REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE OF AVOPARCIN IN FEEDINGSTUFFS FOR CALVES AND FATTENING CATTLE

Opinion expressed 1 June 1983

TERMS OF REFERENCE (April 1982, expanded in July 1982)

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

1. Does the use of the antibiotic avoparcin under the conditions proposed for milk replacers for calves and feedingstuffs for fattening cattle (see Background) have significant effects on the animal's growth?

2. Does its use under the proposed conditions result in the presence of residues in 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?

3. Could its use affect the development of resistance in bacteria.

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

5. 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-ninth Commission Directive of 15 January 1982 (2), the use of avoparcin is authorized at Community level under the conditions set out in Annex I, Section A, of the Directive :

Species of animal	Minimum content	Maximum content
	ppm (mg/kg) of complete feedingstuffs	
Chickens for fattening	7.5	15
Piglets, up to 4 months	10	40
Pigs, 4 to 6 months	5	20
Turkeys, up to 16 weeks	10	20

The Scientific Committee for Animal Nutrition expressed a favourable opinion on these conditions of use (3,4).

It is proposed that the authorization of use of this additive be extended by the following provisions :

(1) OJ No L 270, 14.12.1970, p. 1
(2) OJ No L 42, 13.02.1982, p. 16
(3) Commission of the European Communities. Reports of the Scientific Committee for Animal Nutrition. Second Series (1980) EUR 6918.
(4) Report of the Scientific Committee for Animal Nutrition on the use of avoparcin in feedingstuffs for turkeys, 7 October 1981 (unpublished).

Milk replacers for calves (up to 6 months), minimum and maximum content : 40-80 ppm (mg/kg).
Complementary feedingstuffs for fattening cattle, minimum and maximum content expressed on the basis of complete feedingstuffs : 15-45 ppm (mg/kg).

OPINION OF THE COMMITTEE

1. The use of avoparcin in milk replacers for calves (up to 6 months old) was the subject of numerous experiments. With pre-ruminant calves a study was carried out on the dose/effect relationship (0, 20, 40, 80, 120 mg/kg of milk replacer in powder form), on the basis of 9 trials involving a total of 420 animals. The number of calves on which the dose of 120 mg/kg was tested was, however, too small to permit a reliable assessment.

   Examination of the results reveals that the dose of 80 mg/kg is not justified because it does not provide results which differ statistically from those provided by 40 mg/kg. Statistical analysis involving the calves treated with 20 mg/kg (Duncan test), however, showed a difference in the efficacy of avoparcin which was statistically significant compared with the controls (0 mg/kg). The results obtained showed that the addition of avoparcin has appreciable effects on daily weight gain and on the feed conversion ratio. However, the dose/effect relationship does not appear to be a linear one.

   According to these data, avoparcin is effective in milk replacers at dose-levels of 20 and 40 mg/kg.

   The use of avoparcin in the feed for beef cattle with a partially or fully functioning rumen was the subject of a total of 32 experiments performed on 3 365 animals. A study of the dose/effect relationship

was carried out with the following doses (mg/kg of feedingstuff) : 0, 10, 15, 30, 45, 60 and 90. The research was performed on cattle of different breeds and initial weights, for varying periods, and with different energy levels, feeding patterns and bioclimatic conditions. The results obtained showed that the addition of avoparcin has appreciable effects on average daily weight gain and on feeding efficiency at doses of between 15 and 45 mg/kg of feedingstuff, even though the dose/effect ratio is not linear either in the case of weight gain or in the case of feeding efficiency.

In the light of these figures, the minimum and maximum content proposed for complementary feedingstuffs for fattening cattle (15 and 45 mg/kg of compound feedingstuff) are thus appropriate. In order to prevent incorrect use of avoparcin in ruminant cattle receiving complementary feedingstuffs, however, it is considered useful to establish a maximum daily dose per animal based on live weight. It is accepted that feed intake of ruminant cattle does not increase in direct proportion to body weight. This necessitates an adjustment of the amount of additive in the ration. In view of the foregoing, the maximum amount in the daily ration should not exceed 90 mg (constant value) + 65 mg/100 kg live weight. The values obtained according to this formula are as follows :

Weight of the animal (kg)	Average daily consumption of feed (kg)	mg avoparcin/ head/day (90 mg + 65 mg/100 kg live weight)	ppm equivalent (mg avoparcin/kg complete feedingstuff)
100	3.4	155.00	45.00
150	4.4	187.50	42.60
200	5.6	220.00	39.30
250	6.7	252.50	37.70
300	7.6	285.00	37.50
350	8.3	317.50	38.30
400	9.0	350.00	38.90
450	9.6	382.50	39.20
500	10.4	415.00	39.90
550	10.5	447.50	42.60
600	10.9	480.00	44.00

2. In its opinion given on 11 July 1979 (Commission of the European Communities, 1980) the Committee stated that avoparcin added to feed was virtually unabsorbed by the digestive system in rats, chickens and pigs and that its use in feed for chickens and pigs did not produce any detectable residues in the tissues.

Studies performed on calves, steers and bulls under the proposed conditions and at higher doses and with the use of molecules labelled with ^{14}C lead to the same conclusions.

