SCIENTIFIC OPINION

# Scientific Opinion on the safety of a zinc chelate of hydroxy analogue of methionine (Mintrex®Zn) as feed additive for all species[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

## 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 for the target animals and consumers.

Tolerance studies in piglets, laying hens and calves for rearing were submitted. Piglets showed the same degree of intolerance to Mintrex®Zn when supplied at the same overdose level as the authorised zinc sulfate. In laying hens, there is sufficient evidence to conclude that zootechnical parameters were unaffected by the zinc (Zn) supplementation and source at three times the maximum level authorised in the EU; the small differences observed in haematology and blood biochemistry between Zn levels and source were considered being of limited relevance. In calves for rearing there was no reason to consider Mintrex®Zn unsafe compared to zinc sulfate.

The FEEDAP Panel concluded that the use of Mintrex®Zn up to the maximum authorised Zn content in feed would not pose a greater safety concern for the target species studied than the authorised inorganic Zn sources. Taking also into account the already assessed safety of Mintrex®Zn for chickens for fattening, the FEEDAP Panel concludes that Mintrex®Zn is safe for all species up to the maximum authorised Zn content in feed.

Tissue/products Zn deposition data were submitted for piglets (muscle, liver, kidney, skin/fat), laying hens (eggs) and dairy cows (milk). There was no indication that Mintrex®Zn would lead to any higher Zn concentration in tissues/products compared to inorganic Zn. Consequently, differences in Zn exposure of the consumer due to the use of Mintrex®Zn are not expected. The FEEDAP Panel concluded that no specific concerns for consumer safety would arise from the use of Mintrex®Zn in feed for all species.

[1] On request from the European Commission, Question No EFSA-Q-2009-00667, adopted on 11 November 2009.

[2] Panel members: Gabriele Aquilina, Georges Bories, Paul Brantom, Francesca Caloni, Andrew Chesson, Pier Sandro Cocconcelli, Joop de Knecht, Noël Albert Dierick, Mikolaj Antoni Gralak, Jürgen Gropp, Ingrid Halle, Nils-Gunnar Ilbäck, Reinhard Kroker, Lubomir Leng, Sven Lindgren, Anne-Katrine Lundebye Haldorsen, Alberto Mantovani, Miklós Mézes, Derek Renshaw and Maria Saarela. Correspondence: FEEDAP@efsa.europa.eu

[3] Acknowledgement: The European Food Safety Authority wishes to thank the members of the Working Group on Trace Elements including Bogdan Debski, Christer Hogstrand and Carlo Nebbia for the preparation of this opinion.

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**KEY WORDS**

Nutritional additive, trace element, zinc, chelate, hydroxy methionine analogue, tissue deposition, safety

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## BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Regulation (EC) No 1831/2003[4] establishes rules governing the Community authorisation of additives for use in animal nutrition and in particular, Article 9 defines the terms of the authorisation by the Commission.

The company Novus Europe S.A.[5] is seeking Community authorisation of its product, Zinc chelate of hydroxy analogue of methionine, as nutritional additive for all species.

On 16th April 2008, the Scientific Panel on Additives and Products or Substances used in Animal Feed of the European Food Safety Authority (FEEDAP) adopted an opinion on the efficacy and safety of Mintrex®Zn (Zinc chelate of hydroxy 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 animals and
- on the zinc deposition in other edible tissues and products than liver from chickens and milk from dairy cows fed with the product.

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

The Commission has now received a supplementary report from the applicant, Novus Europe S.A., for this nutritional additive on the safety for the most sensitive animal species and the impact on zinc exposure to the consumer once the product is incorporated in diets for all species.[6]

## TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In view of the above, the Commission asks to the European Food Safety Authority to deliver an opinion on the safety for the target animals and consumers of this product as nutritional additive for all species taking into account its earlier opinions on 16th April 2008 and 2nd April 2009, and the new dossier received as specified in the Background.

