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Efficacy of RONOZYME® WX (endo-1,4-β-xylanase) as a feed additive for laying hens

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Abstract

RONOZYME® WX is an additive that contains endo-1,4-β-xylanase which is authorised for use as a feed additive in poultry for fattening, weaned piglets and pigs for fattening. The Panel on additives and Products or Substances used in Animal Feed (FEEDAP) delivered in 2012 an opinion on the safety and efficacy of RONOZYME® WX when used as a feed additive for poultry, piglets (weaned) and pigs for fattening and another one in 2016 on the change of the production strain proposed by the applicant. In those opinions, the FEEDAP Panel concluded that the use of the product as a feed additive raise no concerns for consumer safety or for the environment. Considering the safety for the user, the Panel concluded that the additive is not a skin or eye irritant but could not conclude on the skin sensitisation potential of the additive, however, and owing to the proteinaceous nature of the active substance the additive was considered a potential respiratory sensitiser. In a further application, the applicant requested the use of the additive in laying hens. The tolerance trial provided for that assessment allowed to conclude that the additive is safe for laying hens under the recommended conditions of use. In the same application and in order to support the efficacy of the additive in laying hens, the applicant submitted three long-term trials. In all three trials, the groups receiving the xylanase at the recommended dose showed a lower feed intake and a better feed to egg mass ratio. However, in one of the three trials, these reductions were seen concurrently with a decrease in the laying rate. This result casted doubts on the efficacy of the additive, and therefore, the Panel considered that there was not sufficient evidence to conclude on the efficacy of the product. The applicant provided a further efficacy trial in which the results showed that the hens that received the additive had a better laying performance at the recommended level of 100 FXU/kg and allowed the Panel to conclude that the additive is efficacious as a zootechnical additive in laying hens.

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Keywords: safety, efficacy, zootechnical additives, endo-1,4-β-xylanase, laying hens

Requestor: European Commission

Question Number: EFSA-Q-2019-00429

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Regulation (EC) No 1831/2003 establishes rules governing the Community authorization of additives for animal nutrition and, in particular, Article 9 defines the terms of the authorization by the Commission.

The applicant, DSM Nutritional Products Ltd, Switzerland/represented in EU: Novozymes A/S Denmark is seeking a Community authorization of endo-1,4-beta-xylanase as a feed additive to be used as a digestibility enhancers for laying hens (Table 1).

Table 1: Description of the substances

Category of additive	Zootechnical additive
Functional group of additive	Digestibility enhancers
Description	Endo-1,4-beta-xylanase
Target animal category	Laying hens
Applicant	DSM Nutritional Products Ltd., Switzerland/represented in EU: Novozymes A/S Denmark
Type of request	New opinion

On 26 September 2017, the Panel on Additives and Products or Substance used in Animal Feed of the European Food Safety Authority ("Authority"), in its opinion on the safety and efficacy of the product, could not conclude on the efficacy of endo-1,4-beta-xylanase as a feed additive for laying hens.

The Commission gave the possibility to the applicant to submit complementary information in order to complete the assessment and to allow a revision of Authority's opinion. The new data have been received on 30 March 2019.

In view of the above, the Commission asks the Authority to deliver a new opinion on endo-1,4-beta-xylanase as a feed additive for laying hens based on the additional data submitted by the applicant.

1.2. Additional information

The additive RONOZYME® WX[1] is a preparation of endo-1,4-β-xylanase which is produced by a genetically modified strain of *Aspergillus oryzae* (DSM 26372) and is authorised in the European Union as a feed additive for poultry for fattening, weaned piglets and pigs for fattening.[2]

EFSA delivered an opinion on the safety and efficacy of RONOZYME® WX when used as a feed additive for poultry, piglets (weaned) and pigs for fattening (EFSA FEEDAP Panel, 2012a). In 2016, the FEEDAP Panel assessed the proposal made by the applicant in order to change the production strain to *A. oryzae* DSM 26372 (EFSA FEEDAP Panel, 2016). The authorisation of this additive is currently linked to the production strain *A. oryzae* DSM 10287.

In 2017, the FEEDAP Panel adopted an opinion on the use of the additive in laying hens in which the Panel was able to conclude that the additive is safe for laying hens but could not conclude on the efficacy of the product due to the insufficient evidence available.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of supplementary information[3] to a previous application on the same product.[4]

[1] Also known as BioFeed® Wheat.

[2] COMMISSION IMPLEMENTING REGULATION (EU) No 1206/2012 of 14 December 2012 concerning the authorisation of a preparation of endo-1,4-beta-xylanase produced by *Aspergillus oryzae* (DSM 10287) as a feed additive for poultry for fattening, weaned piglets and pigs for fattening and amending Regulations (EC) No 1332/2004 and (EC) No 2036/2005 (holder of the authorisation DSM Nutritional Products), OJ L 347, 15.12.2012, p. 12. Amended by COMMISSION IMPLEMENTING REGULATION (EU) 2017/1006 of 15 June 2017 amending Implementing Regulation (EU) No 1206/2012 as regards the change of the production strain of the preparation of endo-1,4-beta-xylanase, produced by *Aspergillus oryzae* (DSM 10287) as feed additive for poultry for fattening, weaned piglets and pigs for fattening (holder of authorisation DSM Nutritional Products Ltd). OJ L 153, 16.6.2017, p. 9.

