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MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 64348-1
BSP Lime-Sulfur Solution

FROM: William S. Woodrow WSW 5-692
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C) E 1/8/93

TO: S. Lewis / Robert Rose (PM 21)
Fungicide-Herbicide Branch
Registration Division (H75-05C)

APPLICANT: Best Sulfur Products, Inc.
1540 E. Shaw, Suite 101
Fresno, CA 93710

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Calcium Polysulfide	29.0
Inert Ingredient(s):	71.0
Total	100.0%

12/17

BACKGROUND

The Best Sulfur Products, Inc. Co. submitted acute oral, acute inhalation and dermal sensitization studies to support registration of BSP Lime-Sulfur Solution (EPA Reg. No. 64348-1). MRID NOS. used were 421132-01, and 421132-02.

Mary Waller (9-27-88) reviewed and accepted acute dermal and skin irritation studies for this product.

RECOMMENDATION

1) The acute oral, acute inhalation, and dermal sensitization studies currently reviewed are acceptable. The oral and inhalation studies were classified Guideline studies, while the sensitization study was classified Core Minimum; because the challenge and re-challenge concentrations of test material used were the same used for induction. The challenge

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applications should have been reduced compared to the induction application.

2) Current acute toxicity profile for BSP Lime-Sulfur Solution:

study	Classification toxicity Category
acute oral LD_{50} 820 mg/kg	Guideline III
acute dermal LD_{50} >2000 mg/kg	Guideline III
acute inhalation LC_{50} 3.1 mg/l	Guideline III
eye irritation — (missing)	— —
skin irritation Vs erythema slight FR 72hrs	Guideline IV
dermal sensitization did not sensitize	Minimum —

3) The Registrant must submit an acute eye irritation study.

4) The pH of BSP Lime-Sulfur Solution must be submitted; if the product pH is ≤ 2.0, or greater than 11.5, an eye study will not be necessary. A WAIVER MAY BE GRANTED IF REQUESTED ON FORM 8570-6.

PM Note: A CSF (Confidential Statement of Formula) was not (is not) now in the product File Jacket.

LABELLING

A Precautionary Labeling review will be conducted upon receipt of the requested eye irritation study.

PM NOTE: Unless the Registrant can substantiate the corrosive nature of BSP Luna-Sulfur, the Precautionary Labelling and DANGER signal word IS NOT WARRANTED. I

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DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (21) 11-13-91 Reviewer: Woodrow
MRID No.: 421132-01 Report Date: 5-5-92
Testing Facility: Northview Pacific Labs. Report No. XIG004G
Author(s): R. O'meara
Species: Rat, female Sprague Dawley, males also
Age: ~~not given~~ Observation Days (Post Exposure): (14); other ( )
Weight: 150-200g
Source: Simonsen's Labs, Gilroy CA.
Test Material: Lime Sulfur Solution
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Conclusion:

1. LD50 (mg/kg): Males = 820 mg/kg (745-902) ; Females = 920 mg/kg (773-1095) ; Combined =
2. The estimated LD50 is 820 mg/kg (745-902)
3. Tox. Category: III. Classification: Guideline

Procedure (~~Deviations from §81-1~~): Animals fasted 16 hrs prior to test. 5M&5F rats per dose level were dosed by gavage by gavage with different levels of test material, using a volume of 10ml/kg b.wt. Control groups

Results:

Reported Mortality

DOSAGE (/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined

Symptomology & Gross Necropsy Findings:

Rats were dosed (10 ml/kg) with water. Animals escaped on day 7, 14 days, or death.
Clinical observations: Higher dose levels - death, (within 2 days) death, lacrimation, mucoid diarrhea, + wt. loss.

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dead/dosed

Dose	mg/kg	males	Females
1	100	0/5	0/5
2	250	0/5	0/5
3	700	—	1/5
4	750	1/5	2/5
5	850	4/5	—
6	950	4/5	3/10
7	1200	—	4/5
8	2500	5/5	5/5
9	3500	5/5	5/5
10	5000	5/5	4/5

Necropsy: Darkened or enlarged adrenals, dark red lungs, pale kidneys, discolored livers, darkened spleens & fat matter/gas in stomach & intestines. Controls: No abnormalities

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: (21) 7-10-91 Reviewer: W. Woodrow
MRID No.: 421132-02 Report Date: 5-5-92
Testing Laboratory: Product Safety Labs. Report No. T-802
Author(s): B. Shapiro
Species: Rat, Sprague-Dawley
Sex: 15M+15F Weight: M222-250, F221-243 g
Source: Hilltop Lab. Animals
Test Material: Lime Sulfur Sol. - aqueous liquid (calcium polysulfides)
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Summary: Animals acclimated (2, 21 or 26 days.

1. LC_{50} (mg/kg): Males = 3.9 mg/L ; Females = 3.1 mg/L (4-17-2-3) ; Combined = 3.6 mg/L (4-12-2-93)
2. The estimated LC_{50} is 3.1 (4-17-2-3) mg/L
3. Mean Concentration:
4. Tox. Category: III. Classification: Guideline

Procedure (~~Deviations from §81-3~~): 3 groups of 5M & 5F each were separately exposed to three different dose levels of test material aerosols for 4 hours each. The exposure chamber used was a

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2.41 mg/L	1/5	2/5	3/10
3.78 mg/L	1/5	3/5	4/10
5.08 mg/L	4/5	4/5	8/10

~~Symptomology & Gross Necropsy Findings:~~

rectangular perspex with a volume of 106 litres, operated at slight negative pressure. Animals were observed frequently during exposure, and at least once daily thereafter for Day 14. Body weights were recorded on Days 0, 1, 2, 4, 7, 10 and 14.

