CASWELL FILE

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

005284

JUL 9 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Registration No. 9630-15. 2% Copper Naphthenate [redacted] Review of Acute Toxicity Studies.

Caswell No. 245
Accession No. 257437
Project No. 1158

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TEST TYPE: Acute Toxicology; Oral, Skin, Eye, Dermal, and Inhalation. (No test numbers are supplied)

SPONSOR: Mooney Chemicals, Inc.
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Cleveland, OH 44113

TESTING FACILITY: Applied Biological Sciences Laboratory, Inc.
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P.O. Box 3218
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SUBMITTED: February 22, 1985

LABORATORY REPORT NO.: Code No. 2585

The submission contains a description of five toxicity tests (studies), namely: I. Acute Oral Single Dose, II. Skin Irritation, III. Eye Irritation Test, IV. Dermal Acute Toxicity,

and V. Inhalation Toxicity (4-hour exposure period). Each study will be considered in sequence, including Procedures, Results, Conclusions, Evaluation Ratings, Classification, Toxicity Category, and Comments.

I. ACUTE ORAL TOXICITY TEST - EPA. 40 CFR 163.81-1 (PROPOSED) (§81-1)

METHOD:

Sample Preparation: Sample density was 0.87 gm/mL.

Procedure: Sprague-Dawley rats weighing 200 to 300 gm were used, five male (M) and five female (F) rats, treated at a dosage level of 5 gm/kg, by gavage. Animals were housed in a temperature controlled room in subgroups according to sex, and food was withheld for 24 hours prior to intubation. Water was allowed ad libitum, and following the dosing, both food and water were provided ad libitum. The rats were observed twice daily for 14 days for visible signs of physical and behavioral changes, and weight changes were observed at 7 days and at 14 days. Duration of the study was November 7 through November 21, 1984. Date, time, and weight of all animals dying on study were recorded and autopsies were performed. All surviving rats were sacrificed at 14 days and autopsies were performed.

RESULTS:

Behavioral and Physical Characteristics: All rats were lethargic at 1 hour, 2 hours, 4 hours, and 24 hours following intubation: at 2 hours, two rats were hunched over, with piloerection. At 4 hours, three rats were hunched over with piloerection, with one rat showing sanguineous nasal discharge. At 18 hours, one rat (No. 20, F) died. At 24 hours, four rats had wet anal areas, with one rat showing piloerection. At 48 hours, one rat had a wet anal area and lethargy. The remaining animals appeared normal at 48 hours and no abnormal behavioral or physical signs were observed for the remainder of the 2-week observation except for a slight weight loss in one animal at 7 days. By 14 days all weights were normal.

Mortality Data: One rat (No. 20, F) died at 18 hours.

Autopsy Findings: One rat (No. 20) dead at 18 hours, had dark kidneys and hemorrhagic lungs. At the end of 2 weeks, autopsy of the remaining animals showed one (No. 11, M) with a slightly hollow right kidney. All other tissues and organs appeared normal in this animal. All tissues and organs in other remaining animals appeared normal.

CONCLUSION: Under the conditions of this test 2% Copper Naphthenate, Solvent, had an oral LD_{50} greater than 5 gm/kg and, therefore, does not require further testing.

CLASSIFICATION: Core Guideline.

Toxicity Category IV.

COMMENT: No assurance was given that the sample used was a normal commercial batch or formulation. This should be certified to EPA by letter.

II. SKIN IRRITATION TEST, 2% COPPER NAPHTHENATE, SOLVENT - EPA (PROPOSED) (§81-5)

PROCEDURE: Six adult NZ albino rabbits were used to evaluate the degree of primary skin irritation produced by 2% Copper Naphthenate, Solvent. The trunk of each rabbit was clipped free of hair. Four areas of the back, approximately 10 cm apart, were designated for positioning the patches. Two of these areas were further prepared by making minor incisions through the stratum corneum but not deep enough to disturb the derma or to produce bleeding. The patches consisted of 2 layers of light gauze cut in squares (2.5 cm) with a clear plastic between the layers, to retard evaporation of the volatile substances during the 24-hour exposure. The material to be tested was 0.5 mL, introduced beneath each patch. Patches were secured to the area by bands of adhesive tape, forming a trunk band. The test sample was applied to 2 intact and 2 abraded areas on each rabbit, and the patches were removed after 24 hours. Evaluations were made at removal (24 hours) and again at 72 hours following application. If irritation persisted for 72 hours, animal reactions were evaluated every day thereafter until all reversible irritation subsided. Duration of the study was from December 27, 1984 through January 7, 1985.

