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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: November 6, 1981

SUBJECT: Registration No. 45987-R; No Go (Animal Repellant)
CASWELL#526, [redacted] 1328 Accession#245190

FROM: Winnie Teeters, Pharmacologist
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TO: William Miller (16)
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THRU: William Burnam, Acting Chief
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Recommendations:

Toxicology Branch considers these acute studies invalid because of uncertainty concerning identification of the material tested. In these studies the material tested is stated to be "Monogram Animal Repellant No. 100". The relationship of this material to "No Go", the product which the applicant wishes to register and for which adequate chemical composition has been provided, is not explained. This registration action cannot be toxicologically supported by these data until this relationship is explained and documented. The studies can be upgraded upon clarification of the composition of the test substance.

Additional aspects of the studies cause concern:

1. For the acute dermal toxicity test the product, a dry formulation, was not moistened for application. Also, microscopic evaluation of skin sections revealed the presence of acute inflammation and focal purulent crusting, both of which should have been obvious upon gross examination of the animals, yet all gross observations for dermal affects were reported as completely negative.

2. The dose administered in the primary dermal irritation test was not adequately defined since a specific volume of an unknown concentration was administered.

3. The acute inhalation study was run with material which had been triturated so as to pass through a sieve having openings of 297 microns. Particles of this size certainly are not respirable by rats. Since the material used had been sieved the particles could have been any size up to the maximum which would pass through the openings. Average particle size or particle size distribution was not stated. Without such particle size information, results of this completely negative test cannot be properly interpreted.

The following studies submitted in support of Registration No. 45987-R, No Go, have been reviewed and core classified as invalid.

1. Acute Dermal Toxicity - LD_{50} > 5 gm/kg (using dry formulation)

2. Acute Oral Toxicity - LD_{50} > 5 gm/kg

3. Primary Eye Irritation - Washed and unwashed eye scores = 0.0

4. Acute Inhalation Toxicity - LD_{50} > 5 mg/L (using particle size up to 297 microns)

5. Primary Dermal Irritation - Primary Irritation Index = 0.0

6. Dermal Sensitization - Not a dermal sensitizer using Draize procedure.

2

001158

Review:

1. Acute Dermal Toxicity of Monogram Animal Repellant No. 100 in Rabbits (Bio-Technics Laboratories Test No. 1-2-27836-A; August 21, 1980)

Test Material: Monogram Animal Repellant No. 100.

Method: Five (5) male and five (5) female rabbits weighing 2.10-2.56 kg were dosed dermally with 5 grams/kg, dry formulation, applied to lightly abraded skin, clipped free of hair. Application sites were occluded by a rubber sleeve. After 24 hours' exposure the skin was wiped clean. The animals were observed 5 days/week for two weeks then sacrificed and necropsied; tissue taken from the application site was preserved and examined histopathologically. Initial and terminal body weights were recorded.

Body weight data and necropsy findings were reported for 5 male and 5 female control rabbits; dermal sections from 5 control rabbits were evaluated histologically. Treatment of these controls was not described.

Results: All rabbits survived and gained weight during the holding period. No abnormal behavior nor physical characteristics were noted*; organs and tissues appeared normal upon gross examination. Tissues from test sites were similar to controls with quality and quantity of chronic inflammatory cells similar, except for one test site where inflammation was greater and acute inflammation was present*. In another test site, a granuloma was seen near a hair follicle. The skeletal muscle and subcutis were essentially unremarkable, as was the epidermis, which showed no necrosis. Focal purulent crusting was noted in one test and one control site.*

The dermal LD_{50} of the dry formulation was greater than 5 grams/kg to rabbits.

This study is core classified as invalid because of uncertainty concerning composition of the material tested.

*Observations, including those for the skin, were completely negative for all animals yet the pathology report stated acute inflammation and focal purulent crusting were present.

3

2. Acute Oral Toxicity of Monogram Animal Repellant No. 100 in Rats (Bio-Technics Laboratories Test No. 1-2-27836-2; August 21, 1980)

Test Material: Monogram Animal Repellant No. 100

Method: Ten Sprague-Dawley rats (5 males and 5 females) weighing 210-258 grams were dosed orally with 5 grams/kg of the test material prepared in distilled water at a concentration of 1 gram/ml. No statement was made about fasting prior to dosing. The rats were examined for toxicity 2 hours after dosing and daily, except weekends, for 14 days. Then they were weighed, sacrificed, and necropsied, during which the heart, lungs, spleen, kidneys, liver and gastrointestinal tract were examined grossly.

Body weight, dosage data, and necropsy findings for 10 controls (5 males and 5 females) were reported, but treatment of these controls was not described in the report.

Results: All animals survived and gained weight during the holding period. There were no abnormal behavioral or physical characteristics noted and all organs and tissues appeared normal.

The oral LD_{50} was greater than 5 grams/kg to rats.

This study is core classified as invalid because of uncertainty concerning composition of the material tested.

3. Primary Eye Irritation of Monogram Animal Repellant No. 100 in Rabbits (Bio-Technics Laboratories Test No. 1-2-27836-3; August 21, 1980)

Test Material: Monogram Animal Repellant No. 100

Method: Nine (9) rabbits, 2 1/2-3 1/2 months old, were used. Approximately 100 mg were instilled into the conjunctival sac, the lids held together for 1 sec., then the animals were returned to their cages. For 3 of the rabbits the material was flushed from the eye with 50 ml. of water after an exposure period of 10 sec. All rabbits were examined daily for ocular irritancy for 3 days following exposure.

