

**REPEATED INSULT PATCH TEST DATA  
IN SUPPORT OF THE SAFETY AND  
TOLERABILITY OF 5% MENTHOL ICY HOT<sup>®</sup>  
PATCH TOPICAL ANALGESIC**

**Prepared for  
CHATTEM, INC.**

**September 26, 2003**

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# **REPEATED INSULT PATCH TEST DATA IN SUPPORT OF THE SAFETY AND TOLERABILITY OF 5% MENTHOL ICY HOT® PATCH TOPICAL ANALGESIC**

## **BACKGROUND**

The safety and efficacy of topical analgesics containing menthol and/or methyl salicylate has been well established over many decades of wide-spread use in the U.S. and abroad. Although cutaneous reactions such as local skin irritation and allergic reaction occasionally occur after exposure to these compounds, these analgesics have been concluded Generally Safe and Effective (Category I) for external analgesia, within certain limitations of concentration, by the Advisory Review Panel of OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products. These and other recommendations have been incorporated into the Tentative Final Monograph (proposed rule) External Analgesic Drug Products for Over-the-Counter Human Use [68 FR 42324 (July 17, 2003)]. Safety and efficacy for these analgesics in patch, plaster or poultice delivery form is the issue raised by FDA, although commercial use of topical patch products has not been recognized to create toxicities different from those of other non-patch formulations.

To compare tolerabilities of two patch analgesic formulations containing menthol, Chattem, Inc. (Chattem) sponsored a Repeated Insult Patch Test with two developmental patch products, one utilizing hydrogel vehicle and the other non-hydrogel. This study was conducted in 2000 by Consumer Product Testing Co., Fairfield NJ. The protocol utilized was modeled in part after recommendations in the CDER Guidance for Industry: Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products, December 1999, specifically part B. Recommendations for a Skin Sensitization Study (Modified Draize Test) (CDER Guidance December 1999).

Chattem utilized a study design solely comparing two patch test products, one hydrogel and the other non-hydrogel, with the purpose of determining whether there existed any differences in tolerability. In general, the Chattem study utilized procedures and evaluations similar to those recommended by FDA such that non-immunologic irritant skin responses and/or the induction of allergic contact sensitization would have been detected, if present.

A synopsis of the Repeated Insult Patch Test results from the hydrogel and non-hydrogel sensitization test is provided below. The synopsis combines the findings from Consumer Product Testing Co. final reports identified as C00-0602.01 (Non-hydrogel Study CSE-391) and C00-0602.02 (Hydrogel Study CSE-3912). Complete final reports are attached as appendices.



## PURPOSE OF STUDIES

To examine the potential for cutaneous irritancy and allergic sensitization to two topical menthol-containing analgesic patch products.

## TEST ARTICLES

1. Hydrogel type patches (study CSE 25-392) containing 5% menthol
2. Non-hydrogel type patches ((current commercial Icy Hot<sup>®</sup> (study CSE 25-191) containing 5% menthol

Inactive ingredients in both hydrogel and non-hydrogel patches include acrylic acid, aluminum hydroxide, carmellose sodium, 2-ethylhexyl acrylate, glycerin, isopropyl myristate, methyl acrylate, nonoxynol-30, polyacrylate, polyacrylic acid, polysorbate 80, sorbitan sesquioleate, starch, talc, tartaric acid, titanium dioxide and water. Water content defines the difference between hydrogel and non-hydrogel patches.

## SUBJECTS

Adult ( $\geq 16$  years) male and female subjects without a variety of standard exclusions that included previous history of reactions to cosmetics or other personal healthcare products; recent or concomitant use of antihistamines or topical or systemic corticosteroids; and/or existing skin conditions that could be confused with skin reactions from the test materials.

## TEST PROCEDURES

Volunteer test subjects were simultaneously exposed to each of the patch types according to a Repeated Insult Patch Test (RIPT) protocol incorporating interval exposure. The RIPT procedure combined a repeated exposure induction phase and a subsequent challenge phase. The hydrogel and non-hydrogel test patches were part of a shared panel.

Briefly, subjects had 1 inch by 1 inch menthol patches, hydrogel and non-hydrogel types, placed on left and right scapular skin, and covered with semi-occlusive adhesive dressings. Patches were applied to the same site for 24-hour periods every other day, *i.e.*, 3 times a week (M, W, F), for a total of 9 applications. Patches were removed at home after each 24-hour exposure period, thus generating 1-day (weekday) or 2-day (weekend) rest periods before each subsequent patch application. Scoring of skin reactions was performed at the clinical center prior to each patch application. If moderate skin reactions (evaluation level 2 or greater) were observed during this induction phase, the subsequent patch application was performed at an adjacent skin site. Applications were discontinued if level 2 reactions were noted at the second site or if more marked cutaneous reactivities were observed at either the original or new application sites.



After the three week induction phase of the RIPT, there was a 2-week rest period followed by a challenge phase. Patches were applied to virgin skin sites adjacent to the original induction patch sites for 24 hours, and scoring for cutaneous reactions performed 24 hours and 72 hours after exposure.

## **EVALUATIONS**

Scoring was according to a 6-point scale, as follows:

No visible skin reaction (0); Barely perceptible or spotty erythema (+); Mild erythema covering most of the test site (1); Moderate erythema, possible presence of mild edema (2); Marked erythema, possible edema (3), Severe erythema, possible edema, vesiculation, bullae and/or ulceration (4).

## **DESCRIPTION OF SUBJECTS**

Subjects were studied in two panels (two groups, initiated a few days apart) identified as #20000325 and #20000334 in the Consumer Product Testing Reports. Each subject received both a hydrogel and non-hydrogel patch, as well as several other test articles.

113 subjects, males (n=22; 19.5%) and females (n=91; 80.5%), were qualified for this study. The average age was 51 years (range: 18 to 79 years).

102 subjects (90.3%) completed the study (83 females, 19 males). The average age of these subjects was 52.7 years (range: 18 to 79 years).

The remaining 11 subjects discontinued their participation in the study for reasons reportedly unrelated to the application of the test material. These subjects consisted of 8 females and 3 males; the average age was 37.5 years (range: 18 to 66 years).

Studies were conducted by Consumer Product Testing Company, Fairfield, NJ

## **SUMMARY OF FINDINGS WITH HYDROGEL FORMULATION**

The vast majority of both male and female subjects did not develop skin reactions at any time during the repeated exposure induction phase or subsequent challenge phase. This prominent lack of reaction was similar for both younger subjects (<50 years) and an older cohort (≥50 years). Table 1 below shows the percentage of subjects by gender and age demographics who had no cutaneous reactions to Hydrogel during any of the eleven patch applications.



