US EPA ARCHIVE DOCUMENT

5 80AA

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

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

010810

MAR - 3 1994

PC 063502

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: EPA ID # 063502: Mineral Oil - Review of Acute Toxicity Studies
MRID No.:416853-07 to 416853-10
DP barcode: D196004
PC Code: 063502
Submission No.: S451290
Casewell No.: 580AA

From: Paul Chin, Ph.D. Paul Chin 2/23/94
Section 2
Toxicology Branch I
Health Effects Division (H7509C)

To: Kathryn Davis/Bonnie Adler, PM 52
Reregistration Division (H7508W)

Thru: Joycelyn Stewart, Ph.D. 3/1/94 KB 3/1/94
Section Head
Section 2, Toxicology Branch I
Health Effects Division (H7509C)

Registrant: Exxon Co.

CONCLUSIONS:

Four acute toxicity studies with mineral oil were reviewed by the Toxicology Branch I. All studies are classified as acceptable and they satisfy the guideline requirements (81-1), (81-2), (81-3) and (81-4) for acute oral, dermal, and inhalation toxicity studies and primary eye irritation study, respectively.

The summaries of the reviews are shown on the attached table. [Detailed reviews are appended to this memorandum.]

REQUESTED ACTION:

The Reregistration Division requested that the Toxicology Branch review the above acute toxicity studies with mineral oil.

a:\mo-acute.mem 2/11/94

Recycled/Recyclable
Printed with Soy/Canola ink on paper that contains at least 50% recycled fiber

ACUTE TOXICITY DATA FOR MINERAL OIL

Citation	MRID No.	Results	Tox. Categ.	Coregrade
81-1 Acute Oral Species: rat	416853 -07	LD50 > 5 g/kg for males and females	IV	acceptable
81-2 Acute Dermal Species: rabbit	416853 -08	LD50 > 2 g/kg for males and females	III	acceptable
81-3 Acute inhalation Species: rat	416853 -09	LC50 > 4.7 mg/L	III	acceptable
81-4 Primary eye irrit. Species: rat	416853 -10	Slight eye irritant. Eye irritation (slight conjunctival redness) did not clear at day 14 (last day of observation).	III	acceptable

¶▼

2

Primary Reviewer: Paul Chin, PhD Paul Chin 2/4/94
Section 2, Tox. Branch 1 (H7509C)
Secondary Reviewer: Joycelyn Stewart, PhD, Section Head JS 2/23/94
Section 2, Tox. Branch 1 (H7509C)

DATA EVALUATION REPORT

STUDY TYPE:	Acute Oral (81-1)/Rat
P. C. No:	063502
MRID No:	416853-07
TEST MATERIAL:	MRD-87-984
SYNONYMS:	Mineral Oil
SPONSOR:	Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873
TESTING FACILITY:	Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873
Study NO:	298401
REPORT TITLE:	Orchex 796 - Acute Oral Toxicity Study in the Rat
AUTHOR(S):	R. T. Plutnick
REPORT ISSUED:	Feb. 18, 1987

CONCLUSIONS: MRD-87-984 (Mineral Oil) was administered orally by gavage to 5 Sprague Dawley rats per sex per dose level at 5000 mg/kg in an oral acute toxicity study. All animals were free of significant signs of toxicity and no deaths occurred at 5000 mg/kg.

Toxicity category: IV.
Core classification: Acceptable.
LD50 > 5000 mg/kg for males and females.

A: MATERIALS:

1. Test compound: MRD-87-984, Batch No. 1, a light yellow liquid, and the specific gravity of 0.84 g/ml.

3

2. Test animals: Species: Rat, Strain: Sprague-Dawley, Age: 9 weeks, Weight: Males: 272-286 g; Female: 175-181 g, Source: Charles River Breeding Lab., Kingston Facility, Stone Ridge, NY, Acclimation period: 15 days.

