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DATA EVALUATION REPORT

STUDY TYPE: Dermal Toxicity/Carcinogenicity - Mice. **GUIDELINE No.:** None

DP BARCODE: D225072 **SUBMISSION:** S503609

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

TEST MATERIAL: Pelargonic acid **MRID No.** 43961801

CITATION: Barkley, W *"Chronic Mouse Dermal Toxicity Study. Test Material C-182 = Pelargonic acid"*. Kettering Laboratory, University of Cincinnati Medical Center, Cincinnati, OH. Study ID: None. 7/85. **MRID No. 43961801.** Unpublished.

EXECUTIVE SUMMARY: The chronic toxicity and the carcinogenic potential of pelargonic acid was evaluated by repeated dermal applications to male C3H/Hej mice. Four treatment groups each consisting of 50 mice included: an untreated control; undiluted pelargonic acid at 50 mg applied twice weekly; a vehicle control treated with 50 mg of mineral oil twice weekly; and a positive control treated with 50 mg of a 0.05% solution of benzo(a)pyrene in mineral oil twice weekly. Mice received the treatment for 80 weeks. At termination, a complete gross necropsy was performed and histopathological examinations of all tissues from all mice were conducted. No treatment-related clinical signs of toxicity were seen at any dose level. Mean body of mice treated with pelargonic acid was similar to that of the untreated controls. No treatment-related non-neoplastic or neoplastic lesions were seen either in the skin or other organs. A total of 180 skin tumors seen in 45 of 50 mice treated with the positive control benzo(a)pyrene included 45 papillomas, 53 keratoacanthomas, 81 squamous cell carcinomas, and 1 fibrosarcoma. A NOEL/LOEL was not established since only a single dose was tested.

This study is classified as **supplementary** because it does provide scientifically valid information and was not designed to fulfill a Guideline requirement. This study, however, addresses the study objective which was to assess the chronic toxicity and the carcinogenic potential of pelargonic acid by the dermal route.

Based on the results of this study (i.e., lack of dermal or systemic toxicity) and the unlikelihood of prolonged human exposure via the skin (i.e., not used in swimming pool or impregnating clothing), the Registrant's request for a data waiver of the 90-day dermal toxicity is granted.

I. INTRODUCTION

This Data Evaluation Report (DER) summarizes the experimental procedures and results of a dermal toxicity/carcinogenicity study in mice. The Registrant is citing this study to request a data waiver for a 90-dermal toxicity study (§152-21).

II. MATERIALS AND METHODS

1. Test Material — Pelargonic acid
   - Identification: C-182; CE-81-6
   - Purity: Not specified
   - Lot No.: Not reported
   - Description: Not reported

2. Test Animals — Mice
   - Strain: C3H/HeJ, Jackson Laboratory, Bar Harbor, Maine
   - Sex: Males
   - Age: 6-8 Weeks
   - Weight: 25-26 g (group mean) at 1 week
   - Identification: Ear punch/Toe clip
   - Acclimation: 3 weeks

3. Animal Husbandry
   - Housing: 5/Cage.
   - Food: Certified Rodent Chow 5001 ad libitum
   - Water: Tap water ad libitum
   - Environment: Temperature, 74 ± 2°F; Humidity, 45 ± 10%; Light, 12 hr.light/dark cycle;

4. Study Design

Group	No. Animals	Treatment
	Males	
Control	50	Untreated
Vehicle Control	50	50 mg of mineral oil 2x/week
Pelargonic acid	50	50 mg undiluted 2x/week
Benzo(a)pyrene	50	50 mg of a 0.05% in mineral oil 2 x/week

5. Treatment

Hair was removed from the backs of the mice with electric clippers before dermal applications. Four treatment groups each consisting of 50 mice included: an untreated control; undiluted pelargonic acid at 50 mg applied twice weekly; a vehicle control treated with 50 mg of mineral oil twice weekly; and a positive control treated with 50 mg of a 0.05% solution of benzo(a)pyrene in mineral oil. Mice received the treatment for 80 weeks or until a neoplasm was clinically diagnosed a an "Advanced tumor".

