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MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 10182-150
Vapam Soil Fumigant For All Crops

FROM: William S. Woodrow WSW 1-18-93
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)
E 1/29/93

TO: Susan Lewis / Sidney Jackson (PM 21)
Fungicide-Herbicide I Branch
Registration Division (H75-05C)

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

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Sodium methyldithiocarbamate (anhydrous)	32.7
Inert Ingredient(s):	67.3
Total	100.0%

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BACKGROUND

The Stauffer Chemical Co. submitted a new primary dermal irritation study for VAPAM Soil Fumigant Solution for All Crops (EPA Reg. NO. 10182-150).

Mary Waller previously reviewed a dermal sensitization study Aug. 3, 1982. This product was shown to be a skin sensitizer. Study graded Guideline Data.

Mary also reviewed acute oral, acute dermal, acute inhalation, primary eye and skin irritation studies Sept. 2, 1988. A re-examination of the VAPAM effects reported in Mary's review seem to indicate probable destruction of the skin dermis (corrosive effects), and therefore this study probably should have resulted in a Toxicity Category of I designation; instead of Category II.

RECOMMENDATION

1) The new skin irritation study (MRID #25114-

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, laboratory NO. CTL/P/3793 is acceptable, and was graded Guideline Data. Due to dermal necrosis (tissue destruction), this study was given a Toxicity Category I status. The Tox. I Category will dictate the skin portion of Precautionary Labeling.

2) Current acute toxicity profile for VAPAM (NO. 10182-150):

study	Classification	Tox. Category
acute oral LD_{50} 1294 (1062-1578) mg/kg	Guideline	III
acute dermal LD_{50} = 1012 (720-1421) mg/kg	Minimum	II
acute inhalation LC_{50} > 4.7 mg/l	Guideline	III
eye irritation - irrit. absent by day 2	Guideline	III
skin irritation eschar - in depth destruction - day 21	Guideline	I
dermal sensitization - did sensitize	Guideline	-

LABELING

1) The DANGER signal word is appropriate.
2) Change the Precautionary Statements to read "Corrosive. Causes burns. May be fatal if absorbed through skin. Harmful if inhaled or swallowed. Causes eye injury (irritation). Do not get in eyes,

on skin or on clothing. Wear protective clothing and rubber gloves. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse. PROLONGED OR FREQUENTLY REPEATED SKIN CONTACT MAY CAUSE ALLERGIC REACTIONS IN SOME INDIVIDUALS. E

3) The Statements of Practical Treatment are acceptable:

PM NOTE: This product is intended for uses other than residential or institutional use (40 CFR § 152.170 (2) All other uses, and does meet the requirement for restricted use classification.

"§152.170 (b) (2) (vi) The pesticide, as formulated, is corrosive to the skin (causes tissue destruction into the dermis and/or scarring." (This product caused eschar - in depth destruction in two rabbits through 21 days post treatment).

PM should determine if alternative labeling language is sufficient to offset the hazard and the need for restricted use classifications.

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

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Product Manager: (21) 8-21-92 Reviewer: Woodrow M Waller
MRID No.: 425214-01 Report Date: 1-7-93
Testing Laboratory: ICI Central Tox. Lab. Cheshire, U.K. Report No.: CTL/P/3793
Author(s): P. Robinson
Species: Rabbit
Age: Young adult
Sex: Female
Weight: 3292-4486 g.
Dosage: 0.5ml undiluted
Test Material: "VAPAM", metam sodium (Sodium methyl dithiocarbamate) liquid
Quality Assurance (40 CFR §160.12): both G.L.P. & Q.A.

Summary:

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The Primary Irritation Index = _____

Toxicity Category: I

Classification: Guideline

Procedure (~~Deviations from §81-5~~): Animals acclimated to lab. conditions at least 6 days pre-test. 24 hours before application, hair was removed by clipping to backs of 7x13 cm on left flanks of ~~6 rabbits~~ rabbits. 0.5ml was applied to each prepared site, covered with 2.5x2.5cm gauze patch, secured & taped, & wrapped with impermeable rubber sheeting. Sheeting secured with tape. 4 hour exposure. Each (of 6) dressings removed, treated sites rinsed; collars placed on some animals to prevent site damage. Treated sites scored according to Draize system @ 30-60 min, 1, 2, 3 days post patch removed. Assess erythema & edema scores. Calculated Persistence of irritation in 3 animals (up to 21 days) — from these sites, skin samples were removed, fixed, and scanned for

~~Results~~:

Special Comments:

Histopathology.

2 of 6 animals - necrotic test sites at 21 days: Corrosive (tissue destruct, in into dermis)

Draize Scale: ER 0 ED 0

1 1

2 2

3 3

4 4

Results: Average (6 rabbits) ER & ED scores

	30-60m	1 day	2 days	3 days	4 days	5 days	7 days	8 days	10 days
ER	2.8	2.8	2.5	2.5	1.5	1.5	2.0	0.8	0.6
ED	3.6	3.5	2.6	2.6	1.1	0.8	0	0	0

	11 days	12 days
ER	0.31	0.5
ED	0	0

Two rabbits showed irritation (scored) at 14 days, 15 days, 17 days, and both of these rabbits exhibited 2.0 scores at 21 days post patch removal, for erythema (no edema). 2.0 erythema = well defined erythema.

Three of rabbits showed persistent skin lesions (upto 21 days). Samples of test site and samples from opposite sites were removed & prep and for examination.

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"Improvement during 3 days - (irritation thru 21 days) Moderate to severe erythema - one had completely cleared by 21 days.

Histopathological examination revealed (3 cases) complete loss of hair follicles - fibrous tissue spreading down to subcutaneous muscle layers. Epithelium necrotic with large covering layers of surface debris, a moderate inflammatory reaction at center of lesion and severe acanthosis with slight hyperkeratosis at edges.