B. METHODS:

- Rats (5 male and 5 female) were fasted overnight before dosing.
- Test material, undiluted, was administered orally by gavage at the 5 g/kg level. The dose in grams was calculated by multiplying the specific gravity (0.86 g/ml) times the actual dose received in ml.
- Animals were observed at 1, 2, 4, and 6 hours after dosing and once daily for a total of 14 days.
- Rats were weighed on day 0, 7, and 14.
- Gross necropsy was performed on all survivors which were sacrificed on day 14.
- Doses given and lethality are presented in the table under results and discussion.
- A signed and dated Quality Assurance statement was present.
- A signed and dated GLP statement was present.

C. RESULTS AND DISCUSSION:

	Dose of MRD-87-984 mg/kg	Number Animals that Died (day of death) Male	Total	Female	Total
Test Group	5000	0	0/5	0	0/5

Animals were sacrificed on day 14.

Clinical signs of toxicity observed in all animals during day 0 were unthrifty coat and staining of the ano-genital area. No clinical signs of toxicity were observed in all rats from the day 1 observation through study termination. All animals had increased body weight over their initial values. All animals were free of abnormalities at necropsy.

No deaths occurred at 5000 mg/kg. Since the guideline allows a limit dose of 5000 mg/kg, a repeat study is not required. The LD50 was stated in the report to be > 5000 mg/kg.

Primary Reviewer: Paul Chin. PhD Paul Chin 2/4/94
Section 2, Tox. Branch 1 (H7509C)
Secondary Reviewer: Joycelyn Stewart, Ph.D., Section Head 2/23/94
Section 2, Tox. Branch 1 (H7509C)

DATA EVALUATION REPORT

STUDY TYPE:	Acute Dermal (81-2)/Rabbit
P. C. No:	063502
MRID No:	416853-8
TEST MATERIAL:	MRD-87-984
SYNONYMS:	Mineral Oil, Orchex 796
SPONSOR:	Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873
TESTING FACILITY:	Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873
Study NO:	298406
REPORT TITLE:	Orchex 796 - Acute Dermal Toxicity Study in the Rabbit (MRD-87-984)
AUTHOR(S):	R. T. Plutnick
REPORT ISSUED:	Mar. 3, 1987

CONCLUSIONS: MRD-87-984 (Mineral Oil) was administered dermally to 5 rabbits per sex for 24 hours at 2000 mg/kg. Slight to moderate erythema and edema were noted at the dosed site of all animals at patch removal and by 14 days all signs of irritation had disappeared. Clinical signs of toxicity observed were nasal discharge (3 males and 1 female), unthrifty coat (1 male and 1 female), soft stool (1 male and 1 female), cut mouth (2 males), staining of the ano-genital area (1 male), and emaciation (1 male). No animal died at 2000 mg/kg.

Toxicity category: III.
Core classification: Acceptable.
LD50 > 2000 mg/kg for males and females.

5

010810

A: MATERIALS:

1. Test compound: MRD-87-984, Batch No. 1, a light yellow liquid, and the specific gravity of 0.84 g/ml.

2. Test animals: Species: Rabbit, Strain: New Zealand, Age: 12 weeks, Weight: 2600-3100 g at study initiation, Source: Hazleton Research Products, Inc., Denver, PA, Acclimation period: 15 days.

