



**Report Title: Primary Skin Irritation in Rabbits**

**Test Type:** Skin Irritation

**Conducting Laboratory and Location:** International Research and Development Corporation

**Test Substance(s):** T-7120 – 2% Octopirox in shampoo at pH 4.5

**Species:** Rabbit

**# of Animals:** 1 male, 2 female

**Test Conditions:** 1 male and 2 female New Zealand White rabbits exposed to two patches on the back with 0.4ml applied as a 10% (w/w) solution in distilled water for 24 hr. One patch was applied to intact skin and the other to abraded skin. Test sites were graded at 24 and 72 hr.

**Results:** NOT a primary skin irritant. Primary Irritation Score = 4.7

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

**Report Date:** 10/25/77

**Accession #:** 19198

(5)

Final

11304

*International Research and Development Corporation*

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Primary Skin Irritation Study in Rabbits

SPONSOR: Procter and Gamble Company

TEST MATERIAL: T-7120

STUDY NUMBER: 191-081

DATE: October 25, 1977

PROCEDURE: Animals

Three New Zealand White rabbits (obtained from Kuiper's Rabbit Ranch, Gary, Indiana), one male and two females, weighing from 2726 to 3579 grams, were used in this study. The rabbits 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" and were conditioned for a minimum of 27 days prior to study initiation.

Administration

0.4 milliliter of the test material was applied, as a 10% (w/w) solution in distilled water, to each of two 38 x 38 mm Parke-Davis Readi-Bandages with a 20 x 20 mm felt pad which were then placed on the two sites on the backs of each of the rabbits. One of the sites was abraded while the other remained intact. The patches were secured in place with several wrappings of 75 mm Elastoplast tape and collars were placed on each animal. Following the 24 hour application period, the collars and patches were removed and any test material remaining on the sites was removed with a damp cloth.

Observations

-for irritation of the skin at 24 and 72 hours. (The observations at 24 hours were made 30 minutes following removal of the patches.) (See attached protocol for specific experimental design used.)

RESULTS: Effects of the test material determined at indicated intervals and scored according to the attached grading system. Grade of effect with time is shown in the table below. Individual rabbit scores are presented in Table 1.

191-081

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Primary Skin Irritation (cont.)

RESULTS  
(cont.):

Number of Animals Exhibiting Signs with Scoring "Value"

Observations	Value	Intact Skin		Abraded Skin	
		Hours		Hours	
		24	72	24	72
Erythema,	0				
Eschar	1	1/3		1/3	
Formation	2	2/3	2/3	2/3	1/3
	3		1/3		2/3
	4				
Edema	0				
Formation	1				
	2	2/3	2/3	3/3	1/3
	3	1/3	1/3		2/3
	4				
Blanching		3/3	1/3	3/3	0/3

Primary Irritation Score (Index): 4.7

	<u>Value</u>
<u>Erythema and Eschar Formation:</u>	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
<u>Edema Formation:</u>	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raising approximately 1.0 mm)	3
Severe edema (raised more than 1.0 mm extending beyond the area of exposure)	4

T-7120:

Individual Rabbit Scores and Score Calculation

TABLE 1.

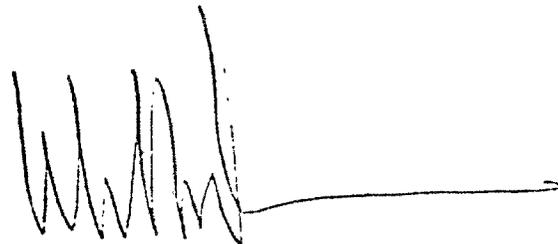
Intact Skin										
Animal No./Sex	Erythema					Edema				
	Observation Period (Hours)					Observation Period (Hours)				
	24	72				24	72			
28738, Female	2.0	3.0				2.0	3.0			
29519, Male	1.5	2.0				2.0	2.0			
29540, Female	2.0	2.5				3.0	2.5			
Total	5.5	7.5				7.0	7.5			
Average (Value)	1.8	2.5				2.3	2.5			

Abraded Skin										
Animal No./Sex	Erythema					Edema				
	Observation Period (Hours)					Observation Period (Hours)				
	24	72				24	72			
28738, Female	2.0	3.0				2.0	3.0			
29519, Male	1.5	2.0				2.5	2.0			
29540, Female	2.0	3.0				2.5	3.0			
Total	5.5	8.0				7.0	8.0			
Average (Value)	1.8	2.7				2.3	2.7			

Calculation for Primary Skin Irritation Score (Score = sum of the values (averages) divided by the number of observation periods used in evaluating the Primary Irritation Score times 2  
 $18.6 \div 4 = 4.7$

Primary Skin Irritation (cont.)

CONCLUSION: Based upon the results obtained, T-7120 would not be considered a primary skin irritant. The test material would be further classified, based upon the Primary Irritation Index, as being moderately irritating to the skin.



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Director of Acute Toxicology  
and Special Studies

Approved by: D. Clifford Jessup, Ph.D.  
Associate Director of Research

Lab Project No. 191-081 Sheet 1 Date 3/5/77 Authorized by J. C. [Signature]  
Dr. Jessup

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<u>Compound</u>	<u>Identification Number</u>	<u>IRDC No.</u>
T-7120	_____	A-326
_____	_____	_____
_____	_____	_____
_____	_____	_____

TITLE: ACUTE TOXICITY STUDIES IN RATS AND RABBITS

Conduct in accordance with the attached protocol.

Proctor & Gamble  
Standard Procedure for Toxicological Evaluation

Primary Skin Irritation - Rabbit Closed Patch

Date: /

Issue #2

**Purpose:** To determine relative levels of primary skin irritation.

**Animals:** Rabbits, three New Zealand albino of either sex, weighing greater than 2 kg and showing no signs of molting.

**Dosage Levels:** Four-tenths (0.4) milliliter of a 10% (w/w) aqueous solution of the compound, using distilled water.

**Procedure:** Before treatment, clip the rabbit backs with an Oster small animal clipper. One test site on each animal is left intact and one test site is abraded with the clipper head so as to penetrate the horny layer of the epidermis, but without causing bleeding.

Apply 0.4 ml of the appropriate concentration of test material to a 38 x 38 mm Parke-Davis Kendi-Bandage with a 20 x 20 mm felt pad. Place coverlets on both the intact and abraded site on each animal. Secure the patches with several wrappings of 75 mm Elastoplast tape around the animals' trunk. Place the animals in a Newmann(1) harness to prevent their removing the wrapping. After 24 hours, remove the harness and patches. Remove any test material remaining on the patch sites with a damp cloth. Thirty minutes after removal of the patches, evaluate the reactions on the basis of the table below. Evaluate again after 72 hours. Record all skin reactions not covered by the scoring table.

**Scoring:** Evaluation of Skin Reactions

(1) Erythema and Eschar Formation

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Highest possible erythema score	<u>4</u>

(2) Edema Formation

No Edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Highest possible edema score	<u>4</u>

(1) Newmann, E. A. (1963) Lab. Animal Care, 13, 207-210.

SPAT Primary Skin Irritation - Rabbit Closed Patch (cont'd)

Report:

The average of all scores (3 animals, 24 and 72 hours, abraded and intact) for erythema readings. The average of all scores for edema readings. The sum of the two averages is the Primary Irritation Index. Descriptive words are correlated with values of the Primary Irritation Index, as follows:

0 - 2 = Mild

2 - 5 = Moderately irritating

5 - 6 = Moderately to severely irritating

6 - 8 = Severely irritating

File the final report within 3 weeks of completing the experimental work.

Principal Investigator: M. J. Winrow

Date: 7/28/77