

US EPA ARCHIVE DOCUMENT



587

008942

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 <sup>4/20/91</sup> <sup>E 5/24/91</sup>  
Precautionary Review Section  
Registration Support Branch  
Registration Division (H75-05C)

TO: Walter Francis/Arvela Saunders Farmer (PM 32)  
Antimicrobial Branch  
Registration Division (H75-05C)

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

FORMULATION FROM LABEL:

<u>Active Ingredient(s):</u>	<u>% by wt.</u>
<u>Naphthalene</u>	<u>99.9</u>
_____	_____
_____	_____
<u>Inert Ingredient(s):</u> . . . . .	<u>0.1</u>
Total	100.0%

**BEST AVAILABLE COPY**

1 *[Handwritten signature]*

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) as the Secondary reviewer (Edwin R. Budd, D.A.B.T. Section Head Section II Toxicology branch) that placed the inhalation toxicity in Category II. The LC50 was found to be greater than 0.4 mg/L or 77.7 ppm.

Texaco claims that all other data submitted in support of the product shows naphthalene to be essentially non-toxic and suggests that perhaps an error was made in assigning the toxicity category, because 0.4 mg/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 category assignment is correct. Any test material in a limit test achieving 0.4 mg/L concentration is assigned to Category II Toxicity. In expressing the estimated LC50, the term greater than 0.4 mg/L is used. This does not mean it is also greater than 0.5, which would place the inhalation toxicity in Category 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 <sup>toxicity</sup> and eye irritation studies were considered core minimum data:

1. The oral study used animals that weighed much less than

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 slough off when only moderate erythema and slight edema was 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	Category III
Dermal Toxicity	Category III
Eye Irritation	Category IV
Dermal Irritation	Category 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 category than category 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 lower toxicity category.

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

BEST AVAILABLE COPY

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

Product Manager: ( 32 ) Reviewer: L. Markarian  
 MRID No.: 25 7902 Report Date: 2/26/91  
 Testing Laboratory: Bucky Run Research Center, Union Carbide Report No. 48-511  
 Author(s): David W. Fair, Donald T. Nachreiner  
 Species: Rat, Wistar Albino [LA (W) BR]  
 Sex: ♂ + ♀ Weight: 240-290g  
 Source: Hilltop Lab Animals, Scottsdale, PA  
 Test Material: Naphthalene (Test Article # 5601-56-1, Order J-229)  
 Quality Assurance (40 CFR §160.12): included

Summary:

- LC50 (mg/kg): Males = \_\_\_\_\_; Females = \_\_\_\_\_; Combined = \_\_\_\_\_
- The estimated LC50 is > 0.4 mg/L (77.7 ppm)
- Mean Concentration: 77.7 pp = 0.4 mg/L
- Tox. Category: II Classification: Core Guideline

Procedure (Deviations From §81-2): Exposure was in 12 liter plexiglass chamber. The aerosol was generated in a compact tube furnace (as vapor) at 101°C. Filtered compressed air was passed through a desiccator + mixed with the vapor and entered into the chamber. The flow rate was maintained at 25 LPM using a Monostat flowmeter (calibrated). Temperature + humidity were recorded continuously and 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. Results: there of sev. Body weights were recorded at initiation and on days 7 + 14. Necropsy

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 hypertrophy of the left kidney and one female showed enlarged cervical lymph nodes. There were no other abnormalities.

BEST AVAILABLE COPY

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. PH 402-TX-002-84  
 Author(s): Victor Mallory  
 Species: Rat, Sprague Dawley  
 Age: Young Adult Observation Days (Post  
 Weight: ♂ 143-205g ♀ 145-200g Exposure): (14); other ( )  
 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<sub>50</sub> (mg/kg): Males = 2009 (1356-2977) mg/kg; Females = 3310 (2617-4185) mg/kg; Combined = 2649 (2074-3376) mg/kg
2. The estimated LD<sub>50</sub> is \_\_\_\_\_
3. Tox. Category: III. Classification: core minimum

Procedure (Deviations From §81-1): A range-finding test was made using 240 males at 500, 1500 + 5000 mg/kg. Based on the results of this animals were initiated at five levels with test material suspended in corn oil and at each level administered at 15 ml/kg. Animals were fasted prior to initiation. Observations were at 1, 2, 4, 8, and 14 days thereafter. Urinary output was twice daily. Body weight was taken at initiation and on days 7, 14, and at death. Necropsy was performed on all animals. Sacrifice was with CO<sub>2</sub> 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	3/5	2/5	5/10
3200	4/5	1/5	5/10
4000	4/5	4/5	8/10

Symptomology & Gross Necropsy Findings:

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

**BEST AVAILABLE COPY**

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

Product Manager: ( 32 ) Reviewer: L. Markarian  
 MRID No.: 257229 Report Date: 2/21/91  
 Testing Laboratory: Pharmakon Research International, Inc. Report No. PH 422-TV-002-84  
 Author(s): Victor Mallory  
 Species: Rabbit, New Zealand White, Spear's Rabbitry, Harvey's Lake Penna.  
 Sex: 5♂ + 5♀ Wt.: 2.83 - 2.71 kg  
 Test Material: Naphthalene (Test article S601-S6-1 Order # 3225) white flakes  
 Quality Assurance (40 CFR §160.12): included

## Summary:

- LD<sub>50</sub> (mg/kg): Males = \_\_\_\_\_; Females = \_\_\_\_\_; Combined = \_\_\_\_\_;
- The estimated LD<sub>50</sub> is Greater than 2.0g/kg
- Tox. Category: III. Classification: Low 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 new dam and ice bandage. At 24 hrs all wrappings 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<sub>2</sub>. 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 &amp; Gross Necropsy Findings:

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

Necropsy revealed no gross pathology.

BEST AVAILABLE COPY

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

Product Manager: (32) Reviewer: L. Markarian  
 MRID No.: 257228 Report Date: 2/26/91  
 Testing Laboratory: Pharmacia Research International Inc. Report No. PH 221-TX-004-24  
 Author(s): Victor Mallory  
 Species: Rabbit, New Zealand white  
 Sex: ♂ + ♀ Weight: 2116 - 3623 gm  
 Source: Sparte's Rabbitry, Harvey's Lake, Pa  
 Dosage: 100mg/kg  
 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: Lowest

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. Erythema was 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	
OBSERVED	Cornea Opacity	-	1/6	2/6	4/6	4/6	4/6		
	Iris	-	1/6	4/6	4/6	4/6	4/6		
	Conjunctivae Redness	-	2/6	4/6	4/6	4/6	4/6		
	Chemosis	-	4/6	4/6	4/6	4/6	4/6		
	Discharge	-	2/6	2/6	2/6	2/6	2/6		
	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		

BEST AVAILABLE COPY

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 )  
 MRID No.: 257227  
 Testing Laboratory: Pharmakon Research International, Inc.  
 Author(s): Victor Mallory  
 Species: Rabbit, New Zealand White, Sargent's Laboratory, Harvey's Lake, Pa  
 Age: Adult  
 Sex: 3 ♂ & 3 ♀  
 Weight: 2064 - 2449 g  
 Dosage: 500 mg  
 Test Material: Naphthalene (Test material S001-56-1 Order # J-226) white flakes  
 Quality Assurance (40 CFR §160.12): included

Reviewer: L. Markarian

Report Date: 2/26/61

Report No. PH420-TX-013-24

## Summary:

The Primary Irritation Index = 0.397Toxicity Category: IVClassification: Guideline

Procedure (Deviations From §81-5): The test material was moistened with acetone and applied to a 6cm<sup>2</sup> 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 semioclusive dressing. Exposure was for 4 hrs. Observations were at 30-60 minutes, 24, 48, 72 hrs and on days 4, 5, 6. Acetone control patches were applied to each animal. All evaluations were according to Draize

## Results:

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

## Special Comments:

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

**BEST AVAILABLE COPY**

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

Product Manager: (32 )  
MRID No.: 257223  
Testing Laboratory: Pharmacia Research International Inc.  
Author(s): Victor Mallory  
Species: Guinea Pig, Hartley  
Sex: 1907 + 1908  
Weight: 351 - 429g  
Source: Hazleton-Dutchland Deaver Pennsylvania  
Test Material: Naphthalene (Toxicologic 5601-56-1 order # J-227) white flakes  
Positive Control Material: DNCB  
Quality Assurance (40 CFR §160.12): included  
Method: Assumed to be Buehler

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

Summary:

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

Procedure (Deviation From §81-6): A pretest screening was made to assess the irritative potential using four guinea pigs (207 + 208) 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 and elicitation concentration. Twenty guinea pigs (1007 + 1008) were used in the test group, ten were used in the positive control group, induced with 0.3% DNCB in ETOH, and four were used as naive control. Test and positive control groups were induced using 0.4g or 0.4ml test or control material. This was applied beneath 3x2cm adhesive ready 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 compounds. Additionally four guinea pigs were challenged with the test material. The challenge was applied in the same manner as the induction. At 24 hrs the challenge sites were depilated and after a minimum of 2 hrs the sites were examined according to what appears to be Buehler.

The naive sites did not show any reaction

All positive controls showed irritation after the induction and the induction, and were positive at challenge at 24 + 48 hrs.

The test group remained normal - There was no irritation

BEST AVAILABLE COPY