[3] FEED dossier reference: FAD-2019-0043.

[4] FEED dossier reference: FAD-2016-0073.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA.

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the efficacy of RONOZYME® WX (endo-1,4-β-xylanase) is in line with the principles laid down in Regulation (EC) No 429/2008[5] and the relevant guidance documents: Guidance on zootechnical additives (EFSA FEEDAP Panel, 2012a) and Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011).

3. Assessment

The additive RONOZYME® WX is a preparation of endo-1,4-β-xylanase produced by a genetically modified strain of *A. oryzae* (DSM 26372). The additive is available in two forms, RONOZYME® WX (CT) and RONOZYME® WX (L), these two formulations were fully characterised in previous opinions (EFSA FEEDAP Panel, 2012b, 2016). RONOZYME® WX (CT) is a coated thermotolerant formulation which ensures a minimum activity of xylanase of 1,000 FXU/g and RONOZYME® WX (L) is a liquid formulation which ensures a minimum activity of xylanase of 650 FXU/mL.

Safety aspects regarding the use of this additive in feed including the safety of the genetic modification of the production strain, target species, the safety for the consumers, for the users and for the environment have been previously evaluated (EFSA FEEDAP Panel, 2012b, 2016). The FEEDAP Panel concluded that there are no concerns for the target species or the consumer and no risks for the environment are expected from the use of the additive in animal nutrition. Considering the safety for the user, the Panel concluded that the additive is not a skin or eye irritant but could not conclude on the skin sensitisation potential of the additive. Because of the proteinaceous nature of the active substance the additive was considered a potential respiratory sensitiser. However, in a previous assessment (EFSA FEEDAP Panel, 2017) data submitted to support the efficacy of the additive were considered as not sufficient to conclude.

The applicant has provided a new trial to support the efficacy of the additive when added to feed for laying hens at 100 FXU/kg feed.

3.1. Efficacy for laying hens

In a previous opinion (EFSA FEEDAP Panel, 2017), the Panel evaluated three long-term trials in laying hens. In all three trials, the hens fed the xylanase from RONOZYME® WX had a significantly lower feed intake and feed to egg mass ratio. In two of these trials, the laying rate of the hens was not different between groups; however, in one of these studies the hens fed the xylanase showed a significantly lower laying rate compared to the control. The Panel considered that the reduction in the laying rate in the latter trial could cast doubts on the overall efficacy of the additive and prevented the Panel to reach a conclusion on the efficacy of the additive in laying hens.

The applicant provided a new efficacy study to support the efficacy of the additive.

A total of 288 23-week-old hens (Hy-Line) were distributed in 36 enriched cages of 8 hens each and allocated to two dietary treatments (18 replicates (cages) per treatment), blocked by the laying rate of the previous week. A basal diet based on wheat, rye and soya bean meal was either not supplemented (control) or supplemented with RONOZYME® WX to provide 100 FXU per kg feed (enzyme activity was confirmed by analysis). The feed was offered on *ad libitum* basis for 168 days. Mortality and general health were monitored throughout the study. Body weight of the hens was recorded at the beginning and at the end of the trial. Feed consumption was recorded every 4 weeks per cage. Egg production per cage was recorded and weighed every second day. Feed to egg mass ratio was calculated. An analysis of variance (ANOVA) was done with the performance data (cage basis) and considering the treatment as the effect. Significance level was set at 0.05.

Mortality was low and no differences were found between treatments. The hens that received the additive showed, a statistically significant higher laying rate, egg to mass production and a significantly better feed to egg ratio compared to the control group (Table 2).

[5] 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.

Table 2: Effect of RONOZYME® WX on the feed intake, laying performance and mortality of laying hens

Groups FXU/kg feed	Daily feed intake (g)	Body weight		Laying rate (%)	Daily egg mass (g/hen)	Feed to egg mass	Mortality (n), %
		Initial	Final				
0	116	1,686	1,930	92.4[b]	55.0[b]	2.11[a]	(3) 2.1
100	115	1,687	1,952	94.0[a]	56.3[a]	2.05[b]	(4) 2.8

a,b: Values within a trial and within a column with a different superscript are significantly different ($p < 0.05$).

3.1.1. Conclusions on efficacy

Based on the results obtained in two studies previously evaluated, in which the hens that received the additive showed positive effects on the feed to gain ratio (with no impact on the laying rate) and the results obtained indicating a better laying performance in the newly submitted study the Panel concludes that the additive has a potential to be efficacious as a zootechnical additive in laying hens at the dose of 100 FXU/kg feed.

4. Conclusions

RONOZYME® WX has a potential to be efficacious as a zootechnical additive in laying hens at 100 FXU/kg feed.

Documentation as provided to EFSA/Chronology

Date	Event
21/06/2019	Dossier received by EFSA. RONOZYME® WX for laying hens. Submitted by DSM Nutritional Products Ltd.
28/06/2019	Reception mandate from the European Commission
10/07/2019	Application validated by EFSA – Start of the scientific assessment
13/11/2019	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

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Abbreviations

ANOVA analysis of variance
FEEDAP EFSA Panel on additives and Products or Substances used in Animal Feed