[4] OJ L 268, 18.10.2003, p.29
[5] Novus Europe S.A. Avenue Marcel Thiry 200. 1200 Brussels, Belgium
[6] EFSA Dossier reference: FAD-2009-0021

# ASSESSMENT

## 1. Introduction

Mintrex®Zn is a chelate containing by weight a minimum of 16 % zinc (Zn) and 80 % hydroxy analogue of methionine ((2-hydroxy-4-methylthio)butanoic acid), according to the specifications provided by the applicant. Mintrex®Zn is intended to supply Zn in final feed within EU legal limits for all species (total maximum content: 150 mg/kg complete feed, except for the following: milk replacer: 200 mg/kg; fish: 200 mg/kg complete feed; pet animals: 250 mg/kg complete feed). Currently, the Zn chelate of hydroxy analogue of methionine is authorised in the EU as a feed additive for chickens for fattening.[7]

The FEEDAP Panel previously adopted an opinion on the efficacy and safety of Mintrex®Zn as feed additive for all species (EFSA, 2008). With regard to the safety for the target species, the FEEDAP Panel could not make any assessment because of lack of data. Based on current knowledge and the limited data submitted by the applicant, the FEEDAP Panel concluded that the use of Mintrex®Zn would be unlikely to affect consumer exposure different to authorised inorganic Zn sources.

In response to the FEEDAP Panel's opinion on Mintrex®Zn (EFSA, 2008), the applicant supplied data to assess the safety of this product for chickens for fattening. EFSA delivered an opinion in which it was concluded that the additive is safe for chickens for fattening (EFSA, 2009). Later on the applicant has supplied additional data to assess the safety for target species other than chickens for fattening, and the safety for consumer of Mintrex®Zn when used as a feed additive for all species.

## 2. Safety for the target animals

In its previous opinion on the same product, the FEEDAP Panel concluded that Mintrex®Zn is safe for chickens for fattening (EFSA, 2009). In the current dossier, the applicant has provided data on the safety of the product for piglets, laying hens and calves for rearing.

### 2.1. Tolerance study with piglets

A 42-day tolerance study with different Mintrex products was carried out on a total of 720 crossbreed (Large white male line x Landrace*Large white, sex ratio 1:1) piglets.[8] Piglets of 26 days (initial weight: 7.4 kg) were allocated to nine treatments with eight replicates per treatment (ten piglets per replicate). Common basal diets (a pre-started feed during the first two weeks and a starter feed for the subsequent four weeks) were supplemented with Zn, Cu and Mn from sulfate and Mintrex at different levels. All diets were adjusted to the same content of the hydroxy analogue of methionine (MHA) as provided by 0.346 % Mintrex®Mn (equivalent to 450 mg Mn/kg and 0.313 % MHA feed supplement) by addition of the calcium salt of MHA.

For the purpose of the dossier provided, the applicant extracted five groups and applied a separate statistical evaluation (ANOVA) on this part of the experiment, expressing all experimental parameters as least square corrected means. The treatments were: a control feed supplemented with Zn, Cu and Mn at NRC requirement levels (T1); a second control group supplemented with Zn, Cu and Mn from sulfate at maximum authorised levels (T2); a Mintrex®Zn group equivalent to T2, in which zinc sulfate was replaced by Mintrex®Zn (T3); an overdose group supplemented with Zn and Mn (three times the level of T2) and Cu (twice the level in T2) from sulfate (T4); and a group corresponding to T4, in which zinc sulfate was replaced by Mintrex®Zn (T5). The dietary content of all three trace elements supplemented was analysed.

Performance parameters (mortality, body weight, weight gain, feed intake, feed/gain) were recorded. Haematological (RBC, Hb, PCV, MCV, MCH, MCHC, WBC, platelet count, mean platelet volume)

[7] Commission Regulation (EC) No 888/2009. OJ L 254, 26.9.2009, p.71
[8] Technical Dossier, Annex III.1.1.

and blood biochemical (total protein, albumin, γ-GT, AST, ALT and urea) parameters were measured (n=8 per treatment, one piglet per replicate).

Table 1 gives an overview on the experimental design and summarises the zootechnical parameters as well as the other endpoints showing significant differences.

