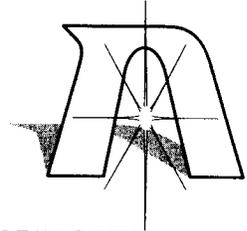


Northview Pacific Laboratories, Inc.

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SPONSOR 4151-0

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NV REPORT NUMBER

X2H376G

MRP NUMBER

R2H013G

REPORT DATE

September 9, 2002

TEST ARTICLE

Experimental Patch Lot 23-1
Sample Code: Lot 23-1
Lot Number: 23-1

TEST PERFORMED

FHSA Primary Skin Irritation/Corrosion

STUDY DIRECTOR

Zobair Musa, Laboratory Technician
In Vivo Services

PERFORMING LABORATORY

Northview Pacific Laboratories, Inc.
551 Linus Pauling Drive
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STUDY DATES

Study Authorization: Signed Protocol
Date Sample Received: August 28, 2002
Study Initiation Date: August 30, 2002
Date On Test: September 4, 2002
Date Off Test: September 7, 2002
Report Date: September 9, 2002

PURCHASE ORDER NUMBER

L-764

TEST ARTICLE IDENTIFICATION

Name: Experimental Patch Lot 23-1
Physical Description: Patch
Total Quantity Received for Testing: 4 pouches of 6 patches each
Total Quantity Used for This Study: 2 patches
Sample Code: Lot 23-1
Lot Number: 23-1
Storage Condition: Room Temperature

PROTOCOL

This test was conducted according to Protocol Number X2H376G, which incorporates by reference Northview Standard Operating Procedure 16F-03 and is on file at Northview Pacific Laboratories, Inc. There were no amendments to the protocol.

DEVIATIONS FROM PROTOCOL

There were no deviations.

DATA DISPOSITION

Raw data and the final report from this study are archived at Northview Pacific Laboratories, Inc., 551 Linus Pauling Drive, Hercules, CA 94547, under Northview Report Number X2H376G. The test article(s) will be disposed of by Northview Pacific Laboratories, Inc., unless the client requests that the test article(s) be returned. It is the responsibility of the client to maintain test articles in accordance with GLP regulations.

SUMMARY OF RESULTS

This test article was non-irritating to the skin of six test animals. This test article was not a primary irritant as defined in the FHSA regulation (16 CFR 1500.3).



FHSA PRIMARY SKIN IRRITATION/CORROSION

INTRODUCTION

This study is designed to show the degree of skin irritation caused by the test article under evaluation.

Six New Zealand White rabbits were used in the test. Twenty four hours prior to dosing, the hair on each animal's back was removed with clippers. One inch square pieces of the test article were cut and applied to intact and abraded areas on the skin of each animal. The squares of test article were held in place with surgical tape. To protect the dosing sites and to promote occlusion, the trunks of each animal were wrapped with gauze, which was held in place with porous tape. The gauze was then wrapped with an elastic bandage.

After 24 hours, the animals were unwrapped and the article removed. The test sites were observed and scored 24 and 72 hours after dosing. Based on the scores, a Mean Primary Irritation Index was calculated in order to evaluate the material's potential to be a primary irritant.

MATERIALS AND METHODS

Test System

Species	Rabbit
Strain	New Zealand White
Source	Western Oregon Rabbit Company, Philomath, OR
Number	Six
Sex	3 Male, 3 Female
Weight	2.2 – 2.3 kg
Age	Young Adult
Housing	Individually; 16 – 22°C and 50 ± 20% relative humidity
Feed	Certified Laboratory Rabbit Diet (approximately 200 grams per day)
Water	Provided <i>ad libitum</i>
Identification	Ear tag
Photoperiod	Diurnal (12 hours on – 12 hours off)
Quarantine Period	Seven days

Justification for Test System

Rabbits are the species required by the Consumer Product Safety Commission and the Federal Hazardous Substance Act.



