REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE OF LERBEK (*) IN FEEDINGSTUFFS FOR POULTRY

Opinion expressed 17 November 1982

TERMS OF REFERENCE (July 1978 expanded in October 1981)

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

A. Chickens

1. Does the use of the coccidiostat Lerbek (*) (premix containing 100 parts of meticlorpindol and 8.35 parts of methylbenzoquate) in feedingstuffs for chickens, under the conditions of use authorized (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 authorized for this additive be maintained or should they be modified?

B. Turkeys

1. Does the use of Lerbek (*) in feedingstuffs for turkeys, under the proposed conditions (see Background), result in residues in animal

(*) registered trade name

products or excreted products which are different from those resulting from its use in chickens?

2. If so, could these residues or excretion products be prejudicial to the consumer or the environment?

3. In the light of the answers to the above questions, are the conditions proposed 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 States are authorized by way of derogation to use Lerbek (*) 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 feedingstuffs : 110 ppm (mg/kg).
Other provisions : use prohibited at least five days before slaughter.

An extension of the use of Lerbek (*) under the following conditions has been proposed :

Species of animal : turkeys for fattening.
Maximum age : 12 weeks.
Minimum and maximum content in complete feedingstuffs : 110 ppm (mg/kg).
Other provisions : use prohibited at least five days before slaughter.

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(1) OJ No L 270, 14.12.1970, p. 1
(2) OJ No L 231, 15.08.1981, p. 30
(*) registered trade name

OPINION OF THE COMMITTEE

A. Chickens

1. The metabolism of meticlorpindol (MCP) has been studied in rats, dogs and rabbits after oral administration. The product is partially absorbed. In rats and dogs, about 38 to 56% of the administered dose was excreted in the urine and 42 to 55% in the faeces. Unchanged MCP was one of the three major compounds identified among the products excreted in the urine. With rabbits, some 98% of the dose was excreted in the urine; almost half was as MCP and the remaining part as a mixture of hydroxylated MCP and its O-glucuronide derivative. Studies using ^{36}Cl-labelled MCP showed that there is virtually no breakdown of MCP in the tissues.

The metabolism of methylbenzoquate (MBQ) has been studied in rats and chickens, using ^{14}C-labelled molecules. In rats, 95% of the administered dose was excreted in the faeces and 0,2 to 1,0% in the urine within 4 days. Within 3 days about 1% of the dose was excreted in the bile, a large part of it in the form of an identified metabolite. In metabolism studies with surgically modified chickens, 80-85% of the radioactivity was excreted in the faeces (the greates part being as MBQ), and 1% in the urine. Several metabolites excreted have been identified.

Various studies on tissue residues have been carried out in rats, chickens and rabbits. In chickens fed Lerbek (at the authorized level of 110 mg active ingredient/kg feedingstuff) for 10 days, tissue levels of MCP after 5 days, but not at 3 days were undetectable (limit of detection : 0.05 mg/kg). Residues of MBQ

were not detected in any sample. The elimination of MCP residues in muscle and liver was confirmed in studies with chickens fed 100 mg MCP/kg feedingstuff for six days. In chickens fed MBQ at 20 mg/kg feedingstuff for up to 13 weeks, no residues were detected in muscle, levels up to 0.11 mg/kg were found in liver and up to 0.04 mg/kg in other tissues (limit of detection : 0.02 mg/kg). After a 24 h withdrawal period, traces of residues (0.04 mg/kg) were still detected in liver only.

