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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 62766-1
Naphthalene Technical

FROM: Lucy D. Markarian 4 2/26/91 E 5/24/91
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

TO: Walter Francis/Arvella Saunder Farmer (PM 32)
Antimicrobials Branch
Registration Division (H75-05C)

APPLICANT: Texaco Chemical Co.
Post Office Box 27707
Houston, TX 77227-7707

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Naphthalene	99.9
Inert Ingredient(s):	0.1
Total	100.0%

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BACKGROUND: It is requested That the inhalation study submitted in support of Texaco Naphthalene Technical (EPA 62766-1) be reviewed again, because Texaco is objecting to the signal word "Warning" based on the inhalation Toxicity study (reviewed by Krystyna K, Locke, Toxicologist in Section II, Toxicology branch (TS-769c) with Secondary review Edwin R. Budd, D.A.B.T. Section Head Section II Toxicology branch) That placed the inhalation Toxicity in Catagory II. The LC_{50} was found to be greater Than 0.4mg/L or 77.7ppm.

Texaco claims That all other data submitted in support of the product shows naphthalene to be essentially non toxic and suggest. That perhaps an error was made in assigning the Toxicity catagory, because 0.4mg/L was the highest attainable chamber concentration.

RECOMMENDATION:

The second review of the inhalation study concurs with the conclusion reached by Krystyna Locke. That the Toxicity catagory assignment is correct. Any Test material in a limit Test achieving 0.4 mg/L concentration is assigned to Catagory II Toxicity. In expressing the estimated LC_{50}, the term greater Than 0.4mg/L is used. This doesn't mean it is also greater Than 0.5, which would place the inhalation Toxicity in catagory III, because it has not been demonstrated, claimed limitations notwithstanding.

As The file lacked a copy of reviews of tests in other areas of toxicity The tests were reviewed again to get a complete profile of the Toxicity of naphthalene.

The oral, dermal (Toxicity) and eye irritation studies were considered core minimum data.

1. The oral study used animals That weighed much less then

the recommended 200-300 gram range by the guidelines

The dermal study did not even address the systemic Toxicity signs. It only addresses manifested dermal Toxicity and in addressing. This does not explain how the skin can sloughoff when only moderate erythema and slight edema were present at the onset of irritation. Sloughing is not considered desquamation.

The eye irritation study has omitted the 1hr. reading required by the guidelines. Also there is no indication that the absence of corneal lesions was confirmed by fluorescein dye.

The profile resulting from the review is as follows.

oral Toxicity	Catagory III
Dermal Toxicity	Catagory III
Eye Irritation	Catagory IV
Dermal Irritation	Catagory IV
Sensitization	not a sensitizer

All the other areas of Testing show naphthalene to be only mildly deleterious, however. This does not mean that naphthalene cannot be more toxic in a specific area such as inhalation. As long as it is not established that the inhalation toxicity is in any other catagory than catagory II, Naphthalene Technical must carry the signal word "warning" and the precautionary statements and the statement of practical treatment that accompany it. The alternative would be a new test with a more concentrated chamber atmosphere for exposure that can establish the LC50 at a higher level, in a lesser toxicity catagory.

The label as recommended before is adequate, but not the new proposed label with signal word "Caution".

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

Product Manager: (32)
MRID No.: 257902
Testing Laboratory: Bushy Run Research Center, Union Carbide
Author(s): David W. Fair, Donald J. Nachreiner
Species: Rat, Wistar Albino [HLA (WI) BR]
Sex: ♂ & ♀ Weight: 240-340g
Source: Hilltop Lab Animals, Scottdale, PA
Test Material: Naphthalene (Test Article # 56C1-56-1, Order I-334)
Quality Assurance (40 CFR §160.12): included

Reviewer: L. Markarian
Report Date: 2/24/91
Report No. 48-511

Summary:

1. LC_{50} (mg/kg): Males = _____; Females = _____; Combined = _____
2. The estimated LC_{50} is > 0.4 mg/L (77.7 ppm)
3. Mean Concentration: 77.7 ppm = 0.4 mg/L
4. Tox. Category: II. Classification: Core Guideline

Procedure (Deviations From §81-2): Exposure was in 120 Liter plexiglass chamber. The aerosol was generated in a compact Tube furnace (as vapor) at 101°C. Filtered compressed air was passed through a dessicator & mixed with the vapor and entered into the chamber. The flow rate was maintained at 25 LPM using a Manostat flowmeter (calibrated). Temperature & humidity were recorded continuously & averaged 24°C and 49%, respectively. Chamber concentration was determined 2 times during exposure using a Perkin-Elmer Sigma 2000 GC. Particle sizing was not necessary because exposure was to vapor. Animals were observed during exposure and daily thereafter. Body weights were recorded at initiation and on days 7 & 14. Necropsy
Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
0.4 mg/L (77.7 ppm)	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:
was performed on all animals.
On the day of exposure observations included closed eyes, lacrimation and mouth breathing. There were no signs of toxicity during the rest of the observation period.
At necropsy one male showed mild hydronephrosis of the left kidney and one female showed enlarged cervical lymph nodes. There were no other abnormalities.