B. METHODS:

- Twenty-four hours before application of test material, rabbits were prepared by clipping the hair of each rabbit on the dorsal and ventral surface from the shoulder region to the lumbar region.
- The test site was not abraded.
- Test material, 2000 mg/kg, was administered dermally to 5 rabbits per sex, the dose in grams was calculated by multiplying the specific gravity (0.86 g/ml) times the actual dose received in ml.
- To retard evaporation, to prevent ingestion of the test material, and to keep the substance in contact with the skin, the gauze patch was secured to the trunk of the animal with tape and a plastic sleeve. The test material remained in contact with the skin for 24 hours. At the end of 24 hours, the bandaging was removed and the skin was wiped with distilled water and paper towels to remove excess test material.
- Rabbits were placed in neck collars and they were observed at 2, 4, and 24 hours post-dosing, then at least once a day for 14 consecutive days. Dermal responses were evaluated 24 hours after application and on Days 3, 7, 10 and 14 according to the Draize Method of scoring.
- Rabbits were weighed at 0, 7, and 14 days following dosing.
- Gross necropsy was performed on all animals that died on study and on all survivors which were sacrificed on day 14.
- A signed and dated Quality Assurance statement was present.
- A signed and dated GLP statement was present.

C. RESULTS AND DISCUSSION:

Clinical signs of toxicity observed were nasal discharge (2 males at 4 hour and on day 1; 1 male on day 8; 3 males and 1 female on day 13; and 1 male on day 14), unthrifty coat (1 male on day 2, 3, 4, 5, 13 and 14; 1 female on day 2), soft stool (1 male on day 2 and 12; 1 males and female on day 13), cut mouth (1 male on day 2; 2 males on day 13; 1 male on day 14), staining of the ano-genital area (1 male on day 12), and emaciation (1 male on day 14).

Eight animals (3 males, 5 females) gained weight and 2 males lost weight between day 0 and 14.

6

Slight to moderate erythema was observed at the dosed site of all animals at patch removal, one animal showed erythema up to day 10 and by day 14, all signs of irritation had disappeared. Very slight edema was observed in four animals (2 males, 2 females) at the 24 hour observation and none was observed thereafter. Desquamation was observed in two females on day 7, 10, and 14.

At gross necropsy, all tissues and organs appeared normal except for lung discoloration commonly found in animals euthanized by sodium pentobarbital cardiac injection. Lung discoloration is probably due to insufficient bleeding. Findings in lung which are not considered treatment-related were as follows: slightly red (1 male, 2 female), moderately red (1 male), moderately bright red (1 male, 2 female), extremely red (1 male), and extremely bright red (1 male, 1 female).

Since no animals died at 2000 mg/kg, a repeat test is not required. The guidelines allow a limit dose of 2000 mg/kg.

a:\adrab-MO.8

7

Primary Reviewer: Paul Chin. PhD Paul Chin 2/14/94
Section 2, Tox. Branch 1 (H7509C)
Secondary Reviewer: Joycelyn Stewart, Ph.D., Section Head 2/23/94
Section 2, Tox. Branch 1 (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation (81-4)/Rabbit

P. C. No: 063502

MRID No: 416853-10

TEST MATERIAL: MRD-87-984

SYNONYMS: Mineral Oil, Orchex 796

SPONSOR: Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873

TESTING FACILITY: Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873

Study NO: 298413

REPORT TITLE: Orchex 796 - Ocular Irritation Study in the Rabbit

AUTHOR(S): R. T. Plutnick

REPORT ISSUED: Mar. 9, 1987

CONCLUSIONS: MRD-87-984 (Mineral Oil) was administered to one eye of each of 6 rabbits and observed for 14 days. Ocular irritation of all animals was limited to slight to moderate conjunctival redness (grades 1 to 2). Five animals (2 males, 3 females) had conjunctival redness throughout the observation period and one female had moderate conjunctival redness until 24 hours post-instillation but the irritation was cleared during the remaining observation period.

The test material is considered slightly irritating with a primary eye irritation score of 2 out of a possible maximum score of 110 at day 14. Although the eye irritation was limited to slight conjunctival redness, the response did not clear at day 14, the last day of observation. This study didn't examine until

8

eyes were normal or 21 days (whichever is shorter).

Toxicity category: III.
Core classification: Acceptable.

A : MATERIALS:

1. Test compound: MRD-87-984, Batch No. 1, a light yellow liquid, and the specific gravity of 0.86 g/ml.

2. Test animals: Species: Rabbit, Strain: New Zealand White, Age: 13 weeks old, Weight: 2.7-3.2 kg at study initiation, Source: Hazleton Research Products, Inc., Denver, PA. Acclimation period: 21 days.

