EFFICACY AND TOLERABILITY OF AN ITCH RELIEF PRODUCT AND COMPARING ITCH RELIEF PERFORMANCE VS A COMPETITOR

Quality Assurance Statement

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in 21CFR , part 50 (Protection of Human Subjects Informed Consent) and part 56 (Institutional Review Boards).

For the Purpose of this clinical study,
× Informed Consent was obtained:
_ Informed Consent was not obtained:
×An IRB review was not required:
_ An IRB review was conducted and approval to conduct the proposed clinical research was granted:
This study report has been reviewed to assure that it correctly describes the methods of testing and that the reported results accurately reflect the data obtained during the clinical study.

(Testing Facility Study Number: 4157454340)

Name Date
Quality Assurance Manager

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I. SUMMARY OF RESULTS

Under the conditions of this study, a total of 33 healthy male and female subjects completed the clinical study evaluating the efficacy and tolerability of two investigational itch relief products, under normal use conditions (split-body application) with mild-to-moderate itch severity, eczema/atopic dermatitis-prone skin.

A. Clinical Assessment for the Time to Itch Relief (time in seconds)

Statistic	**Galderma**	**CeraVe**
N	33	33
Mean (SD)	28.48 (16.15)	41.84 (21.72)
Median	30	37
Min, Max	5, 66.56	7, 108
***p*-value**	0.0026	

Clinical findings:

- Galderma provided itch relief as early as 5 seconds with an average of 28.48 seconds. CeraVe provided itch relief as early as 7 seconds with an average of 41.84 seconds. From statistical analysis comparison, Galderma was significantly faster than CeraVe in providing itch relief (*p*-value of 0.0026).

B. Tolerability Assessment for Itch Severity

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	4.36 (1)	4.36 (1)
	Median	4	4
	Min, Max	3, 6	3, 6
8 hours	N	33	33
	Mean (SD)	1.39 (1.83)	2.58 (2.14)
	Median	0	3
	Min, Max	0, 7	0, 7
	p-value from baseline	0	0.0002
	Comparison	0.0023	
12 hours	N	33	33
	Mean (SD)	1.91 (2.52)	2.42 (2.96)
	Median	2	2
	Min, Max	0, 6	0, 7
	p-value from baseline	0	0.0002
	Comparison	0.1672	
24 hours	N	33	33
	Mean (SD)	1.91 (1.81)	2.36 (1.95)
	Median	2	2
	Min, Max	0, 6	0, 7
	p-value from baseline	0	0
	Comparison	0.1652	

Clinical findings:

- Galderma and CeraVe significantly improved itch severity at each timepoint post-baseline. At 8 hours, Galderma was able to significantly better than CeraVe in decreasing itch severity.

C. Tolerability Assessment for Burning/Stinging

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	1.55 (0.94)	1.52 (0.91)
	Median	1	1
	Min, Max	0, 3	0, 3
24 hours	N	33	33
	Mean (SD)	0.79 (0.65)	1.18 (0.68)
	Median	1	1
	Min, Max	0, 2	0, 3
	p-value from baseline	0	0.0057
	Comparison	0.0003	

Clinical findings:

- Galderma and CeraVe significantly improved burning/stinging at 24 hours post-baseline. Galderma outperformed CeraVe in decreasing burning/stinging sensation after 24 hours post-application.