Short- and long-term toxicity studies on laboratory animals were carried out on MCP and MBQ. Both compounds showed low acute toxicity (oral LD_{50} in the rat higher than 16 g/kg b.w. for MCP and 3 g/kg b.w. for MBQ). From two-year oral studies in rats and dogs and a reproduction study on three generations in the rat, the no-effect levels for MCP were respectively 30 mg/kg b.w. and higher than 200 and 300 mg/kg b.w. Changes in the testes were observed in the rat at dosages higher than 30 mg/kg b.w. For MBQ, the no-effect level in the rat, established from a two-year oral study and a reproduction study on three generations, was higher than 200 mg/kg body weight. No mutagenic activity for MCP or MBQ could be detected in in vitro assays with microorganisms. From these data, ADI's for man were estimated at 0.015 mg/kg b.w. for MCP and 2 mg/kg b.w. for MBQ.

For the combined product, Lerbek, LD_{50}'s for rats and chickens are respectively 10 and 4.64 g/kg b.w. In short term studies with

chickens fed at 1, 2, 4 or 10 x the recommended dose level, feed intake and liveweight gain were depressed significantly at the highest dose level by 21 days. No mutagenic activity of Lerbek could be demonstrated in an Ames test.

It is clear from the foregoing that MCP is appreciably absorbed from the digestive tract of rats, dogs and rabbits. Similar pharmacokinetic data are not available for the chicken. MCP appears to undergo little metabolism within the tissues of all the species examined and chickens would be unlikely to behave differently. With MBQ there is little absorption of the product but some metabolism of the small amount that is absorbed does take place within the body. It is the MCP component of Lerbek that gives rise to measurable tissue residues although none are found after 5 days. A 5-day withdrawal period would therefore ensure the absence of any risk to the consumer.

2. In experiments with soils fertilized with poultry litter from chickens receiving MCP in their diet at levels up to 275 mg/kg, residues of MCP in grass decreased from 7 mg/kg to less than 0.1 mg/kg after 26 months. Over this period of time MCP concentrations in the soil fell by two thirds. Studies on lucerne (Medicago sativa), ryegrass (Lolium perenne), lettuce (Lactuca sativa), carrots (Daucus carota) and dwarf beans (Phaseolus vulgaris) grown in soils intimately mixed with Lerbek (at a level considered to reflect the use of poultry manure from birds fed the product) and harvested 3-4 months later have shown that MCP residues in these crops did not exceed 0.2 mg/kg. These values in general agree with the residues observed in a considerable range of vegetables grown in

soils fertilized before planting with 5 tonnes/ha chicken litter containing 124 or 258 mg MCP/kg. After a 3-4 month period of growth, residues were undetectable with the exception of cabbage (Brassica oleracea) and corn fodder (Zea mais), where they amounted 1.1 and 0.2-0.6 mg/kg respectively. In no instance was any phytotoxicity observed.

The presence of MCP in forages is of no consequence for cattle. Studies on beef cattle fed a predominantly hay diet containing from 5 to 50 mg MCP/kg have shown that MCP residues in muscle tissues never exceeded 0.2 mg/kg. In Holstein cows fed diets containing respectively 3 and 10 mg MCP/kg there were no residues of MCP detectable in the milk. With 30 and 100 mg MCP/kg, MCP residues averaged 0.07 and 0.25 mg/l in milk. No residues were detected after a 36 hour withdrawal period.

Lerbek has no effect on soil nitrifying bacteria; in anaerobic sludge there appears to be a small stimulating effect of the product on methanogenic bacteria. Lerbek has no methane-inhibiting influence on rumen contents. Neither of the components of Lerbek is very soluble in water; solubility values are 40 mg/l for MCP and 0.4 mg/l for MBQ. The LC_{50}'s of MCP and MBQ for a number of aquatic organisms are 7 mg/l and 1 mg/l respectively. The foregoing data suggest that contamination of the environment is unlikely.

3. In the light of the available information, the Committee is of the opinion that the use of Lerbek in feedingstuffs for chickens, at a use-level of 110 mg active ingredient/kg, should be maintained subject to a withdrawal period of not less than five days before slaughter.

B. Turkeys

The Committee proposes to express its opinion when data on metabolism of Lerbek in turkeys, its residues and excreted products become available.

REFERENCES

Dossiers Dow Chemicals.