European Food Safety Authority

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SCIENTIFIC OPINION

Safety of Mintrex®Zn (Zinc chelate of hydroxy analogue of methionine) as feed additive for chickens for fattening[1]

Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed

(Question No EFSA-Q-2008-424)

Adopted on 2 April 2009

PANEL MEMBERS

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SUMMARY

Following a request from the European Commission, the European Food Safety Authority (EFSA) was asked to consider additional data provided by the applicant subsequent to its former opinion on the efficacy and safety of Mintrex®Zn for all animal species.

The Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) assessed the supplementary information supplied by the applicant on the safety of Mintrex®Zn for chickens for fattening. A tolerance study was provided.

Due to the experimental design, it was difficult to attribute the findings to higher dietary zinc, either from Mintrex®Zn or sulphate, because potential interactions of high levels of zinc, copper and manganese given together could not fully be excluded.

Considering the maximum authorised content (150 mg Zn kg^{-1} complete feed for food-producing animals, except fish), a margin of safety for zinc from Mintrex®Zn could not be calculated.

Zinc from Mintrex®Zn was tested under the same conditions as the authorised zinc source (zinc sulfate). No evidence was seen that an overdose of zinc from Mintrex®Zn could exert additional or different adverse effects than those observed for zinc from sulfate.

[1] For citation purposes: Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on a request from the European Commission on the safety of Mintrex®Zn (Zinc chelate of hydroxy analogue of methionine) as feed additive for chickens for fattening. *The EFSA Journal* (2009) 1042, 1-8

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Therefore, the FEEDAP Panel concludes that zinc from Mintrex®Zn is as safe as the inorganic sources of Zn for chickens for fattening when supplemented up to the authorised maximum total dietary Zn. This conclusion cannot be extended to other poultry categories or to other species because of the limitations of the experimental design.

Key words: nutritional additive, trace element, Mintrex®Zn, zinc, chelate, hydroxy analogue of methionine, safety, chickens for fattening

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BACKGROUND AS PROVIDED BY EC

Regulation (EC) No 1831/2003[2] establishes rules governing the Community authorisation of additives for animal nutrition and in particular, Article 9 defines the terms of the authorisation by the Commission.

The company Novus Europe S.A[3] is seeking Community authorisation of its product, Zinc chelate of hydroxy analogue of methionine, as nutritional additive for chickens for fattening (Table 1).

Table 1. Description of the substance:

Category of additive	Nutritional additive
Functional group of additive	compounds of trace elements
Trade name	Mintrex®Zn
Description	Zinc chelate of hydroxy analogue of methionine
Target animal category	Chickens for fattening
Applicant	Novus Europe S.A.
Type of request	Update opinion

On 16th April 2008, the Scientific Panel on Additives and Products or Substances used in Animal Feed of the European Food Safety authority adopted an opinion on the efficacy and safety of Mintrex®Zn (Zinc chelate of hydroxyl analogue of methionine) as feed additive for all species (Question No EFSA-Q-2007-098). It was concluded that there were not enough data to demonstrate the safety of the product for the target animals.

Therefore, the Commission gave the possibility to the company to submit complementary information to complete the assessment.[4]

The Commission has now received supplementary dossier from the applicant, Novus Europe S.A., with information on this substance on the safety for chickens for fattening as target species. The data generated by the company and compiled in the above mentioned supplementary dossier have been sent directly to the Authority.

TERMS OF REFERENCE AS PROVIDED BY EC

In view of the above, the Commission asks to the European Food Safety Authority to deliver an opinion on the safety of this product as nutritional additive for chickens for fattening taking into account its earlier opinion on 16th April 2008 and the supplementary information submitted.

[2] OJ L 268, 18.10.2003, p. 29
[3] Novus Eurpe S.A. Avenue Marcel Thiry 200, 1200 Brussels, Belgium
[4] Dossier reference: FAD-2008-0036

ACKNOWLEDGEMENTS

The European Food Safety Authority wishes to thank the members of the Working Group on Trace Elements for the preparation of this opinion.

ASSESSMENT

1. Introduction

Mintrex®Zn is a chelate containing a minimum of 16 % zinc and 80 % hydroxy analogue of methionine ((2-hydroxy-4-methylthio)butanoic acid, HMTBa), according to the specifications provided by the applicant, intended to be used in chickens for fattening as source of Zn up to the maximum authorised content (150 mg kg^{-1} complete feed).

The FEEDAP Panel previously adopted an opinion on the efficacy and safety of Mintrex®Zn as feed additive for all species (EFSA, 2008). Due to the lack of specific experimental data on animal tolerance to a potential overdose of the additive under assessment, the Panel could not conclude on the safety of the product for the target species.

In response to the FEEDAP Panel's opinion on Mintrex®Zn, the applicant supplied further data on the safety of Mintrex®Zn for chickens for fattening. Consequently, in the current opinion the FEEDAP Panel considered only the safety of Zn from Mintrex®Zn for this target species.

2. Safety of Zn from Mintrex®Zn for chickens for fattening

According to the most recent data (NRC, 2005), the maximum tolerable level of dietary zinc is 500 mg Zn kg^{-1} for poultry feed.