D. Assessment of Consumer Perception (immediately post-application)

	T2B	
Immediately post-application	Galderma	Cera Ve
Q1. The product quickly soothed my itchy skin	30	27
Q2. My skin felt an instant cooling sensation upon application	31	29
Q3. The product immediately helped calm my eczema prone skin	29	30
Q4. The product delivers a great application experience with its unique packaging	29	25
Q5. I like the product texture	27	27
Q6. I had the most pleasant experience using the product	27	25
After 8 hours		
Q1.The product continuously relives my itch	26	24
Q2. My skin does not feel irritated since the product application	28	24
Q3.The product helps soothe my eczema-prone skin	26	24
Q4. My skin still feels comfortable	27	25
After 12 hours		
Q1. The product continuously soothes my eczema-prone skin	22	23
Q2. This product consistently keeps my skin comfortable	24	24
Q3. My itchiness is still much relieved	22	23
After 24 hours		
Q1. This is the best product to relieve my itch	20	21
Q2. I have not noticed an urge to scratch my skin	23	22
Q3. My skin comfort is completely maintained	24	24
Q4. The product is a game changer for my itchy skin	24	20
Q5. The product keeps my irritated skin at ease throughout the day	23	22

Clinical findings:

Galderma and CeraVe were both well-perceived by the subjects at every timepoints post-application.

E. Assessment on product preference

TIMEPOINT	QUESTIONS	GALDERMA	CERAVE	NONE
BASELINE (After Application)	Q1. Which product provides better immediate relief?	17	10	6
24 Hrs	Q2. Of the 2 samples which one do you prefer overall?	19	10	4
24 Hrs	Q3. Which one would you recommend?	16	11	6
24 Hrs	Q4. Which one would you purchase?	16	9	8
24 Hrs	Q5. Which product delivered more than your itch relief expectations?	17	11	5

Clinical findings:

Galderma was numerically preferred by the subjects compared to CeraVe. However, there was no statistically significant different in preference results.

CCID #	CeraVe	Galderma	**Subject Comments**
1	L	R	I preferred the gel because it stayed dry and soft
2	R	L	The left product made my skin feel clean and invigorating and cool. The right product was also nice soothing and creamy on skin
3	L	R	Left side was under the sun while driving and it made it itchy with the cream.
4	L	R	
5	L	R	I really enjoyed the roller product, mainly the idea of the roller is great for the product. The amount of itch was not felt at all with the roller. The cream side was noticeable during the day but not the rolling product. The cream is very moisturizing.
6	R	L	The left product was easy to apply with roller and was thin enough to absorb in the skin quickly.
7	L	R	I liked the cream because I felt something soft and refreshing on my skin. I didn't feel the burning or itch.
8	R	L	
9	L	R	
10	R	L	Instant relief upon application of product gel.
11	L	R	The left side felt better than the right side, the whole 24 hrs.
12	R	L	The gel has a cool feeling but is to watery. The cream is very good.
13	L	R	
14	R	L	Although both gave relief, left side actually helped with redness and a previous light swelling.
15	L	R	I felt an itch on another part of my left hand, 4 hours after application.
16	R	L	
17	L	R	
18	R	L	Loved the gel applicator, cool to the touch. And non-greasy, did not need hand washing.
19	L	R	
20	R	L	The product used on the left had a better absorbing feel compared to the right side. It was instant relief to the touch, didn't feel greasy. However, I feel I would like to apply more throughout the day.
21	L	R	I Did not feel much on my skin.
22	R	L	Gel was a nice sensation. The cream was just regular lotion to me.
23	L	R	I preferred the texture of the right side. It was less greasy. I also preferred the roller with right side.
24	R	L	
25	L	R	
26	R	L	
27	L	R	I like the applicator of the new product but it did not feel as effective in reducing the itchiness.
28	R	L	The cool touch applicator is easier to apply, more cool upon application so faster relief. Lighter texture finger application took longer for cooling effect, thicker texture, not as sanitary since dipping fingers. But both are good and would use both.
29	L	R	The right side felt cool and a little itchy at first but later on it made my skin soft and not dry and itchy.
30	R	L	Liked the cooling sensation on right side, think it would help relief eczema.
31	L	R	I liked everything about it. I would recommend everyone to use it, really helps.
32	R	L	I Liked the right product better but left one is better packaged which will help it store properly.
33	L	R	

II. ADVERSE EVENTS

No adverse events or unexpected reactions of any kind were observed on any of the subjects during the study.