Table 1: Supplies

Reagents/Equipment	Lot Number	Manufacturer	Expiration Date
Gauze – Sof Kling Conforming Bandage	200104011803	Johnson & Johnson	2/03
Zonas Porous Tape	NA	Johnson & Johnson	NA
Dental dam/rubber sheeting	NA	VWR	NA
Micropore surgical tape	002	3M	NA
Nu Gauze general-use sponges	NA	Johnson & Johnson	NA
25 gauge needle	2062119	Becton Dickinson	NA

Table 2: Study Design

Number of Animals	Sex	Route of Administration	Dose/Site	Duration of Exposure	Scoring (Hours Post-Dosing)
6	3 Male 3 Female	Topical	1 in ²	24 hours	24 and 72

Table 3: Study Schedule

Time	Procedure
Day -1	Clipping and weighing
Day 0	Dosing and wrapping
Day 1	24 hours after dosing, unwrapping and wiping
Day 1	Scoring
Day 3	Scoring

Sample Preparation and Dosing Procedure

Sample Preparation – The test article was applied to the skin as received from the sponsor.

Animal Preparation – During the 24 hours prior to exposure, the entire dorsal surface of each animal was clipped free of hair. Only animals with healthy, intact skin were used. There was one intact test site and one abraded skin site on each animal. The abraded site was prepared by scoring the skin with the point of a 25 gauge needle. This was done in a way so as to penetrate the stratum corneum, but not the dermis.

Dosing Procedure – One inch square pieces of test article were cut and placed on a four inch square piece of surgical tape. The patches were then applied to the backs of the animals at sites according to the diagram below:



Head
Intact Site Abraded Site
Tail

After the patches were applied to the appropriate test sites, the entire trunk of each animal was wrapped with a six inch wide gauze bandage, which was held in place with porous tape. The trunk of each animal was then wrapped with an elastic bandage and secured with staples so that complete occlusion was obtained.

The test sites were uncovered after 24 hours of exposure. Any residual test article was removed by gently wiping with lukewarm water.

Observation and Scoring

Clinical Observations – The test sites were observed at 24 and 72 hours after application of the test article.

At least once daily, all animals were observed for mortality, signs of ill health, or reaction to treatment.

Scoring – All of the animals were scored at 24 and 72 hours after application of the test article. Signs of edema, erythema and/or eschar formation were scored as shown in Table 4. Separate scores were recorded for the intact and abraded sites.

Weights – All of the animals were weighed prior to study initiation.

Interpretation and Analysis

The Primary Irritation score was calculated as follows:

The values for the erythema and edema scores taken at the 24 and 72 hour observations for both the intact and abraded skin were added together. The sum of the eight erythema and edema values was divided by four (2 observations periods and 2 sites/animal) to give a Primary Irritation Score for each animal. The Mean Primary Irritation Score was determined by dividing the sum of the individual Primary Irritation Scores by six, the number of test animals. As defined in FHSA regulations (16 CFR 1500.3), a primary irritant is a substance that results in an empirical score of ≥ 5 when tested by this method.

RESULTS AND DISCUSSION

Clinical Observations – All animals remained healthy throughout the test period.

Scoring – The individual primary irritation scores are presented in Table 5. Primary and average scores are shown in Table 6. Only one animal showed a score of 1 during the 24 hour scoring period.

Mean Primary Irritation Score – The Mean Primary Irritation Score was 0. This test article is not a primary skin irritant.



CONCLUSION

This test article was non-irritating to the skin of six test animals. This test article was not a primary irritant as defined in the FHSA regulation (16 CFR 1500.3).

Table 4: Evaluation of Skin Reactions

Erythema and Eschar Formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate erythema	3
Severe erythema (beet-redness) to eschar formation (preventing grading of erythema)	4
Edema Formation	Value
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised about 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

Adapted from 16 CFR Part 1500.41.