**Table 1.**  
**NON-RESPONSE RATES FOR**  
**HYDROGEL BY SEX AND AGE GROUP**

<b>Age Group</b>	<b>Male</b>	<b>Female</b>
<b>&lt;50 years</b>	6/6 (100%)	36/42 (86%)
<b>≥50 years</b>	14/16 (88%)	45/49 (92%)

All male subjects under the age of 50 years and 86% of female subjects under the age of 50 years had no cutaneous reactions at all to the hydrogel patch during repeat irritancy and allergic sensitization exposures. Similarly, 88% of males ≥50 years and 92% of females ≥50 years had no cutaneous reactions to hydrogel during repeat irritancy and allergic sensitization exposures.

Table 2 shows the distribution of maximum cutaneous reaction ratings among the 102 subjects who completed the study, as well as among the 11 subjects who discontinued the study. The complete study report is in the appendix beginning on p. 11 of this document.

**Table 2.**  
**SKIN REACTIONS TO HYDROGEL:**  
**SUMMARY OF SEVERITY OF RESPONSE**

<b>Rating</b>	<b>Among subjects who completed the study</b>	<b>Among subjects who discontinued the study</b>	<b>All subjects</b>
0 (No visible skin reaction)	91	10	101
+ (Barely perceptible or spotty erythema)	5	1	6
1 (Mild erythema covering most of the test site)	4	0	4
2 (Moderate erythema, possible presence of mild edema)	2	0	2
3 (Marked erythema, possible edema)	0	0	0
4 (Severe erythema, possible edema, vesiculation, bullae and/or ulceration)	0	0	0
<b>TOTAL</b>	102	11	113

As shown, 101 of 113 total subjects had no skin reactions during multiple patch applications. The remaining twelve subjects developed demonstrable skin reactions. Ten of the twelve total subjects with cutaneous responses had single time-point, barely perceptible or only minor, reactions which had resolved by the following observation. None of the 102 panelists who completed the study, or of the 113 total subjects enrolled, were observed as having anything more than moderate (*i.e.*, level-2) reaction when exposed to the hydrogel patch. Level 3 or level 4 reactions were not observed (95% CI: 0-2.9%); specifically, there was no blistering as is characteristic of a more significant cutaneous allergic response. There was only 1 instance of barely perceptible erythema in the group of 11 panelists who failed to complete the study, thus demonstrating that discontinuations were not the result of cutaneous responses to patch



materials. The reasons for discontinuations were not specified though were reported by the testing facility as unrelated to application of test material.

The rate of adverse reactions to hydrogel was 10.6% (95% CI: 5-17%) (12/113 enrolled subjects, including subjects who did not complete the study). A closer look at the 12 panelists who showed barely perceptible (+) to moderate (level 2) patch test irritant responses to hydrogel is provided in the following table.

**Table 3.**  
**SUMMARY OF SKIN REACTIONS TO HYDROGEL:**  
**INDIVIDUAL SUBJECT RESPONSES**

Subject Number (Panel <sup>1</sup> )	Age	Sex	Maximum Rating	Completed Study	When reaction noted
2 (1)	61	M	+	Yes	24 hours following virgin challenge site
9 (2)	69	F	2	Yes	Days 3 and 5 of induction phase; at 24, 72, and 96 hours following virgin challenge
22 (1)	42	F	+	Yes	24 hour assessment after initial patch placement
23 (2)	22	F	1	Yes	24 hours following virgin challenge
25 (2)	40	F	+	Yes	24 hour assessment after initial patch placement
26 (2)	43	F	+	Yes	24 hour assessment after initial patch placement
28 (2)	76	F	1	Yes	24 hours following virgin challenge
31 (2)	62	F	2	Yes	24 hour assessment after initial patch placement; days 1 to 3 of induction phase; at 72 and 96 hours following virgin challenge
49 (1)	54	M	1	Yes	24 hours following virgin challenge site
50 (2)	37	F	1	Yes	24 hour assessment after initial patch placement
52 (1)	47	F	+	No	24 hour assessment after initial patch placement
54 (2)	76	F	+	Yes	24 hour assessment after initial patch placement

<sup>1</sup>Panel 1 corresponds to #20000326 and Panel 2 corresponds to #20000334 in the study report (study reports presented in the appendices)

Of the 12 panelists who had reactions, 10 were females and 2 were males. The average age was 52.4 years (range: 22 to 76 years). All participants exhibiting reactions, with the exception of subject number 52 (a 47-year-old female who developed barely perceptible or spotty erythema),



completed the study. The immediate response of subject 31 during induction (minor erythema at 24 hours, increasing to moderate erythema/possible mild edema at day 2) is most consistent with presensitization or “excited skin”, perhaps related to concomitant test patches in this non-exclusionary study. In approximately 2% of study subjects (subject numbers 9 and 31 of panel 2), level-2 challenge reactions developed at 72 hours, characterized by moderate erythema and possibly including mild edema.

## SUMMARY OF FINDINGS WITH NON-HYDROGEL FORMULATION

The vast majority of both male and female subjects did not develop skin reactions to non-hydrogel at any time during the repeated exposure induction phase or subsequent challenge phase. This prominent lack of reaction was similar for both younger subjects (<50 years) and an older cohort (≥50 years). Table 4 below shows the percentage of subjects by gender and age demographics who had no cutaneous reactions to non-hydrogel during any of the eleven patch applications.

**Table 4.**  
**NON-RESPONSE RATES FOR**  
**NON-HYDROGEL BY SEX AND AGE GROUP**

<b>Age Group</b>	<b>Male</b>	<b>Female</b>
<b>&lt;50 years</b>	6/6 (100%)	36/42 (86%)
<b>≥50 years</b>	15/16 (94%)	45/49 (92%)

All male subjects under the age of 50 years and 86% of female subjects under the age of 50 years had no cutaneous reactions at all to the non-hydrogel patch during repeat irritancy and allergic sensitization exposures. Similarly, 94% of males ≥50 years and 92% of females ≥50 years had no cutaneous reactions to non-hydrogel during repeat irritancy and allergic sensitization exposures.

Table 5 shows the distribution of maximum ratings for non-hydrogel among the 102 subjects who completed the study, as well as among the 11 subjects who discontinued the study. The complete study report can be found in the appendix beginning on p. 11.



