Clinical
Research
Laboratories, Inc.

# Final Report

## Repeated Insult Patch Test
## (Marzulli and Maibach Method)

**CLIENT:** Dizolve Group Corporation
290 Baig Blvd. Suite B10
Moncton, NB, E1E 1C8
Canada

**ATTENTION:** Irina Bogdanova, Ph.D

**TEST MATERIAL:** 2X (BLIZARD-6X) SHEETS

**CRL STUDY NUMBER:** CRL114512-1

**AUTHORIZED SIGNATURES:**

Bruce E. Kanengiser, M.D.
President/Medical Director

Michael J. Muscatiello, Ph.D.
Executive Vice President/COO

Anita Lee Cham, M.D.
Dermatologist

**REPORT DATE:** January 11, 2013

Clinical
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# Good Clinical Practice
# Quality Assurance Audit Statement

**Clinical Study Number:** CRL114512-1

**Start Date:** November 12, 2012

**Completion Date:** December 21, 2012

The clinical study listed above was conducted in accordance with Clinical Research Laboratories, Inc. Standard Operating Procedures, which incorporate the principles of Good Clinical Practice defined by applicable guidelines and regulations established by U.S. Regulatory Agencies. The conduct of the study was monitored for compliance, and the associated records, including source documents or raw data, were reviewed for documentation practices and accuracy by a Project Manager/Study Director and/or a Quality Assurance representative. Standard Quality Assurance audit procedures for this final report and study related documents were conducted, as indicated below.

Eileen Vogl
Signature of QA Auditor

1/11/13
Date

**Clinical Research Laboratories, Inc.**

# FINAL REPORT

# REPEATED INSULT PATCH TEST
# MARZULLI AND MAIBACH

## PURPOSE

The purpose of this study was to confirm that the application of a cosmetic product to volunteer subjects, under maximized conditions of exposure, does not induce delayed contact sensitization.

## INVESTIGATIVE SITE

Clinical Research Laboratories, Inc.
371 Hoes Lane Suite 100
Piscataway, New Jersey 08854
732-981-1616

## TEST MATERIAL

The following test material was provided by Dizolve Group Corporation and received by Clinical Research Laboratories, Inc. on November 6th, 2012:

| Test Material | Test Condition | Patch Type |
|---|---|---|
| 2X (BLIZARD-6X) SHEETS | Test as an aqueous dilution of 1gm. In 30.2oz of water. | Semi-occlusive* |

The test material was coded with the following CRL identification number:

CRL114512-1

## STUDY DATES

This study was initiated on November 12, 2012 and was completed on December 21, 2012.

* Semi-occlusive Strip (Brady Medical, Mesquite,TX)

**Clinical Research Laboratories, Inc.**

## PANEL SELECTION

Each subject was assigned a permanent CRL identification number. All subjects signed an Informed Consent Form in compliance with 21 CFR Part 50: "Protection of Human Subjects" and a HIPAA Authorization Form in compliance with 45 CFR Parts 160 and 164. All subjects completed a Panelist Profile/Medical History Form provided by Clinical Research Laboratories, Inc. prior to the study (Subject Demographics - Appendix I). Subjects who met the following inclusion criteria were selected for study participation.

- Male and female subjects between the ages of 18 and 70;
- Subjects who have completed a Panelist Profile/Medical History Form;
- Subjects in general good health as determined by the Panelist Profile/Medical History Form;
- Subjects who do not exhibit any skin diseases that might be confused with a skin reaction from the test material;
- Subjects willing to sign an Informed Consent Form in conformance with 21 CFR Part 50: "Protection of Human Subjects";
- Subjects who have signed a HIPAA Authorization Form in conformance with 45 CFR Parts 160 and 164;
- Females who are not pregnant or lactating;
- Subjects who demonstrate dependability and intelligence in following directions;
- Subjects who are not currently using any systemic or topical corticosteroids, anti-inflammatory drugs, sympathomimetics, antihistamines and/or immunosuppressive medication;
- Subjects who do not have any known allergies to cosmetics, skin care products or topical related drugs as related to the product(s) being tested.

## TEST METHOD

Prior to the application of the patch, the test area was wiped with 70% isopropyl alcohol and allowed to dry. The test material, which was prepared as described in the Test Material section of the report, was applied to the upper back, between the scapulae and the waist, lateral to the midline.

