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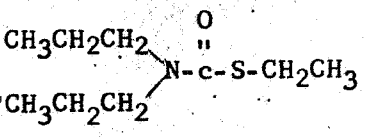
CASWELL FILE

RDCoberly:deg
November 30, 1967

Chemical Name	:	S-Ethyl dipropylthiocarbamate
Trade Name	:	Eptam
Chemical Structure	:	
Physical State	:	Liquid
Boiling Point	:	232°C at 760 mm
Solubility	:	Very slightly soluble in water, miscible with most organic solvents.
Available Formulations	:	2.3, 5.0, and 10% Granular and 75.4% EC.
Use	:	Herbicide (ornamentals, crops)
Company	:	Stauffer Chemical Company
Reason	:	New Chemical to PHS
Deadline	:	December 15, 1967

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Acute Rat Oral (R-1608)	:	LD_{50} = 1.71 ml/Kg (~1.71 gm/Kg). Physical signs included depression, closed eyes, lacrimation and labored respiration.
Acute Mice Oral (Tech) (99%)	:	LD_{50} = 3.16 gm/Kg. No toxicity noted at 215 mg/Kg. Toxicity signs noted at 464 mg/Kg and higher.
Acute Dog Oral (99% Tech)	:	Levels tested were 1.59, 2.51, 6.31 gm/Kg. No deaths. Emesis occurred at both high levels.
Acute Rabbit Dermal (R-1608)	:	LD_{50} = > 2.15 ml/Kg. Mild erythema noted.
Acute Rabbit Dermal (Tech)	:	LD_{50} = ~10 gm/Kg. Mild erythema noted.
Acute Rabbit Eye Irritation (R-1608)	:	A moderate degree of eye irritation was noted.
Skin Sensitization (Guinea Pig) (Tech)	:	Did not produce skin sensitization.
21 Day Rat Feeding (Tech)	:	Tested only at 326 mg/Kg/day. Some excitability noted. No deaths. No effect level is = 326 mg/Kg/day.

Summary

These data indicates the chemical to have a low degree of acute and subacute toxicity in experimental animals by the routes investigated. The subacute no effect can be based only on one study at one dosage level. This level, 326 mg/Kg/day produced very little if any effects. Thus we can assume the no effect level in rats is approximately 326 mg/Kg/day. Accordingly the safe consumption for man in food is approximately 15 ppm in food.

Information pertaining to the results of inhalation exposure was not submitted.

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S-Ethyl Dipropylthiocarbamate

Acute Rat Oral (R-1608)

Five male rats were doses with the undiluted test material or a 10% volume/volume solution at dosage levels of 0.215, 0.464, 1.00, 2.15, and 4.64 ml/Kg (assuming the specific gravity to be 1.0, these dosage levels are equal to 215, 464, 1,000, 2,150, and 4,640 mg/Kg). Animals were fasted for a period of three to four hours.

Results

The LD_{50} = 1.71 ml/Kg (confidence limits from 1.05 to 2.78 ml/Kg).

Within 24 hours the following mortality was observed: 60% at 1.0 ml/Kg; 20% at 2.15 ml/Kg; 80% at 4.64 ml/Kg.

Immediately following administration of the test material the animals on all dosage levels appeared depressed and showed squinting or closed eyes, lacrimation, preening, and labored respiration. Additional gross signs of systemic toxicity among the animals at the three higher dosage levels included salivation, sprawling of the hind limbs, ataxia, and depressed placement, righting, and pain reflexes. Death was preceded by gasping, LABORED respiration, and coma. Three of the four surviving animals at the 2.15 ml/Kg level appeared depressed and exhibited nasal discharge, wheezing, and labored respiration throughout the study.

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Gross autopsies performed on the animals that died showed a bright red coloration of the lungs, irritation of the gastrointestinal tract and peritenoneum, and congested kidneys and adrenals. The animals of the three lower levels showed no pathology. Three of the animals at the 2.15 ml/Kg dosage level showed consolidated and abscessed areas present in the lungs.

Comment

The material used in this study is assumed by the reader to be 100% pure chemical.

Acute Rabbit Dermal (R-1608)

Four rabbits were tested per dosage level of 1.00 and 2.15 ml/Kg.

Results

No mortalities were observed. LD_{50} = >2.15 ml/Kg.

The single application produced a mild degree of irritation characterized by mild erythema which subsided in four to six days. At autopsy all the organs appeared to be within normal limits.

Acute Rabbit Eye Irritation (R-1608)

A single application of 0.05 ml of the undiluted test material was placed in the conjunctival sac of the left eye of each of three rabbits. The eye was held closed for approximately 30 seconds after which an immediate reading was made. Additional observations were made at 1, 4, and 24 hours post-treatment, and daily thereafter for 6 days.

Results

Within four hours following the application there was a moderate degree of irritation which was characterized by erythema, vascularization of the sclera and nictitating membrane, edema of the lids and nictitating membrane, mild iritis and corneal dullness, accompanied by lacrimation and exudate. These signs gradually subsided within four days post-treatment.

Acute Mice Oral (99% Tech)

Five male albino mice were tested per dosage level of 215, 464, 1,000, 2,150, 4,640, and 10,000 mg/Kg. The animals were fasted for a period of three to four hours prior to treatment.

Results

LD_{50} = 3.16 gm/Kg. The levels of 4,640 and 10,000 mg/Kg produces 100% mortality within 24 hours. The lower dosage levels produced no mortality. The animals of the lowest level exhibited normal appearance and behavior. Within 15 minutes or less the remaining animals appeared depressed and showed lacrimation, labored respiration, and ataxia. In addition, the animals at the three highest dosage levels showed signs including ptosis, jerky body movements, and vasodilation of the ears, feet and tail, and around the nose and mouth. The moribund animals at the two top levels also exhibited sprawling followed by stiffening of the limbs, depressed

and/or absent righting, placement and pain reflexes, and intermittent clonic convulsions. Death was preceded by coma and gasping.