Table 5: Dermal Irritation Scores

Rabbit Number	Sex	Weight (kg)	Time	Intact		Abraded	
				Erythema	Edema	Erythema	Edema
33305	F	2.3	24 hours	0	0	0	0
33292	M	2.3		0	0	0	0
33310	F	2.3		0	0	0	0
33304	F	2.3		1	0	0	0
33277	M	2.2		0	0	0	0
33293	M	2.2		0	0	0	0
33305	F		72 hours	0	0	0	0
33292	M			0	0	0	0
33310	F			0	0	0	0
33304	F			0	0	0	0
33277	M			0	0	0	0
33293	M			0	0	0	0

Table 6: Cumulative Primary Dermal Irritation Scores

Rabbit Number	Sum of 24 & 72 hr scores		Primary Irritation Score (C)
	Erythema (A)	Edema (B)	
33305	0	0	0
33292	0	0	0
33310	0	0	0
33304	1	0	0.25
33277	0	0	0
33293	0	0	0
Mean Primary Irritation Scores (MPIS):			0
Descriptive Rating:			Non-irritant

REFERENCES

NV SOP 16F-03, *Primary Skin Irritation/Corrosion*
 16 CFR Part 1500.41



QUALITY ASSURANCE UNIT GLP INSPECTION AND AUDIT SUMMARY

This study, X2H376G, was inspected by Quality Assurance at intervals adequate to assure the integrity of the study. The SOP/protocol that the study followed, the phase(s) of the study inspected, and the date(s) of the inspection are provided below.

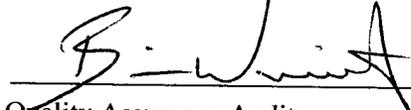
<u>SOP/Protocol</u>	<u>Phase of Study</u>	<u>Date</u>
16F-03	24 Hour Scoring	9/5/02

QAU inspection findings are routinely reviewed by the management of Northview Pacific Laboratories. Management is notified immediately if there are any deviations which might affect the integrity of the study data.

QAU inspection findings for this study were reported to the Study Director and Management on the following date(s): September 5, 2002

FINAL REPORT AUDIT

Quality Assurance has conducted a thorough audit of the test data generated during this study. Northview Report Number X2H376G represents an accurate description of the conduct and final results of the study.



 Quality Assurance Auditor

9/10/02

 Date



NORTHVIEW PACIFIC LABORATORIES STAFF PARTICIPATING IN THIS STUDY

Some or all of the following staff were involved in the conduct of this study:

1. Gurpreet Ratra, Ph D., Toxicology Manager, *In Vivo* Services
2. Angela Cologross-Schouten, D.V.M., M.P.V.M., Manager, Veterinary Services
3. Cheryl Loughery, Supervisor, *In Vivo* Services
4. Robert Noonan, Ph.D., LATg, Senior Scientist, *In Vivo* Services
5. Roger O'Meara, LATg, Laboratory Technician 3, *In Vivo* Services
6. Fernando D. Salangsang, Laboratory Technician 2, *In Vivo* Services
7. Leah Wilcox, Laboratory Technician 2, *In Vivo* Services
8. Blanca Ramirez, Laboratory Technician 1, *In Vivo* Services
9. Jade David, Laboratory Technician 1, *In Vivo* Services
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16. Jessica Houghton, Laboratory Technician 1, *In Vivo* Services
17. Joseph Johnson, Assistant Laboratory Technician 1, *In Vivo* Services
18. Apryl Carlton, Assistant Laboratory Technician 1, *In Vivo* Services
19. Noe Gonzales, Assistant Laboratory Technician 1, *In Vivo* Services
20. Melvin Parker, Assistant Laboratory Technician 1, *In Vivo* Services
21. Darlene Magee, Assistant Laboratory Technician 1, *In Vivo* Services
22. Erin Hung, Laboratory Technician 1, *In Vivo* Services

STATEMENT OF COMPLIANCE

This study, Northview Report Number X2H376G, has been conducted in accordance with applicable Good Laboratory Practice Regulations.

 Study Director

9/10/02
 Study Completion Date

 Quality Assurance Unit

9/10/02
 Date

 Management

9/10/02
 Date

:cw, 9/10/2002 9:23 AM