Results: No signs of corneal involvement, iritis or conjunctivitis were observed throughout the 72-hour period, thus the test material should be classified as a non-irritant.

The mean unwashed eye score was 0.0.

The mean washed eye score was 0.0.

This study is core classified as invalid because of uncertainty concerning composition of the material tested.

4. Acute Inhalation Toxicity of Monogram Animal Repellant No. 100 in Rats (Bio-Technics Laboratories Test No. 1-2-27836-4; August 21, 1980)

Test Material: Monogram Animal Repellant No. 100

Method: Ten (10) Sprague-Dawley rats (5 males and 5 females) weighing 222-248 grams were used. They were exposed for 4 hours to an average concentration of 5.5-6.1 mg/L of the test material having a particle size of 297 or less microns, determined by passage through a U.S. Standard Sieve Series No. 50 mesh (opening 0.0116 inches). Average particle size was not stated.

The air chamber, volume 14.086 L, was designed for head-only exposure. Approximately 4 grams of test material was introduced into the chamber every 15 min. to create and maintain a concentration equal to or greater than 5 mg/L. Air samples were obtained from the chamber environment every 10 min. to monitor particulate concentration. Chamber temperature was 25 $\pm$ 0.5°C.

Following exposure the rats were returned to their cages and observed daily, except weekends, for 14 days, after which they were weighed, sacrificed and necropsied, during which the heart, lungs, spleen, kidneys, liver and gastrointestinal tract were examined grossly.

Terminal weight data and necropsy findings were reported for 10 controls (5 males and 5 females) but treatment was not described in the report for these controls.

Results*: All rats exposed to the test material survival and gained weight during the holding period. No abnormal behavioral or physical characteristics were observed. All tissues and organs appeared grossly normal; the bronchial passages were clear with no evidence of irritation. (This last statement appeared only in the Summary, and was not present in the gross pathology raw data sheets.)

The inhalation LC_{50} is greater than 5 mg/L to rats, using a particle size of 297 or less microns. Particles larger than 10 microns in diameter are not considered respirable.

This study is core classified as invalid because of uncertainty concerning composition of the material tested.

*On pages 46 through 55 of Test Report 1-2-27836-4, the dose is listed as 5 gm/l; yet in the text and tables of the inhalation study the dose is stated as milligrams per liter. The latter is assumed to be the correct dose.

5

001158

5. Primary Dermal Irritation of Monogram Animal Repellant No. 100 to Rabbits (Bio-Technics Laboratories Test No. 1-2-27836-5; August 21, 1980)

Test Material: Monogram Animal Repellant No. 100

Method: Six (6) rabbits, aged 2 1/2 -3 1/2 months old, were used. The trunk was clipped free of hair and half of the clipped area was abraded. The sample was moistened with deionized water and a portion, 0.5 ml.*, was applied on the abraded and unabraded sites, which were then covered with gauze squares, securely taped and wrapped. The rabbits were immobilized in restraining devices for an exposure period of 24 hours, after which bandages were removed and the remaining test material washed from the skin. Dermal reactions was evaluated by the Draize scoring system at 24, 48 and 72 hours following application.

Results: There was no erythema, edema or eschar formation observed at the 24- or 72-hour evaluation.

The Primary Dermal Irritation Score was 0.0.

This study is core classified as invalid because of uncertainty concerning composition of the material tested.

*The correct dose for this procedure should have been 0.5 gram moistened with water and applied to the abraded site and a similar amount moistened with water then applied to the intact site. From description of the dosing procedure used, the amount of the product applied cannot be determined since concentration of the applied volume was not stated.

The irregularity in dose is not considered critical to the overall evaluation of this product for there is provided a dermal toxicity study in which 10 rabbits were dosed with 5 gm/kg on abraded skin for 24 hours' exposure. Erythema, eschar and edema were graded.

4

6. Sensitization Study of Monogram Animal Repellant No. 100 in Guinea Pigs (Bio-Technics Laboratories Test No. 1-2-27836-6).

Test Material: Monogram Animal Repellant No. 100

Method: Ten (10) male guinea pig, each weighing between 300 and 500g, were used. Initially they received a intracutaneous injection on the shaved anterior dorsal region of 0.05 ml of a 0.1% suspension of the test material in physiological saline; 9 succeeding injections of 0.1 ml were given on alternate days. After a two-week rest, the pigs were challenged by a final intracutaneous injection of 0.05 ml of a fresh suspension (0.1%) of the test material. Injection sites were evaluated for erythema and edema 24 and 48 hours after each injection using the Draize scoring system.

Results: Average scores for inducing injections were 1.83 for erythema and 0.87 for edema; for the challenge injection the average scores were 1.25 and 0.7; respectively for these parameters. Additionally, the average challenge score was less than the average score for any single inducing injection other than the initial one, where the scores were 1.0 for erythema and 0.5 for edema. Thus the test material is not considered to be a sensitizer in guinea pigs when tested by this procedure. However, it is common knowledge that this technique is sensitive only to strong, but not moderate and weak, sensitizers.

The test material was not a dermal sensitizer to guinea pigs when tested by the Draize injection technique.

This study is core classified as invalid because of uncertainty concerning composition of the material tested.

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7