SUMMARY OF FINDINGS:

At 24 hours all rabbits showed slight erythema and edema. At 72 hours the erythema was slightly worse and the edema was subsiding. There was little change at 96 hours. At 5 days the edema had disappeared, but most of the skin on all the rabbits was thickened, and the surface was hard and cracked. The skin condition remained unchanged until day 11, when the skin was healed and all that remained was a little flakiness.

24-Hour Score = 3.0/8
72-Hour Score = 3.5/8
96-Hour Score = 2.7/8
120-Hour Score = 2.6/8
6-Day Score = 2.6/8

7-Day Score = 2.6/8
8-Day Score = 2.6/8
11-Day Score = 0.0/8

CONCLUSION: Under the conditions of this test, 2% Copper Naphthenate, Solvent, caused some moderate irritation for at least 8 days after application of the test material. All signs and manifestations of irritation, except flakiness, subsided by day 11.

CLASSIFICATION: Core Guideline.

Toxicity Category II.

COMMENT: No assurance was given that the sample used was a normal commercial batch or end-use formulation. This should be certified by the sponsor, in a letter to EPA.

III. EYE IRRITATION TEST - EPA, 40 CFR 163.81-4 (PROPOSED) (RABBIT) (§81-4)

2% Copper Naphthenate, Solvent.
Duration of the test, December 17 through December 24, 1984 (7 days).

PROCEDURE: Nine adult albino rabbits were used to evaluate the degree of eye irritation produced by 2% Copper Naphthenate, Solvent. The eyes of all rabbits were stained with fluorescein 24 hours prior to testing, and examined with an illuminated magnifying glass. One-tenth mL of the product was instilled into one eye of each rabbit, the other eye serving as a control. In six of the nine rabbits (Group A) the product was instilled in the conjunctival sac of the lower lid and the eyelids were gently held together for 1 second, and the rabbit released. In the remaining 3 rabbits (Group B) the test sample was introduced in the same manner, but each eye was flushed for 1 minute with lukewarm water starting no sooner than 20 to 30 seconds after instillation.

Ocular reactions were read with the naked eye. Readings were made at 24, 48, and 72 hours, and at 4 and 7 days after treatment.

RESULTS:

There was at no time, for any animal, a score above zero, for eyes in Group A and in Group B.

CONCLUSION: Under the conditions used for this test, 2% Copper Napthenate, Solvent, was considered to be nonirritating to the rabbit eye. No irritation was observed.

CLASSIFICATION: Core Guideline.

Toxicity Category IV.

COMMENT: No assurance was given that the sample used was a normal commercial batch or end-use formulation. The sponsor should certify this to EPA by letter.

IV. DERMAL TOXICITY - EPA - 2% COPPER NAPHTHENATE, SOLVENT (§81-2) DURATION OF TEST - DECEMBER 6, 1984 through DECEMBER 21, 1984.

Sample density measured 0.85 gm/mL.

PROCEDURE: Adult NZ albino rabbits were used for this study, five M, five F. Dosage level was 2 gm/kg, and the test sample was held in contact with skin of the trunk by a sleeve of impervious material for a 24-hour period. The trunks of the rabbits were clipped free of hair, and abraded by making epidermal abrasions every 2 to 3 cm, longitudinally over the area of exposure. Abrasions were deep enough to penetrate the stratum corneum, but not deep enough to disturb the derma or to obtain bleeding.

The sleeve was slipped onto the animal and one end secured. The appropriate dose was introduced under the sleeve and the remaining end secured to prevent leakage. The rabbits were returned to their cages for 24 hours, and at that time the sleeves were removed and the volume of unabsorbed material was estimated, and the skin reactions were noted. Rabbits were cleaned by thoroughly wiping with dry paper towels and examined for gross signs of toxicity, then observed for 2 weeks. Weight changes were recorded at 7 days and at 14 days. At the end of the 2-week observation period the rabbits were sacrificed and autopsied for gross pathological changes in tissues and organs. Any animals dying during the study were to be weighed and autopsied. An untreated control group of 5M, 5F was run concurrently.

RESULTS:

Behavioral and Physical Characteristics:

Test animals: Rabbits appeared normal following administration of the sample. After 24 hours exposure the wrappings were removed. At least 80 percent of the sample

appeared to have been absorbed. All animals showed moderate erythema at 24 and 48 hours. At 72 hours slight to moderate erythema persisted in all treated rabbits. No edema was observed. By 7 days all signs of irritation subsided except for flaky skin which persisted until day 14, on all rabbits. One rabbit, No. 12014 (M) had diarrhea at day 7 and 8 and showed slight weight loss at day 7, but showed a gain at day 14. Two rabbits, No. 12011 (M) and No. 12036 (F) lost a small amount of weight between day 7 and day 14. Rabbit No. 12037 (F) showed a small weight loss at the end of the 14-day observation period. No other abnormal signs were observed during the 14-day observation period.

