

Report Title: Acute Dermal Toxicity Study in Rabbits

Test Type: Acute Dermal Toxicity

Conducting Laboratory and Location: International Research and Development Corporation

Test Substance(s): #T7121 – 2% Placebo shampoo at pH 4.5. Undiluted test substance used for dosing.

Species: Rabbit

of Animals: 3 male, 3 female

Test Conditions: 3 male and 3 female New Zealand White Rabbits exposed to 2000 mg/kg on abraded skin for 24 hours. Rabbits were observed for 14 days.

Results: Minimum lethal dermal dose in both male and female rabbits was >2.0 g/kg.

Study #: 191-082; see related studies 191-080 and 191-081

Accession #: 19624

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International Research and Development Corporation

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I. SYNOPSIS

The minimum lethal dermal dose of T-7121 in the male and female albino rabbit was found to be greater than 2000 mg/kg.

II. TEST MATERIAL

The test material was received from The Procter and Gamble Company, Cincinnati, Ohio on August 4, 1977. It was identified as "T-7121" and was received as a slightly yellow viscous liquid.

III. METHOD

Three male and 3 female New Zealand White rabbits (obtained from Kuiper's Rabbit Ranch, Gary, Indiana) were used for this study. The rabbits weighed from 2260 to 2750 grams at the beginning of the study. They were individually housed in metal metabolism cages in temperature and humidity controlled quarters. They were maintained in accordance with the recommendations contained in H.E.W. Publication No. 74-23 (N.I.H.) entitled "Guide for the Care and Use of Laboratory Animals". The rabbits were conditioned for a minimum of 6 days prior to study initiation. Water and Purina Rabbit Chow were available ad libitum.

The hair was clipped from the backs of the rabbits (20-30% of the body surface) with an electric clipper. The skin was abraded for one male and two females with a clipper head. The abrasions penetrated the stratum corneum, but were not deep enough to cause bleeding. The test material was applied to the back, as received, at a dosage level of 2000 mg/kg. The application site was then covered with 8-ply gauze bandaging, rubber dam and several wrappings of 75 mm Elastoplast tape. A collar was also applied. Following the 24 hour application period, the collars and wrappings were removed and any remaining test material was wiped from the rabbits' backs with a wet disposable paper towel.

At 24 hours and daily thereafter for a total of 14 days, the rabbits were observed for pharmacotoxic signs, dermal irritation (in accordance with the scale found on page 4) and mortality. Body weights were recorded initially and at 7 and 14 days of the observation period. All rabbits which died on study were subjected to gross necropsy examination as were all survivors at the end of the 14-day observation period.

EVALUATION OF SKIN REACTIONS (CODE)

Erythema

- 0 - None
- 1 - Slight (barely perceptible)
- 2 - Moderate (well defined)
- 3 - Severe (beet red)

Edema

- 0 - None
- 1 - Slight (barely perceptible to well defined by definite raising)
- 2 - Moderate (raised approximately 1 mm)
- 3 - Severe (raised more than 1 mm)

Atonia (not including eschar area)

- 0 - Normal
- 1 - Slight (slight impairment of elasticity)
- 2 - Moderate (slow return to normal)
- 3 - Marked (no elasticity)

Desquamation (not including eschar area)

- 0 - None
- 1 - Slight (slight scaling)
- 2 - Moderate (scabs and flakes)
- 3 - Marked (pronounced flaking with denuded areas)

Coriaceousness

- 0 - None
- 1 - Slight (decrease in pliability)
- 2 - Moderate (leathery texture)
- 3 - Marked (tough and brittle)

Fissuring

- 0 - None
- 1 - Slight (definite cracks in epidermis)
- 2 - Moderate (cracks in dermis)
- 3 - Marked (cracks with bleeding)

Eschar

- N - No
- Y - Yes

Exfoliation (sloughing of the eschar tissue)

- N - No
- Y - Yes

IV. RESULTS

A. MORTALITY:

Dose - Mortality Data

Dosage Level mg/kg	Number of Deaths														Total Mortalities			
	Hrs.		Day															
	0-4	1	2	3	4	5	6	7-14	Male	Female	Total							
	M	F	M	F	M	F	M	F	M	F	M	F	M	F				
2000																0/3	0/3	0/6

The minimum lethal dermal dose of T-7121 in the male and female albino rabbit was found to be greater than 2000 mg/kg.

B. PHARMACOTOXIC SIGNS:

The following pharmacotoxic signs were observed during the 14-day observation period. (See the following page.)

