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

006005

JUL 20 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Naphthalene (5601-56-1) - Evaluation of Five Acute Toxicity Studies

Record No. 195503
EPA ID No. 4413-1
TOX Chem No. 587
TOX Br. Proj. No. 7-0665

FROM: Krystyna K. Locke, Toxicologist Krystyna K. Locke 7/8/87
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TO: Jeff Kempter/Walter Francis, PM Team 32
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THRU: Edwin R. Budd, D.A.B.T., Section Head
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7/14/87
7/19/87

Toxicology Branch/HED has completed an evaluation of five acute toxicity studies as follows:

Study Type	Accession Number	Test Animal	LD_{50}/LC_{50}	Toxicity Category	Core Classification
Acute Oral	257224	Rat	M 2009 mg/kg F 3310 mg/kg C 2649 mg/kg	III	Guideline
Acute Dermal	257229	Rabbit	> 2000 mg/kg (M and F)	III	Guideline
Acute Inhalation	257902	Rat	> 0.4 mg/L (M and F)	II	Guideline

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Study Type	Accession Number	Test Animal	LD_{50}/LC_{50}	Toxicity Category	Core Classification
Primary Dermal Irritation	257227	Rabbit	---	III	Guideline
Primary Eye Irritation	257228	Rabbit	---	III	Guideline

No special review trigger was noted in any of the above studies.

Reviewed By: Krystyna K. Locke, Toxicologist
Section II, Toxicology Branch (TS-769C)
Secondary Reviewer: Edwin R. Budd, D.A.B.T., Section Head
Section II, Toxicology Branch (TS-769C)

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DATA EVALUATION REPORT

Study Type: Acute Oral (Rat)

TOX Chem No.: 587

Accession Number: 257224

MRID No.: None

Record Number: 195503

Project No.: 7-0665

EPA ID Number: 4413-1

Test Material: Naphthalene (white flakes); Order No. J-225

Synonyms: 5601-56-1

Study Number: PH 402-TX-002-84

Sponsor: Texaco, Inc., Beacon, NY

Testing Facility: Pharmakon Research International, Inc.
Waverly, PA

Title of Report: Acute Exposure Oral Toxicity

Authors: Mallory, J.T.; Naismith, R.W.

Report Issued: March 4, 1985

Conclusions:

The test material was moderately toxic in this study (Toxicity Category III). LD_{50} and (95% Confidence Limits):

Males 2009 (1356 to 2977) mg/kg
Females 3310 (2617 to 4185) mg/kg
Combined 2649 (2079 to 3376) mg/kg

Classification: Core-Guideline

Experimental Procedures

Young adult Sprague-Dawley rats, 5/sex/dose level, received single doses of the test material as follows (mg/kg of body weight): 1000, 1600, 2500, 3200, and 4000. The test material was administered by gavage in corn oil and the animals were observed for toxic signs for 14 days. The dose levels were based on the results of a range-finding study in which the same test material (500, 2500, or 5000 mg/kg) was administered to one male and one female Sprague-Dawley rat/level. The rats were obtained from Charles River Breeding Labs, Wilmington, MA; acclimated for 5 days before treatment; assigned randomly to groups based on body weight; housed in groups according to sex or individually; and received unrestricted amounts of food (Wayne Lab Blox®) and water. Body weights were recorded initially, on days 7 and 14, and at death.

Results

Range-Finding Study

Both rats died at the 5000 mg/kg dose level, but there were no deaths at the 500 or 2500 mg/kg level.

Acute Oral Toxicity Study

1. Mortality occurred at all dose levels as follows:

Dose (mg/kg)	Deaths	Sex
1000	1	M
1600	1	M
2500	7	5M and 2F
3200	5	4M and 1F
4000	8	4M and 4F

With the exception of one female in the 4000 mg/kg group, which died on day 5, all of the remaining animals died within the first 2 days after treatment.

2. Toxic signs observed included decreased activity, diarrhea, poor grooming, increased or decreased muscle tone, chromodacryorrhea, piloerection, ptosis, cyanosis, dyspnea, abnormal gait and stance, tremors, preconvulsive behavior, and prostration.

3. Necropsy of animals dying during the course of the study revealed multiple lesions in the stomach mucosa and discolored lungs, adrenals, and intestines.

