UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

003763

MEMORANDUM

OFFICE OF TOXIC SUBSTANCES

SUBJECT: EPA Reg.#241-EAR; 241-EAN; Amdro - 20 insecticide; Amdro fire ant insecticide; PP#0F2374, tolerance for Amdro of 0.05 ppm in/on forage grasses. CASWELL#642AB; Accession#099464, 099487, 099489

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Recommendations:

1) Since certain types of toxicology studies are currently in progress (i.e., oncogenicity, chronic toxicity, reproduction), certain toxicological aspects of the pesticide have not as yet been fully evaluated. Consequently, all of the potential risks to humans from use of the pesticide are not known. Final reports of the toxicology studies in progress are normally required for permanent tolerances on raw agricultural commodities, such as forage grasses. However, in light of the fact that the requested tolerance on forage grasses may not require a tolerance for any human dietary food items, the submitted toxicity data may be given consideration as a basis of support for the conditional registrations and permanent tolerance on forage grasses. If permanent tolerances were required in meat or milk, the tolerances would not be supported.

2) Toxicity data submitted on Amdro technical include the following:

- °Rat Oral LD50 (both sexes) = 1213 mg/kg
- °Ames Test: negative
- °Dominant Lethal in Rats: negative at 30 mg/kg/day
- °Rat Teratology: negative at 30 mg/kg; NOEL = 3 mg/kg for fetotoxicity
- °90-Day Rat Feeding: NOEL = 50 ppm
- °90-Day Dog Feeding: NOEL = 3 mg/kg/day
- °26-Week Dog Feeding: NOEL = .33 mg/kg/day
- °3-Generation Rat Reproduction (in progress): F_0 generation reported
- °18-Month Mouse Oncogenicity (in progress): 6-month status report
- °24-Month Rat Chronic Toxicity/Oncogenicity (in progress): 6-month status report

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Relative and absolute testes weights were decreased ($p < 0.05$) at both the 200 and 400 ppm levels. Histopathologic evaluation of the testes showed that lesions ascribable to CL 217,300 were still evident and slightly more r umerous after a four-week recovery period. The corresponding restricted control groups were unremarkable histologically.

Conclusion:

The testicular lesions noted in previous studies were the result of ingestion of CL 217,300 and not to reduced food intake. The testicular lesions observed were not reversible within a four-week recovery period.

Classification: Supplementary Data

7) CL 217,300: An 8-Week Feeding and Recovery Study in Mature Rats (AC Report No. AX80-4; Experimental L-1781)

The purpose of this experiment was twofold: (1) To determine if pathologic changes of the testes even seen in previous studies with rats fed CL 217,300 were due to reduced food intake or CL 217,300; (b) To determine if these pathologic changes in the testes were reversible upon removal of CL 217,300 from the diet.

Charles River CD rats (Sprague-Dawley derived) were divided into the following test groups: Group 1, unrestricted control; Group 2, 200 ppm of CL 217,300; Group 3, restricted control, food intake restricted to that of the 200 ppm group; Group 4, 400 ppm of CL 217,300; Group 5, restricted control, food intake restricted to that of the 400 ppm group. The rats received CL 217,300 in the diet for four weeks (groups 2 and 4) or had their food intake restricted during the treatment phase of the test. At the end of the treatment phase 6 rats per group were sacrificed and examined histologically. During the recovery phase the remaining rats were returned to control diet and unrestricted feeding for four weeks. At the end of the 4-week recovery period the rats were sacrificed and examined histologically. The rats were observed twice daily for signs of overt toxicity, moribidity, and mortality. Detailed observations and individual body weights were recorded weekly. Food intake was recorded daily during the treatment phase and weekly during the recovery phase.

Results:

Symptoms of toxicity (anorexia and weight loss) were observed at both the 200 and 400 ppm levels of CL 217,300. Two rats at the 400 ppm level and one rat in the unrestricted control group died during the treatment phase of the study. Decreases ($p < .01$) in weight gains and food intake were observed during the treatment phase of the study at the 200 and 400 ppm levels as well as in the corresponding restricted control groups.

Histopathologic evaluation of the testes indicated that lesions ascribable to CL 217,300 (giant cells, cellular debris in the tubules) were present at the 400 ppm dose level. Hepatic cell degeneration was also observed at the 400 ppm level. The 200 ppm group and the two restricted control groups were unremarkable histologically.

Weight gains and food intake were increased during the recovery phase at the 200 and 400 ppm levels as well as in the corresponding restricted control groups.

Hepatocellular degeneration was not observed in the 400 ppm group indicating that this effect was reversible. Relative and absolute testes weights were decreased ($p < 0.05$) at the 400 ppm level.

Histopathologic evaluation of the testes showed that lesions ascribable to CL 217,300 were still evident and slightly more severe after a 4-week recovery period. The 200 ppm group and the two corresponding restricted control groups were unremarkable histologically.

Conclusion: The testicular lesions noted in previous studies were the result of ingestion of CL 217,300 and not reduced food intake. The testicular lesions observed were not reversible within a four-week recovery period.

Classification: Supplementary Data

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