



**Opinion of the Scientific Committee for Animal Nutrition
on the safety of Potassium - and Sodium ferrocyanide
used as anticaking agents.**

(ADOPTED ON 3 DECEMBER 2001)

1. BACKGROUND

Council Directive 70/524/EEC foresees the possibility to authorise anticaking agents in animal feedingstuffs.

The Commission receives regularly dossiers for authorisation of such substances. Recently, two dossiers respectively on potassium ferrocyanide and sodium ferrocyanide have been submitted by the "Verein für Deutsche Salzindustrie" in accordance with the clock running authorisation procedure laid down in Directive 70/524/EEC.

Both dossiers have been checked by the Standing Committee on Animal Nutrition and considered by Member States in compliance with the requirements of Council Directive 87/153/EEC on 13 September 2000.

2. TERMS OF REFERENCE (FEBRUARY 2001)

The Scientific Committee for Animal Nutrition is therefore requested to assess the data provided and to evaluate the safety for the target animals, the users, the workers, the consumers and the environment of the two above mentioned products.

3. OPINION OF THE COMMITTEE

3.1. Previous evaluation and current authorisations of the products

Sodium and potassium ferrocyanide are complex cyanides that belong to the ferrocyanide salts that have been in use for many years for anticaking in salt for human consumption. The compounds are approved by JECFA/WHO (1975) and were evaluated by the SCF (1990)(E 535 /E 536) which fixed an ADI of 0-0.025 mg/kg body weight. Both products are authorised in food for human consumption by the European Parliament and Council Directive 95/2/EC¹ on food additives other than colours and sweeteners.

¹ OJ EC n° L 248 of 14/10/1995, p. 60

Sodium ferrocyanide (E 535), potassium ferrocyanide (E 536) and calcium ferrocyanide (E 538) are permitted in salt and its substitutes at the level of 20 mg/kg (calculated as anhydrous potassium ferrocyanide) individually or in combination. They have to fulfill a purity criterion as laid down in Commission Directive 96/77/EC² of 2 December 1996 laying down specific purity criteria on food additives other than colours and sweeteners amended by 2000/63/EC³.

3.2. Safety for the animals and for the human consumers

No specific safety studies for animal feed application have been supplied. The firm has submitted summarised information packages that have been used for human use approval and that are publicly available to a large extent. In addition, the UK Committee on the Toxicity of Chemicals in Food, Consumer Products and the Environment (COT; 1994) has further supplied data on reports of carcinogenicity, mutagenicity and reproductive toxicity studies.

In laboratory animal studies the toxicity of these compounds appeared to be limited. The compound is excreted via urine through glomerular filtration. Feeding studies in rats demonstrated kidney damage attributed to crystal formation at 5% and to a lesser extent at 0.5% dietary incorporation in a 90-day study. A carcinogenicity study in rats with doses up to 5000 ppm (0.5%) and a teratogenicity study did not indicate carcinogenic or teratogenic potential. There was no or slight skin and eye irritation, and no sensitisation potential. For genotoxicity testing an Ames was carried out, as well as an *in vitro* cytogenetics assay with human lymphocytes and a mouse lymphoma L5178Y cell assay. All these tests pointed towards absence of genotoxicity. Although many of these studies were, due to the period of performance, not according to GLP, the methodology was sufficient not to invalidate the study results. The NOAEL can be set at 50 ppm in the diet based on urinary cell excretion in the chronic rat study; as that effect was inconsistent and therefore of questionable significance, it confers another conservative factor in safety assessment. Thus a group ADI for ferrocyanides of 0-50 µg/kg bw / day was proposed by the COT.

The proposed application as a feed additive is also as anticaking agent in feed salt with a maximum proposed concentration of 100mg/kg salt, and for poultry 80 mg/kg. The estimated daily intake for livestock (for instance finishing pig, 100 kg) fed 0.3% salt containing 100 mg/kg ferrocyanide and a daily feed intake of 3 kg would yield a daily intake of 0.009 mg/kg BW / day. For poultry (for instance a 2 kg layer) these resulting intake would be (at 0.3% salt, 80 mg/kg ferrocyanide and 100 g daily feed intake) 0.012 mg of ferrocyanide /kg body weight. As the NOAEL in rat studies can be set at 50 ppm (equivalent to around 2.5 mg/kg/bw/day), there is an adequate margin of safety based on laboratory animal experiments. In comparison, the human ADI is set by SCF at 0.025 mg/kg BW. Therefore, also in view of the

² OJ EC n° L 339 of 30/12/1996 p.1

³ OJ EC n° L 277 of 30/10/2000, p.1

absence of specific biological activity, further toxicity / tolerance studies in target animals are not deemed necessary.

No specific studies to residues in animal produce have been submitted. However, it can be assumed that due to the renal clearance of these salts accumulation in animal produce is not expected and will not significantly contribute to authorised human intake.

Based on this assessment and relying on the human food application data the SCAN is of the opinion that the use of these food grade ferrocyanide salts as anticaking agents in animal feed salt can be considered safe for animals and consumers of animal produce.

3.3. Workers' exposure (including users at the farm level)

As the risk for workers in production plants is considered low due to the biological properties, it is recommended to maintain the same conditions as applied in premises for human food salt preparation. In view of the low toxicity and the low levels in final feed, no special precautions are considered necessary at the farm level.

3.4. Impact on environment

Ferrocyanides are excreted in faeces and urine, mainly unchanged, although most studies on metabolism and kinetics were performed using IV injection. The feed levels are low and biological effects in the environment may be negligible. Ferrocyanides are also used in salt for road de-icing at levels up to 200 ppm, which is a far more important source of environmental exposure. Nevertheless some assessment on the environmental fate and impact should be provided.

3.5. Conclusion

Principally on the basis of data compiled for food application as anticaking agent in salt, the use of these ferrocyanides in salt for feed use is acceptable as regards safety for target animals and human consumer. However, some assessment for environmental fate and impact is lacking.

Note: The SCAN recognises that the requested level of use in feed of this technological additive is considerably higher than in human food sector; in addition, a further distinction is made between livestock and poultry feed (20, 100 and 80 ppm in salt for man, livestock and poultry, respectively). The rationale behind this discrepancy remains unclear. As the higher levels and the differentiation are not justified, the SCAN would recommends reconsideration of the dose levels. Ideally the same dose levels should be used for humans and animals.

4. REFERENCES

Dossier submitted by the company

COT evaluation TOX/94/45 with annexes