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CASWELL FILE

RDCoberly:deg
March 25, 1968

Acute Rat Oral (6-E)	:	Male LD_{50} = 1.59 gm/Kg Female LD_{50} = 1.367 gm/Kg No systemic toxicity noted at levels up to and including 1.0 ml/Kg.
Acute Rabbit Dermal (6-E)	:	Male and female LD_{50} = >4.64 gm/Kg
Acute Rat Inhalation (6-E)	:	LC_{50} = >31.5 mg/L Reddening and consolidation was noted in the lungs at both levels ie: 3/10 at 7.2 and 6/10 at 31.5 mg/L.
Twenty-One Day Rabbit Dermal (6-E)	:	Tested at 150 and 300 mg/Kg/day No mortality. Some cholinesterase inhibition. Some body weight loss. No effect level = ~150 mg/Kg/day.
Thirteen Week Rat Feeding (Tech)	:	Levels were 8, 16, and 32 mg/Kg/day No effect level = >16 mg/Kg/day and <32 mg/Kg/day. Toxic effects at the 32 mg/Kg/day were not outstanding.
Fifteen to Sixteen Week Dog Feeding (Tech)	:	Levels were 450, 900, and 1,800 ppm. No mortality. Some brain cholinesterase inhibition and gastric mucosal changes noted at 1,800 ppm. No effect level = >900 and <1,800 ppm.

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S-Ethyl Dipropylthiocarbamate EPTAM

Acute Rat Oral (6-E)

Five males and five females were tested per dosage level of 464, 1,000, 2,150, and 4,640 µl/Kg. Animals were fasted overnight prior to dosage.

Results

Male LD_{50} = 1,710 µl/Kg or 1.59 gm/Kg. Female LD_{50} = 1,470 µl/Kg or 1.367 gm/Kg.

The dosage levels of 1.0 ml/Kg showed no systemic toxicity. The higher levels showed inactivity, depression and lacrimation. Onset was from two to ten hours after dosing.

The animals which succumbed showed lung erythema and congested kidneys and adrenals. Survivors showed no gross findings.

Acute Rabbit Dermal (6-E)

Single doses of the undiluted formulation were applied to the intact abdominal skin at the levels of 1,000 and 4,640 mg/Kg. Two males and two females were used per dosage level. Exposure was 24 hours.

Results

No mortality was recorded. LD_{50} = >4.64 gm/Kg. Severe erythema and slight edema were noted. Two to three days later the area appeared red-brown in color and thickened with a few hard black eschars forming.

Desquamation followed and scar tissue was noted in five of eight animals.

Acute Rat Inhalation (6-E)

Five males and five females were exposed to a chamber concentration of 7.2 or 31.5 mg/L. Duration of exposure was one hour. The droplets were between one and five microns in size.

Results

During the exposure the animals at the 31.5 mg/L level showed some signs of distress, lacrimation, and slight ataxia. No unusual signs were noted at the 7.2 mg/L level. There were no deaths.

Autopsy findings showed reddening and consolidations in the lungs of six of ten animals at the higher level and three of ten animals at the low level. A no effect level was not reached in this study.

Twenty-One Day Rabbit Dermal (6-E)

The dose levels in this study were set at 2.0 ml/Kg/day of a 20% aqueous dilution and at 2.0 ml/Kg/day of a 10% aqueous dilution, equivalent in terms of active ingredient to approximately 300 and 150 mg/Kg/day respectively. Ten males and ten females were used per dosage level with half of each sex on each level being abraded. The animals were held in stocks until the material had either dried or penetrated the skin. After 24 hours of exposure the exposed area was washed to remove the remaining compound. This procedure was repeated daily for five days a week for three weeks.

RESULTS:

Two intact females at the high level lost 600 and 300 gms respectively. At the low level one male lost 220 gms and one female lost 410 gms. Both animals had intact skin. The mean body weight gain of the two test levels was moderately lower than the corresponding control value.