**Table 5.**  
**SKIN REACTIONS TO NON-HYDROGEL:**  
**SUMMARY OF SEVERITY OF RESPONSE**

Rating	Among subjects who completed the study	Among subjects who discontinued the study	All subjects
0 (No visible skin reaction)	92	10	102
+ (Barely perceptible or spotty erythema)	7	1	8
1 (Mild erythema covering most of the test site)	1	0	1
2 (Moderate erythema, possible presence of mild edema)	2	0	2
3 (Marked erythema, possible edema)	0	0	0
4 (Severe erythema, possible edema, vesiculation, bullae and/or ulceration)	0	0	0
<b>TOTAL</b>	102	11	113

As shown, 102 of 113 total subjects had no skin reactions during multiple patch applications. The remaining eleven subjects developed demonstrable skin reactions. None of the 102 panelists who completed the study, or of the 113 total subjects enrolled, were observed as having anything more than moderate (*i.e.*, level 2) irritation when exposed to the nonhydrogel patch. Nine of the 11 total subjects with cutaneous responses had single time-point, barely perceptible or only minor, reactions which had resolved by the following observation. Level 3 or level 4 reactions were not observed (95% CI: 0-2.9%); specifically, there was no blistering as is characteristic of a more significant cutaneous allergic response. There was only 1 instance of barely perceptible erythema in the group of 11 panelists who failed to complete the study, thus demonstrating that discontinuations were not the result of cutaneous responses to patch materials. The reasons for discontinuations were not specified though were reported by the testing facility as unrelated to application of test material.

The rate of adverse reactions to non-hydrogel was 9.7% (95% CI: 4-15%) (11/113 enrolled subjects, including subjects who did not complete the study). A closer look at the 11 panelists who showed barely perceptible (+) to moderate (level 2) patch test irritant responses to non-hydrogel is provided in the following table.



**Table 6.**  
**SUMMARY OF SKIN REACTIONS TO NON-HYDROGEL:**  
**INDIVIDUAL SUBJECT RESPONSES**

Subject Number (Panel <sup>1</sup> )	Age	Sex	Maximum Rating	Completed Study	When Reaction Noted
2 (1)	61	M	+	Yes	24 hours following virgin challenge site
9 (2)	69	F	2	Yes	Days 3 and 5 of induction phase; at 24, 72, and 96 hours following virgin challenge
22 (1)	42	F	+	Yes	24 hour assessment prior to induction phase
23 (2)	22	F	+	Yes	24 hours following virgin challenge
25 (2)	40	F	+	Yes	24 hour assessment prior to induction phase
26 (2)	43	F	+	Yes	24 hour assessment prior to induction phase
28 (2)	76	F	1	Yes	24 hours following virgin challenge
31 (2)	62	F	2	Yes	24 hour assessment prior to induction phase; days 1 to 3 of induction phase; at 72 hours following virgin challenge (minimal + reaction at this challenge)
37 (1)	24	F	+	No	24 hour assessment prior to induction phase
50 (2)	37	F	+	Yes	24 hour assessment prior to induction phase
54 (2)	76	F	+	Yes	24 hour assessment prior to induction phase

<sup>1</sup>Panel 1 corresponds to #20000326 and Panel 2 corresponds to #20000334 in the study report (study reports presented in the appendices)

Of the 11 panelists who had reactions, 10 were female and 1 was male. The average age was 50.2 years (range: 22 to 76 years). All participants exhibiting reactions, with the exception of subject number 37 (a 24 year old female who developed barely perceptible or spotty erythema), completed the study. The immediate response of subject 31 (minor erythema at 24 hours, increasing to moderate erythema/possible mild edema at day 2) is most consistent with presensitization or “excited skin”, perhaps related to concomitant test patches in this non-exclusionary study. Subject 9 of panel 2 developed a level-2 challenge reaction at 24 hours and 72 hours, characterized by moderate erythema and possibly including edema. This is the subject who responded similarly to the hydrogel patch. Subject 31 of panel 2, who exhibited a level-2 challenge reaction to hydrogel, had only a + (barely perceptible) erythematous reaction at 72 hours post-challenge.



## COMPARISON OF REACTIONS TO HYDROGEL AND NON-HYDROGEL

The prominent low cutaneous reactivity to hydrogel and non-hydrogel patches demonstrated in Tables 1 and 4 are further supported by directly comparing the rates of no visible reactions and the similar severities of noted reactions in those few subjects with positive cutaneous responses. The distribution of skin reactions to hydrogel and non-hydrogel are compared in Table 7 below.

**Table 7.**  
**SEVERITY OF CUTANEOUS REACTIONS BY PATCH TYPE**

Rating	Hydrogel	Non-Hydrogel
0 (No visible skin reaction)	101 (89%)	102 (90%)
+ (Barely perceptible or spotty erythema)	6 (5%)	8 (7%)
1 (Mild erythema covering most of the test site)	4 (4%)	1 (1%)
2 (Moderate erythema, possible presence of mild erythema)	2 (2%)	2 (2%)
3 (Marked erythema, possible edema)	0 (0%)	0 (0%)
4 (Severe erythema, possible edema, vesiculation, bullae and/or ulceration)	0 (0%)	0 (0%)
<b>TOTAL</b>	<b>113 (100%)</b>	<b>113 (100%)</b>

Among 113 subjects tested with hydrogel and non-hydrogel, 89-90% had no cutaneous reactions at all during repeated induction phase and challenge exposures. Most of the positive cutaneous responses were minimal, consisting of barely perceptible or spotty erythema.

The table below compares the maximum observed ratings for hydrogel to that of non-hydrogel.

**Table 8.**  
**COMPARATIVE REACTIONS TO PATCHES**

Maximum Reaction to Hydrogel	Maximum Reaction to Non-Hydrogel Exposure						Total
	0	+	1	2	3	4	
0	100	1	0	0	0	0	101
+	1	5	0	0	0	0	6
1	1	2	1	0	0	0	4
2	0	0	0	2	0	0	2
3	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0
<b>TOTAL</b>	102	8	1	2	0	0	113
McNemars test (null hypothesis: adverse event patterns are similar): p=0.18							

As shown in the shaded diagonal cells above, 108 of 113 total subjects experienced identical reactions to non-hydrogel versus hydrogel. Most of these 108 subjects reacted to neither the hydrogel nor the non-hydrogel (n=100; 92.6%). Eight subjects reacted equivalently to both



patches. Maximum reactions to hydrogel and non-hydrogel for all 113 subjects were not significantly different ( $p=0.18$ , McNemars test).

Five subjects did not experience identical maximum ratings to the hydrogel and non-hydrogel patches. Specifically, as shown below, subject number 37 had a mild reaction to non-hydrogel but no reaction to hydrogel, while four subjects showed at most mild erythematous responses to both test patches with a slightly more severe reaction to hydrogel. None of these differences are more than slight, and none are considered of any clinical significance.

