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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SEP 24 1987

MEMORANDUM

SUBJECT: EPA Pesticide Petition No. 7F3472. EPA File Symbol 9018-A. Propel® (80% a.i.) [L(+)] Lactic Acid. Request for Waiver of Toxicity Data. Accession No. 265645

Caswell No. 517R

FROM: William S. Woodrow, Ph.D., Section VII, WSW 9-11-87
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Hazard Evaluation Division (TS-769C)

TO: J. Miller/R. Taylor, PM Team 25
Fungicide-Herbicide Branch
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THRU: Albin B. Kocialski, Ph.D., Supervisory Pharmacologist
Section VII, Toxicology Branch
Hazard Evaluation Division (TS-769C) ABK 9/21/87

Petitioner: Brea Agricultural Services, Inc.
Drawer I
Stockton, CA 95201

Action Requested

Brea Agricultural Services, Inc. requests that EPA waive the following toxicity requirements for Propel [L(+)] lactic acid:

- All Subchronic Toxicity studies;
- All Chronic Toxicity studies; and
- All Mutagenicity studies.

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Background

Brea Agricultural Services, Inc. was granted a temporary exemption from tolerances for L-Lactic acid and an EUP for Propel® used as a plant growth regulator to increase nut and fruit set in: almonds, walnuts, apples, beans (green and dry), broccoli, cabbage, cauliflower, cherries, citrus, corn (sweet and field), grapes, lettuce, peppers (green and chili), pineapples, prunes, strawberries, sugarcane, tomatoes, and cotton.

No permanent tolerances for Propel® (80% active ingredient) or lactic acid on RACs currently exist.

Lactic acid is a natural, widely-distributed constituent of plant and animal tissues and is involved in glycolytic reactions. Many plants have the ability to accumulate large amounts of lactic acid; barley grain can have a typical concentration of pyruvic and lactic acid at 15 meq/100 grams fresh weight. Lactic acid is found in man and other animals; the normal lactic acid concentration in arterial blood ranges from 5 to 20 mg/dl (100 mL). The basic lactic acid reaction in animals is the same as occurs in plants.

Recommendations

1. The following toxicity data will be required:

   - Acute Inhalation Toxicity.

2. Acceptable acute toxicity studies previously submitted by Brea Agricultural Services, Inc. include (see attached one-liner list):

Study	Toxicity Category
Rat Acute Oral LD_{50}	III
*Primary Dermal Irritation	I
Rabbit Acute Dermal LD_{50}	III

3. It will not be necessary to conduct subchronic or chronic toxicity testing using lactic acid:

   Rationale to Support Waiver of Mutagenicity, Subchronic, and Chronic Toxicity Data for Lactic Acid

* eye irritation study waived based on pH < 2.0.

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Lactic acid has been approved as an inert ingredient by the Agency for application to plants (40 CFR 180.1001(c)). Thus, residues of lactic acid were exempted from the requirement of a tolerance when used in accordance with good agricultural practices as an inert or occasionally applied as an active ingredient in pesticide formulations to growing crops or to RACs after harvest.
FDA approved the use of lactic acid as a generally recognized as safe (GRAS) ingredient in human foods. There is no limitation on amount used other than good manufacturing practice (21 CFR 184.1061).

The metabolism of lactic acid is the same in plants and animals. Data (provided by the petitioner) show that residues of lactic acid from the proposed use will not exceed physiological normal lactic acid levels in RACs, or that which is allowed from inert ingredient applications, or that which is allowed in food production as a GRAS ingredient.*

Normal human urine generally contains 50 to 200 mg of lactic acid per 24 hours. Once lactic and pyruvic acids are formed in muscle (glycolysis), they can be removed by the kidney or reconverted by the liver to glucose and glycogen.

Thus, lactic acid is a normal constituent of plants and animals. The fact that lactic acid residues resulting from the uses proposed in the present petition will not be higher than is presently allowed in food production, and that such residues will not exceed normal physiological lactic acid levels in RACs or that which is allowed from inert ingredient applications, or that which is allowed in food production as a GRAS ingredient provides justification for not requiring subchronic and chronic toxicity data.

Attachments

4. Add to the precautionary statements the phrase "May be harmful or fatal if swallowed or inhaled.

*EPA Accession Nos. 265692, Vol. III Residue Chemistry Data Req., and 072330, Experimental Use Permit for SY-83. USDA Agricultural Statistics, 1982.

