9-26-78

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

000105

DATE: September 26, 1978

SUBJECT: Registration No: 201-Gov, AZODRIN, CASWELL NO: 377

FROM: J.D. Doherty
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TO: W. Miller
Product Manager

Previous reviews of the delayed neurotoxicity study with Azodrin considered the existing studies inadequate and not establishing the lack of a potential of Azodrin to cause delayed neurotoxic effects. The Shell Oil Company conducted a new hen demyelination study and this test is reviewed herein.

Title: Toxicity of organophosphorous insecticide AZODRIN: Investigation of the neurotoxic potential of AZODRIN-5 to adult domestic hens.

Shell Toxicology Laboratory (TUNSTALL), May 1978, study number TLGR 0066. 78.

By D.E. Owen, S.T.G. Butterworth, (reviewed by Shell employees V.K.H. Brown, and E. Thorpe.)

Healthy Warren Studdler laying hens, 9 months old were pretreated with atropine (17.4 mg/kg) and pralidoxime chloride (50 mg/kg), one hour later groups of 6 hens each were dosed as:

Group I 6.7 mg/kg AZODRIN (this group was supplemented with 8 additional hens to give a total of 14). The dose was repeated after 21 days.

Group II 0.5 ml/kg of Tri-o-tolyl phosphate

Group III No further treatment.

All birds were observed dailyand at intervals tested for their ability to land without staggering when forced to fly. Birds displaying ataxia were sacrificed and examined. The surviving birds were sacrificed and sent for autopsy three weeks after the completion of the second period of dosing (42 days total).

Results

3 of the original six hens treated with AZODRIN 6.7 mg/kg (the LD 50) died after the first dose within 4 days of dosing. Of the eight supplementary hens, 5 died after the first dose of AZODRIN. One of the original hens died after the second dose. Thus of 14 hens, 5 survived the acute dosing). These hens showed no signs of delayed neurological disturbance and were found to be free from histological lesions in the nervous system.

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All hens in the positive control group developed signs of neurological disturbance 15 days after dosing Foci of axonal and myelin degeneration were revealed histologically.

No signs of neurological disturbance was noted in the control birds (Group III).

Conclusion: AZODRIN-5 when given at its LD 50 dose did not develop persistant ataxia or histological evidence to indicate it caused delayed neurotoxicity.

This test is CORE MINIMUM.

Recommendation

This experiment will be acceptable when the detailed scorings on histopathology on the positive control groups are submitted.

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