

HUMAN REPEAT INSULT PATCH TEST

Prepared For:

024™ Zone

Richard Weise

Stephens & Associates Study Number: C05-C031C

TABLE OF CONTENTS

	<u>Page</u>
PURPOSE.....	3
GENERAL INFORMATION.....	3
SUMMARY.....	4
STORAGE, HANDLING, AND DOCUMENTATION OF TEST MATERIALS	5
TEST MATERIAL DESCRIPTION	5
INFORMED CONSENT	5
ATTRITION	5
ADVERSE EVENTS.....	5
SUBJECT DEMOGRAPHICS	5
PROCEDURES AND METHODS	5
BIostatISTICS AND DATA MANAGEMENT	6
MAINTENANCE OF RECORDS	7
RESULTS.....	7
DISCUSSION AND CONCLUSIONS.....	7
STATEMENT OF QUALITY ASSURANCE	8
REPORT APPROVAL.....	9
TABLE	
Table 1: Score Frequencies for Site 1/A: 024™ Pain Neutralizer	7
APPENDICES	10
I. Biostatistics	
II. Protocol: Human Repeat Insult Patch Test	
III. Sample Forms	
IV. Copy of Attrition Form	
V. Copy of Subject Demographics Form	
VI. Copy of Site Form	
VII. Copies of Observation Records	

PURPOSE

This human repeat insult patch test was conducted for 024™ Zone to assess the potential of the Sponsor's test material to induce contact sensitization by repetitive applications to the skin of healthy volunteers.

GENERAL INFORMATION

Study Number: C05-C031C
Test: Human Repeat Insult Patch Test
Test Material: 024™ Pain Neutralizer

Staff

Investigator/Study Physician: Nathan S. Trooman, M.D., Board Certified Dermatologist
Sub-Investigator: Ronald L. Rizer, Ph.D.
Site Manager: Sarah K. Shipp, B.A.
Biostatistics Supervisor: Paul Kavanaugh, M.S.
Quality Assurance Manager: Patricia G. Pierce, M.Ed., CCRA
Testing Facility: Thomas J. Stephens & Associates, Inc.
Colorado Research Center
5050 Edison Avenue, Suite 202
Colorado Springs, Colorado 80915
Administrative Facility: Thomas J. Stephens & Associates, Inc.
3310 Keller Springs Road, Suite 130
Carrollton, Texas 75006
Sponsor: 024™ Zone
11910 Shiloh Road, Suite 148
Dallas, Texas 75228
Sponsor's Representative: Richard Weise, Director of Manufacturing & Quality Assurance
Experiment Start Date: January 31, 2005
Experiment End Date: March 11, 2005

SUMMARY

This study was conducted for 024™ Zone to assess the potential of the Sponsor's test material, 024™ Pain Neutralizer, to induce contact sensitization by repetitive applications to the skin of healthy volunteers. One hundred eight subjects completed the study. The following test material was tested:

024™ Pain Neutralizer

For the induction period, subjects were semi-occlusively patched with the Sponsor's test material nine times at approximately 48 to 72-hour intervals. Subjects were informed that the test material may cause a strong warming sensation for a few hours after application. Subjects removed the patches approximately 48 hours after application or two hours prior to a study visit, and sites were graded approximately 48 to 72 hours after each application. Twelve to 24 days after application of the last induction patches, challenge patches were applied to original and alternate (naïve) sites. Subjects removed the patches approximately 48 hours after application (approximately two hours prior to grading), and sites were graded approximately 48 and 96 hours post-application.

Under the exposure conditions of this test, test material 024™ Pain Neutralizer did not induce delayed contact sensitization (allergic contact dermatitis) in any subject completing the study.

STORAGE, HANDLING, AND DOCUMENTATION OF TEST MATERIALS

The receipt of test materials by Stephens & Associates was documented in a log book, which serves as a permanent record of the receipt, storage, return, and disposition of all study materials. All study materials were kept in a locked product storage room accessible to clinical staff members only. At the conclusion of the clinical study, the remaining study materials were destroyed according to city, state, and federal regulations.

TEST MATERIAL DESCRIPTION

Test Material Identification Number (TMIN): 0015-05CC
Sponsor Test Material Identification: 024™ Pain Neutralizer
Physical Description: Colorless, transparent liquid
Concentration Tested: Neat
Patch Type: Semi-occlusive

INFORMED CONSENT

Written informed consent conforming to 21 CFR 50.25 was obtained from each subject prior to enrollment in the study. An original signed copy for each subject participating in the study will be retained in the study file. Each subject received a copy of the agreement. Please see Appendix III for a sample form.

ATTRITION

One hundred twenty-seven subjects were enrolled to participate in this study. One hundred eight subjects completed the study. Nineteen subjects discontinued participation in the study for reasons unrelated to the test material. The attached attrition form (Appendix IV) documents the dates of and reasons for the attrition of the 19 subjects.

ADVERSE EVENTS

No adverse events occurred over the course of the study.

SUBJECT DEMOGRAPHICS

One hundred eight subjects completed the study. Please see Appendix V for a copy of the subject demographics form, which lists each subject's ethnicity, gender, and date of birth. Ethnicity information was obtained from each subject's eligibility and health questionnaire.

PROCEDURES AND METHODS

At Visit 1, prospective subjects completed an eligibility and health questionnaire and read and signed a confidentiality agreement and an informed consent agreement. Qualified subjects were prepared for patch application by having the test sites wiped with alcohol and air-dried. For the induction period, subjects were semi-occlusively patched with the Sponsor's test material nine times at approximately 48 to 72-hour intervals. Subjects were informed that the test material may cause a strong warming sensation for a few hours after application. Subjects were instructed to remove and discard the induction patches 48 hours after application or two hours prior to a study visit. Reactions at the application sites were graded approximately 48 to 72 hours after each application by a trained clinician.