**Table 9.**  
**COMPARATIVE MAXIMUM REACTIONS TO PATCHES**

Subject Number (Panel <sup>1</sup> )	Age	Sex	Completed Study?	Maximum Hydrogel Rating	Maximum Non-Hydrogel Rating
37 (1)	24	F	No	0	+
52 (1)	47	F	No	+	0
49 (1)	54	M	Yes	1	0
23 (2)	22	F	Yes	1	+
50 (2)	37	F	Yes	1	+

<sup>1</sup>Panel 1 corresponds to #20000326 and Panel 2 corresponds to #20000334 in the study report (study reports presented in the appendices)

## SPONSOR CONCLUSIONS OF THE REPEATED INSULT PATCH TESTS

This study was conducted as is standard industry practice to determine the relative tolerability of two topical analgesics. In general, reactions were few, mild and transient. These are expected findings with this type of repeated skin testing of a counterirritant analgesic. The results favorably support the safe use and generally good tolerability of the Icy Hot<sup>®</sup> Patch topical analgesic. Some additional, more specific observations follow.

- The study was conducted with patch applications and evaluations in general accordance with the recommendations of the FDA guidance on skin irritation and sensitization testing (CDER Guidance December 1999). However, removal of patches for 24 hours prior to skin evaluations and subsequent applications was a potential limitation to sensitivity.
- The majority of test subjects (approximately 90%) completed the repeat exposure and challenge without demonstrable skin reaction.
- Among subjects who reacted to study patches, the majority (83%) had irritation at only a single observation time point.
- A minority of subjects (10-11%) had barely perceptible to moderate, transient erythematous reactions consistent with irritation. Ten subjects had reactions to both



hydrogel and non-hydrogel patches, and three other subjects reacted slightly (barely perceptible to mild erythematous responses) to one patch but not the other. Neither definite induration (edema) or visiculation were noted in any subject, although two subjects (1.8% of all study subjects) developed level-2 lesions (moderate erythema, possible presence of mild edema). The sponsor's conservative interpretation is that the scoring system does not allow one to rule out a mild allergic hypersensitivity response in these two subjects.

- Irritation reactions occurred predominantly in female subjects.
- Irritation reactions were relatively equally distributed between ages 22 and 76 years.
- Irritation reactions occurred equally with hydrogel and non-hydrogel test products.

## REFERENCES

Food and Drug Administration (FDA). 2003. Proposed Rule: External Analgesic Drug Products for Over-the-Counter Human Use; Reopening of the Administrative Record and Amendment of Tentative Final Monograph. Federal Register 68(137):42324-42326.

Food and Drug Administration (FDA). 1999. Guidance for Industry: Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products. Center for Drug Evaluation and Research, December 1999.



**APPENDIX 1.**  
**REPEATED INSULT PATCH TEST**  
**STUDY CSE-391 NON-HYDROGEL TYPE PATCH**  
(Consumer Product Testing Co. reports for hydrogel and non-hydrogel patches)





EST. 1975

# Consumer Product Testing Co.

## FINAL REPORT

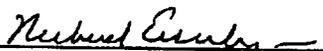
**CLIENT:** Chattem, Inc.  
1715 West 38<sup>th</sup> Street  
Chattanooga, Tennessee 37409

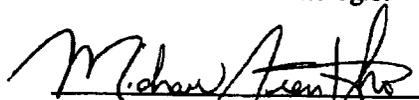
**ATTENTION:** William J. Durkin  
Manager,  
Product Safety & Regulatory Affairs

**TEST:** Repeated Insult Patch Test  
Protocol No.: 1.01

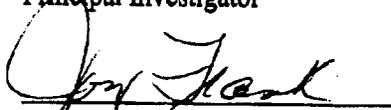
**TEST MATERIAL:** Study CSE 25-<sup>397</sup>191 Non Hydrogel Type Patch Lot # E010

**EXPERIMENT  
REFERENCE NUMBER:** C00-0602.01

  
Richard R. Eisenberg, M.D.  
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EST. 1975

# Consumer Product Testing Co.

## QUALITY ASSURANCE UNIT STATEMENT

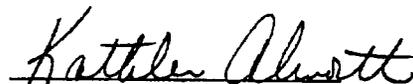
**Study No.:** C00-0602.01

The objective of the Quality Assurance Unit (QAU) is to monitor the conduct and reporting of clinical laboratory studies. The QAU maintains copies of study protocols and standard operating procedures and has inspected this study on the date(s) listed below. Studies lasting six months or more are inspected at time intervals to assure the integrity of the study. The findings of such inspections are reported to management and the Study Director. All materials and data pertinent to this study will be stored or disposed of in accordance with current Standard Operating Procedures.

<b>Date(s) of inspection:</b>	June 16, 2000	July 31, 2000
	June 20, 2000	August 1, 2000
	June 28, 2000	August 7, 2000
	June 30, 2000	August 11, 2000

**Senior personnel involved:**

OnChi Cheung, B.S.	-	Quality Assurance Associate
Titilayo Bello, B.S.	-	Quality Assurance Associate

  
Kathleen Alworth, B.A.  
Director of Quality Assurance

The representative signature of the Quality Assurance Unit signifies that this study has been performed in accordance with standard operating procedures and study protocol as well as government regulations regarding such procedures and protocols as outlined in the Federal Register (Vol. 46, No. 17 of Tuesday, January 27, 1981).

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Clinical • Toxicology • Analytical Chemistry • Microbiology

**Objective:** To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

**Participants:** One hundred thirteen (113) qualified subjects, male and female, ranging in age from 18 to 79 years, were selected for this evaluation. One hundred two (102) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

**Inclusion Criteria:**

- Male and female subjects, age 16<sup>a</sup> and over.
- Absence of any visible skin disease which might be confused with a skin reaction from the test material.
- Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
- Completion of a Medical History form and the understanding and signing of an Informed Consent form.
- Considered reliable and capable of following directions.

**Exclusion Criteria:**

- Ill health.
- Under a doctor's care or taking medication(s) which could influence the outcome of the study.
- Females must not be pregnant or nursing.
- A history of adverse reactions to cosmetics or other personal care products.

**Test Material:** Study CSE 25-191 Non Hydrogel Type Patch Lot # E010

<b>Study Schedule:</b>	<b>Panel #</b>	<b>Initiation Date</b>	<b>Proposed Completion Date</b>	<b>Actual Completion Date</b>
	20000326	June 19, 2000	July 27, 2000	July 28, 2000
	20000334	June 21, 2000	July 27, 2000	August 3, 2000

*patches assembled in pps of 50's - subjects  
non-exclusive patches - could be tested for 12 products  
Simultaneous Chatterm.*

<sup>a</sup>With parental or guardian consent

*Angy Shi Tanos*

**Methodology:**

The upper back between the scapulae served as the treatment area. Prior to the initiation of this study, the test material was cut into approximately 1" x 1" pieces. This sample was then placed over the absorbent pad portion of an adhesive dressing\*. When applied to the appropriate treatment site, this dressing formed a semi-occlusive patch.

