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DATA EVALUATION RECORD

TRICHLORFON

Subchronic Toxicity in Dogs

CITATION: Doull J, Vaughn G. 1958. Measurement of the safe dietary level of Dipterex for dogs. (Unpublished study, Chemagro No. 2105, submitted by K.P. DuBois, Department of Pharmacology, University of Chicago, to Chemagro Agricultural Division, Mobay Chemical Corporation).

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ACCESSION NUMBER: 090786.

MRID NUMBER: Not available.

LABORATORY: Department of Pharmacology, University of Chicago.

TEST MATERIAL: Dipterex "50 percent soluble powder" supplied by Chemagro Corporation.

PROTOCOL:

1. Adult male and female mongrel dogs weighing between 15 and 26 pounds were used. The animals were housed in individual cages with outside runs and were provided water and food ad libitum. The animals were kept under observation prior to the study to insure they were disease-free.
2. The dogs were assigned to four test groups of 1 dog/sex/group. During the first five weeks, all dogs were fed the control diet, and weekly determinations of serum and erythrocyte cholinesterase activities were made on each dog to obtain baseline values. The dogs were then fed test material incorporated into the diet at 20, 100, 300, and 500 ppm. The treatment period lasted 12 weeks; the dogs were then returned to the control diet for a four week recovery period. During the treatment and recovery periods, weekly serum and erythrocyte cholinesterase determinations were made on each dog. In addition, the animals were weighed weekly and observed daily for pharmacotoxic signs.
3. Cholinesterase activity was measured using the manometric method of DuBois and Mangun (1947. Proc. Soc. Exper. Biol. Med. 64:137). Duplicate samples were analyzed.

RESULTS:

The variation in serum and erythrocyte cholinesterase activity among the weekly repeated samplings for each dog prior to test material feeding was less than ± 10 percent. The results of the effects of treatment on cholinesterase activity were presented graphically as a percent of control values. Values for males and females were averaged "since there was little difference in the inhibition of the cholinesterase activity" between sexes.

At the lowest dose, 20 ppm, serum and erythrocyte cholinesterase activities were not inhibited, and were increased relative to controls. At 100 ppm, erythrocyte cholinesterase activity was not inhibited, and serum cholinesterase activity was inhibited about 10 percent beginning at 2 weeks after the initiation of treatment. At 300 ppm, erythrocyte cholinesterase activity was reduced about 20 percent by week 4 and 30 percent by week 8, and serum cholinesterase activity was reduced about 35 percent beginning at week 3. At 500 ppm, serum and cholinesterase activity were both reduced about 55 percent after 3 weeks of treatment. During the recovery period, serum cholinesterase activity in the treatment groups returned to near control levels after 1-2 weeks. Erythrocyte cholinesterase activity in the 300-ppm groups returned to control levels after 3 weeks, but in the 500-ppm group the activity remained reduced by about 15 percent 4 weeks after termination of treatment.

"There was no indication of any adverse effects" due to treatment, and none of the dogs lost weight during the treatment period.

DISCUSSION:

This study was reported in summary fashion; data for individual dogs were not reported. In addition, only one dog/sex was used at each treatment level, food consumption data were not obtained, and the dogs were mongrels. Consequently, the results can only be used as supplementary data on the subchronic toxicity of Dipterex in dogs. It is apparent from the data that ingestion of Dipterex ("50 percent soluble powder") at ≥ 100 ppm produced a dose-related decrease in erythrocyte and serum cholinesterase activities.

CONCLUSIONS:

The administration of Dipterex "50 percent soluble powder" via the diet to mongrel dogs (2 animals/dose level) produced a dose-related depression in serum cholinesterase activities at dietary levels of 100, 300, and 500 ppm, and in erythrocyte cholinesterase activities at 300 and 500 ppm. Based on the cholinesterase activities reported, the LEL for Dipterex "50 percent soluble powder" administered in the diet to mongrel dogs was 100 ppm and the NOEL was 20 ppm.

CORE CLASSIFICATION: Supplementary data.

This core classification is based on the following deficiencies:

1. Only one dog/sex was used at each treatment level.
2. Food consumption data were not obtained.
3. Individual animal data were not presented.
4. Tissues were not examined for possible gross or microscopic pathologic lesions.
5. The dogs were mongrels.