Control Animals: Animal No. 12017 (M) showed diarrhea on days 5 and 6. Two rabbits, No. 12017 (M) and No. 12021 (F) showed some weight loss at 7 days but showed a weight gain at 14 days. No other abnormal signs were observed during the 14-day observation period.

MORTALITY DATA: There were no deaths among either the test animals or the controls.

AUTOPSY FINDINGS:

Test Animals: At the end of the 2-week observation period all animals were sacrificed, weighed and autopsied. Rabbit No. 12016 (M) showed several small white areas in the liver and small white round specks embedded in the surface of the entire cecum. All other tissues and organs appeared normal in No. 12016, and in the other 9 rabbits.

Control Animals: On day 14 all animals were weighed and grossly examined. No abnormalities were found. Two males and two females were sacrificed and autopsied. All organs and tissues appeared normal.

CONCLUSION: Under the conditions of this test, 2% Copper Naphthenate, Solvent had a dermal acute LD_{50} in rabbits greater than 2 gm/kg. No animals died. No further testing is required.

CLASSIFICATION: Core Guideline

Toxicity Category III

COMMENT: No assurance was given that the sample used was a normal commercial batch or the end-use formulation. The sponsor should certify this to EPA by letter.

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V. INHALATION TOXICITY - EPA 40 CFR 163.81-3 (§81-3)

METHOD:

Sample Preparation: 1021 gm of the sample was placed in a sprayer. Sample was sprayed into chamber with Burgess Thermo-Fogger Model F-982, at 5-minute intervals for 15 seconds for first 15 minutes and at 5-minute intervals for 5 seconds for the remaining part of 4 hours.

PROCEDURE: Sprague-Dawley rats weighing 200 to 300 gm were used for this study, five M and five F. Rats were placed in individual restrainers in an inhalation chamber with a volume of 392 liters, and exposed to the aerosolized sample for a 4-hour exposure. The rats were observed during the exposure period for changes in behavior, physical appearance, symptoms of toxicity, and death. At the end of the 4-hour exposure period surviving rats were returned to their cages for a 2-week observation period. The rats were housed in groups according to sex, in a temperature-controlled room (70 ± 2 °F). Any animals dying on this study were weighed and autopsied. Rats were observed twice daily, and weighed at 2, 3, 4, and 7 days. A control group of 10 rats (5M, 5F) was held for a 2-week observation period under the same conditions.

At the end of 2 weeks the surviving rats were sacrificed, weighed and autopsied. The lungs and trachea were removed and preserved in 10 percent formalin.

Measurement of Chamber Concentration: The weight of sample aerosolized into the chamber was measured to determine nominal concentration. Chamber concentrations were also measured by taking samples of chamber air near the breathing zone at 45, 105, and 165 minutes after beginning exposure. The chamber atmosphere was measured by pulling air from the chamber through 70 mL [redacted] for 15 minutes at a rate of 3 L/min. Analysis of the resulting [redacted] was done using atomic absorption. The results of these tests indicated a nominal concentration in the chamber of 17.5 mg/L (total weight of sample was 84 gm, pulled through at 20 mL/min for 240 minutes). At the three sampling times (45, 105, and 165 minutes after starting) the analytical concentration of 2% Copper Naphthenate, Solvent (the sample) was 0.15 mg/L of air.

Anderson sampler data indicated that 53.8 percent of particles obtained were 5.8 μ or larger and that 46.2 percent were less than 5.8 μ.

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RESULTS:

Behavioral and Physical Characteristics: The rats sat quietly in a curled position during exposure. After 2 hours and 40 min into the test the rats had ruffled fur. At the end of 4 hours of exposure the animals appeared alert and normal except for green tinge to the fur. The fur appeared normal at 24 hours. No abnormal behavior or physical characteristics were observed during the 2-week observation period, in either test or control rats.

Mortality Data: There were no deaths in this study.

Autopsy Findings: At the end of 14 days the rats were sacrificed, weighed and autopsied. All tissues and organs in the test animals appeared normal. One rat in the control group (No. 25, M) showed hypervacuolization of the center of the right kidney. All other tissues and organs appeared normal.

CONCLUSION: This study, although well performed, used only one dosage level of 0.15 mg/L of air (analytical concentration), a level at which none of the animals died. This level is not a limit level of exposure. Additional (higher) dosage levels should have been used in order to estimate an LC_{50}. The available information only indicates the Toxicity Category may be I, II, III, or IV.

CLASSIFICATION: Core Supplementary.

Toxicity Category - Not Determined (I, II, III, or IV).

COMMENT: The sponsor should certify to EPA by letter that the sample used in this test was a regular batch of the end-use product.