**Induction Phase:**

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. It was noted that due to a holiday weekend which occurred during the Induction Phase, subjects who required a makeup day experienced a delay between applications. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications are discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

**Challenge Phase:**

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy-two hours post-application.

\*Manufactured by TruMed Technologies, Inc., Burnsville, MN

**Evaluation Key:**

- 0 = No visible skin reaction
- + = Barely perceptible or spotty erythema \*
- 1 = Mild erythema covering most of the test site
- 2 = Moderate erythema, possible presence of mild edema
- 3 = Marked erythema, possible edema
- 4 = Severe erythema, possible edema, vesiculation, bullae and/or ulceration

**Results:**

The results of each participant are appended (Table 1).

Barely perceptible (+) to moderate (2-level) patch test irritant/cumulative irritant responses were observed on eleven ~~(11/102)~~ test panelists (Subject's #2, 22, 37 [discontinued], Panel #20000326; 9, 23, 25, 26, 28, 31, 50, 54, Panel #20000334) during the Induction and/or Challenge phases of the study. It was noted that Subject's #9 and 31 (Panel# 20000334) exhibited skin response patterns suggestive of a hyperirritability to one or more of the test product components. Based on the lack of any other observed dermal sequelae, neither of these response patterns was considered indicative of induced allergic contact sensitization.

**Summary:**

Under the conditions of a repeated insult (semi-occlusive) patch test, test material, Study CSE 25-191 Non Hydrogel Type Patch Lot # E010, was a patch test irritant/cumulative irritant to approximately 11% (11/102) of the test population. There was no evidence of induced allergic contact dermatitis.

Table 1  
 Panel #20000326

Individual Results

Study CSE 25-191 Non Hydrogel Type Patch Lot # E010

Subject Number	24*hr	Induction Phase									Virgin Challenge Site		
		1	2	3	4	5	6	7	8	9	24*hr	72 hr	
1	0	0	DID NOT COMPLETE STUDY										
2	0	0	0	0	0	0	0	0	0	0	0	0	
3	0	0	0	0	0	0	0	0	0	0	+	0	
4	0	0	0	0	0	0	0	0	0	0	DNC		
5	0	0	0	0	0	0	0	0	0	0	0	0	
6	0	0	0	0	0	0	0	0	0	0	0	0	
7	0	0	0	0	0	0	0	0	0	0	0	0	
8	0	0	0	0	0	0	0	0	0	0	DNC		
9	0	0	0	0	0	0	0	0	0	0	0	0	
10	0	0	0	0	0	0	0	0	0	0	0	0	
11	0	0	0	0	0	0	0	0	0	0	0	0	
12	0	0	0	0	0	0	0	0	0	0	0	0	
13	0	0	0	0	0	0	0	0	0	0	0	0	
14	0	0	0	0	0	0	0	0	0	0	0	0	
15	0	0	0	0	0	0	0	0	0	0	0	0	
16	0	0	0	0	0	0	0	0	0	0	0	0	
17	0	0	0	0	0	0	0	0	0	0	0	0	
18	0	0	0	0	0	0	0	0	0	0	0	0	
19	0	0	0	0	0	0	0	0	0	0	0	0	
20	0	0	0	0	0	0	0	0	0	0	0	0	
21	0	0	0	0	0	0	0	0	0	0	0	0	
22	+	0	0	0	0	0	0	0	0	0	0	0	
23	0	0	0	0	0	0	0	0	0	0	0	0	
24	0	0	0	0	0	0	0	0	0	0	0	0	
25	0	0	0	0	0	0	0	0	0	0	0	0	
26	0	0	0	0	0	0	0	0	0	0	0	0	
27	0	0	0	0	0	0	0	0	0	0	0	0	
28	0	0	0	0	0	0	0	0	0	0	0	0	

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
 DNC = Did not complete study

*48 hrs after 5<sup>th</sup> induction*

Table 1  
(continued)  
Panel #20000326

Individual Results

Study CSE 25-191 Non Hydrogel Type Patch Lot # E010

Subject Number	24*hr	Induction Phase									Virgin Challenge Site			
		1	2	3	4	5	6	7	8	9	24*hr	72 hr		
29	0	0	0	0	0	0	0	0	0	0	0	0	0	
30	0	0	0	0	0	0	0	0	0	0	0	0	0	
31	0	0	0	0	0	0	0	0	0	0	0	0	0	
32	0	0	0	0	0	0	0	0	0	0	0	0	0	
33	0	0	0	0	0	0	0	0	0	0	0	0	0	
34	0	0	0	0	0	0	0	0	0	0	0	0	0	
35	0	0	0	0	0	0	0	0	0	0	0	0	0	
36	0	0	0	0	0	0	0	0	0	0	0	0	0	
37	+	0	0	0	0	0	0	0	0	DNC				
38	0	0	0	0	0	0	0	0	0	0	0	0	0	
39	0	0	0	0	0	0	0	0	0	0	0	0	0	
40	0	0	0	0	0	0	0	0	0	0	0	0	0	
41	0	0	0	0	0	0	0	0	0	0	0	0	0	
42	0	0	0	0	0	0	0	0	0	0	0	0	0	
43	0	0	0	0	0	0	0	0	0	0	0	0	0	
44	0	0	0	0	0	0	0	0	0	0	0	0	0	
45	0	0	0	0	0	0	0	0	0	0	0	0	0	
46	0	0	0	0	0	0	0	0	0	0	0	0	0	
47	0	0	0	0	0	0	0	0	0	0	0	0	0	
48	0	0	0	0	0	0	0	0	0	0	0	0	0	
49	0	0	0	0	0	0	0	0	0	0	0	0	0	
50	0	0	0	0	0	0 <sup>m</sup>	0	0	0	0	0	0	0	
51	0	0	0	0	0	0	0	0	0	0	0	0	0	
52	0	0	0	DID NOT COMPLETE STUDY										
53	0	0	0	0	0	0	0	0	0	0	0	0	0	
54	0	0	DID NOT COMPLETE STUDY											
55	0	0	DID NOT COMPLETE STUDY											
56	0	0	0	0	0	0	0	0	0	0	0	0	0	

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
DNC = Did not complete study  
m = Additional makeup day granted at the discretion of the clinic supervisor