In veal calves which had received feedingstuffs with 40, 80 and 400 mg of avoparcin per kg for 10 to 19 weeks no residues detectable by microbiological assay (detection limit : 0.20 to 0.25 mg/kg) and no antibiotic activity were found in the muscles, liver, kidneys or subcutaneous fat. The withdrawal periods before slaughter were respectively 0, 1 and 3 days.

In steers to which 2 mg/kg body weight of avoparcin labelled with ^{14}C had been administered orally for eight consecutive days, and which had been slaughtered two hours after the last administration, the radioactivity administered was recovered quantitatively (88% in faeces, 20% in the rumen, 4.5% in the contents of the digestive system, 0.1% in the urine and 0.5% in the wash water from the metabolism cages). The blood, liver, muscles and fatty tissues were free of radioactive residues (detection limit expressed in terms of avoparcin : 0.05 mg/kg); there were traces in the kidneys (0.05 to 0.06 mg/kg).

Other studies on steers which had received feed containing 97 mg of avoparcin per kg for 56 days and bulls which had received feed containing 200 mg of avoparcin per kg for five months showed that the blood, liver, kidneys, muscles and fat of the animals were free of residues which could be detected either by microbiological assay (detection limit : 0.25 to 0.50 mg/kg according to substrate) or by thin layer chromatography (detection limit : 0.1 mg/kg).

Since the proposed uses of avoparcin do not cause detectable residues in edible products, they do not entail any risks for the consumer.

3. The microbiological effects of the addition of avoparcin to feed for calves and fattening cattle were the subject of several experiments.

In a ten-week experiment on four groups of nine calves each, which were fed doses of 0, 40, 80 and 400 mg/kg of feedingstuff respectively, a marked reduction in gram-positive bacteria (enterococci and lactobacilli) was observed, depending on the dose, and there was a slight increase, irrespective of the dose, in gram-negative bacteria

(E. coli). All the calves in the experiment were fed a combined antibiotic for three days before the start of the experiment. As could be expected, the E. coli strains (143 strains) isolated at the start of the experiment were mostly multi-resistant, whereas those isolated at the end of the experiment (142 strains) showed a considerable reduction in the number of multi-resistant strains.

In an experiment lasting six weeks which included among others two groups of eight yearling steers, one given no avoparcin and the other 60 mg avoparcin/kg of feedingstuff, the number of intestinal bacteria (E. coli and enterococci) did not seem to be affected by the use of avoparcin. The resistance pattern in general remained unchanged throughout the experiment.

The effects of administering avoparcin to calves on certain salmonellae strains was also studied. In a six-week experiment which included four groups of ten calves, two of the groups were infected with S. thypimurium and fed diets containg 0 and 80 mg of avoparcin/kg of feedingstuff. The infected animals excreted S. typhimurium between the seventh and the thirty-fifth day independently of the administration of avoparcin. This additive did not lead to colonization by salmonellae.

In another six-week experiment four groups of nine calves received doses of 0, 20 , 40 and 80 mg of avoparcin/kg of feedingstuff. At the end of the experiment two calves had died and 20 of the remaining 34 were found to be infected with S. dublin. Avoparcin was not observed to have any effect.

These residues show that the use of avoparcin as an additive in feed for calves and steers does not lead to the development of resistance in intestinal bacteria and does not influence the effects of S. typhimurium and S. dublin on the organism of these animal species.

4. In pre-ruminant calves and fattening cattle most of the avoparcin added to the feed is eliminated as such in the faeces. In this environment avoparcin breaks down fairly rapidly. Its half-life has been estimated on the basis of antibiotic activity at 8 to 16 days at temperature of 28 and 37°C.

The use of faeces of pre-ruminant calves or fattening cattle containing avoparcin as manure has no apparent phytotoxic effects or any disadvantages for aquatic organisms. The incorporation of 22 tonnes/ha of faeces containing 15 or 150 mg of avoparcin per kg in the soil does not affect the microbial nitrification process. At 150 mg/kg (=10 times the quantity excreted by the animal after administration of 40 mg/kg of feed) there is even a stimulant effect on the production of nitrates. Methanogenesis is not affected by the faeces of pre-ruminant calves of cattle receiving feed containing 40 or 45 mg of avoparcin/kg.

These observations confirm those reported for pigs. They lead to the conclusion that under the proposed conditions of use avoparcin cannot have harmful effects on the environment.

5. In the light of the figures available, the Committee is of the opinion that, for the sake of effectiveness the minimum and maximum avoparcin contents of milk replacers for calves should be reduced to 20 and 40

mg/kg. As regards complementary feedingstuffs for fattening cattle, the Committee takes the view that the minimum and maximum contents proposed (15 and 45 mg/kg of complete feedingstuff) are acceptable. However, to avoid incorrect use of the additive for ruminating cattle the following provision should be added concerning doses : "For ruminant cattle receiving complementary feedingstuffs the maximum dose in the daily ration shall be adjusted so as not to exceed 90 mg + 65 mg/100 kg live weight".

If used under these conditions avoparcin added to milk replacer feeds for calves and complementary feedingstuffs for fattening cattle involves no risks either for the consumer or for the environment.

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