



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

HUMIC ACIDS AND THEIR SODIUM SALTS

SUMMARY REPORT

1. Humic acids are a class of compounds resulting from decomposition of organic matter, particularly plants, and are natural components of drinking water, soil and lignite. They are three dimensional macrocolloidal molecules with a polyaromatic center containing iso- and heterocyclic structures and peripheral side-chains. The humic acids under consideration are extracted from lignite (brown coal) and have an average molecular mass of 20 000 to 150 000. They include humocarb with a humic acid content of $55 \pm 10\%$, concentrated humic acid and a humic acid-iron(II)-carboxymethylcellulose-complex.

Humic acids are used in horses, ruminants, swine and poultry at a oral doses level of 500 to 2000 mg/kg bw for the treatment of diarrhoea, dyspepsia and acute intoxications. They exert an protective action on the mucosa of the intestine and have antiphlogistic, adsorptive, antitoxic and antimicrobial properties. They are not used in humans.

2. The intramuscular injection of the humic acid sodium salt (1 mg/kg bw) to rabbits had no effects on haematological parameters and the glucose concentration in blood, but affected the albumine/globuline *ratio* in plasma (marked increase of the gammaglobuline fraction).
3. The absorption of humic acids from the intestine after oral administration is very low. The rate of absorption in the isolated gastrointestinal tract of the rat ranged from less than 0.05 to 0.07%.
4. Humic acids are of low toxicity after oral administration. The LD₅₀ in rats is greater than 11 500 mg/kg bw. However they are toxic after parenteral administration with LD₅₀ values of 54.8 to 58.5 mg/kg bw after intravenous administration in mice and 163.5 to 205.8 mg/kg bw after intraperitoneal administration in rats.
5. In a 30-day toxicity study in rats oral dose levels of 100 to 1000 mg/kg bw/day of concentrated humic acid or of its sodium salt had no effects on the behaviour and induced no clinical disturbances. The same results were obtained in dogs which received daily doses of 300 mg/kg bw for 90 days. Humocarb or concentrated humic acid administered with feed for 90 days at the dose of 1000 mg/kg bw/day had no effects on the pH in the gastrointestinal tract of rats and rabbits.
6. Groups of 10 pregnant rats were treated orally with 500 sodium humate/kg bw/day on days 5 to 17 of pregnancy or with 1000 mg/kg bw/day on days 5 to 9 or on days 11 to 15 of pregnancy. No teratogenic effects were seen. After intraperitoneal administration of 50 mg/kg bw/day on days 5 to 9, days 11 to 15 or days 5 to 17 of pregnancy the resorption rate was higher (13.2 to 13.6%) than in negative controls (3.2%). No teratogenic effects were noted.
7. The concentrated humic acid (50 to 150 µg/ml) and the sodium salt (500 to 15 000 µg/ml) did not induce an increase of spontaneous aberrations in kidney cells of rabbits and baby hamsters or in diploid human fibroblasts. Both formulations had no mutagenic activity in *Salmonella typhimurium* TA98 and TA100 in concentrations between 0.1 and 0.5% with and without metabolic activation. It can be concluded that humic acids are not mutagenic.

8. No carcinogenicity studies were provided. Considering the structure of the substance, the fact that long-term administration gave no indications for a carcinogenic potential of the compounds and that they are devoid of mutagenic activity in the test systems used, such data are not required.
10. In residue studies swine orally received a mixture of humocarb and concentrated humic acid (ratio 16:1) at a dose level of 500 (n = 2) and 2000 mg/kg bw/day (n = 3) for 30 days and sheep (n = 3) orally received 1000 to 2000 mg/kg bw/day. At the end of the treatment periods no humic acid could be detected by a photometric method (limit of detection: 10 to 50 µg/ml) in blood plasma and muscle, liver and kidney. However, due to the inadequacies of the analytical method the results are of limit relevance.

Conclusions and recommendation

Having considered the criteria laid down by the Committee for the inclusion of substances in Annex II of Council Regulation (EEC) No 2377/90 and in particular that:

- humic acids are part of the human diet as they are contained in drinking water,
- humic acids have low oral toxicity,
- humic acids are poorly absorbed after oral administration,
- humic acids are used for infrequent and non-regular treatments;

the Committee concludes that there no need to establish an MRL for humic acids and their sodium salts and recommends their inclusion in Annex II of Council Regulation (EEC) No.2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Humic acids and their sodium salts	All food producing species	For oral use only