Table 1  
(continued)  
Panel #20000334

Individual Results

Study CSE 25-191 Non Hydrogel Type Patch Lot # E010

Subject Number	24*hr	Induction Phase									Virgin Challenge Site		
		1	2	3	4	5	6	7	8	9	24*hr	72 hr	
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	2 <sup>A</sup>	2 <sup>X</sup>	-	-	-	2	2	2 <sup>**</sup>
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0	0
21	DID NOT COMPLETE STUDY												
22	0	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	+	0
24	0	0	0	0	0	0	0	0	0	0	0	0	0
25	+	0	0	0	0	0	0	0	0	0	0	0	0
26	+	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0	0

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
A = Changed to adjacent site  
X = Patching discontinued  
\*\* = 96 follow-up evaluation

Table 1  
(continued)  
Panel #20000334

Individual Results

Study CSE 25-191 Non Hydrogel Type Patch Lot # E010

Subject Number	24*hr	Induction Phase									Virgin Challenge Site		
		1	2	3	4	5	6	7	8	9	24*hr	72 hr	
29	0	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0	0
31	+	+	2 <sup>A</sup>	2 <sup>X</sup>	-	-	-	-	-	-	0	+	0**
32	0	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	DID NOT COMPLETE STUDY										
44	0	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0	0
50	+	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0	0
52	0	DID NOT COMPLETE STUDY											
53	0	0	0	0	0	0	0	0	0	0	0	0	0
54	+	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0	0

*Handwritten notes:*  
 31 - 36  
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 55 - 36  
 56 - 36  
 57 - 36

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
 A = Changed to adjacent site  
 X = Patching discontinued  
 \*\* = 96 follow-up evaluation

Table 2  
Panel #20000326

Subject Data

Subject Number	Initials	Age	Sex
1	CS	40	M
2	DC	61	M
3	KW	66	F
4	RM	74	F
5	MS	68	F
6	DN	51	F
7	MB	31	F
8	ES	50	M
9	CV	63	F
10	JP	56	F
11	AB	43	F
12	AL	72	F
13	OU	73	F
14	WM	32	F
15	EG	56	F
16	KM	54	F
17	KS	53	F
18	DL	23	F
19	SC	51	M
20	DL	43	F
21	EW	53	F
22	DB	42	F
23	KL	22	F
24	MK	52	F
25	LD	67	F
26	MD	74	F
27	SM	24	F
28	MM	21	F

Table 2  
(continued)  
Panel #20000326

Subject Data

Subject Number	Initials	Age	Sex
29	JC	66	F
30	CT	32	F
31	LS	53	F
32	JB	50	F
33	RL	63	F
34	EL	67	M
35	JR	73	M
36	SR	68	F
37	TU	24	F
38	DB	51	F
39	EB	53	M
40	DL	56	M
41	LP	32	F
42	TL	52	F
43	SB	38	F
44	DS	69	F
45	HS	72	M
46	EG	36	M
47	SG	71	F
48	AS	18	F
49	MG	54	M
50	LH	35	F
51	DR	40	F
52	AF	47	F
53	PV	48	F
54	DW	18	M
55	JR	20	F
56	CD	31	F

Table 2  
(continued)  
Panel # 2000334

Subject Data

Subject Number	Initials	Age	Sex
1	CA	56	F
2	ED	33	F
3	CP	39	F
4	EK	78	F
5	CF	39	F
6	SV	47	F
7	LG	53	F
8	RG	56	M
9	EH	69	F
10	HH	73	M
11	AH	77	F
12	LR	49	F
13	CD	29	F
14	JT	70	F
15	LL	71	F
16	AL	73	M
17	MB	67	F
18	CS	38	F
19	MB	74	F
20	NV	53	F
21	KM	22	F
22	JD	51	F
23	JM	22	F
24	DH	25	M
25	LM	40	F
26	MP	43	F
27	AA	79	F
28	ID	76	F

**APPENDIX 2.**  
**REPEATED INSULT PATCH TEST**  
**AND STUDY CSE-392 HYDROGEL TYPE PATCH**  
(Consumer Product Testing Co. reports for hydrogel and non-hydrogel patches)





# Consumer Product Testing Co.

EST. 1975

## FINAL REPORT

**CLIENT:** Chattem, Inc.  
1715 West 38<sup>th</sup> Street  
Chattanooga, Tennessee 37409

**ATTENTION:** William J. Durkin  
Manager,  
Product Safety & Regulatory Affairs

**TEST:** Repeated Insult Patch Test  
Protocol No.: 1.01

**TEST MATERIAL:** Study CSE 25-392 Hydrogel Type Patch Lot # E050

**EXPERIMENT  
REFERENCE NUMBER:** C00-0602.02

Richard R. Eisenberg, M.D.  
Board Certified Dermatologist

Michael J. Frentzko, B.A.  
Director, Clinical Evaluations

Robert W. Shanahan, Ph.D.  
Principal Investigator

Joy Frank, R.N.  
Study Director

This report is submitted for the exclusive use of the person, partnership, or corporation to whom it is addressed, and neither the report nor the name of these Laboratories nor any member of its staff, may be used in connection with the advertising or sale of any product or process without written authorization.

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234



EST. 1975

# Consumer Product Testing Co.

## QUALITY ASSURANCE UNIT STATEMENT

Study No.: C00-0602.02

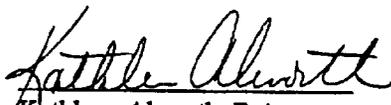
The objective of the Quality Assurance Unit (QAU) is to monitor the conduct and reporting of clinical laboratory studies. The QAU maintains copies of study protocols and standard operating procedures and has inspected this study on the date(s) listed below. Studies lasting six months or more are inspected at time intervals to assure the integrity of the study. The findings of such inspections are reported to management and the Study Director. All materials and data pertinent to this study will be stored or disposed of in accordance with current Standard Operating Procedures.

<b>Date(s) of inspection:</b>	June 16, 2000	July 31, 2000
	June 20, 2000	August 1, 2000
	June 28, 2000	August 7, 2000
	June 30, 2000	August 11, 2000

### Senior personnel involved:

OnChi Cheung, B.S. - Quality Assurance Associate

Titilayo Bello, B.S. - Quality Assurance Associate

  
Kathleen Alworth, B.A.  
Director of Quality Assurance

The representative signature of the Quality Assurance Unit signifies that this study has been performed in accordance with standard operating procedures and study protocol as well as government regulations regarding such procedures and protocols as outlined in the Federal Register (Vol. 46, No. 17 of Tuesday, January 27, 1981).

**Objective:** To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

**Participants:** One hundred thirteen (113) qualified subjects, male and female, ranging in age from 18 to 79 years, were selected for this evaluation. One hundred two (102) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

**Inclusion Criteria:**

- a. Male and female subjects, age 16<sup>a</sup> and over.
- b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
- c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
- d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
- e. Considered reliable and capable of following directions.