Within three to six hours post-treatment the animals on the 464, 1,000, and 2,150 mg/Kg dosage levels exhibited normal appearance and behavior.

Gross autopsies performed upon the animals that died showed hyperemic or hemorrhagic lungs and congested kidneys, adrenals, and pancreas.

Acute Dog Oral (99% Tech)

Two males and two females were tested per dosage level of 1.59, 2.51, and 6.31 gm/Kg. The compound was given in gelatin capsules on an empty stomach.

Results

Approximately one hour following administration of 1.59 gm/Kg emesis was observed in two dogs. The dog which did not vomit produced formed excreta approximately one and a half hours following administration; the fecal material showed a mucous coating and had an intensely pungent odor resembling the odor of the material administered.

Approximately one hour following oral administration of the 2.51 gm/Kg emesis occurred in all four dogs. All four dogs appeared normal when sacrificed after seven days.

Emesis was observed in all dogs 25 to 55 minutes following treatment with 6.31 gm/Kg of the test material. Other signs observed were excitability, tremors, salivation and lacrimation. One dog produced

soft excreta which had a pungent odor resembling the odor of the test material. On the following morning one dog was mildly ataxic; the remaining three animals appeared normal. Gross autopsies performed at ten days revealed no pathological changes which could be attributed to the test material.

Acute Rabbit Dermal (Tech)

Four rabbits were tested per dosage level of 2.51, 3.98, 6.31, and 10 gm/Kg. The test material was used in the undiluted form.

Results

The 10 gm/Kg level produced 50% deaths. As these were the only deaths in the study the LD_{50} is calculated to be approximately 10 gm/Kg. The animals on the three lower dosage levels appeared normal throughtout the study. At 24 hours the high level animals appeared depressed and exhibited unsteadiness and labored respiration. In one of these rabbits which was moribund, there was sprawling of the limbs, depressed righting and placement reflexes, prostration, and intermittent clonic convulsions. The eyes of this animal showed erythema and iritis. After 48 hours the animals on this level appeared normal.

Gross autopsies performed upon the animals that died showed hemorragic lungs. The internal organs of one of the animals that died appeared pale, while the remaining animals showed congested kidneys and adrenals,

irritation of the intestinal track, and a granular liver. The autopsy of the surviving animals showed no significant gross pathological findings.

Skin Sensitization (Guinea Pig) (Tech)

Intracutaneous injections of a 0.1% weight/volume suspension of the test material in 3% volume/volume propylene glycol/physiological saline were made on the left trunk area of ten animals, while the vehicle alone was injected on the right trunk area. Two animals received intracutaneous injections of a 0.1% volume/volume solution of 1-chloro-2,4-dinitrobenzene in sesam oil. The control and test materials were injected in the trunk areas of the animals every other day until a total of ten injections had been given. Sixteen days following the tenth injection, a challenge injection was given. The doses were 0.05 ml for the first injection, 0.1 ml for the next nine injections, and 0.05 ml for the challenge injection. Readings of irritation of the sites of injection were made 48 hours following administration of each dose.

Results

Both animals receiving the positive control (1-chloro-2,4-dinitrobenzene showed slight to moderate irritation (the challenge dose produced a reaction in which the erythema and edema were increased over the initial and sensitizing dose. This material does produce skin sensitization.

The animals receiving the vehicle showed signs of very mild erythema. The challenge dose produced the same degree of results.

All animals receiving the test material exhibited mild primary irritation from the first injection. Nine of the ten test animals showed increased irritation following the second to seventh sensitizing doses. The challenge dose produced slight erythema in eight animals and no reaction in two animals. These data indicate that the test material does not produce skin sensitization in the guinea pig.

Twenty-Ond Day Rat Feeding (Tech)

Ten male albino rats were tested at a dosage level of 326 mg/Kg per day. This is approximately one-fifth of the acute LD_{50} for rats.

Results

The mean body weight gain for the experimental animals was significantly lower than the corresponding controls. However, an examination of the body weight gains on a weekly basis indicates that the food was not readily accepted by the test animals during the first week. During the second and third week the test animals ate more food and reduced the difference in the body weight gains. Thus it appears this difference is due to the reduced food consumption during the first week rather than the actual effect of the chemical. No deaths occurred. Approximately one-half of the test animals exhibited excitability during the second or third day of the study; this was the only consistent observation noted. However, this phenomenon was not noted during the remainder of the study.

No gross or microscopic abnormalities were observed in the control or experimentsl animals at termination.

Comment

Based on the results of these data the no effect level in rats is approximately 326 mg/Kg/day.

U.S. DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
PESTICIDES REGULATION DIVISION
WASHINGTON, D. C. 20250

INTERDEPARTMENTAL COORDINATION OF ACTIVITIES RELATING TO PESTICIDES

Referral of Application for Registration under the Federal Insecticide, Fungicide, and Rodenticide Act

APPLICANT

Stauffer Chemical Corp.
366 California Street
San Francisco, California

2. PRODUCT		3. DATE OF REFERRAL
STAUFFER EPTAM 5% GRANULAR	476-1307	11-24 wk of 12-1-67

4. COMMENTS BY COORDINATING AGENCY

5. BY (Name)	6. DATE	7. NAME OF AGENCY

PR FORM 9-230
DEC 1964

REPLACES PR FORM 9-230, OCT 1964, WHICH IS OBSOLETE

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Eptam

Page __13__ is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product inert impurities.

_____ Description of the product manufacturing process.

_____ Description of product quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

__X__ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.