

REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE  
OF HALOFUGINONE IN FEEDINGSTUFFS FOR TURKEYS

Opinion expressed 17 November 1982

TERMS OF REFERENCE (October 1981)

The Scientific Committee for Animal Nutrition is requested to give an opinion on the following questions :

1. Does the use of halofuginone as a coccidiostat under the conditions proposed for feedingstuffs for turkeys (see Background) result in the presence of residues in the tissues and organs of the animal? If so, what is the qualitative and quantitative composition of these residues? Could these residues be harmful to the consumer?
2. Could the excreted products, derived from the additive, be prejudicial to the environment? If so, what is the nature of the risks?
3. In the light of the answers to the above questions, are the proposed conditions of use acceptable?

BACKGROUND

In accordance with the provisions of Council Directive 70/524/EEC of 23 November 1970 concerning additives in feedingstuffs (1), as last amended by the thirty-eighth Commission Directive of 16 July 1981 (2), Member

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(1) OJ No L 270 of 14.12.1970, p. 1

(2) OJ No L 231 of 15.08.1981, p. 30

States are authorized by way of derogation to use halofuginone under the following conditions set out in Annex II, Section B of the Directive :

Species of animal : chickens for fattening.

Minimum and maximum content in complete feedingstuff : 2-3 ppm (mg/kg).

Other provisions : use prohibited at least five days before slaughter.

An extension of the use of halofuginone under the following conditions has been proposed :

Species of animal : turkeys for fattening.

Minimum and maximum content in complete feedingstuff : 2-3 ppm (mg/kg).

Other provisions : use prohibited at least seven days before slaughter.

#### OPINION OF THE COMMITTEE

1. Halofuginone excretion was studied after administration for 15 days to turkeys of a diet containing 3 mg of halofuginone (spiked with <sup>14</sup>C-labelled halofuginone on the 15th day)/kg feedingstuff. Five days after the administration of the final dose there was a slight residual radioactivity in the liver, kidneys, digestive tract and carcass. Expressed in mg of halofuginone per kg of tissue or organ, the residues ranged from 0.005 to 0.053 (detection limit : 0.005 mg/kg). Radioactivity in the bile was much higher (around 0.3 mg of halofuginone/kg), which indicates that excretion is mainly via the enterohepatic cycle. Studies on the nature of the residues have shown that their principal constituents are unchanged halofuginone and a halofuginone conjugate.

In turkeys fed for 16 weeks with a supplemented feedingstuff (3 mg halofuginone/kg) the residues determined by HPLC (detection limit : 0.02 mg halofuginone/kg) were less than 0.1 mg/kg in all tissues immediately after treatment. After three days of withdrawal they were at the analytical detection limit.

2. A comparison of the carbon 14 studies using chickens and turkeys revealed a significant positive correlation between the tissue concentrations and elimination kinetics of halofuginone on the two species.

Because the metabolism is similar it may be assumed that the data concerning the biodegradation of halofuginone and halofuginone metabolites from chicken droppings in soil and water are also valid for the same substances derived from turkey droppings. The data concerning chickens, originally obtained in 1979, have been amplified with the results of several other studies requested by the Scientific Committee, and now dispelled any doubts concerning the effects of halofuginone on the environment (3).

Droppings of chickens fed orally for 15 days with a dose of halofuginone labelled with  $^{14}\text{C}$  (in the quinazolinone nucleus), at a rate of 0.3 mg/kg bodyweight/day, were used for a number of experiments. The droppings were mixed with samples of river water and kept in darkness at 25°C. Tests on the radioactivity of the filtrate showed that the activity never exceeded 76% of the total radioactivity and that the activity associated with unchanged halofuginone, which

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(3) Commission of the European Communities. Reports of the Scientific Committee for Animal Nutrition, Second Series (1980) EUR 6918, pp. 11-13.

was initially 20%, had dropped to 4-5% of its original value in the space of 32 weeks. Several breakdown products less polar than halofuginone were also detected in the filtrate and some of them identified.

The same chicken droppings, mixed with two types of soil, either in controlled laboratory conditions or in field plots, showed that halofuginone and halofuginone metabolites are broken down slowly, giving off  $^{14}\text{CO}_2$ . Within 16 weeks the total radioactivity is reduced to less than 30% of its initial value and any quantities migrating to a soil depth exceeding 5 cm do so in very small quantities and only after 32 weeks. This indicates that the risk of leaching are insignificant. The half-life of halofuginone in soil is of the order of 43 days.

In crops of sugar beets, potatoes and carrots grown in pots, no transfer of radioactivity from the soil (treated with 10 tonnes of droppings/ha) to the plants was observed (detection limit of radioactivity expressed as halofuginone : 0.004 mg/kg), except in carrot tops (0.007 mg/kg). The presence of residues of halofuginone in soil therefore presents no risk for the crops.

3. In view of the foregoing, the Committee has no objections to the use of halofuginone under the conditions of use proposed for turkeys. However, it is unable to issue a final opinion before the results of the additional mutagenicity tests requested previously are available.

#### REFERENCES

Dossiers Roussel Uclaf and Huntingdon Research Centre.