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# Safety and efficacy of ECONASE® XT (endo-1,4-β-xylanase) as a feed additive for pigs for fattening

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## Abstract

ECONASE® XT is an enzyme preparation with endo-1,4-β-xylanase which is authorised as a feed additive for chickens for fattening or reared for laying, turkeys for fattening or reared for breeding, laying hens, weaned piglets, pigs for fattening and minor poultry species. The authorisation of the additive for pigs for fattening is at 24,000 BXU/kg feed. The applicant asked for a modification on the conditions of use in pigs for fattening, which consists in the reduction of the minimum recommended level from 24,000 BXU/kg feed to 16,000 BXU/kg feed. In previous opinions, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) assessed the safety of the product when used as a feed additive and concluded that the use of the product raises no concerns for consumer safety and no risks for the environment are expected. The Panel also concluded that the additive is non-irritant to the skin, and the liquid form is non-irritant to the eyes and is not a dermal sensitiser; however, it is considered a respiratory sensitiser. Regarding the use of the additive in pigs for fattening, the Panel concluded that under the conditions of use, the additive is safe for pigs for fattening and that it can be efficacious at 24,000 BXU/kg. In the current application, the applicant provided three efficacy trials to support the efficacy at 16,000 BXU/kg feed. Two of these studies had been previously evaluated by the FEEDAP Panel and supported the efficacy at 16,000 BXU/kg feed. The third study revealed a significant effect of the additive on the feed to gain ratio in pigs for fattening at 20,000 BXU/kg feed (analysed content). The FEEDAP Panel concluded that the additive has a potential to be efficacious in pigs for fattening as a zootechnical additive at the dose of 20,000 BXU/kg feed.

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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 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 Roal Oy[2] for a modification of the terms of the authorisation of the product ECONASE® XT (endo-1,4-β-xylanase), when used as a feed additive for pigs for fattening (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). 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 28 November 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 ECONASE® XT (endo-1,4-β-xylanase), when used under the newly proposed conditions of use for pigs for fattening (see Section 3).

## 1.2. Additional information

The EFSA Panel on Additives and Products or Substances used in Animal feed (FEEDAP) released two opinions on the safety and efficacy of ECONASE® XT P/L as a feed additive for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding and piglets (weaned) (EFSA, 2008, 2009), which included the assessment of the safety for the consumer, the user and the environment as well as the safety aspects of the genetic modification of the production strain. The FEEDAP Panel adopted a further opinion on the safety and efficacy of ECONASE® XT when used as a feed additive for laying hens, minor poultry species and pigs for fattening (EFSA FEEDAP Panel, 2011a). The additive is currently authorised for use in chickens for fattening or reared for laying, turkeys for fattening or reared for breeding, laying hens, weaned piglets, pigs for fattening and minor poultry species.[3,4] The additive is authorised in pigs for fattening at the dose of 24,000 BXU/kg feed. The applicant has now requested a modification of the conditions of use in pigs for fattening which consists in lowering the minimum recommended dose from 24,000 BXU/kg feed to 16,000 BXU/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 dossier[5] in support of the authorisation request for the use of ECONASE® XT as a feed additive. The technical dossier was prepared following the provisions of Article 13 of Regulation (EC) No 1831/2003, Regulation (EC) No 429/2008[6] and the applicable EFSA guidance documents.

[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, pp. 29–43.
[2] Roal Oy, Tykkimäentie 15, 05200 Rajamäki, Finland.
[3] Commission Regulation (EC) No 902/2009 of 28 September 2009 concerning the authorisation of an enzyme preparation of endo-1,4-ß-xylanase produced by *Trichoderma reesei* (CBS 114044) as a feed additive for weaned piglets, chickens for fattening, chickens reared for laying, turkeys for fattening and turkeys reared for breeding (holder of authorisation Roal Oy). OJ L 256, 29.9.2009. pp. 23–25.
[4] Commission Implementing Regulation (EU) No 1110/2011 of 3 November 2011 concerning the authorisation of an enzyme preparation of endo-1,4-ß-xylanase produced by *Trichoderma reesei* (CBS 114044) as a feed additive for laying hens, minor poultry species and pigs for fattening (holder of authorisation Roal Oy). OJ L 287, 4.11.2011, pp. 27–29.
[5] FEED dossier reference: FAD-2016-0058.
[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, pp. 1–65.