Dermal irritation was comparable for the control and low level animals. For these animals a slight erythema was observed by the third day and persisted for the duration of the study. Parching of the skin followed by a flaking and sloughing of the epithelial debris was noted during the second week of the study. A fissuring of the treated area, dryness, and sloughing of the skin persisted until termination. For some rabbits layers of dry skin could be pealed from their backs. These changes were also noted for the high level rabbits. However, erythema was more marked and the pealing of dry skin was more pronounced and frequent.

Hematological values of the test animals were comparable to the control values.

The erythrocyte, plasma, and brain cholinesterase activity of the test levels was slightly reduced from that of the controls. The low level test animals showed a lesser reduction than the high level.

Gross autopsy findings showed no significant difference between the test and the control animals.

Histopathological Observations - In some sections of liver mild glycogen depletion and slight irregularity of hepatic cell size were more distinct in the treated rabbits than in the control rabbits.

From these data it can be concluded that the test material caused borderline to slight effects such as erythrocyte and plasma cholinesterase inhibition, mild glycogen depletion and slight irregularity in hepatice cell size. It is also obvious that these findings are somewhat increased for the high level. It can be concluded that the no effect level for this material dermally is in the immediate area of 150 mg/Kg/day.

Thirteen Week Rat Feeding (Tech)

Fifteen males and fifteen females were tested per dosage level of 8, 16, and 32 mg/Kg/day.

Results

The general appearance behavior and survival of the treated animals was comparable to the control animals.

The body weight of the 32 mg/Kg females was statistically significantly less than the corresponding control females. However, the mean body weights of the animals fed the 8 mg/Kg level was elevated over that of the corresponding control values. Food intake for these groups varied according to the weight gain or weight loss.

Hemograms and clinical determinations and brain cholinesterase determinations of the 32 mg/Kg/day rats was comparable to the control values.

Histopathological observations showed a slightly greater frequency of very slight irregularity in hepatic cell size with some glycogen depletion in the high level test animals as compared to the control animals.

Fifteen to Sixteen Week Dog Feeding (Tech)

Three males and three females were tested per dosage level of 450, 900, and 1,800 ppm.

Results

The pharmacologic and toxicologic effects were limited to, slight reduction of brain cholinesterase at 1,800 ppm, small areas of hair loss for two dogs in each of the 1,800 and 900 ppm levles, and gastric mucosal changes for one male at the 1,800 ppm level.

The aforementioned loss of hair has been noted on occasion for four other dogs from the same supplier. If we assumed this hair loss at the 900 ppm level was not due to the chemical then the no effect level is equal to greater than 900 and less than 1,800 ppm.

Washington, D. C.
November 28, 1967

Mr. Kenneth Nash
Pesticide Regulation Division
Agricultural Research Service
U. S. Department of Agriculture
Washington, D. C. 20250

Dear Mr. Nash:

The toxicological data on S-ethyl dipropylthiocarbamate has been reviewed in connection with Reg. No. 476-1307.

These data show the chemical to exhibit a low degree of acute and subacute toxicity in experimental laboratory animals. Information resulting from inhalation exposure was not included in these data. We would appreciate receiving a copy of it.

We concur with you in the registration of this chemical for uses stated on the aforementioned Reg. No.

Sincerely,

Robert D. Coberly
Biologist
Registration Section
Pesticides Program

RDCoberly:mw

March 25, 1968

Mr. Kenneth B. Nash
Pesticide Regulation Division
Agricultural Research Service
U. S. Department of Agriculture
Washington, D. C. 20250

Reg. No. 476-1620
Referral Date: 2/23/68

Dear Mr. Nash:

The acute rat inhalation study using the 6-E formulation of S-Ethyl dipropylthiocarbamate (Eptam) received from the Stauffer Chemical Company has been reviewed. These data were requested in my letter to you of November 28, 1967.

These data show the LC_{50} of the formulation to be greater than 31.5 mg/L. They also show the no-effect level to be less than the lowest level tested i.e. 7.2 mg/L.

As this level produced reddening and consolidation in the lung of 3/10 animals, it would be helpful in the evaluation of this chemical to know the approximate no-effect inhalation level.

This does not constitute an objection to the registration of the chemical as used in Reg. No. 476-1198 or 476-1620.

Sincerely,

Robert D. Coberly
Biologist
Registration Section
Pesticides Program

cc: Tox File
Mildred Workinger

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