III. PROTOCOL DEVIATION

All procedures were followed according to the protocol. There were no deviations from the original protocol.

IV. STATISTICAL SUMMARY

Since this was a small sample experiment with 33 patients, a paired T-test was used to decide equality/inequality between Galderma and CeraVe means, using alpha = 0.5. These are two sided tests, so p-values are compared to half of alpha, that is 0.025.

V. DEMOGRAPHICS: STUDY POPULATION

	N	%
Subjects completed	33	100%
Gender		
Female	24	72.7
Male	9	27.2
Age		
Mean	49.7	
Minimum	25	
Maximum	69	
Race/Ethnicity		
White/Caucasian	3	9.1%
Black/African American	7	21.2 %
Hispanic/Latin American	8	24.24%
Asian/Indian	13	39.39%
Native American/Alaskan		
Native Hawaiian/Pacific Islander		
Other (MIXED)	2	6.1%
Fitzpatrick		
I	2	6.1%
II	4	12.1%
III	5	15.2%
IV	7	21.21%
V	8	24.2%
VI	7	21.2%

References for the following tables and text:

Galderma - Galderma Itch Relief Gel
CeraVe - CeraVe Itch Relief Moisturizing Cream
Baseline – Immediately post application

The following tables represent the Top 2 responses of the Questionnaire, such that the original values of the results were converted to: 1 for top two responses, and 0 for others, and the statistics were calculated using the converted values

Table 1: Summary of statistics for responses to question 1 of the Questionnaire

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.91 (0.29)	0.82 (0.39)
	Median	1	1
	Min, Max	0, 1	0, 1
8 hours	N	33	33
	Mean (SD)	0.79 (0.42)	0.73 (0.45)
	Median	1	1
	Min, Max	0, 1	0, 1
12 hours	N	33	33
	Mean (SD)	0.67 (0.48)	0.70 (0.47)
	Median	1	1
	Min, Max	0, 1	0, 1
24 hours	N	33	33
	Mean (SD)	0.61 (0.50)	0.64 (0.49)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 2: Summary of statistics for responses to question 2 of the Questionnaire

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.94 (0.24)	0.88 (0.33)
	Median	1	1
	Min, Max	0, 1	0, 1
8 hours	N	33	33
	Mean (SD)	0.85 (0.36)	0.73 (0.45)
	Median	1	1
	Min, Max	0, 1	0, 1
12 hours	N	33	33
	Mean (SD)	0.73 (0.45)	0.73 (0.45)
	Median	1	1
	Min, Max	0, 1	0, 1
24 hours	N	33	33
	Mean (SD)	0.70 (0.47)	0.67 (0.48)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 3: Summary of statistics for responses to question 3 of the Questionnaire

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.88 (0.33)	0.91 (0.29)
	Median	1	1
	Min, Max	0, 1	0, 1
8 hours	N	33	33
	Mean (SD)	0.79 (0.42)	0.73 (0.45)
	Median	1	1
	Min, Max	0, 1	0, 1
12 hours	N	33	33
	Mean (SD)	0.67 (0.48)	0.70 (0.47)
	Median	1	1
	Min, Max	0, 1	0, 1
24 hours	N	33	33
	Mean (SD)	0.73 (0.45)	0.73 (0.45)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 4: Summary of statistics for responses to question 4 of the Questionnaire

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.88 (0.33)	0.76 (0.44)
	Median	1	1
	Min, Max	0, 1	0, 1
8 hours	N	33	33
	Mean (SD)	0.82 (0.39)	0.76 (0.44)
	Median	1	1
	Min, Max	0, 1	0, 1
24 hours	N	33	33
	Mean (SD)	0.73 (0.45)	0.61 (0.50)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 5: Summary of statistics for responses to question 5 of the Questionnaire

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.82 (0.39)	0.82 (0.39)
	Median	1	1
	Min, Max	0, 1	0, 1
24 hours	N	33	33
	Mean (SD)	0.70 (0.47)	0.67 (0.48)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 6: Summary of statistics for responses to question 6 of the Questionnaire

