2-17-83

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

002504

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: William H. Miller, PM #16
Registration Division (TS-767)

THRU: R. Bruce Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

SUVJECT: CYTHION® Malathion, EPA Reg. No. 241-208;
Two-Year Rat Feeding Study. Acc. No. 76252
CASWELL #535

Registrant:

American Cyanamid Company
Agricultural Research Division
Princeton, N.J. 08540

The Evaluaiton of the Chronic Toxicity Effects of Cythion Administered in the Diet to Sprague-Dawley Rats for 24 Consecutive Months by G. Rucci, P.J. Becci and R.A. Parent, Food and Drug Research Laboratories, Inc., Study No. 5436, May 13, 1980; Acc. No. 76252

Test Material:

Cythion Tech., Lot #W70225-1, 92.1% (The Premium Grade Malathion).

Test Animals:

Male and female Sprague-Dawley rats weighing 50-75 gm.

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Experimental Design:

Animals were acclimated for ten days at FDRL and assigned to 4 treatment groups each of 50 males and 50 females. Cythion was blended with the basal laboratory diet to obtain concentrations of 0, 100, 1000 and 5,000 ppm cythion. These diets and tap water were provided ad libitum to respective treatment groups throughout the study. Weekly diet samples were taken for cythion feed retention analysis.

All animals were observed daily for gross signs of toxicity and palpated weekly for tissue masses. Individual body weights and food consumption were recorded at the end of weeks 1 through 13, 24, 53, 79 and 103 of the study. Blood samples were collected from 5 rats/sex/group during weeks 12, 26, 53 and 104 of the study for hematological and cholinesterase determinations. Urine was collected during the same time periods for analysis.

All animals that died or were sacrificed moribund during the study and all survivors at termination underwent a complete gross necropsy. A variety of tissues and organs were stored in 10% neutral buffered formalin. Fresh organ weights were recorded for the adrenal glands, brain, gonads (testes or ovaries), heart, kidneys, liver, pituitary, spleen, and thyroid (including parathyroids).

Results:

Daily observations (appearance, behavior, absence of overt signs of toxicity) and the incidence of palpable tissue masses of cythion treated rats were comparable to the respective controls. Mortality/survivability were unaffected by dose.

Mean body weight of males were significantly suppressed at the 1000ppm dose level at weeks 3-8, 13, 79 and 103, and were consistently lower than controls at all other intervals. Females at the 1000 ppm dose level had significantly suppressed mean body weights only at weeks 79 and 103. Mean body weights of males and females at the 5000 ppm dose level were significantly suppressed throughout the study. There was no dose-related trend or pattern of food consumption among dosage groups; however, several sporadic significant differences in mean weekly food consumption did occur.

Erythrocyte cholinesterase was significantly depressed in both males and females at 1000 ppm and above. Other hematologic and urinalysis parameters and blood chemistry (BUN, SGOT, SGPT, glucose) indicate no effects of cythion in treated animals at any dose level.

Significant increases were observed in mean liver weight and mean relative liver weight of males at the 5000 ppm dose level. However, microscopic examination revealed no differences in tissue structure compared to controls. Other selected organs were of normal weight.

Gross and microscopic examination of tissues and organs revealed no definite morphologic effects attributable to the presence of dietary cythion at dosage levels up to 5000 ppm. Lesions, both neoplastic and non-neoplastic, that did occur were equally distributed among all dose levels and sexes and considered to be naturally occurring and age-associated but not unusual for this strain of rat.

Conclusion:

There were sufficient numbers of animals (found dead, sacrificed moribund and survivors) examined to evaluate the oncogenic potential. In this study Cythion was not an oncogen in rats.

Chronic NOEL = 100 ppm. Mean body weight gain and RBC ChE significantly depressed at 1000 ppm.

Oncogenic NOEL $\geq$ 5000 ppm

Classification:

Core-Guideline

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