The test material was applied to the same site three times per week (Monday, Wednesday, and Friday) for a total of nine applications. However, the schedule may have been modified to accommodate inclement weather, holidays, or missed applications. At the discretion of the Study Director, the test material may have been applied on two consecutive days during the Induction Phase or a makeup day may have been added at the end of the Induction Phase.

The sites were graded by a CRL technician for dermal irritation and sensitization 48 hours after application of the patches on Monday and Wednesday and 24 hours after removal of the patches on Sunday, unless the patching schedule was altered as described above.

The sites were graded according to the following scoring system:

### Dermal Scores

| | |
|---|---|
| - | = No reaction |
| ? | = Minimal or doubtful response, slightly different from surrounding normal skin |
| + | = Definite erythema<br>No edema |
| ++ | = Definite erythema<br>Definite edema |
| +++ | = Definite erythema<br>Definite edema and vesiculation |

If a "++" reaction or greater occurred, the test site did not receive any further Induction Phase patches, and the test material was instead applied to an adjacent virgin site. If a "++" reaction or greater occurred on the new site, the subject was not patched again during the Induction Phase but was challenged on the appropriate day of the study. At the discretion of the Study Director, patch sites with scores less than "++" may have been changed.

## TEST METHOD (Continued)

Following a 2-week rest period, the challenge patches were applied to the previously treated test sites on the back (original) and to newly defined sites, previously unexposed (virgin). After 48 hours, the patches were removed by a CRL technician, and the test sites were evaluated for dermal reactions. The test sites were re-evaluated at 72 and 96 hours.

## RESULTS

This study was initiated with 56 subjects. Three subjects discontinued study participation for reasons unrelated to the test material. A total of 53 subjects completed the study.

Individual dermal scores recorded during the Induction and Challenge Phases appear in Table I.

## CONCLUSION

Based on the test population of 53 subjects and under the conditions of this study, the sample identified as 2X (BLIZARD-6X) SHEETS did not demonstrate a potential for eliciting dermal irritation or sensitization.

## REFERENCES

Marzulli, F. N. and Maibach, H. I. 1973. *Antimicrobials: Experimental contact sensitization in man. J. Soc. Cosmet. Chem.* 24:399-421

Marzulli. F. N. and Maibach, H. I. 1974a. *Status of topical parabens: Skin hypersensitivity. Int. J. Dermatol.* 13:397-399

Marzulli, F. N. and Maibach, H. I. 1974b. The use of graded concentrations in studying skin sensitizers: Experimental contact sensitization in man. *Food Cosmet. Toxicol. 12:219-227. Human Patch Tests, Proc. Sci. Sect. Toilet Goods Assoc.*, 19:46-49, 1953.

## RETENTION

Test materials and all original forms of this study will be retained by Clinical Research Laboratories, Inc. as specified in CRL Standard Operating Procedures 30.6 and 30.6C, unless designated otherwise by the study Sponsor.

**Clinical Research Laboratories, Inc.**

## TABLE I

### Tabulation of Individual Scores

| Test Material: | 2X (BLIZARD-6X) SHEETS |
|---|---|

| | Induction Scores | | | | | | | | | Challenge Scores | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 48 Hours | | 72 Hours | | 96 Hours | |
| Subject Number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | O | V | O | V | O | V |
| 1 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 2 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 3 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 4 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 5 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 6 | ? | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 7 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 8 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 10 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 11 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 13 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 14 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 15 | - | - | - | ? | - | - | - | - | - | - | - | - | - | - | - |
| 16 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 17 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 18 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 19 | - | ? | ? | - | - | - | - | - | - | - | - | - | - | - | - |
| 20 | - | Discontinued | | | | | | | | | | | | | |
| 21 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 22 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 23 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 24 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 25 | - | - | Discontinued | | | | | | | | | | | | |

R = Subject number reassigned due to subject's early discontinuation.
O = Original Site
V = Virgin Site