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

Product Manager: (32) Reviewer: L. Markarian
MRID No.: 257224 Report Date: 2/26/91
Testing Facility: Pharmakon Research International, Inc. Report No. PH443-TX-003-84
Author(s): Victor Mallory
Species: Rat, Sprague Dawley
Age: Young Adult . Observation Days (Post Exposure): (14); other ( )
Weight: ♂ 143-205g ♀ 145-200g
Source: Charles River Breeding Laboratories, Wilmington, Mass
Test Material: Naphthalene (Test article 5601-56-1, Order # J-225 (white flake
Quality Assurance (40 CFR §160.12): included

Conclusion:

1. LD_{50} (mg/kg): Males = 2009 (1356-2977) mg/kg ; Females = 3310 (2617-4185) mg/kg ; Combined = 2649 (2074-3376) mg/kg
2. The estimated LD_{50} is
3. Tox. Category: III . Classification: core minimum

Procedure (Deviations From §81-1): A range finding Test was made using 2 animals at 500, 2500 & 5000 mg/kg. Based on the results of this animals were intubated at five levels with Test material suspended in corn oil and at each level administered at 15ml/kg. Animals were fasted prior to intubation. Observations were at 1 & 4 hrs and daily thereafter. Viability check was twice daily. Body weight were taken at initiation and on days 7 & 14, and at death. Necropsy was performed on all animals. Sacrifice was with CO_2 inhalation

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
1000	1/5	0/5	1/10
1600	1/5	0/5	1/10
2500	5/5	2/5	7/10
3200	4/5	1/5	5/10
4000	4/5	4/5	8/10

Symptomology & Gross Necropsy Findings:

Symptoms of toxicity includes decreased activity, diarrhea, poor grooming, changes in muscle tone chromodacryorrhea, piloerection, ptosis, cyanosis dyspnea, abnormal gait and stance, Tremors, preconvulsive behaviors, and prostration. All deaths occurred within 48 hrs with the exception of one dying at 5 days. Necropsy of the deceased revealed lesions of the gastric mucosa, discoloration of lungs & intestines.
Necropsy of the survivors showed no remarkable gross pathology

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: (32) Reviewer: L. Markarian
MRID No.: 257229 Report Date: 2/26/91
Testing Laboratory: Pharmakon Research International, Inc. Report No. PH 222-TX-002-84
Author(s): Victor Mallory
Species: Rabbit, New Zealand White, Spartak's Rabbitry, Harvey's Lake Penna.
Sex: 5♂ & 5♀ Wt.: 2.83 - 3.11 g
Test Material: Naphthalene (Technical 5601-56-1 Order # 3225) white flakes
Quality Assurance (40 CFR §160.12): included

Summary:

1. LD_{50} (mg/kg): Males = _____; Females = _____; Combined = _____;
2. The estimated LD_{50} is Greater Than 2.0 g/kg
3. Tox. Category: III. Classification: Core minimum

Procedure (Deviations From §81-2): The test material was applied to an area on the shaved backs of animals no less than 10% of the entire body surface. A layer of gauze was wrapped around the animals followed by a sheet dam and an bandage. At 24 hrs all wrapping were removed. Observations were at 2 hrs after application & daily for 14 days. Body weights were recorded at initiation and on days 7 & 14. Euthanasia was with CO_2. Necropsy was performed for all animals.

Results:

Reported Mortality

DOSAGE (g /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2.0	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

No signs of systemic toxicity were noted. Dermal toxicity is reported as slight to moderate erythema, slight edema, fissures and slougning of the skin at the application site.

Necropsy revealed no gross pathology.

