



Report of the Scientific Committee for Animal Nutrition on the Extension of Use of Diclazuril (E-771) to the Feedingstuffs for Chickens Reared for Laying

(Expressed, 26 September 1997; Text consolidated 5 November 1997)

TERMS OF REFERENCE (July 1995)

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

1. Has the use as of Diclazuril (E-771: 2,6-dicloro-alpha-(4-chlorophenyl)-4-(4,5 dihydro-3,5-dioxo-1,2,4-triazin-2(3H)-yl) benzeneacetonitrile) under the conditions proposed for its use as an additive for chickens reared for laying (see background) significant effects on the prevention of coccidiosis in the chickens reared for laying?
2. Is this use safe for the chickens reared for laying?
3. Does the proposed use result in residues on the eggs? If so, what is the qualitative and quantitative composition of these residues?
4. 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 (1) the use of Diclazuril (E-771) is authorized at Community level in the Annex I, according to the conditions set up by Commission Directive 93/107/EEC (2), as follows (See Table I)

1. Concerning additives in feedingstuffs (OJ No L270, 14.12.70 p.1.) as amended by Directives 84/58/EEC (O.J. No. L319 8/12/84 p 13) and 93/114/EC (OJ L334 31.12.93, p. 24)
2. O.J. No. L219, 4/12/93, p. 44.

Table I. Annex I, Part D (Coccidiostats). Diclazuril (E-771)

Species or category of animal	Maximum age	Minimum / Maximum content mg/kg of complete feedingstuffs	Other provisions
Chickens for fattening	-	1 / 1	Used prohibited at least five days before slaughter

The Scientific Committee for Animal Nutrition has expressed its favourable opinion in its reports of 10 July 1991 on the use of Diclazuril in feedingstuffs for Chickens (3). It has been requested an extension of the use of Diclazuril (E-771) to chickens reared for laying under the following conditions of use (See Table II):

(3) Eight Series of reports, page 51. ISBN 92-826-7975-6

Table II. Annex I, Part D (Coccidiostats). Diclazuril

Species or category of animal	Maximum age	Minimum / Maximum content mg/kg of complete feedingstuffs	Other provisions
Chickens reared for laying	16 weeks	1 / 1	-

A registration file has been submitted by the applicant firm

OPINION OF THE COMMITTEE

The favourable opinion of the SCAN expressed on July 1991 (SCAN reports - 8th series) came from the answers to different questions posed by the Commission, relative to the efficacy and safety of the additive for the target species and category (i.e. chickens for fattening) as well as to its toxicological characteristics, in view of possible risks for the consumer, the user and the environment.

To support the quoted extension of use of Diclazuril in chickens reared for laying, the firm has prepared a short dossier with data relevant to:

- egg production
- egg hatchability
- egg fertility
- eggshell deformation
- residues of the additive in the edible components of eggs layed by treated hens
- a short summary of experiments on the development of immunity.

1. As far as the efficacy of Diclazuril is concerned some relevant studies have been performed in order to demonstrate the anticoccidial activity of this additive, at the requested level of inclusion in feedingstuffs, for the control of coccidiosis from different *Eimeria* strains in pullets for replacement. Moreover, the possible interference of Diclazuril in the development of a protective immunity against *E. acervulina*, *E. maxima*, *E. necatrix* and *E. brunetti* has been investigated.

The results of these investigations show that Diclazuril at the proposed level of inclusion of 1 mg/kg in feedingstuffs provides both a good control of the disease (comparable to that in broilers) and does not markedly interfere with immunity, an important feature for pullets as they live longer than broilers.

2. The safety of the additive for both male and female pullets has been investigated through a comparative study in which the animals where fed with diets containing 0, 1.0 and 5.0 mg/kg of Diclazuril. These diets were given to 39 week old male birds for 46 days (from day 14 up to day 32) and to 54 week old hens for 32 days (from day 0 to day 32).

