8-22-96

PRIMARY REVIEWER: Jess Rowland, M.S, Toxicologist
Section I, Toxicology Branch II

SECONDARY REVIEWER: Alan C. Levy, Ph.D., Toxicologist
Section I, Toxicology Branch II

DATA EVALUATION REPORT

STUDY TYPE: 14-Day Feeding - Rat. **GUIDELINE:** None

DP BARCODE: D225072 **SUBMISSION:** S503609

PC CODE: 217500 **TOX.CHEM.No:** 637C

TEST MATERIAL: Pelargonic acid **MRID No.** 43843507

CITATION: Kuhn, J.O *"Pelargonic acid-Range-Finding for a 90-Day Rat Oral Toxicity (Diet)"*. Stillmeadow, Inc., Sugar Land, Texas, Study ID: 1941-95. 8/29/95. **MRID No. 43843507.** Unpublished.

EXECUTIVE SUMMARY: In a range-finding study, pelargonic acid (93%) was administered in the diet for 2 weeks to male and female Sprague-Dawley rats (3/sex/dose) 0, 1500, 2500, 4000, 6300, 7500, or 20,000 ppm or 0, 145, 267, 423, 633, 753 or 1834 mg/kg/day, respectively. No systemic toxicity was seen in either sex at any dose level; treatment had no adverse effect on survival, clinical signs, body weight, body weight gain, food consumption, hematology, clinical chemistry or gross pathology. Organ weights were not obtained and histopathology was not performed.

This study is determined to be deficient because of an inadequate number of animals tested (i.e., 3/sex/dose instead of 10/sex/dose recommended in the Guideline) and the lack of organ weights as well as histopathology data. Consequently, this study is classified as **Unacceptable** and does not satisfy Guideline Requirement §152-20.

The Registrant's request for data waiver of a 90-day feed study is denied. A 90-day feeding study must be conducted because: (i) the 14-day range-finding study is determined to be unacceptable; (ii) the use-pattern (food-use) meets the criteria specified in the 40 CFR 158.690 (i.e., *a 90-day study is conditionally required when the use requires a tolerance or an exemption from requirement of tolerance, use of the herbicide will result in repeated human exposure by the oral route, and pelargonic acid is a secondary food additive*; (iii) no long-term studies via the oral route are available; and (iv) results of a 90-day feeding study will be used in dietary risk assessments. **Therefore, a 90-day feeding study must be conducted.**

I. INTRODUCTION

1

This Data Evaluation Report (DER) summarizes the experimental procedures and results of a 14-day range-finding dietary study of pelargonic acid in rats. The Registrant is citing this study to request a data waiver for a 90-day feeding study in rats (§152-20).

II. MATERIALS AND METHODS

1. Test Material — Pelargonic acid
   - Purity: 93%
   - Reference No: Emery 1202
   - Lot No.: 4H006
   - Description: Pale yellow liquid

2. Test Animals — Rats
   - Strain: Sprague-Dawley, Harlan Sprague-Dawley, Houston, TX
   - Sex: Males and Females
   - Weight: 154 - 174 M and 131 - 160 F
   - Identification: Ear punch
   - Acclimation: 6 days quarantine, 7 days on pretest

3. Animal Husbandry

   - Housing: 1/Cage.
   - Food: Certified Rodent Chow 5002 ad libitum
   - Water: Tap water ad libitum
   - Environment: Temperature, 72 ± 5°F; Humidity, 30-80%; Light, 12 hr.light/dark cycle; Air changes, 10-12/hour

2

4. Study Design

Group	No. Animals		Dose [ppm]
	Males	Females	
1	3	3	0
2	3	3	1500
3	3	3	2500
4	3	3	4000
5	3	3	6300
6	3	3	7500
7	3	3	10,000/20,000[a]

a = The dose of 10,000 ppm on Week 1 was increased to 20,000 ppm during Week 2.

