4-27-82

Memorandum

Date: 27 April 1982

Subject: EPA Reg. No. 476-1713 ASPON 6-E
Caswell 845A

From: B. T. Backus
IRB/TSS

To: Mr. William Miller
Product Manager 16

Registrant: Stauffer Chemical Co.
1200 South 47th St.
Richmond, CA 94804

Active Ingredient:
0,0,0,0-tetrapropyl dithiopyrophosphate.....67.64%
Inert Ingredients:.....32.36%

Background:

The registrant has submitted Acute Oral LD50, Dermal LD50, Primary Dermal and Eye Irritation studies on this formulation as data required to support its reregistration.

Comments and Recommendations:

1. The Acute Oral LD50, Dermal LD50, Primary Dermal and Eye Irritation studies received 3-4-82 on this product are acceptable.

2. A short summary of an Acute Inhalation LC50 study was submitted, but the actual study was not received. According to the summary sheet, this study is in final report preparation.

Labeling:

1. "Atropine by injection is antidotal" should be revised to "Atropine by injection is antidotal only if symptoms of cholinesterase inhibition are present."

2. The IF SWALLOWED statement of practical treatment could be revised to something like the following:

IF SWALLOWED: Contact your local Poison Control Center, Physician or hospital immediately. Give water, but do not induce vomiting. Do not give anything by mouth to an unconscious or convulsing person. If the patient is unconscious, maintain breathing and heart rate (CPR: cardiopulmonary resuscitation).

3. The Statement of Practical Treatment for IF ON SKIN should be:

   IF ON SKIN: Wash with plenty of soap and water.

   (although not necessary, we can accept the additional wording: "Remove contaminated clothing and shoes. Get medical attention if irritation occurs. Wash clothing before re-use.").

4. The appropriate Statement of Practical Treatment for IF IN EYES would be:

   IF IN EYES: Flush with water for 15 minutes. Get medical attention if irritation persists.

   alternatively, we can accept a modification of the statement proposed in the labeling received 3-4-82. Note that we prefer IF IN EYES to FOR EYE CONTACT.

   IF IN EYES: Hold eyelids apart and flush eyes with large amounts of running water for at least 15 minutes. Get medical attention if irritation persists.

5. The recommended Statement of Practical Treatment for IF INHALED is:

   IF INHALED: Remove victim to fresh air. If not breathing, give artificial respiration, preferably mouth-to-mouth. Get medical attention.

6. The signal word WARNING has been proposed, apparently because of the oral LD50 in female rats (475 mg/kg). We can accept this. The appropriate Hazards to Humans and Domestic Animals statement would tentatively then be:

   WARNING: May be fatal if swallowed. Harmful if absorbed through skin. Do not breathe vapors or mist. Avoid contact with eyes, skin or clothing. Wash thoroughly after handling. Avoid drift to food or forage crops.

   (according to the summary sheet, the inhalation LC50 for this product is greater than 5 mg/L for 4-hour exposure. If this study is acceptable, the product may then be in toxicity category IV by this exposure route, and the proposed "May be fatal if inhaled." would be inappropriate.

Review:

The following studies were conducted on a representative sample (containing 68.1% active; label declaration = 67.64%) of the registered product. Studies were conducted at the Stauffer Chemical Co. Richmond Toxicology Laboratory, Richmond CA 94804 under Laboratory Report T-10610. Studies were received at EPA 3-4-82 and are in Acc. 246893.

1. Acute Oral LD50 - Rat. Laboratory Report T-10610; dated 11-17-81.

Procedure: Groups of 10M SD rats received oral dosages of 1259, 1381, 1585, 1995, 2239 and 2500 mg/kg. Groups of 10F SD rats received oral dosages of 398, 422, 500 or 631 mg/kg. Subjects were observed for 14 days.

Results: Mortalities:

Dosage Level (mg/kg)	Mortalities/Animals Dosed M	F
398	-	0/10
422	-	3/10
500	-	6/10
631	-	8/10
1259	0/10	-
1381	6/10	-
1585	4/10	-
1995	6/10	-
2239	10/10	-
2500	10/10	-

Oral LD50(M) = 1685 (1505-1886) mg/kg.
Oral LD50(F) = 475(413-546) mg/kg.
Symptoms: depression, diarrhea, shallow breathing, ataxia, salivation, lacrimation, tremors and stained fur. Necropsy findings on animals which died included bloated discolored intestines, reddened lungs, discolored spleens, enlarged purple testes. Most survivors seemed normal by day 5, and post-sacrifice necropsies were unremarkable.

Study Classification: Core Minimum Data

Product Classification: Because of the considerable sensitivity of female animals, Tox. Cat. II

2. Acute Dermal LD50 - Rabbit. Laboratory Report T-10610; dated 11-17-81.

Procedure: A group of 10 Stauffland albino rabbits, of which at least 4 were M, 4 were F, received a 24-hr occluded dermal exposure to a dosage level of 2000 mg/kg with subsequent 14-day observation.

Results: 3 animals (sex unspecified) died. Symptoms included depression, diarrhea, shallow breathing, ataxia, excessive urination and nasal discharge. Survivors still appeared depressed on day 14. Necropsies showed reddish-black intestines in one rabbit, reddish-yellow fluid filled intestines of another and reddened lungs in another. Survivors were unremarkable. Deaths were at days 10, 12 and 14.

Study Classification: Core Minimum Data (study is borderline, but the considerable time elapsed between exposure and death - if death was caused by this formulation - indicates the dermal LD50 value is above 2 gm/kg).

Product Classification: Tox. Cat. III

3. Primary Dermal Irritation - Rabbit. Laboratory Report T-10610; dated 11-17-81.

   Procedure: 0.5 mls was placed at each of 2 sites, one intact, one abraded, on each of 6 rabbits, with 24-hr occluded dermal exposure.

   Results: PDIS = 1.75, with improvement between 24 and 72 hrs.

   Study Classification: Core Minimum Data

   Product Classification: Tox. Cat. IV

4. Primary Eye Irritation - Rabbit. Laboratory Report T-10610; dated 11-17-81.

   Procedure: 0.1 ml test material was placed in one eye of each of 9 rabbits, with 3 eyes being flushed out with water starting 20-30 seconds after instillation. Remaining 6 eyes were unwashed.

   Results: Slight irritation present in all of unwashed eyes at 24 hrs; no irritation (all scores zero) in washed eyes at all times. All unwashed eyes had cleared at 4 days.

   Study Classification: Core Minimum Data

   Product Classification: Tox. Cat. III

Byron T Backus 04/27/82

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