On eggs collected after inseminations performed weekly for 6 consecutive weeks, the different parameters of safety evaluation previously quoted were recorded together with embryonic mortality in fertile eggs during 3 weeks, the number of eggs vs fertile eggs, the number of weak chickens from fertile eggs and the number of dead chickens from fertile eggs.

No significant differences were recorded among treatments groups, although the number of eggs laid by animals fed the 5 mg/kg Diclazuril diet (i.e. fivefold the recommended dose) was reduced by 12% and the proportion of the dead chicks from fertile eggs increased from 0.1 to 0.6%.

These findings not only agree with the high tolerability shown to Diclazuril by poultry and in mammalian species (as reported in the dossier already examined for the application of use in broilers) but also warrant the absence of harmful effects of the additive on the health and productivity of chickens reared for laying.

3. Diets containing 0 (controls), 1.0 and 5.0 mg/kg (5 times the recommend use level) of Diclazuril were given to laying hens for 32 days. The animals were then maintained on a Diclazuril-free diet for 20 days.

The eggs collected during the whole 32 + 20 days period were analyzed for their content of residual Diclazuril

with a GC analytical method assuring a sensitivity of 50 ppb (0.05 µg/g).

Because of the limited metabolism of the additive by the chickens (from 7.6 to 10,3% of the dose) the data obtained refer to unchanged Diclazuril both in yolk and albumen. During the administration of the diet at 1 mg/kg Diclazuril residues became detectable on day 9 in yolk and on day 11 in the albumen. From this point steady state of concentrations of residues were detected in eggs until 2-3 days following discontinuation of treatment.

The maximum levels of Diclazuril found in yolk and in albumen were 0.322 µg/g at the 3rd day of withdrawal (=322 ppb) and 0.082 µg/g at the 14th and the 29th day of treatment (=82 ppb), the ratio yolk/albumen being always at a constant range of 3.7-3.9.

Treatment discontinuation was followed by a rapid decline of Diclazuril in albumen (below detection limit at the 4th day after withdrawal) and by a longer decline in yolk (below detection limit at the 15th day after the withdrawal).

The steady state concentrations of Diclazuril in eggs laid by hens on a 5 mg/kg diet was very close to that found by using the 1 mg/kg diet (10-11 days) even though residues became detectable (i.e. 3rd day in albumen earlier and 4th day in yolk). The presence of residues was higher in the eggs from these highly dosed animals, the maximum values being reached at the 4th day after the withdrawal in yolk and at the 26th day of treatment in albumen. These values amounted to 1.28 and 0.325 µg/g respectively. The depletion of residues was slower in eggs from these highly dosed animals, lasting up to the 10th day of withdrawal in albumen and still longer in yolk where residues were detectable even after 20 days of withdrawal.

In another study evidence was obtained which confirms the absence of residues (<0.05 µg/g) in the eggs laid by hens reared on a 1 mg/kg diet for 16 weeks before their start of laying.

This finding could justify the claim for 0 day of withdrawal to onset of laying.

Because of the very low level of inclusion in feedingstuffs, an uneven distribution in mixing the additive into diets cannot be ruled out. This is addressed by the following calculation.

Taking into account the maximum values for residues in yolk and white of the 5 mg/kg trial (x5 the recommended dose), and assuming eggs of 35g albumen and 20g yolk, the total egg residue will be a maximum of 37 µg. It can be therefore calculated that a 60kg person consuming 3 eggs a day would ingest a maximum of 111µg of Diclazuril residues. This represents 6.3% of the ADI (1740 µg/person)

Taking into account the results of the 1 mg/kg experiment, a 60 kg consumer eating 3 eggs a day will ingest the 1.5% of the ADI.

4. Conclusively in the light of the answers to the questions posed by the Commission the SCAN is of the opinion that the proposed extension of use of Diclazuril to pullets reared for laying (at the same conditions already approved for broilers) can be accepted without any risk for the target animals or the consumers.

REFERENCES

- Registration file submitted by the firm in 1995
- Diclazuril (RO64433) Documentation assembled and submitted for evaluation by the 50th JECFA (1998) as reply to questions remaining after the 45th JECFA (1995).