B. METHODS:

- Test material (undiluted) was administered at 0.1 ml in one eye of each of 6 rabbits (2 males, 4 females) and remained unwashed. Animals were observed at 1, 4, 24, 48, and 72 hours after dosing, and once per day on days 4, 7, 10, and 14. At each interval the eye was examined and scored for ocular reactions according to the method of Draize (1959).
- Gross necropsy was not performed.
- Fluorescein was used to confirm whether ulceration was present.
- A signed and dated Quality Assurance statement was present.
- A signed and dated GLP statement was present.

C. RESULTS AND DISCUSSION:

Ocular irritation of all animals was limited to slight to moderate conjunctival redness (grades 1 to 2). Five animals (2 males, 3 females) had slight to moderate conjunctival redness (grades 1 to 2) throughout the observation period and one female had moderate conjunctival redness (grade 2) until 24 hours post-instillation but the irritation was cleared during the remaining observation period.

The test material is considered slightly irritating with a primary eye irritation score of 2 out of a possible maximum score of 110 at day 14. The eye irritation (slight conjunctival redness) did not clear at day 14, the last day of observation. This study didn't examine until eyes were normal or 21 days (whichever is shorter).

The toxicity category for eye irritation is III.

Primary Reviewer: Paul Chin, Ph.D. Paul Chin 2/4/94
Section 2, Tox. Branch 1 (H7509C)
Secondary Reviewer: Joycelyn Stewart, Ph.D., Section Head
Section 2, Tox. Branch 1 (H7509C) 2/23/94

DATA EVALUATION REPORT

STUDY TYPE:	Acute Inhalation (81-3)/Rat
P. C. No:	063502
MRID No:	416853-09
TEST MATERIAL:	MRD-87-984
SYNONYMS:	Mineral Oil; Orchex 796
SPONSOR:	Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873
TESTING FACILITY:	Exxon Biomedical Sciences, Inc., Toxicol. Lab., East Millstone, NJ 08873
Study NO:	298415
REPORT TITLE:	Acute Inhalation Toxicity Study of Orchex 796 (MRD-87-984) in the Rat
AUTHOR(S):	J. P. Hinz
REPORT ISSUED:	Mar. 4, 1987

CONCLUSIONS: MRD-87-984 (Mineral Oil) was administered in an acute inhalation study for 4 hours to 5 Sprague-Dawley rats per sex at 4.7 mg/L. The LC50 was found to be greater than 4.7 mg/L. The particle size of the test material was reported as a mass median aerodynamic diameter (MMAD) of 6.2 micrometers (um) which is not in the respirable range. However, a repeat test is not required because of the following reasons: Subdivision F guideline 81-3 allows a limit dose of 2 mg/L and approximately 38% (estimated from the Table 3 of the Study Report) of the test material was in the respirable range (1-4 um in diameter).

Toxicity category: III.
Core classification: Acceptable.
LC50 = greater than 4.7 mg/L

A. MATERIALS:

1. Test compound: MRD-87-984, Batch No. 1, a light yellow liquid, and the specific gravity of 0.86 g/ml.

2. Test animals: Species: Rat, Strain: Sprague Dawley, Age: 7-8 weeks, Weight: 200-288 g, Source: Charles River Breeding Lab., Inc., Kingston Facility, Kingston, NY, Acclimation period: 15 days.
3. Environment of Chamber : Temperature: 69-74 degrees F, Humidity: 45-53%.