**Table 1:** Tolerance study in piglets with Mintrex®Zn (42 days)

| Group | T1[1] | T2[2] | T3[2] | T4[3] | T5[3] |
|---|---|---|---|---|---|
| Zn source | Sulfate | Sulfate | Mintrex®Zn | Sulfate | Mintrex®Zn |
| Zn supplementation (mg/kg)* | 100/80 | 150 | 150 | 450 | 450 |
| Zn analysed (mg/kg)* | 194/119 | 195/180 | 192/184 | 454/398 | 503/435 |
| Cu analysed (mg/kg)* | 15/11 | 149/145 | 159/144 | 319/271 | 321/300 |
| Mn analysed (mg/kg)* | 34/39 | 159/162 | 165/163 | 416/417 | 466/427 |
| Mortality (n out of 80) | 4 | 3 | 6 | 6 | 7 |
| Daily weight gain (g) | $346^{a}$ | $346^{a}$ | $349^{a}$ | $295^{b}$ | $277^{b}$ |
| Daily feed intake (g) | $534^{a}$ | $510^{a}$ | $521^{a}$ | $451^{b}$ | $405^{c}$ |
| Feed/gain ratio | 1.54 | 1.48 | 1.50 | 1.54 | 1.48 |
| Haemoglobin (g/dl) | $10.60^{a}$ | $8.16^{bc}$ | $8.98^{b}$ | $7.66^{c}$ | $7.73^{c}$ |
| Packed cell volume (%) | $28.80^{a}$ | $23.47^{bc}$ | $25.54^{b}$ | $21.48^{c}$ | $21.53^{c}$ |
| Mean corpuscular Hb (pg) | $15.3^{a}$ | $13.0^{b}$ | $12.3^{bc}$ | $11.4^{cd}$ | $11.0^{d}$ |
| Plasma total protein (g/dL) | $5.75^{b}$ | $5.81^{b}$ | $6.12^{ab}$ | $6.36^{a}$ | $6.26^{ab}$ |
| Plasma albumin (g/dL) | $2.63^{b}$ | $3.03^{a}$ | $2.95^{a}$ | $3.02^{a}$ | $3.16^{a}$ |
| Serum urea (mg/dL) | $18.4^{ab}$ | $14.6^{b}$ | $18.7^{ab}$ | $20.6^{ab}$ | $21.7^{a}$ |

* Pre-starter/starter feed

1: Supplemented also with 6/5 mg Cu and 4/3 mg Mn/kg pre-starter/starter feed from sulfates

2: Supplemented also with 170 mg Cu and 150 mg Mn/kg feed from sulfates

3: Supplemented also with 340 mg Cu and 450 mg Mn/kg feed from sulfates

a, b, c, d: Different letter superscripts in the same row indicate significant differences ($P < 0.05$).

The design of the experiment, namely the high doses of Cu and Mn in the Zn overdose groups (T4 and T5), does not allow assessing the influence of high Zn levels as the only experimental variable and particularly that of the overdosed Mintrex®Zn. The only correct comparisons that could be done are those between T2 and T3 and between T4 and T5. The high level of supplemental Cu (170 mg/kg in T2/T3 and 340 mg in T4/T5) would have required an adjustment of dietary iron (Fe). However, Fe was supplemented to all diets at the same level (100 mg/kg) and from a poorly available source (Fe-carbonate). It should be also noted that, according to the analysed values, the supplementation rate of Zn in the intermediate dose groups T2/T3 exceeded the maximum content set for the total dietary content by EU legislation (150 mg/kg).

Mortality/culls was not significantly affected by the treatments; results of necropsies were not reported. However, daily weight gain and feed intake were depressed in the overdose groups (T4 and T5). Differences in these parameters between the sulfate and the Mintrex®Zn groups were not observed except a lower feed intake in the Mintrex®Zn overdose group (T5) compared to the sulfate overdose group (T4).

Haemoglobin and mean corpuscular haemoglobin showed the highest values in the control group (T1) (with a low supplementation level of Zn, Cu and Mn) and the lowest values in the overdose groups (T4 and T5). This may be related to the low and constant supplementation rate of Fe, in combination with high Zn and Cu supplementation. Zinc and Cu are known to interact with Fe metabolism. Within the overdose groups, no differences were seen between Zn from sulfate and from Mintrex®Zn. It should be noted that the above haematological parameters declined during the study in all experimental groups.

Plasma total protein and urea showed a tendency to increase with increasing Zn levels (T2/T3 compared to T4/T5). Differences between the two Zn sources did not occur.

## 2.2. Tolerance study with laying hens

An 8-week tolerance study with different Mintrex products was carried out with a total of 392 laying hens (commercial brown Hy-Line layers, initial body weight 1940 g).[9] The hens were allocated to 14 treatments with seven replicates per treatment (four birds per replicate). A common basal diet was supplemented with Zn, Cu and Mn from sulfate and Mintrex at different levels. All diets were adjusted to the same content of the MHA as provided by 0.346 % Mintrex®Mn (equivalent to 450 mg Mn/kg and 0.313 % MHA feed supplement) by addition of the calcium salt of MHA.