**Clinical Research Laboratories, Inc.**

## TABLE I
## (Continued)

### Tabulation of Individual Scores

| Test Material: | 2X (BLIZARD-6X) SHEETS |
|---|---|

| | Induction Scores | | | | | | | | | Challenge Scores | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 48 Hours | | 72 Hours | | 96 Hours | |
| Subject Number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | O | V | O | V | O | V |
| 26 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 27 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 28 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 29 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 30 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 31 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 32 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 33 | ? | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 34 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 35 | - | ? | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 36 | - | Discontinued | | | | | | | | | | | | | |
| 37 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 38 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 39 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 40 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 41 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 42 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 43 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 44 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 45 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 46 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 47 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 48 | - | ? | - | ? | - | - | - | - | - | - | - | - | - | - | - |
| 49 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 50 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

O = Original Site
V = Virgin Site
X = Subject Absent

**Clinical Research Laboratories, Inc.**

## TABLE I
## (Continued)

### Tabulation of Individual Scores

| Test Material: | 2X (BLIZARD-6X) SHEETS |
|---|---|

| | Induction Scores | | | | | | | | | Challenge Scores | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 48 Hours | | 72 Hours | | 96 Hours | |
| Subject Number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | O | V | O | V | O | V |
| 51 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 52 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 53 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 54 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 55 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| 56 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

O = Original Site
V = Virgin Site

**Clinical Research Laboratories, Inc.**

## Appendix I

### Subject Demographics

| Subject Number | Subject Initials | CRL ID # | Age | Sex |
|---|---|---|---|---|
| **1** | RS | 27934 | 51 | F |
| **2** | SS | 28239 | 58 | F |
| **3** | AL | 26675 | 22 | F |
| **4** | ML | 15956 | 48 | M |
| **5** | SW | 28214 | 30 | M |
| **6** | MK | 28209 | 30 | F |
| **7** | PH | 22490 | 53 | F |
| **8** | VD | 23036 | 55 | F |
| **9** | SR | 23160 | 31 | F |
| **10** | EH | 21115 | 64 | F |
| **11** | PN | 28923 | 20 | F |
| **12** | JA | 5348 | 63 | F |
| **13** | CR | 28785 | 55 | F |
| **14** | JJ | 28713 | 24 | M |
| **15** | AC | 28568 | 22 | F |
| **16** | LE | 13314 | 30 | F |
| **17** | LT | 22440 | 48 | M |
| **18** | RC | 23752 | 37 | F |
| **19** | TA | 24249 | 21 | F |
| **20** | JP | 28661 | 50 | F |
| **21** | SR | 26943 | 46 | M |
| **22** | RO | 27909 | 37 | F |
| **23** | RL | 27571 | 48 | F |
| **24** | EC | 19900 | 51 | M |
| **25** | MC | 25724 | 22 | F |
| **26** | CB | 12833 | 37 | F |
| **27** | KT | 21206 | 30 | F |
| **28** | TC | 7969 | 38 | F |

| Subject Number | Subject Initials | CRL ID # | Age | Sex |
|---|---|---|---|---|
| **29** | RH | 4483 | 66 | F |
| **30** | MF | 15462 | 28 | F |
| **31** | CB | 24254 | 37 | F |
| **32** | EK | 22508 | 50 | M |
| **33** | DP | 24464 | 41 | F |
| **34** | LL | 25728 | 66 | F |
| **35** | MS | 23662 | 55 | F |
| **36** | SI | 4174 | 69 | F |
| **37** | PL | 28191 | 23 | F |
| **38** | DL | 21572 | 47 | F |
| **39** | CD | 27957 | 63 | F |
| **40** | SB | 22179 | 48 | F |
| **41** | PT | 27362 | 58 | F |
| **42** | DI | 29384 | 55 | F |
| **43** | AA | 23089 | 46 | F |
| **44** | XX | 27426 | 57 | F |
| **45** | JC | 28618 | 22 | F |
| **46** | SH | 28871 | 19 | F |
| **47** | SG | 24997 | 21 | F |
| **48** | GC | 564 | 55 | M |
| **49** | DB | 20814 | 49 | M |
| **50** | EA | 17153 | 43 | M |
| **51** | JB | 26047 | 53 | M |
| **52** | MM | 26626 | 39 | F |
| **53** | EU | 28891 | 45 | F |
| **54** | LB | 28105 | 42 | F |
| **55** | SS | 5948 | 49 | F |
| **56** | AC | 23736 | 43 | F |