**Exclusion Criteria:**

- a. Ill health.
- b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
- c. Females must not be pregnant or nursing.
- d. A history of adverse reactions to cosmetics or other personal care products.

**Test Material:** Study CSE 25-392 Hydrogel Type Patch Lot # E050

<b>Study Schedule:</b>	<u>Panel #</u>	<u>Initiation Date</u>	<u>Proposed Completion Date</u>	<u>Actual Completion Date</u>
	20000326	June 19, 2000	July 27, 2000	July 28, 2000
	20000334	June 21, 2000	July 27, 2000	August 3, 2000

<sup>a</sup>With parental or guardian consent

**Methodology:**

The upper back between the scapulae served as the treatment area. Prior to the initiation of this study, the test material was cut into approximately 1" x 1" pieces. This sample was then placed over the absorbent pad portion of an adhesive dressing\*. When applied to the appropriate treatment site, this dressing formed a semi-occlusive patch.

**Induction Phase:**

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. It was noted that due to a holiday weekend which occurred during the Induction Phase, subjects who required a makeup day experienced a delay between applications. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications are discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

**Challenge Phase:**

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy-two hours post-application.

---

\*Manufactured by TruMed Technologies, Inc., Burnsville, MN

**Evaluation Key:**

- 0 = No visible skin reaction
- + = Barely perceptible or spotty erythema
- 1 = Mild erythema covering most of the test site
- 2 = Moderate erythema, possible presence of mild edema
- 3 = Marked erythema, possible edema
- 4 = Severe erythema, possible edema, vesiculation, bullae and/or ulceration

**Results:**

The results of each participant are appended (Table 1).

Barely perceptible (+) to moderate (2-level) patch test irritant/cumulative irritant responses were observed on twelve (12/102) test panelists (Subject's #2, 22, 49, 52 [discontinued], Panel #20000326; 9, 23, 25, 26, 28, 31, 50, 54, Panel #20000334) during the Induction and/or Challenge phases of the study. It was noted that Subject's #9 and 31 (Panel# 20000334) exhibited skin response patterns suggestive of a hyperirritability to one or more of the test product components. Based on the lack of any other observed dermal sequelae, neither of these response patterns was considered indicative of induced allergic contact sensitization.

**Summary:**

Under the conditions of a repeated insult (semi-occlusive) patch test, test material, Study CSE 25-392 Hydrogel Type Patch Lot # E050, was a patch test irritant/cumulative irritant to approximately 12% (12/102) of the test population. There was no evidence of induced allergic contact dermatitis.

Table 1  
 Panel #20000326

? analysis by demographics?

Individual Results

Study CSE 25-392 Hydrogel Type Patch Lot # E050

Subject Number	24*hr	Induction Phase									Virgin Challenge Site		
		1	2	3	4	5	6	7	8	9	24*hr	72 hr	
1	0	0	DID NOT COMPLETE STUDY										
2	0	0	0	0	0	0	0	0	0	0	0	0	
3	0	0	0	0	0	0	0	0	0	0	DNC		
4	0	0	0	0	0	0	0	0	0	0	0	0	
5	0	0	0	0	0	0	0	0	0	0	0	0	
6	0	0	0	0	0	0	0	0	0	0	0	0	
7	0	0	0	0	0	0	0	0	0	0	DNC		
8	0	0	0	0	0	0	0	0	0	0	0	0	
9	0	0	0	0	0	0	0	0	0	0	0	0	
10	0	0	0	0	0	0	0	0	0	0	0	0	
11	0	0	0	0	0	0	0	0	0	0	0	0	
12	0	0	0	0	0	0	0	0	0	0	0	0	
13	0	0	0	0	0	0	0	0	0	0	0	0	
14	0	0	0	0	0	0	0	0	0	0	0	0	
15	0	0	0	0	0	0	0	0	0	0	0	0	
16	0	0	0	0	0	0	0	0	0	0	0	0	
17	0	0	0	0	0	0	0	0	0	0	0	0	
18	0	0	0	0	0	0	0	0	0	0	0	0	
19	0	0	0	0	0	0	0	0	0	0	0	0	
20	0	0	0	0	0	0	0	0	0	0	0	0	
21	0	0	0	0	0	0	0	0	0	0	0	0	
22	+	0	0	0	0	0	0	0	0	0	0	0	
23	0	0	0	0	0	0	0	0	0	0	0	0	
24	0	0	0	0	0	0	0	0	0	0	0	0	
25	0	0	0	0	0	0	0	0	0	0	0	0	
26	0	0	0	0	0	0	0	0	0	0	0	0	
27	0	0	0	0	0	0	0	0	0	0	0	0	
28	0	0	0	0	0	0	0	0	0	0	0	0	

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
 DNC = Did not complete study

Table 1  
 (continued)  
 Panel #20000326

Individual Results

Study CSE 25-392 Hydrogel Type Patch Lot # E050

Subject Number	24*hr	Induction Phase									Virgin Challenge Site			
		1	2	3	4	5	6	7	8	9	24*hr	72 hr		
29	0	0	0	0	0	0	0	0	0	0	0	0	0	
30	0	0	0	0	0	0	0	0	0	0	0	0	0	
31	0	0	0	0	0	0	0	0	0	0	0	0	0	
32	0	0	0	0	0	0	0	0	0	0	0	0	0	
33	0	0	0	0	0	0	0	0	0	0	0	0	0	
34	0	0	0	0	0	0	0	0	0	0	0	0	0	
35	0	0	0	0	0	0	0	0	0	0	0	0	0	
36	0	0	0	0	0	0	0	0	0	0	0	0	0	
37	0	0	0	0	0	0	0	0	0	0	DNC			
38	0	0	0	0	0	0	0	0	0	0	0	0	0	
39	0	0	0	0	0	0	0	0	0	0	0	0	0	
40	0	0	0	0	0	0	0	0	0	0	0	0	0	
41	0	0	0	0	0	0	0	0	0	0	0	0	0	
42	0	0	0	0	0	0	0	0	0	0	0	0	0	
43	0	0	0	0	0	0	0	0	0	0	0	0	0	
44	0	0	0	0	0	0	0	0	0	0	0	0	0	
45	0	0	0	0	0	0	0	0	0	0	0	0	0	
46	0	0	0	0	0	0	0	0	0	0	0	0	0	
47	0	0	0	0	0	0	0	0	0	0	0	0	0	
48	0	0	0	0	0	0	0	0	0	0	0	0	0	
49	0	0	0	0	0	0	0	0	0	0	0	0	0	
50	0	0	0	0	0	0 <sup>m</sup>	0	0	0	0	0	0	0	
51	0	0	0	0	0	0	0	0	0	0	0	0	0	
52	+	0	0	DID NOT COMPLETE STUDY									0	0
53	0	0	0	0	0	0	0	0	0	0	0	0	0	
54	0	0	DID NOT COMPLETE STUDY									0	0	
55	0	0	0	DID NOT COMPLETE STUDY									0	0
56	0	0	0	0	0	0	0	0	0	0	0	0	0	