4. Inhalation conditions: Exposure was by whole body for 4 hours. Figure 1 attached presents a schematic of the exposure/generation system used for this study. The test material was metered to the atomization nozzle using FMI Lab Pump. Compressed air, delivered to the atomizer at 20 psi back pressure, caused the resulting liquid droplet aerosol to be expelled toward the top of the chamber. The aerosol mixed with incoming room air was dispersed throughout the chamber volume. The exposure chamber was operated at an exhaust flowrate of 200 liter per minutes (L/min), providing one air change every 5 minutes and theoretical equilibration time (T99) of 23 minutes.

B. METHODS:

Concentrations (nominal and actual) of test material in the breathing zone were determined during each hour of the 4-hour exposure through removal of gravimetric samples from the chamber. Samples were collected using glass-fiber filters. Filters were weighed before and after collection to determine the mass collected.

The particle size range in the test atmosphere was determined in a Sierra Model 210 Cascade Impactor periodically during 4 hour exposure. A bulk estimation technique was employed to characterize the particle size distribution of the test atmosphere. The change in weight of the filter for each stage was measured and the cumulative percent of the sample collected on each stage was calculated. This information plus the stage constants for the impactor were used to calculate the 15.9%, 50%, and 84.1% particle sizes (equivalent aerodynamic diameter), the geometric standard deviation and the estimated percent of the aerosol less than or equal to 10 um in size.

Nominal atmospheric concentrations was determined by the total amount of test material delivered to the chamber divided by the total volume of air passing through the chamber.

- Animals were observed every 15 minutes during the first exposure hour and every hour thereafter through exposure termination.
- Rats were weighed on day 0 and on days 7 and 14 post-exposure.
- Gross necropsy was performed on all animals that died on study

and on all survivors which were sacrificed on day 14. Organ weights were recorded for lungs plus trachea prior to being perfused with preservative (10% neutral buffered formalin) by means of a constant pressure perfusion device.
-Statistical analyses were performed on body weight data, organ weight data, and organ to body weight ratios using the t-test for equal variances and the Smith-Satterthwaite Correction for unequal variances.
- A signed and dated Quality Assurance statement was present.
- A signed and dated GLP statement was present.

C. RESULTS and DISCUSSION:

The particle size of the test material was reported as MMAD of 6.2 um with a GSD of 5.4 based on four samplings. The report stated that 61.3% of the test material had a particle size of less than or equal to 10 um in diameter.

The homogeneity of test material distribution in the chamber was good based on the coefficient of variation (CV) of 6.2% for the four samples.

The gravimetric chamber concentration was 4.7 mg/L and the nominal chamber concentration was 35.3 mg/L based on four samplings. Although not reported, the ratio of nominal/analytical concentration (approx. 7.5) indicates a loss of the test material from the exposure atmosphere due to the observed occurrence of impaction on animals, on cages and the walls of the chamber.

MRD-87-984 (Mineral Oil) administered via inhalation for 4 hours to 5 rats per sex per group at 0 mg/L (served as a control group for the study) and 4.7 mg/L resulted in no mortality. After removal from the chamber and on day 1 post-exposure, all treated animals of both sexes had wet and matted fur and yellow ano-genital stains. These signs disappeared between day 10 and day 14. The mean body weights of the treated group were significantly different from the control group at the day 7 and day 14 intervals in the males ($p<0.01$) and the day 14 interval in the females ($p<0.05$). The mean lungs (plus trachea) to body weight ratio of the males ($p<0.01$) was statistically significantly higher than the control group. Necropsy finding was lung discoloration in two females in the control group and one male and one female in the treated group. In addition, one female had dilated renal pelvises in both kidneys. All other tissues and organs were unremarkable.

The Toxicity Category is III.

No animals died at 4.7 mg/L. Although the particle size of the test material was reported as MMAD of 6.2 um, which is not in the respirable range, a repeat test is not required because of the following reasons: Subdivision F guideline 81-3 allows a limit dose of 2 mg/L and approximately 38% (estimated from the Table 3 of the Study Report) of the test material was in the respirable range (1-4 um in diameter). The LC50 was stated in the report to be greater than 4.7 mg/L.