

10-10-75

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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SUBJECT: EP#6F1657: Counter 15G soil insecticide, AC-92,100,  
G-[[[(1,1-dimethylethyl)thio]methyl]o,o-diethyl  
phosphorodithioate and its cholinesterase inhibiting  
metabolites - proposal for a tolerance of 0.5 ppm in corn  
forage and fodder (field, popcorn and sweet) and of 0.05 ppm  
in corn grain (field, popcorn and sweet), kernels plus cob  
with husk removed.

TO:  
FROM: TB

TO: M.A. Mautz, PM# 16, IRB  
and Chemistry Branch

American Cyanamid Co.  
Princeton, N.J.

Related Petitions  
471495 361340

No new toxicity data accompany the petition. A final report of  
a two year rat feeding-carcinogenic study was submitted under the  
registration jacket (#241-238) but TB declined to review it for  
technical reasons (see my comments of 8/14/75, #241-238). This  
study is now considered for these tolerance purposes.

Counter 15 G Rat two year chronic and carcinogenic feeding study

(Biodynamics Incorp. # 71R-725) Final report:

The initial three month report was reviewed in detail in the TB  
review of 2/6/73, W.E. Parkins PP#361340; we will only summarize  
the present findings:

Methods:

Groups of female and male rats were offered diets containing 0,  
0.25, 1 or 2 ppm (raised to 4 ppm at week six, then to 8 ppm at  
week 12 with females being returned to 4 ppm at week 16) for two  
years.

Parameters noted and results:

Mortality - total overall mortality incidence prior to termination  
was significantly higher in high-dose males and females and in  
middle dose males.

Thrift - (checked initially, weekly, biweekly and then monthly)  
rate-of-body-weight-gain and feed consumption was significantly  
reduced in high-dose males and females throughout the study.

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Several reduced values occurred early in the study in the middle and low-dose females; this was not noted later on and is not therefore considered to be significant.

Clinical Evaluation: (3 and 24 months)

Hematology - no compound-related differences between groups was noted for Hb., Hct., RBCs, and WBCs. A mild elevation was noted in clotting times at 3 and 6 months in the treated females but we do not consider this to be a significant finding.

Clinical Chemistry - SGPT, APL, Glucose and BUN values were of middle and low dose groups were comparable to those of the controls but glucose was significantly reduced, and BUN was significantly increased in the high-dose females at the three month period.

Cholinesterase - Plasma and RBC ChE values were consistently and significantly reduced in the high and middle dose group males; females showed a similar but less pronounced response in these groups.

Brain ChE values at termination were significantly reduced in the high and middle dose females while the males showed a significant decrease in the high dose group only.

Urinalyses (3, 6, 12, 18, and 24 months)

No significant findings attributable to treatment with LC 92, 199 were noted in protein, glucose, pH, ketones, bilirubin or occult blood.

Pathology (termination)

Organ weight ratios - A slight elevation in liver, kidney and heart-to-body weight ratios was noted in the treated females; there was a slight increase in the kidney ratio for the males. No differences were noted in this parameter for the thyroid gland.

Ophthalmic examination - (23 and 24th months)

The incidence of corneal scarring and cataracts was comparable for the control, lower and middle dose males and females. The high dose females showed a marked increase in the incidence of these abnormalities.

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Microscopic examination of representative tissues

There were no lesions detected microscopically which could be attributed directly to administration of AC92,100.

Discussion and conclusions:

The principle toxicological effect of AC 92, 100 in the diet of rats for two years is that of Cholinesterase inhibition as seen in the middle and high dose RBC and Brain ChE values. The induction of ophthalmic lesions subsequent to the apparent loss of normal lacrimal gland function is a most unusual effect of an organophosphate; indeed, no other such compound has been implicated in this type of lesion so far as we know. However, the appearance of these lesions in the controls (but to a much lesser extent) would seem to indicate an endemic epizootic involving the eyes - not unheard of in rat colonies in which the husbandry is less than perfect, and this may have been exacerbated by treatment with AC 92, 100.

Accordingly, we conclude that the ChE NEL for this study is 0.25 PPM based on RBC and Brain ChE values.

Recommendations:

On the basis of the results of this study and of previously submitted toxicity information, we recommend that the proposed tolerance for residues of AC 92,100 and its cholinesterase-inhibiting metabolites in corn forage and fodder at 0.5 ppm, and in corn grain (kernels and cobs with husks removed) at 0.05 ppm be established.

We defer to CB the question of secondary residues occurring in eggs, meat and milk of livestock and poultry fed such residues-bearing feedstuffs.

*David L. Ritter* 10/10/75  
David L. Ritter, Toxicologist  
Toxicology Branch  
Registration Division

cc: Branch File:EEEB:CB:PP#6F1657

Init: O.E. Paynter 10/8/75

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DLRitter:gac:10/8/75

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