For the purpose of the dossier provided, the applicant extracted six groups and applied a separate statistical evaluation (ANOVA) on this part of the experiment, expressing all experimental parameters as least square corrected means. The treatments were: two low Zn diets (35 mg supplemental Zn/kg either from sulfate (T1) or from Mintrex®Zn (T2)), two intermediate Zn diets (150 mg supplemental Zn/kg either from sulfate (T3) or from Mintrex®Zn (T4)), and two Zn overdose diets (450 mg supplemental Zn/kg either from sulfate (T5) or from Mintrex®Zn (T6)). The low Zn diets were also supplemented with 6 mg Cu and 25 mg Mn/kg from sulfates, the intermediate and the overdose Zn diets with 25 mg Cu and 150 mg Mn/kg. The data for the analytical contents of Zn, Cu and Mn were provided.

Performance parameters (mortality, body weight, weight gain, feed intake), egg production (egg weight, egg numbers, egg mass, egg mass/feed ratio), egg quality (yolk colour, egg-shell thickness) were recorded. Haematological (PCV, RBC, Hb, MCV, MCH, MCHC, WBC, heterophils, lymphocytes and monocytes) and blood biochemical (ALT, AST, APT, γ-GT, albumin, globulins, glucose and total protein) parameters were measured (n=10 per treatment) only for the groups with the low Zn-supply (T1 and T2) and the overdose groups (T5 and T6). Table 2 gives an overview on the experimental design and summarizes the zootechnical parameters.

**Table 2:** Tolerance study in laying hens with Mintrex®Zn (56 days). Zootechnical parameters

| Group | T1 | T2 | T3 | T4 | T5 | T6 |
|---|---|---|---|---|---|---|
| Zn source | Sulfate | Mintrex®Zn | Sulfate | Mintrex®Zn | Sulfate | Mintrex®Zn |
| Zn supplementation (mg/kg) | 35 | 35 | 150 | 150 | 450 | 450 |
| Zn analysed (mg/kg) | 82 | 101 | 186 | 197 | 256 | 504 |
| Cu analysed (mg/kg) | 11 | 14 | 36 | 24 | 31 | 39 |
| Mn analysed (mg/kg) | 69 | 62 | 145 | 164 | 160 | 164 |
| Daily feed intake (g) | 127 | 126 | 127 | 127 | 126 | 126 |
| Laying rate (%) | 94.1 | 92.4 | 94.9 | 95.2 | 94.7 | 92.9 |
| Egg weight (g) | 62.5 | 64.0 | 62.1 | 64.4 | 63.4 | 64.4 |
| Daily egg mass (g/bird) | 58.8[a] | 59.1[ab] | 58.9[a] | 61.3[b] | 60.1[ab] | 59.8[ab] |
| Egg mass/feed ratio (g/g) | 0.464 | 0.471 | 0.465 | 0.484 | 0.476 | 0.476 |

a, b: Different letter superscripts in the same row indicate significant differences (P < 0.05)

No health problems were observed, no mortality occurred. The hens increased their weight during the study by about 195 g. Feed intake, laying rate, egg weight and egg mass/feed ratio did not show significant differences between the treatments. Differences in the daily egg mass were small, but significant in favour of 150 mg Zn from Mintrex®Zn compared to 150 mg Zn from sulfate. No differences were observed in egg quality parameters (egg shell thickness, soft shells, cracked shells, yolk colour).

9 Technical Dossier, Annex III.1.2.

The interpretation of the findings is hampered by the facts that (i) the intended Zn content in the overdose group T5 was not confirmed by analysis (256 instead of intended >450 mg/kg feed), and (ii) the hens of the intermediate Zn groups were not examined for haematology and blood biochemistry.

RBC and PCV were not affected by Zn level and source. The other parameters showed significant differences, the most severe were observed in the Zn overdose sulfate group (T5). Zinc overdose decreased WBC and heterophiles, consistent with known effects of Zn toxicity (Stefanidou et al., 2006. Table 3 summarises the main blood biochemical parameters.