6. Observations

Animals were observed twice daily for mortality and clinical signs. Body weights were

obtained once prior to initiation and weekly during the first month, and every two weeks thereafter. All clinical observations of the skin were recorded daily. A complete gross necropsy was performed on all mice that were scarified moribund, died on study and those sacrificed at termination between Weeks 80-83. At necropsy, skin neoplasms were measured and recorded. Tissues from each organ was preserved in 10% neutral formalin. A complete histopathological examination was performed on all tissues from all mice in the untreated, vehicle, and positive control and pelargonic acid groups.

7. Regulatory Compliance

Although this study was conducted in 1985, it did not meet the requirements of EPA's Good Laboratory Practices.

III. RESULTS

1. Survival

Survival data are presented in Table 1.

Table 1. Survival Data in Mice Treated with Undiluted Pelargonic Acid.

Treatment	Percent Survival (Weeks)						
	13	26	39	52	65	78	84
Untreated Control	100	98	98	96	84	52	Survivors sacrificed between Weeks 80-83
Vehicle Control	100	98	92	88	84	64	
Pelargonic Acid	100	100	88	88	82	66	
Positive Control	100	100	96	72	14	0	

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 weight data reported only in the form of "growth curves" indicated that the weight curve of mice treated with pelargonic acid was similar to that of the untreated controls.

4. Histopathology - Skin

Non-neoplastic lesions observed in the skin are presented in Table 2. No skin tumors were seen in any mice treated with pelargonic acid, mineral oil (vehicle control) or untreated controls. A total of 180 skin tumors were seen in 45 of 50 mice treated with the positive control benzo(a)pyrene included 45 papillomas, 53 keratoacanthomas, 81 squamous cell carcinomas, and 1 fibrosarcoma.

Table 2. Non-neoplastic Lesions of the Skin in Mice Treated with Pelargonic Acid.

Lesions	Untreated Control	Vehicle Control	Pelargonic Acid	Positive Control
No. Examined	49	47	48	49
Ulcer	8	9	7	2
Abscess	2	5	0	23
Pigment	2	2	41	4
Fibrosis	37	40	48	49
Scar	13	13	14	23
Folliculitis	6	0	0	1
Acanthosis	37	39	48	49
Hyperkeratosis	29	24	40	32
Keratosis	0	0	0	1
Dysplasia	0	0	0	11
Cyst	0	0	3	1

5. Histopathology - Systemic

No treatment-related non-neoplastic or neoplastic lesions were seen. A variety of lesions seen both in the treated and control groups are presented in Table 3.

Organ/Lesion		Untreated Control	Vehicle Control	Pelargonic Acid	Positive Control
No. Mice Examined		49	47	48	49
Lung-	Pneumonia	10	11	15	7
	Abscess	4	1	1	0
	Fibrosis	3	5	2	4
	Atelectasis	6	3	3	1
	Edema/hemorrhage	2	3	1	1
Kidney-	Nephritis	9	6	4	6
Spleen-	Hemosiderin	5	7	5	3
	Leukemia or Lymphoma	0	0	3	1
Liver- Hepatocarcinoma		18	11	23	5
GI tract-	Gastritis/entero-colitis	3	8	6	11
Testis-	Atrophy	2	3	1	1

IV. DISCUSSION

Repeated dermal application of 50 mg of undiluted pelargonic acid twice a week for 80 weeks to male mice did not cause any dermal or systemic toxicity and there was no evidence carcinogenicity via the dermal route.

This study is classified as **supplementary** because it does provide scientifically valid information and was not designed to fulfill a Guideline requirement. This study, however, addresses the study objective which was to assess the chronic toxicity and the carcinogenic potential of pelargonic acid by the dermal route.

V. CONCLUSION

Based on the results of this study (i.e., lack of dermal or systemic toxicity) and the unlikely prolonged human exposure via the skin (i.e., not used in swimming pool or impregnating clothing), the Registrant's request for a data waiver of the 90-day dermal toxicity is granted.

Sign-off date: 08/22/96
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