Report of the Scientific Committee for Animal Nutrition on the use of lasalocid sodium in feedingstuffs for turkeys. (Opinion expressed: 10 July 1991).

Terms of reference (March 1984):

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

1. Does the use of lasalocid sodium under the conditions proposed for feedingstuffs for turkeys (see Background) result in residues in animal products or excreted products which are qualitatively or quantitatively 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 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 Commission Directive 84/587/EEC[2], the use of lasalocid sodium is authorized at Community level under the conditions set out as follows in Annex I, Section D, of the Directive

- Species of animal: chickens for fattening.
- Minimum and maximum content in complete feedingstuffs: 75-125 ppm (mg/kg).
- Other provisions: withdrawal period of at least five days before slaughter.

The Scientific Committee for Animal Nutrition has expressed a favourable opinion on this use in its report of 14 December 1982

At present it is proposed to extend the authorization of use of this additive under the following conditions:

- Species or category of animals: Complete feedingstuffs for turkeys
- Maximum age: up to 16 weeks.
- Minimum and maximum content in complete feedingstuffs: 90-125 ppm (mg/kg).
- Other provisions: withdrawal period of at least three days before slaughter.

Opinion of the committee (July 1991)

Much of the basic information about lasalocid sodium has already been reviewed and evaluated in the Fourth Series of Reports of SCAN (see references). The proposal to extend the use to feedingstuffs for turkeys therefore requires only an evaluation of information specifically related to turkeys.

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[1] O.J. n° L 270, 14.12.1970, p. 1

[2] O.J. No. L 319, 8.12.1984, p. 13

1. After administration for 8 weeks of 125 or 200 mg of lasalocid sodium per kg in feedingstuffs to groups of 5 or 6 turkeys as from one day, old residues of unchanged lasalocid were determined by HPLC/TLC (limit of detection 25 ppb) in muscle, liver, kidney, fat and skin after a 1, 2 and 3 day withdrawal period. Residues at 125 mg/kg dosage ranged from less than 0.025 to 0.085 mg/kg fresh tissue and at 200 mg/kg dosage from 0.025 to 2.25 mg/kg fresh tissue. No residues of unchanged lasalocid were detectable in any tissue after a 48 hour withdrawal period at 125 mg/kg, while for 200 mg/kg only skin contains detectable levels (0.038 mg/kg fresh tissue) after a 3 day withdrawal period.

   The liver was identified as the target organ in terms of total residues when radiolabelled lasalocid was administered. After 5 days withdrawal total labelled residues were 0.85-0.89 mg/kg tissue lasalocid equivalents in the liver, 0.12 mg/kg in the abdominal fat and 0.07-0.11 mg/kg tissue in the kidney, skin and fat from non-abdominal sites.

   These figures are very close to those reported for chickens. Unchanged lasalocid represents only 3.8% of the total residues in the liver, while extractable and non-extractable residues account for about 40% and 50% respectively.

   Turkey excreta contained about 10% of lasalocid in unchanged form, the remainder representing a large number of different metabolites. This figure compares well with the 12% unchanged lasalocid present in chicken excreta. Chromatography confirmed a similar pattern of faecal metabolites for turkeys and chicken.

   The metabolic fate of lasalocid in the turkey has been studied using ^{14}C-lasalocid labelled in three stable positions of the carbon skeleton. A metabolic balance determination established after the administration of daily doses (127 mg/kg feed) for 14 days that after 5 days of withdrawal from some 83.4% and 80.2% of the total administered dose had been were excreted in the droppings of the males and females respectively. Biliary excretion was considerable, indicating a significant absorption of the lasalocid.

   The metabolic fate of lasalocid was compared in chickens and rats. Methodological difficulties arose because the molecule is metabolized into a very large number of metabolites, none of which accounts for more than 1% of the total radioactivity in the tissues or excreta. It may reasonably be concluded that lasalocid is metabolized similarly in the turkey and chicken but differently in the rat.

   In view of the analytical difficulties in identifying the precise nature of the hepatic residues the Committee took into account exceptionally the very low bioavailability of these residues in addition to the above findings.

2. The Committee concluded in the light of the metabolic data that the residues of lasalocid in the liver of turkeys would not present a danger to the health of the consumer. As reported previously (see references) lasalocid has been found to be non phytotoxic and not to have herbicidal, insecticidal or insect growth regulatory activity. Concentrations of drug related material in the excreta are at least of an order of magnitude lower than the acutely toxic levels for aquatic species. There are no data on the end points of the breakdown of the molecule in the environment nor on the environmental effects of the metabolites of lasalocid present in turkey excreta. However the instability of lasalocid in aqueous systems at all pH values, particularly in the presence of light or heat, and in soil, particularly in the presence of chicken

manure, permits the Committee to conclude that lasalocid related material in turkey excreta is unlikely to be prejudicial to the environment.

3. The Committee is of the opinion that the proposed conditions of use are acceptable i.e. a minimum and maximum content of lasalocid sodium of 90-125 mg/kg of complete feedingstuff for turkeys up to the age of 16 weeks but with a withdrawal period of at least 5 days before slaughter. This withdrawal period, which is similar to that recommended for chickens treated with lasalocid sodium, has been chosen because of the close comparability of the level and composition of the residues in the liver of the two species. Although the consumption of turkey liver from birds subject even to a zero withdrawal period would not lead to intakes exceeding the ADI of 0.005 mg/kg b.w., established on the basis of long-term studies in rats, the Committee nevertheless considered a withdrawal period of 5 days necessary because of the differences in metabolic handling of lasalocid by the rat and poultry.

REFERENCES:

- Dossiers submitted by Hoffmann La Roche in 1983 and 1990.
- Report of the Scientific Committee for Animal Nutrition on the use of Lasalocid Sodium in feedingstuffs for chickens. Fourth Series (1984). Report EUR 8769. Catalogue N° CD-NK-83-010-EN-C. Opinion expressed : 14 December 1982; p.106.