**Table 3:** Tolerance study in laying hens with Mintrex®Zn (56 days). Key blood biochemical parameters

| Group | T1 | T2 | T5 | T6 |
|---|---|---|---|---|
| Zn source | Sulfate | Mintrex®Zn | Sulfate | Mintrex®Zn |
| Zn supplementation (mg/kg) | 35 | 35 | 450 | 450 |
| Zn analysed (mg/kg) | 82 | 79 | 256 | 504 |
| Cu analysed (mg/kg) | 11 | 14 | 31 | 39 |
| Mn analysed (mg/kg) | 69 | 62 | 160 | 164 |
| AST (IU/L) | 188.6$^{b}$ | 186.5$^{b}$ | 160.0$^{a}$ | 163.2$^{ab}$ |
| APT (IU/L) | 410$^{a}$ | 550$^{a}$ | 1024$^{b}$ | 744$^{ab}$ |
| Blood glucose (mmol/L) | 12.99$^{b}$ | 12.92$^{b}$ | 12.58$^{b}$ | 11.56$^{a}$ |
| Plasma albumin (g/L) | 19.8$^{a}$ | 20.9$^{a}$ | 23.6$^{b}$ | 19.9$^{a}$ |
| Plasma total protein (g/L) | 50.5$^{a}$ | 54.2$^{a}$ | 49.8$^{a}$ | 62.3$^{b}$ |

a, b, c: Different letter superscripts in the same row indicate significant differences ($P < 0.05$)

Blood glucose was lower, and both plasma albumin and total protein higher in the Mintrex overdose group (T6) than in the zinc sulfate overdose group (T5) as well as in both controls (T1 and T2). The relevance of these significant differences as regards to a potential lower tolerance of laying hens for Zn from Mintrex is limited, because all these values are within a physiological range. No significant differences in other measured biochemistry parameters appeared between zinc sulfate and Mintrex®Zn overdose groups.

## 2.3. Tolerance study with calves for rearing

A 57-day tolerance study with different Mintrex products was carried out on a total of 60 male Holstein calves for rearing.[10] After a 11 day pre-period the calves of an age of about 50 days (initial weight about 54 kg) were allocated to ten treatments with six calves per treatment. Common basal diets (a milk replacer fed at a restricted level (2 x 250 g/day) and a wheat, oat, soybean meal, corn based starter) were supplemented with Zn, Cu and Mn from sulfate and Mintrex at different levels. All diets were adjusted to the same content of the MHA as provided by 0.346 % Mintrex®Mn (equivalent to 450 mg Mn/kg and 0.313 % MHA feed supplement) by addition of the calcium salt of MHA.

For the purpose of the dossier provided, the applicant extracted four groups and applied a separate statistical evaluation (ANOVA) on this part of the experiment, expressing all experimental parameters as least square corrected means. The treatments were: a control feed supplemented with 30 mg Zn, 10 mg Cu and 40 mg Mn/kg as sulfates (NRC requirement levels, T1); a high Zn control group supplemented with 150 mg Zn/kg from Mintrex, 15 mg Cu and 150 mg Mn from sulfate (T2); a Zn sulfate overdose (T3), and a Zn Mintrex overdose group (T4), both diets supplemented with 450 mg Zn, 15 mg Cu and 150 mg Mn/kg. The contents of Zn, Cu and Mn in the diets and the unsupplemented basal diet were analysed.

Feed intake was registered daily; body weight at days 0, 30 and 57. At the end of the trials, haematology (RBC, PCV, Hb, MCV, MCH, MCHC, WBC, neutrophils, lymphocytes, monocytes,

[10] Technical Dossier, Annex III.1.3.

eosinophils, basophils and platelets) and blood biochemistry (ALT, AST, γ-GT, total serum protein, albumin, glucose and urea) were performed.

The health status of the calves was monitored daily. One calf in the Mintrex®Zn overdose group (T4) died because of bloat. Four calves of the control group (T1) and two calves of the high Mintrex®Zn group (T2) were treated against respiratory disease. The study design and the results for the zootechnical parameters are given in Table 4.

**Table 4:** Tolerance study in calves for rearing with Mintrex®Zn (57 days)

| Group | T1 | T2 | T3 | T4 |
|---|---|---|---|---|
| Zn source | Sulfate | Mintrex®Zn | Sulfate | Mintrex®Zn |
| Zn supplementation (mg/kg) | 30 | 150 | 450 | 450 |
| Zn analysed (mg/kg)* | 70/89 | 175/235 | 496/552 | 518/534 |
| Cu analysed (mg/kg)* | 11.5/18.2 | 10.4/25.1 | 15.6/21.6 | 10.4/23.9 |
| Mn analysed (mg/kg)* | 43/89 | 169/232 | 174/239 | 183/236 |
| Body weight (kg) | 105.9 | 98.7 | 103.9 | 103.2 |
| Body weight gain (kg/day) | 0.91 | 0.78 | 0.87 | 0.86 |
| Total feed intake (kg DM)** | 100.9 | 99.8 | 102.1 | 97.8 |
| Feed : gain (kg DM/kg BW) | 1.96 | 2.04 | 2.27 | 2.00 |

