

US EPA ARCHIVE DOCUMENT

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TOXICOLOGY BRANCH: DATA REVIEW

Chemical: Trichlorfon

Caswell No.: 385
Shaughnessey No.: 057901

Study Type: Acute (delayed) Neurotoxicity in Hens

Citation: Olajos E.G., Rosenblum, I., Coulston, F., Strominger, N., 1979. The dose-response relationship of trichlorfon neurotoxicity in hens. Ecotox. Environ. Safety 3:245-255.

Accession No./MRID No.: NA/GS0104128

Sponsor/Contracting Lab.: N/A (published report)

Report No./Date: N/A

Test Material: Dipterex from Bayer Chemical AG, purity not stated, dissolved in 0.85% saline for assay.

Procedures: Atropinized adult White Leghorn (WL) hens (8/group) were administered test compound once orally or s.c. at doses of 50 and 100 mg/kg (LD₅₀ = 75 mg/kg, established in other studies), while adult Rhode Island Red (RIR) hens were dosed s.c. only at 200 mg/kg (3 hens) or divided schedules of 200 + 100 mg/kg 3 days apart (19 hens). All birds were observed for 12 hr (RIR) or 24 hr (WL) for acute effects, 3 RIR/group and 1 WL/group sacrificed 24 hr post-treatment for neurotoxic esterase (NTE), while the remaining hens were observed for 32 days (RIR) or 35 days (WL) for development of delayed neurotoxicity. All survivors were examined histopathologically (brain, spinal cord and sciatic nerve) and assayed for NTE. Five WL hens served as control (given saline only by unstated route). No concurrent positive controls (TOCP, DFP) were run.


Results: 3/8 WL and 1/8 WL hens given oral trichlorfon (100 and 50 mg/kg, respectively) died during the 5-wk observation period; there was no mortality among WL or RIR birds treated s.c. Dose-related acute muscarinic and nicotinic effects were noted, more severe by the oral than the s.c. route, as well as delayed neurological dysfunction (ataxia) 12-18 days posttreatment and thereafter. 24-Hr brain NTE activity in WL hens was inhibited by approximately 22% at 100 mg/kg by either route, and by 11.5% at 50 mg/kg s.c. (no inhibition was noted orally at this level); among 100 mg/kg-treated birds sacrificed at 5 weeks, NTE inhibition was approximately 9% (both routes), and 4.3% for 50 mg/kg s.c., i.e., near normal (still no inhibition for the lower oral dose). Among s.c.-treated RIR birds, 24-hr NTE was inhibited 43-46% by the single dose but 63-64% by the divided dosage regimen, recovering in the latter group a month later (29-32 days post-treatment) to levels of 22-32% inhibition.

Multifocal neuropathy affecting both the central and peripheral nervous system was evident at the HDT (200 + 100 mg/kg, s.c., 3 days apart), as diffuse degenerative changes in the cerebellar cortex (Purkinje cells), plus some demyelination in brainstem and striatum fibres and sciatic nerve sections. A slighter degree of neurological damage was found in hens given 100 mg/kg trichlorfon orally or s.c.

Hence, the authors concluded that trichlorfon produced dose-responsive acute and delayed neurotoxicity in adult hens, a mild but definite inhibitory effect on brain neurotoxic esterase, and slight to moderate diffuse neuropathological lesions (most evident at the HDT, s.c.). Minimal neuropathy was found at 100 mg/kg.

TB Evaluation: For histopathological changes, the LEL is 100 mg/kg and the NOEL, 50 mg/kg, for both oral and s.c. routes of administration. Mild but definite functional impairment (2-3 "degrees of ataxia" at 100 mg/kg, approximately 1.5 at 50 mg/kg, on a scale of 1-8) was observed 12-18 days post-treatment and thereafter, however, in birds treated by both routes; consequently no NOEL for acute delayed neurotoxicity was determined in this study.

Core Classification: Although no concurrent positive control was included in the study, and a NOEL for acute delayed functional impairment not determined, this study is graded CORE MINIMAL DATA.


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