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
 DNC = Did not complete study  
 m = Additional makeup day granted at the discretion of the clinic supervisor

Table 1  
 (continued)  
 Panel #20000334

Individual Results

Study CSE 25-392 Hydrogel Type Patch Lot # E050

Subject Number	24*hr	Induction Phase									Virgin Challenge Site		
		1	2	3	4	5	6	7	8	9	24*hr	72 hr	
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	2*	+	2*	-	-	-	-	1	2**	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0	0
21	DID NOT COMPLETE STUDY												
22	0	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	1	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0	0
25	+	0	0	0	0	0	0	0	0	0	0	0	0
26	+	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	1	0	0

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
 A = Changed to adjacent site  
 X = Patching discontinued  
 \*\* = 96 follow-up evaluation

Table 1  
 (continued)  
 Panel #20000334

Individual Results

Study CSE 25-392 Hydrogel Type Patch Lot # E050

Subject Number	24*hr	Induction Phase									Virgin Challenge Site		
		1	2	3	4	5	6	7	8	9	24*hr	72 hr	
29	0	0	0	0	0	0	0	0	0	0	0	0	
30	0	0	0	0	0	0	0	0	0	0	0	0	
31	+	+	2 <sup>A</sup>	2 <sup>X</sup>	-	-	-	-	-	-	0	1**	
32	0	0	0	0	0	0	0	0	0	0	0	0	
33	0	0	0	0	0	0	0	0	0	0	0	0	
34	0	0	0	0	0	0	0	0	0	0	0	0	
35	0	0	0	0	0	0	0	0	0	0	0	0	
36	0	0	0	0	0	0	0	0	0	0	0	0	
37	0	0	0	0	0	0	0	0	0	0	0	0	
38	0	0	0	0	0	0	0	0	0	0	0	0	
39	0	0	0	0	0	0	0	0	0	0	0	0	
40	0	0	0	0	0	0	0	0	0	0	0	0	
41	0	0	0	0	0	0	0	0	0	0	0	0	
42	0	0	0	0	0	0	0	0	0	0	0	0	
43	0	0	DID NOT COMPLETE STUDY										
44	0	0	0	0	0	0	0	0	0	0	0	0	
45	0	0	0	0	0	0	0	0	0	0	0	0	
46	0	0	0	0	0	0	0	0	0	0	0	0	
47	0	0	0	0	0	0	0	0	0	0	0	0	
48	0	0	0	0	0	0	0	0	0	0	0	0	
49	0	0	0	0	0	0	0	0	0	0	0	0	
50	1	0	0	0	0	0	0	0	0	0	0	0	
51	0	0	0	0	0	0	0	0	0	0	0	0	
52	0	DID NOT COMPLETE STUDY											
53	0	0	0	0	0	0	0	0	0	0	0	0	
54	+	0	0	0	0	0	0	0	0	0	0	0	
55	0	0	0	0	0	0	0	0	0	0	0	0	
56	0	0	0	0	0	0	0	0	0	0	0	0	
57	0	0	0	0	0	0	0	0	0	0	0	0	

24\* = Supervised removal of 1<sup>st</sup> Induction and Challenge Patch  
 A = Changed to adjacent site  
 X = Patching discontinued  
 \*\* = 96 follow-up evaluation

Table 2  
Panel #20000326

Subject Data

Subject Number	Initials	Age	Sex
1	CS	40	M
2	DC	61	M
3	KW	66	F
4	RM	74	F
5	MS	68	F
6	DN	51	F
7	MB	31	F
8	ES	50	M
9	CV	63	F
10	JP	56	F
11	AB	43	F
12	AL	72	F
13	OU	73	F
14	WM	32	F
15	EG	56	F
16	KM	54	F
17	KS	53	F
18	DL	23	F
19	SC	51	M
20	DL	43	F
21	EW	53	F
22	DB	42	F
23	KL	22	F
24	MK	52	F
25	LD	67	F
26	MD	74	F
27	SM	24	F
28	MM	21	F

Table 2  
(continued)  
Panel #20000326

Subject Data

Subject Number	Initials	Age	Sex
29	JC	66	F
30	CT	32	F
31	LS	53	F
32	JB	50	F
33	RL	63	F
34	EL	67	M
35	JR	73	M
36	SR	68	F
37	TU	24	F
38	DB	51	F
39	EB	53	M
40	DL	56	M
41	LP	32	F
42	TL	52	F
43	SB	38	F
44	DS	69	F
45	HS	72	M
46	EG	36	M
47	SG	71	F
48	AS	18	F
49	MG	54	M
50	LH	35	F
51	DR	40	F
52	AF	47	F
53	PV	48	F
54	DW	18	M
55	JR	20	F
56	CD	31	F

Table 2  
(continued)  
Panel # 20000334

Subject Data

Subject Number	Initials	Age	Sex
1	CA	56	F
2	ED	33	F
3	CP	39	F
4	EK	78	F
5	CF	39	F
6	SV	47	F
7	LG	53	F
8	RG	56	M
9	EH	69	F
10	HH	73	M
11	AH	77	F
12	LR	49	F
13	CD	29	F
14	JT	70	F
15	LL	71	F
16	AL	73	M
17	MB	67	F
18	CS	38	F
19	MB	74	F
20	NV	53	F
21	KM	22	F
22	JD	51	F
23	JM	22	F
24	DH	25	M
25	LM	40	F
26	MP	43	F
27	AA	79	F
28	ID	76	F

Table 2  
(continued)  
Panel # 20000334

Subject Data

Subject Number	Initials	Age	Sex
29	DB	44	F
30	JP	72	F
31	MG	62	F
32	EP	76	F
33	SW	53	F
34	KD	46	F
35	TD	47	M
36	AH	34	F
37	MK	59	F
38	RC	24	F
39	WH	36	F
40	CM	39	F
41	LE	58	F
42	BW	58	F
43	AB	48	F
44	JC	62	M
45	RC	63	F
46	CF	36	F
47	MM	53	M
48	LM	42	F
49	LG	47	F
50	AP	37	F
51	AC	23	M
52	DS	64	M
53	RK	69	F
54	EC	76	F
55	RD	70	F
56	EH	71	F
57	SN	68	M