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DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (32) Reviewer: L. Markarian
MRID No.: 257228 Report Date: 2/23/91
Testing Laboratory: Pharmaceutical Research International Inc. Report No. PH 421-TX-004-84
Author(s): Victor Mallory
Species: Rabbit, New Zealand White
Sex: ♂ + ♀ Weight: 2116 - 3033 gm
Source: Sparlet's Rabbitry, Harvey's Lake, Pa
Dosage: 100mg/eye
Test Material: Naphthalene (Test material 5601-56-1 order# J-226) white flakes
Quality Assurance (40 CFR §160.12): included

Summary:

Tox. Category: III Classification: Core minimum

Procedure (Deviation From §81-4): The test material was instilled in the conjunctival sacs of nine Rabbits. Six rabbits were observed unwashed and three after washing with lukewarm water 20-30 seconds after instillation. Examinations were at 24, 48, 72 hrs and on days 4 + 7 according to Draize

Results:

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
UNWASHED Cornea Opacity	—	0/6	0/6	0/6	0/6	0/6		
Iris	—	0/6	0/6	0/6	0/6	0/6		
Conjunctivae Redness	—	0/6	0/6	0/6	0/6	0/6		
Chemosis	—	0/6	0/6	0/6	0/6	0/6		
Discharge	—	0/6	0/6	0/6	0/6	0/6		
WASHED Cornea Opacity	—	0/3	0/3	0/3	0/3	0/3		
Iris	—	0/3	0/3	0/3	0/3	0/3		
Conjunctivae Redness	—	0/3	0/3	0/3	0/3	0/3		
Chemosis	—	0/3	0/3	0/3	0/3	0/3		
Discharge	—	0/3	0/3	0/3	0/3	0/3		

washed eyes not required - According to guidelines There should have been an evaluation at 1hr.

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

Product Manager: (32)
Reviewer: L. Markarian
MRID No.: 257227
Report Date: 2/26/91
Testing Laboratory: Pharmakon Research International, Inc
Report No. PH420-TX-013-84
Author(s): Victor Mallory
Species: Rabbit, New Zealand White - Specialty Rabbitry, Harvey's Lake, Pa
Age: Adult
Sex: 3♂ & 3♀
Weight: 2064 - 2449 g
Dosage: 500 mg
Test Material: Naphthalene (Test material 5001-56-1 Order # J-226) white flakes
Quality Assurance (40 CFR §160.12): Indicated

Summary:

The Primary Irritation Index = 0.397

Toxicity Category: IV

Classification: Guideline

Procedure (Deviations From §81-5): The test material was moistened with acetone and applied to a 6 cm² area on the shaved skin of the rabbit, covered with gauze held in place with tape "The patches were loosely held in contact with skin by means of a suitable semiocclusive dressing" Exposure was for 4 hrs. Observations were at 30-60 minutes, 24, 48, 72 hrs and on days 4, 5, 6, & 7. A total of 6 central patches were applied to each animal. All evaluations were according to Draize

Results:

Grade 2 erythema was observed in one or two animals between one hour and Day 4. There was no edema. Fissures were noted at sites with Grade 2 erythema and another site with grade 1 erythema. On day 5 three sites showed grade 1 erythema + fissures. On day 6 all erythema subsided, but fissures were still present. Control site were unremarkable.

Special Comments:

How the animals were wrapped should be made clearer. "Loose wrapping" must be clarified.

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

Product Manager: (32)
MRID No.: 25 7223
Testing Laboratory: Pharmaco Research International Inc.
Author(s): Victor Mallory
Species: Guinea Pig, Hartley
Sex: 10♂ & 10♀ Weight: 351 - 429g
Source: Hazleton-Dutchland Denver Pennsylvania
Test Material: Naphthalene (Test article 5601-56-1 order # J-227) white flakes
Positive Control Material: DNCB
Ouality Assurance (40 CFR §160.12): included

Reviewer: L. Markarian
Report Date: 2/26/91
Report No. PH424-TY-001-84

Method: Assumed to be Buehler

Summary:
1. This product ~~is~~ is not a dermal sensitizer.
2. Classification: Guideline

Procedure (Deviation From §81-6): A pretest screening was made to assess the irritation potential using four guinea pigs (2♂'s 2♀) and the test material as received and in 50, 10, 1 % solutions in acetone. The highest non irritating concentration was 100% (as received) therefore it was used as the induction as elicitation concentration. Twenty guinea pigs (10♂'s 10♀) were used in the Test group. Ten were used in the positive control group, inducted with 0.3% DNCB in ETOH, and four were used as naive control. Test and positive control groups were inducted using 0.4g or 0.4ml Test or Control material. This was applied beneath 3"x3" Duoderm bandage & covered with dental dam secured to the restrainers at both sides of the animals. At 6 hrs. The dam & Patches were removed. The test sites were examined and scored at 24 & 48 hrs after each of the three inductions That were made a week apart. Fourteen days after the last induction Both groups of animals were challenged with their respective on pan fo. Additionally four guinea pigs were challenged with the Test material. The challenge was applied in the same manner as the inductions. At 24 hrs The challenge sites were depilated & after a minimum of 2 hrs the sites were scored according to what appears to be Buehler.

The naive sites did not show any reaction

All positive controls showed irritation after the and Third inductions, and were positive at challenge at 24 & 48 hrs.

The Test group remained normal - There was no irritation