The European Union Reference Laboratory considered that the conclusions and recommendations reached in the previous assessment are valid and applicable for the current application.[7]

## 2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of ECONASE® XT (endo-1,4-β-xylanase) 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) and Technical guidance: Tolerance and efficacy studies in target animals (EFSA FEEDAP Panel, 2011b).

# 3. Assessment

The current assessment deals with the request from the applicant to reduce the authorised minimum recommended dose in pigs for fattening. The additive is intended to be used in diets for pigs for fattening at a minimum dose of 16,000 BXU/kg feed.

## 3.1. Characterisation

ECONASE® XT is an enzyme preparation with endo-1,4-β-xylanase (xylanase) as the main activity. It is available in powder (P) and liquid (L) form ensuring activities of 4,000,000 and 400,000 BXU/g,[8] respectively. The production organism is a genetically modified strain of *Trichoderma reesei* (CBS 114044). The production strain and the final formulations have been described and characterised in previous opinions (EFSA, 2008, 2009).

The applicant has submitted new data on the shelf-life of the two formulations at different temperatures and longer periods of storage than the ones previously reported. The shelf-life was measured in three batches of each formulation.[9] Samples of the solid formulation were stored at 20–23°C in closed containers for 24 months and the enzyme activity recovery after storage was 93%. Other samples were stored at 25 or 30°C in closed or open containers for 12 months. Recovery values were 73% and 63% for closed containers stored at 25 or 30°C, the corresponding values for the open containers were 79% and 68%.

Samples of the liquid formulation were stored at 6, 25 or 30°C for 24 months in closed containers. The mean recovery values were 96%, 95% and 80% for the samples stored at 6, 25 or 30°C.

## 3.2. Safety

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 consumers, for the users and for the environment have been previously assessed (EFSA, 2008, 2009). The Panel concluded that the use of the product as a feed additive raises no concerns for consumer safety or for the environment. Considering the safety for the user, ECONASE® XT P/L is non-irritant to the skin, and the liquid form is non-irritant to the eyes and is not a dermal sensitiser; the additive ECONASE® XT is considered a respiratory sensitiser. The FEEDAP Panel is not aware of any new information that would lead it to reconsider the conclusions drawn previously.

In 2008, the FEEDAP Panel also evaluated a tolerance trial carried out with weaned piglets. Considering the results of that trial and the well-established mode of action of enzymes, the FEEDAP Panel concluded in 2011 that ECONASE® XT is safe for pigs for fattening at the dose of 24,000 BXU/kg feed (EFSA FEEDAP Panel, 2011a). The proposed reduction in the minimum recommended dose would not affect that conclusion.

### 3.2.1. Efficacy

In a previous assessment, the FEEDAP Panel concluded that the additive has the potential to be efficacious at 24,000 BXU/kg feed (EFSA FEEDAP Panel, 2011a). In that assessment, there were two efficacy studies which also showed improvements in the performance of pigs for fattening at 16,000 BXU/kg feed. Now the applicant refers to those two studies and has supplied a new long-term trial.[10]

[7] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0006.pdf
[8] One BXU is the amount of enzyme that produces, under Standard conditions (pH 5.3 and 50°C), one nmol of reducing sugars from birch xylan as xylose in one-second.
[9] Technical dossier/Section II/Annex II.20 and II.21.
[10] Technical dossier/Section IV/Annex IV.2-8 and Supplementary information July 2017 and September 2017.

