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*OK - replaced 8/1/83*

DATA EVALUATION RECORD

TRICHLORFON

Acute Delayed Neurotoxicity Study in Chickens--  
Subcutaneous and Oral Routes

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

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Date: *07.30.83*

*No, this review needs to be re-done. Important findings in study not included. Best to do yourself. IC*

DATA EVALUATION RECORD

STUDY TYPE: Acute Delayed Neurotoxicity Study in Chickens--Subcutaneous and Oral Routes.

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

ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Albany Medical College.

TEST MATERIAL: The test chemical was trichlorfon; purity was not stated.

PROTOCOL:

1. The test species were Rhode Island Red and White Leghorn hens. Age/weight of animals--Adult hens 1.5-2.5 kg body weight.
2. The compound was administered in 0.85 percent saline. Dosing regimen:
  - a. Rhode Island Red hens (3), 200 mg/kg, administered once subcutaneously (sc)
  - b. Rhode Island Red hens (19), 200, 100 mg, administered sc, 3 days apart
  - c. White Leghorn hens (8), 100 mg/kg, administered once orally
  - d. White Leghorn hens (8), 50 mg/kg, administered once orally
  - e. White Leghorn hens (8), 100 mg/kg, administered once sc
  - f. White Leghorn hens (8), 50 mg/kg, administered once sc
3. The experimental parameters investigated were as follows:
  - a. The birds were observed for acute toxicity and "cholinergic crisis" for 12 hours.

- b. Three animals from each group were then killed by decapitation and assayed for brain "neurotoxic esterase."
- c. The remaining hens were observed for 32 days, killed and brain homogenates assayed for "neurotoxic esterase." Histopathologic effects on the brain, spinal cord, and sciatic nerve were also examined.
- d. Brain homogenates, in the presence of inhibitors (20  $\mu$ m paroxon, or 20  $\mu$ m paroxon plus 50  $\mu$ m mipafox), were assayed for esterase activity by measuring the hydrolysis of the substrate phenylvalerate.
- e. Formalin-fixed sections from the brain, spinal cord and sciatic nerve of trichlorfon-treated hens were stained with thionin and hematoxylin-eosin, and examined for histological changes.

### RESULTS:

Oral doses of 100 mg/kg trichlorfon or greater produced severe acute general toxic effects; the effects were less severe with oral doses of 50 mg/kg or subcutaneous doses of 100 or 50 mg/kg. At all doses signs of neurological dysfunction were seen at 12 to 18 days. "Neurotoxic esterase" activity (difference between esterase activity in presence of paroxon and mipafox) was inhibited minimally (0 to 20 percent) 24 hours after dosing with 50 or 100 mg/kg and was normal after 30 days. However, levels of 200 mg/kg trichlorfon subcutaneously, or 200 and 100 mg/kg given 3 days apart, inhibited esterase 46 and 64 percent, respectively. Thirty days after this dose, esterase levels were inhibited 20 to 30 percent.

After 300 mg/kg (subcutaneously or orally, in 2 doses), multifocal neuropathy was seen histologically in both the central and peripheral nervous system. There was a disruption of organization of the Purkinje layer of the cerebrum, distorted plasma membranes of neurons, and some chromatolysis. Some sections of sciatic nerves showed axonal swelling and vacuolization of myelin. Minimal degenerative changes in cerebellum, brain stem, and sciatic nerve were seen in hens given 100 mg/kg trichlorfon.

### CONCLUSIONS:

Large oral or subcutaneous doses of trichlorfon caused acute neurotoxic signs in hens. There was a dose-response muscarinic and nicotinic effect. Signs of neurological dysfunction were seen at 12 to 18 days. "Neurotoxic esterase" was inhibited in 24 hours; at 300 mg/kg (200 and 100 mg/kg administered 3 days apart) the level was still inhibited at 30 days but at 100 mg/kg it returned to normal. Histologically, multifocal neuropathy of both central and peripheral nervous system were caused by high doses. However, minimal changes were seen at 100 mg/kg trichlorfon. For histopathologic changes the LOEL is 100 mg/kg and the NOEL 50 mg/kg for both oral and subcutaneous routes of administration.

*grading of dysfunction included in study and should be covered in review. Mild - but definitely positive*

*and thereafter*

*and thereafter?*

CORE CLASSIFICATION: Supplementary Data.

(Minimum) No. 4-84

This study ~~is Core Supplementary since it~~ contains useful information on delayed neurotoxicity. However, ~~only 8 animals were used in most dose groups and~~ a positive control was not included in the study.

in an adequate number of animals per dose group.