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MEMORANDUM

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

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

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

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

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
<u>Sodium methyldithiocarbamate (anhydrous)</u>	<u>32.7</u>
_____	_____
_____	_____
<u>Inert Ingredient(s):</u>	<u>67.3</u>
<u>Total</u>	<u>100.0%</u>

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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, 1987, 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 425 214-

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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 Toxicity 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 - <u>did</u> 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."

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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.

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 classification.

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

Woodrow 010218

Product Manager: (21) 8-21-92 Reviewer: H. Waller
 MRID No.: 425214-01 Report Date: 1-7-93
 Testing Laboratory: LICentral Tex. Co. Cheski, U.K. Report No. CTL/P/3793
 Author(s): P. Robinson
 Species: Rabbit

Age: young adult
 Sex: female
 Weight: 3392-4486 g.
 Dosage: 0.5ml undiluted liquid
 Test Material: "VAPAM" metam sodium (sodium methyl dithiocarbamate)
 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 the backs of 7x13 cm on left flanks of 6 rabbits. 0.5ml was applied to each prepared site, covered with 2.5x2.5 cm

Results: Gauze patch, secured w/ tape, & topped with impermeable rubber sheeting. Sheeting secured with tape. 4 hour exposure. Each (of 6) dressing 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 removal. Areas erythema & edema scores calculated. Peristome fissulation in 3 animals (up to 21 days) - from these sites, skin samples were removed, fixed, and scanned for

Special Comments: histopathology.

2 of 6 animals - necrotic test sites at 21 days. (tissue destroyed, in into decimis)

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Draze Scale:	ER	ED
	0	0
	1	1
	2	2
	3	3
	4	4

Results: Ammonia (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 no scores at 21 days post patch removal, for erythema (no edema) - 2.0 erythema = well defined erythema.

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

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"Insect using 3 animals - (isolated then 21 days) moderate to severe ecthema - one had completely dead by 21 days."

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