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.82 (0.39)	0.76 (0.44)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 7: Mean comparison between the two products for the top 2 responses of the questionnaire

Timepoint	Question Number	Mean of the Difference (95% Confidence Interval)	P value
Baseline	1	0.09 (-0.045, 0.23)	0.1837
	2	0.06 (-0.09, 0.21)	0.4226
	3	-0.03 (-0.17, 0.11)	0.6617
	4	0.12 (-0.07, 0.31)	0.2108
	5	0 (-0.18, 0.18)	1
	6	0.06 (-0.12, 0.24)	0.488
8 hours	1	0.06 (-0.14, 0.26)	0.5354
	2	0.12 (-0.09, 0.33)	0.2543
	3	0.06 (-0.16, 0.28)	0.5717
	4	0.06 (-0.16, 0.28)	0.5717
12 hours	1	-0.03 (-0.2, 0.14)	0.7116
	2	0 (-0.2, 0.2)	1
	3	0.03 (-0.24, 0.18)	0.7681
24 hours	1	-0.03 (-0.256, 0.1954)	0.7681
	2	0.03 (-0.2, 0.27)	0.7863
	3	0 (-0.22, 0.22)	1
	4	0.12 (-0.09, 0.33)	0.2543
	5	0.03 (-0.2, 0.26)	0.7863

Table 7 shows that every mean of the difference is inside the confidence interval. Additionally, every p-value is greater than 0.025. Based on top 2 responses of the questionnaire, we conclude that means for Galderma and CeraVe are equal.

The following tables represent the Product Preference Self-assessment Questionnaire, such that the original values of the results were converted to: 1 for the preferred product, and 0 for the other, and the statistics were calculated using the converted values.

Table 8: Summary of statistics for question 1 immediately after application

Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	0.82 (0.39)	0.76 (0.44)
	Median	1	1
	Min, Max	0, 1	0, 1

Table 9: Summary of statistics for Self-assessment Questionnaire at 24 hours

	Statistic	Galderma	Cera Ve
Question 2	N	33	33
	Mean (SD)	0.58 (0.50)	0.30 (0.47)
	Median	1	0
	Min, Max	0, 1	0, 1
Question 3	N	33	33
	Mean (SD)	0.48 (0.51)	0.33 (0.48)
	Median	0	0
	Min, Max	0, 1	0, 1
Question 4	N	33	33
	Mean (SD)	0.48 (0.51)	0.27 (0.45)
	Median	0	0
	Min, Max	0, 1	0, 1
Question 5	N	33	33
	Mean (SD)	0.52 (0.51)	0.33 (0.48)
	Median	1	0
	Min, Max	0, 1	0, 1

Table 10: Mean comparison for the self-assessment questionnaire

	Mean of the Difference (95% Confidence Interval)	**P value**
Question 1 at baseline	0.21 (-0.1, 0.53)	0.1819
Question 2 at 24 hours	0.27 (-0.05, 0.6)	0.0951
Question 3 at 24 hours	-0.15 (-0.17, 0.47)	0.3437
Question 4 at 24 hours	0.21 (-0.09, 0.52)	0.1648
Question 5 at 24 hours	0.18 (-0.14, 0.51)	0.2632

Table 10 shows that every mean of the difference is inside the confidence interval. Additionally, every p-value is greater than 0.025. Based on the Product Preference Self-assessment questionnaire, we conclude that means for Galderma and CeraVe are equal.

