

## Nitrite as undesirable substances in animal feed

### Scientific opinion of the Panel on Contaminants in the Food Chain

(Question No EFSA-Q-2005-287)

**Adopted on 25 March 2009**

#### SUMMARY

Nitrite is formed naturally by the nitrogen cycle during the process of nitrogen fixation and it is subsequently converted to nitrate, a major nutrient assimilated by plants. Two main nitrite salt forms occur, namely sodium and potassium nitrite.

In animal tissues, nitrite is naturally present mainly as the result of endogenous nitrate conversion. Animal feed represents a natural source of exogenous nitrite and because of its potential for toxicity at excessive levels of intake, the Directive (EC) No 2002/32/EC on undesirable substances in animal feed established maximum limits for sodium nitrite in complete feedingstuffs excluding feedingstuffs intended for pets except birds and aquarium fish, and fish meal of 15 and 60 mg/kg, respectively (corresponding to 10 and 40 mg/kg for the nitrite ion). Nitrite in drinking water is regulated in Europe, with a maximum level of 0.5 mg/L. Nitrate levels in forages are naturally high and the inter-conversion of nitrate to nitrite is the largest contributor to nitrite exposure in food-producing animals. Dietary intake of nitrite *per se* results from the use of vegetable feeds and forages, fertilisers/manures or when used as an antimicrobial for preservation, for example in silage, processed pet food, and in former times fish meal. Additionally, water can be an important dietary source of nitrite via reduction of nitrate. The main analytical technique used to measure both nitrite and nitrate is colourimetry because of its sensitivity and specificity. Three member states provided analytical results on feedingstuffs and nitrite levels were below the maximum levels in all feed commodities.

Acutely, nitrite is approximately ten-fold more toxic than nitrate and three main toxicological endpoints have been identified: methaemoglobin formation (in a wide range of species including man), hypertrophy of the adrenal zona glomerulosa (rats), and equivocal evidence for carcinogenesis (female mice). The Acceptable Daily Intake (ADI) for nitrite 0-0.07 mg/kg body weight (b.w.) per day has been endorsed by the Panel on Contaminants in the Food Chain (CONTAM Panel) of the European Food Safety Authority during the recent risk benefit assessment of nitrate in vegetables.

In monogastric animals, most nitrite is formed and absorbed in the upper digestive tract. In contrast in ruminants, nitrite and nitrate is metabolised by the rumen flora. Reports of adverse effects after excessive nitrite exposure in livestock exist, and pigs and ruminants, as major food producing animals, are particularly susceptible: this is because of relatively low nitrite

reductase activity and high levels of rumen conversion of exogenous nitrate to nitrite, respectively. Acknowledging diverse husbandry conditions between reported studies, No-Observed Adverse Effect Levels (NOAELs) for pigs and cattle have been estimated from the literature with a value of 3.3 mg/kg b.w. per day in both species. In turn, total daily nitrite intakes were estimated for pigs and cattle using the maximum exposure level in complete feed according to the current legislation (10 mg/kg), typical feeding regimens within the European Union and maximum nitrite level in forages from member states (cattle). Overall, the estimated nitrite intakes for pigs and cattle from feed were 0.37 and 0.65 mg/kg b.w. per day (excluding endogenous formation of nitrite) respectively, corresponding to margins of safety of 9 and 5 in comparison with the respective NOAELs. The CONTAM Panel considered that such levels do not pose concerns for animal health given that livestock are husbanded under good agricultural practices. The protection of livestock health is further reinforced by the awareness of livestock producers, of the conditions that are likely to lead to nitrite poisoning particularly regarding high levels of nitrate in forages and the inter-conversion of nitrate to nitrite.

The CONTAM Panel concluded that the typical daily human dietary exposure to nitrite from fresh animal products (e.g. milk, meat and eggs) is only (2.9 %) of the total daily dietary exposure to nitrite. The CONTAM Panel concludes that such low nitrite levels in fresh animal products do not raise any concern for human health.

**Key words:** nitrite, feedingstuffs, toxicity, exposure, carry-over, animal health, human health.