REPORT OF THE SCIENTIFIC COMMITTEE FOR ANIMAL NUTRITION ON THE USE OF NITROIMIDAZOLE DERIVATIVES IN FEEDINGSTUFFS

Opinion expressed 8 December 1977

Terms of reference

The Scientific Committee for Animal Nutrition was requested to give an opinion on the following questions concerning dimetridazole, ronidazole and ipronidazole :

1. Have carcinogenic or mutagenic effects been noted in experiments with these products ?
2. Does the use of these products as additives in feedingstuffs result in the presence of residues under the authorized conditions of use ? Could these residues be harmful to the consumer ?
3. In view of the answers to the abovementioned questions, should
   - use as additives in feedingstuffs of the products concerned or of some of them be prohibited in Member States ?
   - their conditions of use be modified ?

BACKGROUND

In accordance with the provisions of Council Directive 70/524/EEC (1), of 23 November 1970, concerning additives in feedingstuffs, as last amended by the nineteenth Commission Directive of 26 July 1977 (2), the use of dimetridazole is authorized at Community level under the following conditions set out in Annex I, Section D, of the Directive :

Species of animal : turkeys, guinea fowl.

Minimum and maximum content in complete feedingstuffs : 125 - 150 ppm (mg/kg).

Other provisions : use prohibited from laying age onwards and at least 3 days before slaughter respectively.

Furthermore, Member States are authorized to use, by way of derogation up to 31 December 1977, dimetridazole for animal species other than turkeys and guinea fowl, ronidazole and ipronidazole. These provisions are set out in Annex II, Section B, of the Directive without specific conditions of use for dimetridazole and ronidazole and under the following conditions for ipronidazole :

Species of animal : turkeys

Minimum and maximum content in complete feedingstuffs : 50 - 85 ppm (mg/kg).

Other provisions : use prohibited at least 5 days before slaughter.

(1) OJ No L 270 of 14.12.1970, p. 1
(2) OJ No L 207 of 13.8.1977, p. 53

In pursuance of this derogation, some Member States have authorized the use of dimetridazole in feedingstuffs for swine at levels of 100 to 150 ppm (mg/kg) with a withdrawal period varying between 3 to 5 days, the use of ronidazole in feedingstuffs for turkeys at levels of 50 to 60 ppm (mg/kg) and for swine at 30 to 90 ppm (mg/kg) with a withdrawal period varying between 3 to 5 days, and that of ipronidazole under the conditions laid down in the Directive.

A recent examination of these additives has revealed some uncertainties as regards the safety of their use in animal feeding. The Commission, therefore, considered it as necessary to seek the Opinion of the Scientific Committee for Animal Nutrition.

OPINION OF THE COMMITTEE

1. An increase in the number of benign and malignant mammary tumours and also mutagenic effects were observed in laboratory animals, in particular in rats, to which high doses of dimetridazole, ronidazole and ipronidazole were administered orally over their lifetime.

2. The sensitivity and specificity of analytical methods and also knowledge of the metabolism of these products enable a precise evaluation of their residues to be made. These are made up of the initial compound and oxidation products, which undergo rapid breakdown in animal products after withdrawal of the additive in the diet. Under the conditions of use at present authorized for these additives and, in particular, withdrawal periods varying between 3 to 5 days, it may be stated that, at the lower limit of analytical determination (0.002 mg/kg), there are no significant residues in the edible products (see Table in Annex). Possible traces in muscle or skin are broken down through cooking and during cold storage.

3. The Committee is of the opinion that there is no reason to prohibit the use of dimetridazole, ronidazole or ipronidazole as additives in feedingstuffs.

   Taking into account the similarity of their metabolism, the Committee considers however that withdrawal periods before slaughter should be standardized in order, with an additional safety factor, to ensure the absence of residues in products of animal origin. To this effect, a withdrawal period of at least 6 days is recommended for each of these additives.

   On this condition and account being taken of their efficacy for the various animal species, minimum and maximum dose-levels in mg/kg complete feedingstuffs should not exceed the following limits :

	Dimetridazole	Ronidazole	Ipronidazole
Feedingstuffs for turkeys	100-200	50-60	50-100
Feedingstuffs for guinea fowl	100-150	-	50-100
Feedingstuffs for swine	100-200	60-90	-

ANNEX

Comparison of data from rearing practice and the study of residues in meat derived from animals consuming nutritional doses of nitroimidazole derivatives

Additives	Practical conditions of use			Residues in meat(a)(b) (mg/kg)
	Species of animal	Dose-level (mg/kg feed)	Duration of use (weeks)	
Dimetridazole	Turkeys	100 - 200	12	<0.002
	Guinea fowl	125 - 150	10	<0.002
	Swine	100 - 150	16	<0.002
Ipronidazole	Turkeys	50 - 100	12	<0.002
	Guinea fowl	50 - 100	10	<0.002
Ronidazole	Turkeys	50 - 60	12	<0.002
	Swine	30 - 90	16	<0.002

(a) After a withdrawal period of 6 days

(b) Lower limit of analytical determination : 0.002 mg/kg.