The applicant provided a tolerance study carried out with Mintrex®Zn on chickens for fattening reared according to EU farming conditions. The trial was conducted on 800 chickens for fattening (Ross 308 Broilers) divided into four treatments with ten replicates per treatment (five male and five female replicates) consisting of 20 birds each. Four groups were fed diets supplemented with 50 mg Zn kg^{-1} feed (dose recommended by the applicant) or 450 mg Zn kg^{-1} feed (threefold the total maximum EU authorised level) in the form of zinc sulphate or Mintrex®Zn. All diets were simultaneously enriched also with copper and manganese from sulphate salt sources, which resulted in different final levels of Cu and Mn in the diets of the various treatments (Table 2). The final contents of trace elements in the diets were confirmed by analysis.

Birds were phase fed, starter (0-21 days) and finisher (21-35 days) diets. Diets were nutritionally adjusted for total methionine to account for the hydroxy analogue of methionine from Mintrex®Zn. In diets with no or lower addition of Mintrex®Zn, the calcium salt of hydroxy analogue of methionine was used to balance the hydroxy analogue of methionine. Feed was fed as mash; feed and water were available *ad libitum*. All diets were fully analysed for crude nutrients, minerals and trace elements.

Birds performance was monitored over the entire experimental period; at the end of the experiment, blood was sampled from ten birds per treatment (one bird/pen) for routine haematology (haematocrit, haemoglobin, MCH, MCV, counts of red and white blood cells) and blood biochemistry (serum ALT, AST, AP, CK, GGT, amylase, total protein, albumin, globulin, cholesterol, glucose, creatinine, and electrolytes (Na, K, Cl, Ca, P and Mg)). Clinical observations were done throughout the whole trial. Gross pathology examination was limited to cases of unexplained death.

Due to the experimental design, it was difficult to attribute the findings to higher dietary zinc, either from Mintrex®Zn or sulphate, because potential interactions of high levels of zinc, copper and manganese given together could not fully be excluded.

Considering this caveat, zinc supplementation from both sources reduced significantly final body weight compared to the respective controls (Table 2). However, body weight in the high-dose Mintrex®Zn group was significantly higher than that of the high-dose zinc sulphate group, indicating a better tolerance of chickens for fattening to Zn from Mintrex®Zn than from zinc sulphate.

Parameters of health status (mortality – which was overall low (3 %), haematology, blood biochemistry) did not show significant treatment-related differences between the groups. However, endpoints particularly sensitive to zinc toxicity (pancreatic function and morphology) have not been studied.

Table 2. **Experimental design and results of the tolerance study on chickens for fattening**

	Supplemental levels of zinc (mg kg^{-1} complete feed)			
	Zinc sulphate		**Mintrex®Zn**	
Supplemental Zn	50	450	50	450
Analysed **Zn** (mg kg^{-1} feed), starter/finisher*	60/59	510/454	58/67	437/451
Supplemental Cu from copper sulfate (mg kg^{-1} feed)	8	25	8	25
Analysed **Cu** (mg kg^{-1} feed), starter/finisher*	11/8	35/26	13/10	38/31
Supplemental Mn from manganese sulfate (mg kg^{-1} feed)	60	150	60	150
Analysed **Mn** (mg kg^{-1} feed), starter/finisher*	75/80	185/166	76/96	127/150
Body weight (g)	1875^{ab}	1750^{c}	1900^{a}	1832^{b}
Body weight gain (g bird^{-1} day^{-1})	52^{ab}	49^{c}	53^{a}	51^{b}
Feed intake (g bird^{-1} day^{-1})	79^{a}	74^{b}	79^{a}	78^{a}
Feed to gain ratio (g g^{-1})	1.52	1.52	1.49	1.52

$^{a, b, c}$: Means with different letters in superscripts within a row differ significantly ($P < 0.05$)
*: Original data as mg kg^{-1} DM, recalculated to standard complete feed (88 % DM)

CONCLUSIONS

The data from the tolerance study do not allow confirming the maximum tolerable level of Zn from either Mintrex®Zn or sulphate. Consequently, considering the maximum authorised content (150 mg Zn kg^{-1} complete feed for food-producing animals, except fish), a margin of safety for Zn from Mintrex®Zn could not be calculated.

Zn from Mintrex®Zn was tested under the same conditions as the authorised zinc source (zinc sulphate). No evidence was seen that an overdose of Zn from Mintrex®Zn could exert additional or different adverse effects than those observed for Zn from sulphate.

Therefore, the FEEDAP Panel concludes that zinc from Mintrex®Zn is as safe as the inorganic sources of Zn for chickens for fattening when supplemented up to the authorised

maximum total dietary zinc. This conclusion cannot be extended to other poultry categories or to other species because of the limitations of the experimental design.

DOCUMENTATION PROVIDED TO EFSA

1. Supplementary information on the product Mintrex®Zn. February 2009. Submitted by Novus Europe S.A.

REFERENCES

EFSA (European Food Safety Authority), 2008. Scientific opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on the safety and efficacy of Mintrex®Zn (Zinc chelate of hydroxy analogue of methionine) as feed additive for all species. http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178706516708.htm

NRC (National Research Council). 2005. Mineral Tolerance of Animals: Second Revised Edition.