4. Body weights were unaffected.

5. LD_{50} values and (95% confidence limits):

   Males 2009 (1356 to 2977) mg/kg
   Females 3310 (2617 to 4185) mg/kg
   Combined 2649 (2079 to 3376) mg/kg

   Procedure used to calculate the LD_{50} values was not stated.

6. Toxicity category of the test material: III

7. Classification of Study: Core-Guideline.

8. Quality Assurance and Good Laboratory Practice Statements, and raw data were submitted.

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Secondary Reviewer: Edwin R. Budd, D.A.B.T., Section Head
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DATA EVALUATION REPORT

Stuty Type: Acute Dermal (Rabbit)

TOX Chem No.: 587

Accession Number: 257229

MRID No.: None

Record Number: 195503

Project No.: 7-0665

EPA ID Number: 4413-1

Test Material: Naphthalene (white flakes); Order No. J-225

Synonyms: 5601-56-1

Study Number: PH 422-TX-002-84

Sponsor: Texaco, Inc., Beacon, NY

Testing Facility: Pharmakon Research International, Inc.
Waverly, PA

Title of Report: Acute Exposure Dermal Toxicity

Authors: Mallory, V.T.; Naismith, R.W.

Report Issued: January 8, 1985

Conclusions:

The test material was slightly to moderately toxic in this study (Toxicity Category III).

LD_{50} = > 2000 mg/kg (males and females).

Classification: Core-Guideline

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Experimental Procedures

Young adult rabbits of the New Zealand strain, five males and five females, were treated once with 2000 mg of the test material and then were observed for toxic signs and mortality for 14 days. The test material was applied in acetone (paste) to about 10 percent of the dorsal body surface area (shaved) and the application site was occluded. The exposure time was 24 hours. The animals were obtained from Sgarlat's Rabbitry, Harvey's Lake, PA; acclimated for 5 days before the test; housed singly; and received unrestricted amounts of food (Wayne Rabbit Ration®) and water. Body weights were recorded before the test and on days 7 and 14 thereafter. All animals were necropsied.

Results

There were no deaths and all animals gained weight. Slight to moderate erythema, slight edema, fissuring and, during second week, sloughing of the skin at the application sites were observed. No lesions were observed at necropsy.

Quality Assurance and Good Laboratory Practice Statements, and raw data were submitted.

LD_{50} = > 2000 mg/kg (males and females).

Toxicity Category: III.

Classification of Study: Core-Guideline.

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DATA EVALUATION REPORT

Study Type: Acute Inhalation (Rat)

TOX Chem No.: 587

Accession Number: 257902

MRID No.: None

Record Number: 195503

Project No.: 7-0665

EPA ID Number: 4413-1

Test Material: Naphthalene; 100% pure; Order No. J-229

Synonyms: 5601-56-1

Study Number: 48-511

Sponsor: Pharmakon Research International, Inc.
Waverly, PA

Testing Facility: Bushy Run Research Center,
Export, PA

Title of Report: Naphthalene: Acute Inhalation Toxicity Study

Authors: Fait, D.W.; Nachreiner, D.J.

Report Issued: April 24, 1985

Conclusions:

The test material was an eye irritant during exposure. LC_{50} > 77.7 ppm (0.4 mg/L; analytical concentration); males and females. The test material could not be vaporized to higher concentration under the experimental conditions of this study.

Toxicity Category: II.

Classification: Core-Guideline

Experimental Procedures

Wistar albino rats (weight: 200 to 300 g; age: males, 48 days and females, 62 days), five males and five females, were exposed once to naphthalene vapor for 4 hours (whole body exposure) and then were observed for toxic signs for 14 days. The mean (± SD) naphthalene concentration in the exposure chamber was 77.7 (± 1.79) ppm, which is equivalent to 0.4 mg/L. This concentration was the highest that could be obtained under the conditions of this study. The approximate volume of the chamber was 120 liters and the air flow rate was 25 liters per minute. The concentration of naphthalene was determined every 30 minutes during exposure.

The animals were obtained from Hilltop Lab Animals, Scottdale, PA; acclimated for 8 days prior to test; housed two or three per sex; and received unrestricted amounts of food (Purina Certified Rodent Chow #5002) and water. Body weights were recorded prior to exposure and on days 7 and 14 after exposure. All animals were necropsied.

Results

There were no deaths and all rats gained weight. Toxic signs observed during exposure were keeping eyes closed, lacrimation and mouth breathing. No toxic signs were observed after the termination of the exposure, during the entire study. Necropsy revealed mild hydronephrosis in one male rat and enlarged cervical lymph node in one female rat. Both findings were not attributed to treatment.