5. Treatment

A premix was prepared by adding the appropriate amount of the test material to a small amount of feed (total weight 500 g) and mixing the combination in a Hobart A200 Mixer for 5 minutes. The premix was then added to the remaining feed and mixed for an additional 15 minutes. Stability analysis was conducted on 1000 ppm and 50,000 ppm test material. Concentration analyses were performed on a batch of feed prepared for the first two week of the study for each dose level on Day-7 of the pretest week. Homogeneity analyses were conducted to confirm the concentration of each batch.

Results: The diet mix was stable at room temperature for a period of three weeks. Concentration analyses showed that the percentage of nominal concentration to be 51%, 82%, 137%, 123%, 119%, and 125% for the first two weeks, and 69%, 84%, 82%, 89%, 109%, and 91%, for the third week, respectively at 1500, 2500, 4000, 6300, 7500, and 20,000 ppm dose levels.

6. Observations

Animals were observed daily for mortality and clinical signs. Body weights were obtained once prior to initiation and weekly through Day 21. Food consumption were recorded twice weekly. At termination, blood was drawn by cardiac puncture and hematology (red blood cell, hematocrit, white blood cell count, and hemoglobin) and clinical chemistry (blood urea nitrogen, creatinine, serum alanine aminotransferase, total protein, albumin, alkaline phosphatase, total bilirubin, glucose and triglycerides) parameters were evaluated. At necropsy, all animals were examined for gross pathological alterations; no organ weight measurements were taken. **No histopathology was performed.**

7. Regulatory Compliance

Signed and dated No Data Confidentiality Claim, EPA's Good Laboratory Practice, and Quality Assurance were provided.

III. RESULTS

1. Survival

All rats survived to termination of the study.

2. Clinical Signs

No treatment-related clinical signs of toxicity were seen at any dose level.

3. Body Weight and Body Weight Changes

Mean body weights of treated rats were comparable to those of the controls. Mean body weight gain was similar for all treatment groups and lowest for the control group.

N = 3/Sex/Dose	Dose (ppm)						
	0	1500	2500	4000	6300	7500	20,000
Weight Gain (g) Day -1 to 21	57	79	86	82	81	82	85

4. Food and Compound Consumption

Mean food consumption was similar between treated and control groups. Mean compound consumption was 145, 267, 423, 633, 753, and 1834 mg/kg/day, at 1500, 2500, 4000, 6300, 7500, and 20,000 ppm, respectively.

5. Clinical Pathology

No treatment-related alterations in hematology or clinical chemistry parameters were seen

in either sex at any dose level.

6. Gross Pathology

No treatment-related gross pathological alterations were seen at terminal necropsy.

IV. DISCUSSION

Dietary administration of technical pelargonic acid to male and female rats at doses up to and including 20,000 ppm (1834 mg/kg/day) did not cause any systemic toxicity. Results of this study indicate a NOEL of >20,000 ppm (1834 mg/kg/day).

This study, however, is determined to be deficient because of the inadequate number of animals tested (3 sex/dose instead of 10/sex/dose) and the lack of organ weight as well as histopathology data.

V. DEFICIENCIES

Inadequate numbers of animals were used, organ weights were not determined and histopathological examinations were not conducted.

V. CONCLUSION

This range-finding study is classified as **unacceptable** and does not satisfy Guideline Requirement §152-20. Although this range-findings study was conducted to select the dose levels for a 90-day study, the Registrant is requesting a data waiver for the 90-day feeding study due to the lack of toxicity in the 14-day study. The request for data waiver of a 90-day feed study is denied because: (i) the 14-day range-finding study was determined to be unacceptable, (ii) the use pattern (food-use) satisfies the criteria stated in the 40 CFR 158.690 (i.e., a 90-day study is conditionally required when the use requires a tolerance or an exemption from requirement of tolerance, use of the herbicide will result in repeated human exposure by the oral route, and the active ingredient, pelargonic acid, is a secondary food additive); (iii) no long-term studies via the oral route are available; and (iv) results of a 90-day feeding study will be used in dietary risk assessment. **Consequently, a 90-day feeding study must be conducted.**

Sign-off date: 08/22/96
DP Barcode: D225072
HED DOC Number: 012024
Toxicology Branch: TB2