* Milk replacer/starter feed **Milk replacer plus starter feed during the whole experimental period.
Background levels: Milk replacer: 28 mg Zn, 0.8 mg Cu, 3 mg Mn; Starter: 46 mg Zn, 6.8 mg Cu, 36 mg Mn/kg

No significant differences were observed concerning the zootechnical (Table 4), haematological or biochemical parameters. However, the FEEDAP Panel notes that the study design only allows a comparison between the two Zn sources at the overdose supplementation levels of 450 mg/kg complete feed. Moreover, the statistical power of the study was low since only six animals were allocated to each treatment.

## 2.4. Conclusions on the safety for the target species

For compounds of trace elements already authorised, tolerance studies are not required (Regulation (EC) No 429/2008). A safety assessment of novel compounds of trace elements for target species can therefore be limited to a comparison of the effects of the novel compound with a compound of trace elements already authorised at different supplementation levels.

All three tolerance studies are not conducted in full accordance with the guidelines of the above Regulation. The maximum authorised content in diets was permanently exceeded in the high Zn groups, and did not consider commonly accepted scientific principles required for a proper evaluation of the study variable. The following conclusions on the safety of Mintrex®Zn for target species must take into account these sources of uncertainties.

In piglets, some adverse effects of Zn overdose at 450 mg/kg were observed, but these were not different between the two Zn sources. It is concluded that piglets fed Mintrex®Zn show a comparable degree of intolerance as the authorised zinc sulfate.

In laying hens, there is sufficient evidence to conclude that zootechnical parameters are unaffected by the Zn supplementation and source at three times the maximum level authorised in the EU. Small differences observed in haematology and blood biochemistry between Zn levels and source are considered of limited relevance.

In calves, only limited conclusions can be drawn due to the limitation of the experimental design. However, there was no indication, particularly at the Zn overdose, which would suggest that Mintrex®Zn is any less safe for calves for rearing compared to zinc sulfate.

The FEEDAP Panel concludes that the use of Mintrex®Zn up to the maximum authorised Zn content in feed would not pose a greater safety concern for target species studied than the authorised zinc sulfate. Taking also into account the already assessed safety of Mintrex®Zn for chickens for fattening (EFSA, 2009), the FEEDAP Panel concludes that Mintrex®Zn is safe for all species up to the maximum Zn content authorised in feed.

## 3. Safety for the consumer

### 3.1. Tissue/products deposition

The effect of dietary treatment on tissue Zn deposition was derived from the studies on tolerance, plus a dedicated study on Zn transfer into milk.

#### 3.1.1. Piglets

At the end of the tolerance study (see section 2.1) six piglets per treatment (T1, T2 and T3) were slaughtered. Zinc concentration in muscle, liver, kidney, skin/fat and bone was determined. The relevant data are summarised in Table 5.

The use of Mintrex®Zn did not result in significantly higher tissue concentration than zinc sulfate at the same dietary level (150 mg/kg).

**Table 5:** Zinc deposition in piglet tissues (mg/kg wet tissue) at 68 days of age (42 days of treatment with zinc sulfate or Mintrex®Zn)

| Group | T1 | T2 | T3 |
|---|---|---|---|
| Zn source | Zinc sulfate | Zinc sulfate | Mintrex®Zn |
| Zn supplementation (mg/kg)* | 100/80 | 150/150 | 150/150 |
| Analysed Zn (mg/kg)* | 194/119 | 195/180 | 192/184 |
| Muscle | 11.8 | 12.1 | 12.4 |
| Liver | 46.8 | 53.1 | 58.0 |
| Kidney | 20.6 | 19.7 | 18.8 |
| Skin/fat | 10.0 | 12.4 | 15.3 |

* Pre-starter/starter feed

#### 3.1.2. Laying hens

The eggs from hens fed low and intermediate Zn doses from sulfate and Mintrex®Zn (tolerance study with laying hens, section 2.2, groups T1, T2, T3 and T4) and collected in week 8, were examined for Zn content.

