REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE OF AVOPARCIN IN FEEDINGSTUFFS FOR CHICKEN AND PIGS

Opinion expressed 11 July 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 antibiotic avoparcin in feedingstuffs for chicken and pigs, 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 use of this additive affect the development of resistance in bacteria ?

3. Could the excreted products, derived from the additive, be prejudicial to the environment ? If so, what is the nature of the risks ?

4. 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 avoparcin, by way of derogation up to 31 December 1978, under the following conditions set out in Annex II, Section A, of the Directive :

Species of animal	Minimum content	Maximum content
	ppm (mg/kg) of complete feedingstuffs	
Chicken for fattening	7.5	15
Pigs, up to 10 weeks	10	40
Pigs, more than 10 weeks	5	20

(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. Avoparcin is a glycopeptide antibiotic produced by Streptomyces candidus. The active substance of the mycelian product on the market is avoparcin lauryl sulphate.

   Radiotracer methodology sensitive to 0.05 mg/kg has been used to follow the routes and rates of excretion and the distribution in tissues of 14C-labelled avoparcin administered to rats and to broiler chicken. The radioactivity was quantitatively recovered in the excreta after a few days and there were no measurable residues in muscle, fat, liver and kidneys.

   Investigations on residues in tissues were also carried out in a number of experiments with chicken and pigs receiving avoparcin in their ration according to the conditions of use authorized and also at higher levels. There were no microbiologically detectable residues (limit of detection : 0.2 to 0.5 mg/kg, according to the substrate) nor any antibiotic activity in the muscle, fat, blood, liver, kidneys and skin at slaughter after withdrawal periods of 0, 1 and 3 days. The investigation of the muscle and liver by a gas-chromatographic method confirmed the absence of residues at the detection limit of 0.1 mg/kg.

   Avoparcin has been investigated in short- and long-term toxicity studies in laboratory animals. It had a low acute toxicity (oral LD50 for rat, mouse and chick exceeds 10 g/kg body weight). Long-term studies in rats fed diets containing various doses of the mycelian product did not show any significant dose-related differences from the control groups in the usual parameters nor was there any indication that avoparcin induces specific tumours. A three-generation study in rats showed decreased neonatal survival and lower body weights of the young only at the highest dose investigated (1600 mg avoparcin/kg feedingstuff). No abnormalities were observed in relay toxicity studies in rats fed for 90 days a diet containing 33 % of tissues from chicken reared for nine weeks on feed containing 500 mg avoparcin/kg.

2. Avoparcin is active in in vitro tests against gram-positive but not gram-negative bacteria and has been shown to have no significant influence on the flora of the small intestine of broiler chicken. Despite a slight development of resistance in vitro in strains of enterococci, there is no evidence that the use of avoparcin in the diet of pigs and chicken favours the selection of bacteria with stable resistance in Clostridium welchii, group D streptococci and nasal staphylococci. The development of

cross-resistance between avoparcin and a number of therapeutic antibiotics has been studied in pigs. There was no evidence that avoparcin, at levels of 20 to 200 ppm in the diet, induced the selection of bacteria resistant to avoparcin itself, or to any of the other therapeutic antibiotics tested.

3. The elimination of avoparcin lauryl sulphate in pig and chicken excreta and the stability of the excretion products in manure have been studied. The additive passes through the digestive tract of pigs mostly undegrated, but in chicken only about half of the antibiotic activity of the ingested dose appears in the excreta. Antibiotic activity appears to decline more rapidly in chicken excreta than in pig faeces. After storage at 24°C and 37°C the half life values of avoparcin (based on antibiotic activity) were respectively 9 and 4 days in chicken excreta and 22 and 15 days in pig faeces.
Avoparcin breakdown products are strongly bound in the soil. Hence only very small amounts of the antibiotic and its residues are likely to enter the aquatic environment either by drainage or directly. The results of a study in an ecosystem model and a study of the bioaccumulation potential suggest that manuring with chicken excreta containing avoparcin will not result in the accumulation of avoparcin or related residues in components of the environment, only trace amounts being taken up by plants and animals. Avoparcin has no obvious phytotoxic effect on crop plants and weed species and is of low toxicity to aquatic organisms.

4. The Committee considered all available information, particularly the data showing that avoparcin has a low toxicity for mammals and aquatic life, that it is virtually not absorbed from the gastro-intestinal tract, and the absence of any evidence that its use in feedingstuffs could lead to the development of resistant or cross-resistant bacteria and thereby diminish the effectiveness of therapeutically used antibiotics. In the light of the above information, the Committee is of the opinion that the use of avoparcin in chicken for fattening, piglets and pigs, under the authorized conditions, is not prejudicial to the consumer nor to the environment and should be maintained.

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