Statements of compliance with Toxic Substances Control Act, Good Laboratory Practices, and Quality Assurance were submitted. Individual results of gross necropsy were also submitted.

LC_{50} = > 77.7 ppm (0.4 mg/L; analytical concentration); males and females.

Toxicity Category: II.

Classification of Study: Core-Guideline.

Note

In this submission, the top part (identifying a rat) of each individual necropsy report for the females has been inadvertently cut off during copying (see pages 26 to 30).

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DATA EVALUATION REPORT

Study Type: Primary Dermal Irritation (Rabbit)

TOX Chem No.: 587

Accession Number: 257227

MRID No.: None

Record Number: 195503

Project No.: 7-0665

EPA ID Number: 4413-1

Test Material: Naphthalene (white flakes); Order No. J-226

Synonyms: 5601-56-1

Study Number: PH 420-TX-013-84

Sponsor: Texaco, Inc., Beacon, NY

Testing Facility: Pharmakon Research International, Inc.
Waverly, PA

Title of Report: Primary Dermal Irritation Study in Rabbits

Authors: Mallory, V.T.; Naismith, R.W.

Report Issued: January 9, 1985

Conclusions:

The test material was a moderate skin irritant in this study (Toxicity Category III).

Classification: Core-Guideline

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Experimental Procedures

Young adult rabbits of the New Zealand strain, three males and three females, were treated once with 500 mg of the test material and then were observed for 6 days (that is, until all of the skin reactions disappeared). The test material was applied on intact skin (shaved; area: about 6 cm^2) in acetone (paste) and acetone was also used as a negative control. Skin reactions (erythema and edema) were evaluated by the Draize procedure at 30 to 60 minutes; 24, 48, and 72 hours; and on days 4 and 5, following a 4-hour exposure during which the application sites were occluded.

The animals were obtained from Sgarlat's Rabbitry, Harvey's Lake, PA; acclimated for 5 days prior to test; housed singly; and received unrestricted amounts of food (Wayne Rabbit Ration®) and water.

Results

Very slight to well-defined erythema was observed at the 30 to 60 minute scoring and daily through day 5. Fissuring of the skin at the application site was also observed. One animal had a very slight erythema on the negative control site during the first and second day after treatment. All of the skin reactions disappeared on day 6.

Quality Assurance and Good Laboratory Practice Statements, and raw data were submitted.

Toxicity Category: III.

Classification of Study: Core-Guideline.

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DATA EVALUATION REPORT

Study Type: Primary Eye Irritation (Rabbit)

TOX Chem No.: 587

Accession Number: 257228

MRID No.: None

Record Number: 195503

Project No.: 7-0665

EPA ID Number: 4413-1

Test Material: Naphthalene (white flakes); Order No. J-226

Synonyms: 5601-56-1

Study Number: PH 421-TX-009-84

Sponsor: Texaco, Inc., Beacon, NY

Testing Facility: Pharmakon Research International, Inc., Waverly, PA

Title of Report: Rabbit Eye Irritation Study (WASH)

Authors: Mallory, V.T.; Naismith, R.W.

Report Issued: January 9, 1985

Conclusions:

The test material was a moderate eye irritant in this study (Toxicity Category III).

Classification: Core-Guideline

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Experimental Procedures

The test material (100 mg) was instilled in one eye of nine young adult rabbits (six males and three females of the New Zealand strain). The test material was used as received (flakes). The eyes of six rabbits (three males and three females) remained unwashed, whereas the eyes of the remaining three rabbits were washed with lukewarm water for 1 minute, after 20 or 30 seconds of exposure. All eyes were then examined for irritation (by the Draize procedure) at 24, 48, and 72 hours, and on days 4 and 7 following treatment.

Results

Slight to moderate conjunctival irritation and slight conjunctival irritation were observed at 24 and 48 hours, respectively, after treatment in two nonrinsed rabbits. There was no conjunctival irritation in these animals during the observation days 3 through 7, when the study was terminated. Cornea and iris were unaffected in the nonrinsed group. There was no eye irritation in the rinsed group.

Quality Assurance and Good Laboratory Practice Statements, and raw data were submitted.

Based on the above observations, the test material was a moderate eye irritant.

Toxicity Category: III.

Classification of Study: Core-Guideline.