T-7121:

2000 mg/kg

Males

	Normal	Purulent Nasal Discharge	Impaired Use of Hind Legs	Dyspnea
Days 1-2	3/3			
Days 3-4	2/3	1/3		
Day 5	2/3	1/3		1/3
Days 6-7	2/3	1/3		
Days 8-12	3/3			
Days 13-14	2/3		1/3	

Females

	Normal	Nasal Discharge
Days 1-2	3/3	
Day 3	2/3	1/3
Days 4-14	3/3	

C. DERMAL IRRITATION SIGNS:

The following signs of dermal irritation were observed during the 14-day observation period: (See the following page).

T-7121:

Dermal Irritation

2000 mg/kg

	Erythema				Edema			Atonia					Desquamation					Coriaceousness				Fissuring				Exfoliation	Eschar	
	None	Very Slight	Slight	Moderate	None	Very Slight	Slight	None	Very Slight	Slight	Moderate	Marked	None	Very Slight	Slight	Moderate	Marked	None	Very Slight	Slight	Moderate	None	Very Slight	Slight	Moderate			
Day 1	2/6	3/6	1/6		2/6	4/6		3/6	1/6	2/6			6/6					3/6	2/6	1/6		6/6				0/6	0/6	
Day 2		3/6	3/6			3/6	3/6		2/6		4/6		6/6							5/6	1/6		5/6	1/6			0/6	0/6
Day 3			4/6	2/6		2/6	4/6		1/6	2/6	3/6		6/6							6/6		3/6		3/6			0/6	0/6
Day 4			5/6	1/6		2/6	4/6				3/6	3/6	5/6		1/6					5/6	1/6		2/6	4/6			0/6	0/6
Day 5			5/6	1/6			6/6			2/6	3/6	1/6	3/6	2/6	1/6					2/6	4/6		1/6	5/6			0/6	0/6
Day 6			5/6	1/6			6/6			2/6	3/6	1/6	3/6		3/6					2/6	4/6		1/6	5/6			0/6	0/6
Day 7			5/6	1/6			6/6			1/6	4/6	1/6	3/6		3/6						6/6		5/6	1/6			0/6	0/6
Day 8			5/6	1/6			6/6		2/6	1/6	2/6	1/6	2/6		2/6	2/6	2/6				1/6	5/6		5/6	1/6		0/6	0/6
Day 9				6/6			6/6		2/6	1/6	3/6		2/6		2/6	2/6					1/6	5/6		5/6	1/6		0/6	0/6
Day 10		1/6	5/6				6/6		3/6	1/6	1/6	1/6	2/6		3/6	1/6					3/6	3/6		1/6	5/6		0/6	0/6
Day 11		5/6	1/6		1/6	1/6	4/6		3/6	1/6	2/6		1/6	1/6	1/6	3/6			1/6	1/6	4/6		2/6	4/6			0/6	0/6
Day 12		5/6	1/6		1/6	3/6	2/6		4/6	1/6	1/6		1/6			4/6	1/6	1/6	1/6	1/6	4/6		2/6	2/6	2/6		0/6	0/6
Day 13		5/6	1/6		1/6	3/6	2/6		4/6	1/6	1/6		1/6			3/6	2/6	1/6	1/6	2/6	3/6		3/6	1/6	2/6		0/6	0/6
Day 14	1/6	5/6			1/6	3/6	2/6		4/6	1/6	1/6		1/6			4/6	1/6			3/6	3/6		4/6	2/6			0/6	0/6

D. BODY WEIGHTS:

The following body weights were obtained during the 14-day observation period:

<u>Dosage Level (mg/kg)</u>	<u>Individual Rabbit No.</u>	<u>Sex</u>	<u>Control Weight (grams)</u>	<u>7-Day Weight (grams)</u>	<u>14-Day Weight (grams)</u>
2000	29551	Male	2750	2690	2908
	29555	Male	2245	2410	2660
	29557	Male	2420	2425	2476
	29552	Female	2260	2162	2244
	29570	Female	2595	2437	2669
	29574	Female	2465	2380	2527

E. NECROPSY FINDINGS:

Necropsy observations in rabbits which were sacrificed at the end of the study period were as follows:

2000 mg/kg

No gross lesions	1/3 males	1/3 females
Thickening, application site		1/3 females
Consolidation, lungs	1/3 males	
Yellow focus, liver		1/3 females
Abdominal fat, sublumbar region	1/3 males	