A total of 820 castrated male and 820 female pigs (hybrid breed, approx. 80-days-old and initial body weight 24 kg) were allocated to pens in groups of 20 or 21 pigs each (gender separated) and distributed to four dietary treatments (20 replicate pens per treatment). The study followed a 2 × 2 × 2 factorial design, with gender (male, female), enzyme supplementation (0 or 16,000 BXU/kg feed) and level of added fat in the diet (animal-vegetal blend, 3% or 6%) as factors. During the study, a total of five phase diets were offered to the pigs according to their nutritional requirements. At each phase, the dietary treatments were obtained from two basal diets differing in the added fat (3% or 6%) based on maize, soybean meal and maize dried distillers grains and were either not supplemented (control) or supplemented with ECONASE® XT at 16,000 BXU/kg feed. The average recovery of enzyme activity in the diets was 20,170 BXU/kg feed (126% the intended dose). Feed (mash form) and water were available *ad libitum* over an experimental period of 105 days (80–185 day of life). Health status and mortality were monitored during the study. Feed intake was measured and body weight was recorded at the beginning and every 3 weeks. Feed to gain ratio was calculated for the overall period (80–185 day of life). An analysis of variance was carried out with the data considering the pen as the statistical unit and the model included the effects of gender, xylanase and added fat as well as their interactions. Differences were considered statistically significant at a level of at least $p < 0.05$.

Mortality was low (< 1.2%) and not different between treatments. The statistical analysis revealed no interactions between the main factors studied. Regarding the effect of the xylanase (Table 1), a significantly better feed to gain ratio was found in pigs fed ECONASE® XT, and no significant differences were found in the feed intake or in the average daily gain between the control and the group receiving the xylanase.

**Table 1:** Effect of ECONASE® XT on the performance of pigs for fattening

| Group | Final body weight (kg) | Feed intake (kg/day) | Average daily gain (kg/day) | Feed to gain ratio |
|---|---|---|---|---|
| Control | 121.8 | 2.18 | 0.93 | 2.34[a] |
| ECONASE® XT | 122.0 | 2.16 | 0.93 | 2.31[b] |

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

In three trials, the pigs fed the xylanase at an intended dose of 16,000 BXU/kg feed showed improvements on their performance, body weight gain in two trials and feed to gain ratio in a third study. These improvements were seen at the intended dose of 16,000 BXU/kg feed. However, the analysed dose in the trial submitted in the present dossier was 20,000 BXU/kg feed and, therefore, the Panel concludes that the additive has a potential to be efficacious as a zootechnical additive in pigs for fattening at 20,000 BXU/kg feed.

### 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 Regulation[11] and Good Manufacturing Practice.

## 4. Conclusions

The use of the additive under the new proposed conditions of use is safe for pigs for fattening and raises no concerns for consumer safety or for the environment. ECONASE® XT P/L is non-irritant to the skin, and the liquid form is non-irritant to the eyes and is not a dermal sensitiser, however it is considered a respiratory sensitiser.

The additive has a potential to be efficacious in pigs for fattening at a dose of 20,000 BXU/kg feed.

## Documentation provided to EFSA

1) ECONASE® XT for pigs for fattening. October 2016. Submitted by Roal Oy.
2) ECONASE® XT for pigs for fattening. Supplementary information. July 2017. Submitted by Roal Oy.

[11] 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.

3) ECONASE® XT for pigs for fattening. Supplementary information. September 2017. Submitted by Roal Oy.

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EFSA (European Food Safety Authority), 2008. Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) and of the Panel on Genetically Modified Organisms (GMO) on the safety and efficacy of Econase XT P/L as feed additive for chickens for fattening, chickens reared for laying, turkeys for fattening, turkeys reared for breeding and piglets (weaned). EFSA Journal 2008;6(6):712, 19 pp. https://doi.org/10.2903/j.efsa.2008.712

EFSA (European Food Safety Authority), 2009. Scientific Opinion of the Panel on Genetically Modified Organisms on a request from the European Commission related to the enzyme preparation of trade name 'Econase XT P/L (endo-1,4 ß-xylanase) as a feed additive for chickens and turkeys for fattening, chickens reared for laying, turkeys reared for breeding and piglets (weaned). EFSA Journal 2009;7(4):1058, 6 pp. https://doi.org/10.2903/j.efsa.2009.1058

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2011a. 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), 2011b. Scientific Opinion on the safety and efficacy of Econase XT P/L (endo-1,4-ß-xylanase) as a feed additive for laying hens, minor poultry species (including ducks, geese, quails, pheasants and pigeons) and pigs for fattening. EFSA Journal 2011;9(6):2277, 15 pp. https://doi.org/10.2903/j.efsa.2011.2277

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

## Abbreviation

FEEDAP EFSA Panel on Additives and Products or Substances used in Animal Feed