All animals were subjected to gross necropsy examinations. Air was supplied to the spray atomizing nozzle from a compressed gas cylinder, and altered air was supplied directly to the chamber from a filtered ambient source.

Atmosphere: 1/4 inch JCO atomizer (Spraying systems, Inc.) #2050 fluid cap + #7160 air cap.

Chamber Concentration measurements - gravimetric samples collected on 5 accesions from breathing zone of animals using membrane filters. Filters were pre-weighed.

Particle size distribution determined by use of an eight stage Anderson Cascade Impactor - filter paper collection stages pre-weighed. MMAD + GSD

Air flow measured and controlled using a transducer + linearizer

Results:

1) Chamber Concentrations - Each dose level based on the average of 5 samples collected:

dose levels
2.41 mg/L
3.78 mg/L
5.08 mg/L

2) Particle size distribution

dose level 2.41 mg/L : MMAD GSD

MMAD-GSD sample #1 @ ① 2.5 μ 2.20

② 2.2 μ 2.00

Av. Samples 1 & 2 @ stage 4 (2.1 μ cutoff) = 43.4% cumulative particles.

dose level 3.75 mg/L MMAD GSD

① 2.1 μ 1.91

② 2.1 μ 1.86

Av. Samples 1 & 2 @ stage 4 (2.1 μ cutoff) = 50.3% cumulative particles.

dose level 5.08 mg/L

MMAD GSD

1.9 μ 2.03

1.7 μ 1.58

Av. of Samples 1 & 2 @ stage #4 (2.1 μ cutoff) = 52.1% cumulative particles.

Clinical observations included: abnormal respiration, facial staining, hunched posture, reduced movement, ano-genital staining, alopecia, ocular irritation, decedents lost weight prior to death.

Necropsy: Red discoloration of lungs, gaseous distention of GI tract, stasis, red, edematous lungs, 3 of 5 animals showed dark lines with uneven surfaces.

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DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (21) 11-13-91 Reviewer: Woodrow
MRID No.: 421132-01 Report Date: 5-5-92
Testing Laboratory: Northview Pacific Labs. Report No. XIG004G
Author(s): Roger Ameare
Species: Guinea Pig, Hartley strain
Sex: M&F Weight: >300g.
Source: Trents Company, Modesto, CA
Test Material: Lime Sulfur Solution
Positive Control Material: dinitrochlorobenzene (DNCB)
Quality Assurance (40 CFR §160.12): yes (Q.A. & G. Cert.)

Method: Modified Buehler
should have used reduced conc. for challenge

Summary:
1. This product is / is not a dermal sensitizer.
2. Classification: Core Minimum

Procedure (~~Deviation From §81-6~~): "Pilot Study": 12 g.pigs used to determine the "primary irritancy" of the test material. 10 concentrations from 1% to 50% of test material diluted with water used. Three groups ~~Occlusive~~ of 4 g.p. each dosed with 0.5ml/site in filltop chambers. 6 hour exposure. Chambers removed, sites rated. Results of pilot study: Concentrations of 1-20%, no irritation. Moderate irritation produced from 25% to 50%. Thus, main study employed a concentration of 20% of the test material.

Induction:

Protocol 10 test animals
5 negative controls
5 positive controls
10 naive controls:
(5 challenge controls)
(5 re-challenge controls).

On day prior to dosing, dorsal surface of each animal clipped free of hair. Day of dosing, test site

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~~---~~ ~~se shaved using Braun shaver. 0.5 ml of a 20%~~
~~dilution of test material (in water) placed into each of 10~~
~~Hilltop chambers, and were applied to shaved dorsal~~
~~area of each animal. Chambers secured with gauze and~~
~~tape. 5 positive controls received 0.5 ml of 0.1% DNCB.~~
~~5 negative controls treated similarly, using 0.5 ml~~
~~deionized water. 6 hours skin contact. Chambers~~
~~removed, sites rinsed. 24 hrs post application, test~~
~~sites scored (similar scoring scheme to Buehler).~~
~~This procedure repeated at each site, 3 times per week,~~
~~for two weeks, to total 6 exposures. Animals reshaved~~
~~as needed. Following last induction exposure, animals~~
~~rested two weeks.~~

~~Challenge: Animals reshaved. Each dorsal with~~
~~0.5 ml of the 20% dilution of the test material or~~
~~control materials, as used in the induction~~
~~phase, using a previously unexposed site (naive~~
~~site). Chambers left in place 24 hours.~~
~~Chambers removed, sites scored. Scoring repeated~~
~~at 48 hours later. Naive (re challenge) controls~~
~~also challenged at 48 hr re challenge.~~

Challenge

Results :	24 hr	48 hr
Test:	4/10 = 0.5 scores	6/10 = 0.5 scores
	2/10 = 1.0 scores	3/10 = 1.0 scores
negative controls	3/5 (6/10) @ 0.5 scores	3/5 (6/10) @ 0.5 scores
Naive Controls	3/5 = 0.5 scores (4/10)	3/5 (6/10) = 0.5 scores, 3/5 (4/10) = 1.0 scores

Discussion : A comparison of 24 and 48 hour results with test animals compared to negative controls (animals induced and challenged with distilled water) and naive controls (previously unused animals), indicates that it is not possible to distinguish test from control results.

Conclusion : The test material is not considered a sensitizing agent.