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

Opinion expressed 25 April 1979

TERMS OF REFERENCE

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

1. Does the use of the coccidiostat halofuginone in feedingstuffs for chicken, under the conditions of use authorized by derogation (see Background), result in the presence of residues in animal products ? If so, what is the nature and the amount 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, should the conditions of use already authorized for this additive be maintained or should they be modified ?

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 twentieth Commission Directive of 7 December 1977 (2), Member States are authorized to use halofuginone, by way of derogation up to 31 December 1978, under the following conditions set out in Annex II, Section B, of the Directive :
Species of animal : Chicken for fattening.
Minimum and maximum content in complete feedingstuffs : 2 - 3 ppm (mg/kg)
Other provisions : use prohibited at least 5 days before slaughter.

(1) OJ No L 270, 14.12.1970, p. 1
(2) OJ No L 18, 24.01.1978, p. 7

OPINION OF THE COMMITTEE

1. Studies of the metabolism of halofuginone (dl-trans-7-bromo-6-chloro-[3-(3-hydroxy-2-piperidyl)acetonyl]-4(3H)-quinazolinone hydrobromid) in chicken, using compounds with the 14C-label incorporated either in the piperidine or the quinazolinone nucleus, show that the product does not undergo intensive metabolic degradation in animals. Residues in tissues and organs appear to consist mainly of halofuginone and non-polar metabolites containing the piperidine and quinazolinone nuclei.

   Residues in tissues and organs of chicken which had been fed for several weeks with a ration containing 3 mg halofuginone/kg feedingstuff (maximum authorized level) were determined by measurement of total radioactivity and by high-pressure liquid chromatography. Residues were negligible (less than 0.03 mg/kg) in muscle, skin and fatty tissue 24 hours after withdrawal of the supplemented feedingstuff. Small amounts (less than 0.06 mg/kg) were still present in the liver and kidney 5 days after withdrawal.

   Halofuginone was investigated in short- and long-term toxicological studies in laboratory animals. The Committee considered that certain observed effects, one of which was an increase in the incidence of lymphoreticular tumours in mice, required further investigation. The interpretation of these effects is difficult because of the use of animal strains with a tendency for developing similar tumours spontaneously and because studies on mutagenesis, histopathology and clinical chemistry were limited. The acquisition of more extensive data on these aspects is essential because of the low acceptable daily intake of the product for mice, rats and dogs, and because the metabolites are incompletely known.

2. Studies on the fate of halofuginone in chicken showed that, under the authorized conditions of use, about 80 % of the amount ingested appears in the excreta within the next 24 hours. Excretion continues for about a week. The presence of residues in bile indicates the existence of an enterohepatic cycle. The excreted products appear to be composed mainly of halofuginone and non-polar metabolites of similar structure.

   Tests performed on different types of soil showed that these products are strongly adsorbed, difficult to extract with water and resistant to biodegradation. Halofuginone is not phytotoxic

in tests carried out on tomato, cucumber, lettuce and tobacco crops.

These observations indicate that contamination of the environment is unlikely. However, additional data on biodegradation of excreted products and on their effects on soil microbiology and aquatic life are necessary in order to remove any uncertainties.

3. In the light of the available facts, the Committee is of the opinion that the use of halofuginone in feedingstuffs for chicken, at the levels presently authorized, could be maintained provisionally, provided a withdrawal period of at least 7 days before slaughter is imposed in order to assure the elimination of residues from liver and kidneys. A reassessment of this additive is needed, after a more detailed study of the long-term toxicity in rats and additional studies on the biodegradation of the residues excreted by chicken as well as the possible effects on soil micro-organisms and aquatic life have been carried out.

REFERENCES

Dossiers Roussel Uclaf and Huntingdon Research Center.