Twelve to 24 days after application of the last induction patches, challenge patches were applied to original and to alternate (naïve) sites. Subjects were instructed to remove and discard the challenge patches 48 hours after application or two hours prior to the 48-hour challenge visit. Reactions at the original and alternate sites were graded approximately 48 and 96 hours post-application by a trained clinician.

PROCEDURES AND METHODS (continued)

The following scoring scale and symbols were used to grade the test sites:

Erythema Scale: This scale was used only for grading the degree of erythema (redness). A score on this scale was assigned following every application of a test material.

- 0** No visible erythema
- 1** Mild erythema (faint pink to definite pink)
- 2** Moderate erythema (definite redness)
- 3** Severe erythema (very intense redness)

Designation for Elevated Responses: Edema, papules, vesicles, and bullae, if present, were graded as independent responses.

- E** Edema - definite swelling
- P** Papules - small, red, solid elevations; surface of reaction has granular feeling
- V** Vesicles - small, circumscribed elevations having translucent surfaces so that fluid is visible (blister-like); vesicles are no larger than 0.5 cm in diameter
- B** Bullae - vesicles with a diameter >0.5 cm; vesicles may coalesce to form one or a few large blisters that fill the patch site

Other Response Characteristics

- S** Spreading- evidence of the reaction beyond the pad area (does not include obvious signs of leakage of test material away from pad)
- W** Weeping - evidence of release of fluid from a vesicular or bullous reaction

Other Recording Designations

- T** Marked reaction to adhesive (patch relocated)
- X** Succeeding patch not applied and succeeding grade is for residual reaction. At challenge, an "X" denotes that the patch was not applied.
- R** Subject did not remove the patch at the assigned time.
- L-1** Subject report of lost patch (came off) during first 12 hours of exposure
- L-2** Subject report of lost patch (came off) between 12 and 48 hours of exposure (24 hours for shorter exposures)
- (-)** Subject absent
- N9G** No ninth grade. Subject wore nine induction patches but was not present for scoring following ninth application.

BIostatistics and Data Management

A frequency table of the induction and challenge scores was generated for the test material by grading time point.

Data Interpretation

Persisting reactions with edema, vesicles, papules, or spreading that develop in the induction phase and/or at both challenge sites may be indicative of allergic contact dermatitis. Allergic responses normally do not improve markedly at 72-96 hours. Edema or infiltration that persists or increases in intensity is indicative of allergic contact dermatitis. Other indicators are "flares" at former application sites or responses that develop between induction and challenge.

Exceptions to the typical patterns are known to occur. For example, a subject may show symptoms of allergic contact sensitivity early in the induction period to one or more of the test materials. This usually suggests that the subject had a pre-exposure to a component in the test material or a material having similar chemical cross-reactivity to the test material. Data for such subjects will not be included in the final statistical analysis.

MAINTENANCE OF RECORDS

All original records (including the study protocol, observation records, medical histories, informed consent agreements, attrition form, and any other records or forms used in this study) and a copy of the final report will be retained on file in the Stephens & Associates archives for two years from the date of completion of the study. When the archive time has expired, the study files will be sent to the Sponsor at the Sponsor's expense or destroyed in accordance with the Sponsor's preference.

RESULTS

Table 1 presents the score frequencies observed at each visit during induction and challenge. Note: G=Grading, O=Original site, A=Alternate site, 48=48-hour grading, and 96=96-hour grading.

**TABLE 1
 SCORE FREQUENCIES FOR SITE 1/A: 024™ PAIN NEUTRALIZER**

	Induction Phase									Challenge Phase			
	G1	G2	G3	G4	G5	G6	G7	G8	G9	48 O	96 O	48 A	96 A
0	103	106	106	106	98	99	104	106	107	107	108	107	108
0R	2	0	0	2	1	0	1	1	0	1	0	1	0
1	3	1	2	0	8	9	3	1	1	0	0	0	0
1P	0	0	0	0	1	0	0	0	0	0	0	0	0
1R	0	1	0	0	0	0	0	0	0	0	0	0	0
Total	108	108	108	108	108	108	108	108	108	108	108	108	108

Please see the attached biostatistics (Appendix I) and copies of the observation records (Appendix VII).

DISCUSSION AND CONCLUSIONS

Under the exposure conditions of this test, test material 024™ Pain Neutralizer did not induce delayed contact sensitization (allergic contact dermatitis) in any subject completing the study.

STATEMENT OF QUALITY ASSURANCE

All data and supporting documentation for this study have been audited by the Stephens & Associates, Inc., Quality Assurance Department and found to be accurate, complete, and in compliance with the requirements of the protocol and Stephens & Associates' Standard Operating Procedures. This report has been reviewed and accurately reflects all aspects of the conduct of the study.

All clinical research studies that are performed by Stephens & Associates are in accordance with federal regulations and Good Clinical Practice guidelines.

Patricia G. Pierce, M.Ed., CCRA
Quality Assurance Manager

Date

APPENDICES

- I. Biostatistics**
- II. Protocol: Human Repeat Insult Patch Test**
- III. Sample Forms**
 - Eligibility and Health Questionnaire
 - Confidentiality Agreement
 - Informed Consent Agreement
 - Observation Record(s)
- IV. Copy of Attrition Form**
- V. Copy of Subject Demographics Form**
- VI. Copy of Site Form**
- VII. Copies of Observation Records**