphos® (3-phytase) for minor avian species (quails, pheasants, partridges, guinea fowl, geese, pigeons, ostriches, peacocks, flamingos) and ornamental birds. EFSA Journal 2010;8(1):1427, 9 pp. https://doi.org/10.2903/j.efsa.2010.1427. Available online: http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2010.1427/epdf

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EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2017a. Guidance on the assessment of the safety of feed additives for the target species. EFSA Journal 2017;15(10):5021, 19 pp. https://doi.org/10.2903/j.efsa.2017.5021

EFSA FEEDAP Panel (EFSA Panel on Products or Substances used in Animal Feed), 2017b. Guidance on the assessment of the safety of feed additives for the consumer. EFSA Journal 2017;15(10):5022, 17 pp. https://doi.org/10.2903/j.efsa.2017.5022

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2018. Guidance on the assessment of the efficacy of feed additives. EFSA Journal 2018;16(5):5274, 25 pp. https://doi.org/10.2903/j.efsa.2018.5274

EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2011. Scientific Opinion on Guidance on the risk assessment of genetically modified microorganisms and their products intended for food and feed use. EFSA Journal 2011;9(6):2193, 54 pp. https://doi.org/10.2903/j.efsa.2011.2193

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SCAN (Scientific Committee on Animal Nutrition), 2002. Opinion of the Scientific Committee on Animal Nutrition on the use of certain enzymes in animal feedingstuffs. Available online: https://ec.europa.eu/food/sites/food/files/safety/docs/animal-feed_additives_rules_scan-old_report_out96.pdf

Abbreviations

EURL	European Union Reference Laboratory
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
SCAN	Scientific Committee on Animal Nutrition

Appendix A – List of references retrieved from the literature search provided by the applicant to support safety of the additive