Reviewed by: Joycelyn Stewart, Ph.D.
Section VII, Tox. Branch (TS-769C)
Secondary reviewer: Albin Kocialski, Ph.D.
Section VII, Tox. Branch (TS-769C)

DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization TOX. CHEM. NO.: 517R

ACCESSION NUMBER: 265645 PROJ. NO.: 7-0174

TEST MATERIAL: L(+) Lactic Acid

SYNONYMS: Propel; SY-83

STUDY NUMBER(S): 480-2750

SPONSOR: Brea Agricultural Service
Stockton, Ca 95206

TESTING FACILITY: American Biogenics Corporation
Decatur, Illinois 62526

TITLE OF REPORT: Dermal Sensitization Study in Guinea Pigs with SY-83

AUTHOR(S): J. Krueger and S. Smith

REPORT ISSUED: 9/10/86

CONCLUSION: The test compound is not a dermal sensitizer

Classification: core-Minimum

INERT INGREDIENT INFORMATION IS NOT INCLUDED.

MATERIALS: SY-83 L(+) Lactic Acid 80%; [redacted] 20%) was the test material. Female Hartley outbred guinea pigs were the test animals.

METHODS: Twenty two female Hartley guinea pigs were used in the study. Ten animals received induction and challenge doses of the test compound and ten were used as naive controls. The study method was a modified Buehler technique. A range finding study was conducted in which 0.5 ml of the test compound was applied to prepared skin sites of two guinea pigs at concentrations of 3%, 10%, and 30% in deionized water, and at full strength. The test sites were secured with Blenderm tape and the reactions assessed at 24 and 48 hours post compound application. Very slight erythema was reported in the animals receiving the 100% concentration. Based on the results obtained in this study,the test compound was used at full strength in the main study.

In the induction phase of the main study, SY-83 was applied to prepared skin sites on the test animals at 0.5 ml doses three times/week for nine applications on 4x4 cm Webril patches attached to Blenderm tape. The entire trunk of each animal was wrapped

with an impervious binder consisting of plastic wrap, adhesive tape and masking tape. After a six hour exposure period,the binders were removed and the test sites scored for erythema, edema and other lesions at 24 and 48 hours. Dermal reactions were scored according to the Draize system. Food and water were available ad libitum. Individual body weights were recorded initially and terminally for range finding animals, and on the day of the 48 hour challenge evaluations for the animals in the main study. Clinical observations were made daily. Challenge doses of 0.5 ml of SY-83 were administered to the test animals two weeks after the ninth induction application of the test compound and were evaluated at 24 and 48 hours afterwards. The naive controls were administered 0.5 ml of 100% Propel at the time the test animals received the challenge doses. Historical control data of a dermal sensitizer were included in the submission(0.1% dinitrochlorobenzene).

EVALUATION CRITERIA: The test compound was considered a dermal sensitizer if at least 2 animals had more severe dermal reactions after the challenge doses than were observed after the first induction application, and the dermal reactions of the test group were greater than those of the naive control group. The mean and standard deviation were calculated for the erythema and edema values recorded during the induction and challenge phases.

RESULTS: All animals survived the test and all animals gained weight. Body weight increases were similar in control and treated animals. Very slight erythema in 3 animals, and very slight edema in one animal were repored after the first induction application. Erythema became severe after the second induction dose, therefore the test compound concentration was reduced from 100% to 30% and the induction site was changed from the right flank to the left flank. Grades 1-4 (Draize) erythema reactions were reported after the 7th induction application; however, they were described as seeschar formation and pinpoint pitting of the skin rather than redness, and were considered irritation rather than sensitization reactions. After the challenge dose, the test animals developed skin pitting and scab formation, but little redness. The full strength of the test compound produced pitting and eschar formin 8 of 10 naive control guinea pigs which was similar to that observed in the animals in the main study when the test sites were examined 24 and 48 hours later. Apart from the skin reactions no other toxicity was reported. Based on these observations, the investigators concluded that Propel did not cause dermal senssitization in guinea pigs.

DISCUSSION: The similarity of the dermal response of the naive control animals and the test animals to application of the test compound supports the investigators' conclusion that Propel is not a dermal sensitizer. Previously reported data indicate that Propel is a Category I Dermal irritant (Galvin:Toxicology Branch memorandum dated 7/8/1984).

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