Different doses or sources of Zn supplemented to diets of laying hens did not result in any significant difference in whole egg Zn content (10.3, 10.8, 11.7 and 10.4 mg Zn/kg for T1, T2, T3 and T4 respectively).

#### 3.1.3. Dairy cows

A 60-day study was carried out with 40 Holstein cows divided into four groups (homogeneous in parity and days in lactation) with ten animals in each.[11]

The effect of supplementing diets with Cu, Mn and Zn from Mintrex on the milk content of the element supplemented was examined in comparison to equivalent doses of inorganic sources of the same trace elements (copper sulphate, manganese oxide and zinc oxide). The different trace elements were added to complementary feed limited to 2 kg/cow/day, calculated to provide a concentration of 150 mg Zn and Mn or 35 mg Cu/kg complete feed. A partial mixed ration (PMR) was offered in

[11] Technical Dossier, Annex III.1.4.

addition, probably at 19 kg DM, but intake was not measured. The intake of concentrate was recorded (1.93 kg/day without differences between the treatments).

An estimation of total Zn intake is based on analysed values of the PMR and the complementary feed, on the measured intake of the complementary feed and the assumption that PMR has been quantitatively consumed. The total dietary Zn concentration was estimated to be in the range of 160 to 170 mg/kg complete feed DM for both groups.

Milk yield was not different between the two groups (27.1 and 26.1 kg/day in the control and in the Mintrex®Zn group, respectively). At the end of the study, 4.1 mg Zn/kg milk was found in the control group and 4.0 mg Zn/kg milk in the Mintrex®Zn group.

These findings are in agreement with a study formerly assessed by the FEEDAP Panel (EFSA, 2008) showing no differences in Zn content of milk between inorganic source of Zn and Mintrex®Zn at the level of 69 % of the maximum Zn content authorised.

#### 3.1.4. Conclusions on tissue/products deposition

The FEEDAP Panel concludes that use of Mintrex®Zn as Zn source to supplement feed of different species would not lead to different Zn concentrations in edible tissues/products compared to the use of authorised inorganic Zn sources at a similar dose.

### 3.2. Consumer exposure

Since there was no indication that Mintrex®Zn would lead to different Zn concentrations in foods of animal origin compared to inorganic Zn (mainly zinc sulfate), differences in Zn exposure of the consumers due to the use of Mintrex®Zn are not expected.

## Conclusions

The FEEDAP Panel concludes that the use of Mintrex®Zn up to the maximum authorised zinc content in feed would not pose a greater safety concern for the target species studied than the authorised inorganic sources of zinc. Taking also into account the already assessed safety of Mintrex®Zn for chickens for fattening, the FEEDAP Panel concludes that Mintrex®Zn is safe for all species up to the maximum authorised zinc content in feed.

There was no indication in studies with piglets, laying hens and dairy cows that Mintrex®Zn would lead to different zinc concentrations in muscle, liver, kidney, skin/fat, eggs and milk compared to inorganic zinc (zinc sulfate in case of piglets and laying hens, zinc oxide in dairy cows). Consequently, differences in zinc exposure of the consumer due to the use of Mintrex®Zn are not expected. The FEEDAP Panel concludes that no specific concerns for consumer safety would arise from the use of Mintrex®Zn in feed for all species.

## Documentation provided to EFSA

1. Mintrex®Zn. All species. Supplementary information. May 2009. Submitted by NOVUS® Europe S.A.
2. Mintrex®Zn. All species. Supplementary information. September 2009. Submitted by NOVUS® Europe S.A.
3. Mintrex®Zn. All species. Supplementary information. October 2009. Submitted by NOVUS® Europe S.A.

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## ABBREVIATIONS

γ-GT: Gamma-Glutamyl Transferase

ALT: Alanine Transminase

ANOVA: Analysis Of Variance

APT: Alkaline Phosphatase

AST: Aspartate Aminotransferase

Cu: Copper

EFSA: The European Food Safety Authority

Fe: Iron

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

Hb: Haemoglobin

MCV: Mean Corpuscular Volume

MCH: Mean Corpuscular Haemoglobin

MCHC: Mean Corpuscular Haemoglobin Concentration

MHA: Hydroxy Analogue of Methionine

Mn: Manganese

NRC: National Research Council

UL: Upper intake Level

PCV: Packed Cell Volume

PMR: Partial Mixed Ration

RBC: Red Blood Cells

WBC: White Blood Cells

Zn: Zinc