Table 11: Summary of statistics for the Itch Severity

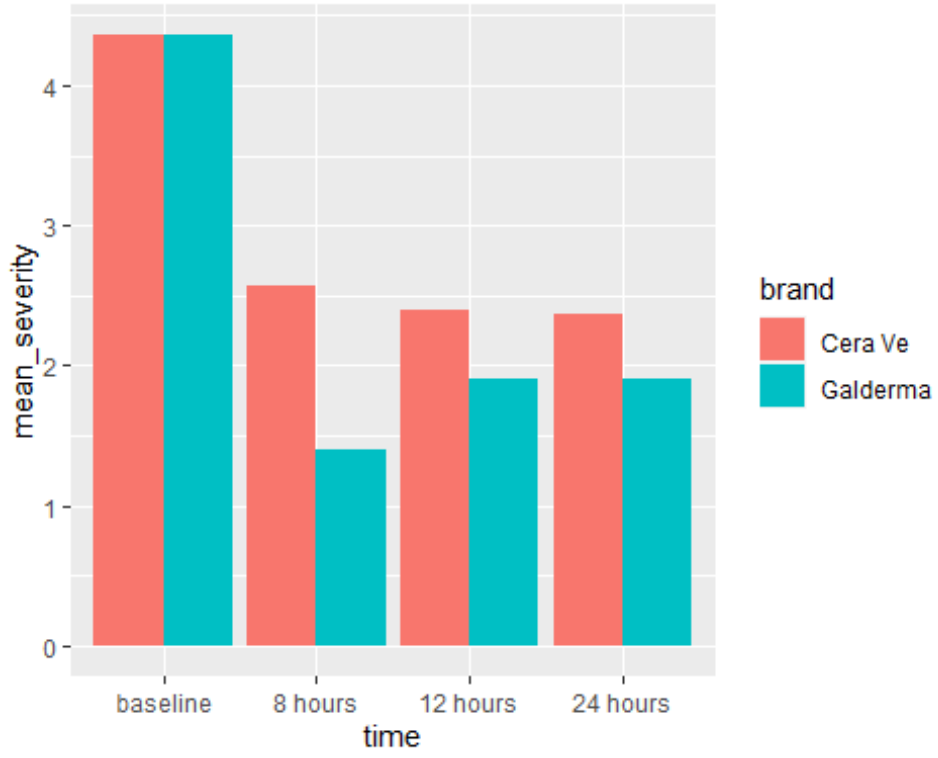
Timepoint	Statistic	Galderma	CeraVe
Baseline	N	33	33
	Mean (SD)	4.36 (1)	4.36 (1)
	Median	4	4
	Min, Max	3, 6	3, 6
8 hours	N	33	33
	Mean (SD)	1.39 (1.83)	2.58 (2.14)
	Median	0	3
	Min, Max	0, 7	0, 7
12 hours	N	33	33
	Mean (SD)	1.91 (2.52)	2.42 (2.96)
	Median	2	2
	Min, Max	0, 6	0, 7
24 hours	N	33	33
	Mean (SD)	1.91 (1.81)	2.36 (1.95)
	Median	2	2
	Min, Max	0, 6	0, 7

Table 12: Mean comparison for the Itch Severity between Galderma and CeraVe

Timepoint	Mean of the Difference (95% Confidence Interval)	P value
8 hours	-1.18 (-1.91, 0.45)	0.0023
12 hours	-0.48 (-1.18, 0.21)	0.1672
24 hours	-0.45 (-1.11, 0.2)	0.1652

Table 12 shows that every mean of the difference is inside the confidence interval. Only the p-value at 8 hours is less than 0.025, but this has low significance as these values are nearly equal. We conclude that means for Galderma and CeraVe are equal, except at 8 hours when there is weak evidence to show that means are different.

Graph 1: Mean Itch Severity post application, 8 hours, 12 hours, and 24 hours



Graph 1 shows that mean severities for the two brands are different at 8 hours, and almost the same at 12 hours and 24 hours. Graph also indicates that there are significant differences in mean itch severity for each brand at every point in time with respect to the baseline.

Table 13: Summary of statistics for the Time to Itch Relief (time in seconds)

Statistic	Galderma	CeraVe
N	33	33
Mean (SD)	28.48 (16.15)	41.84 (21.72)
Median	30	37
Min, Max	5, 66.56	7, 108

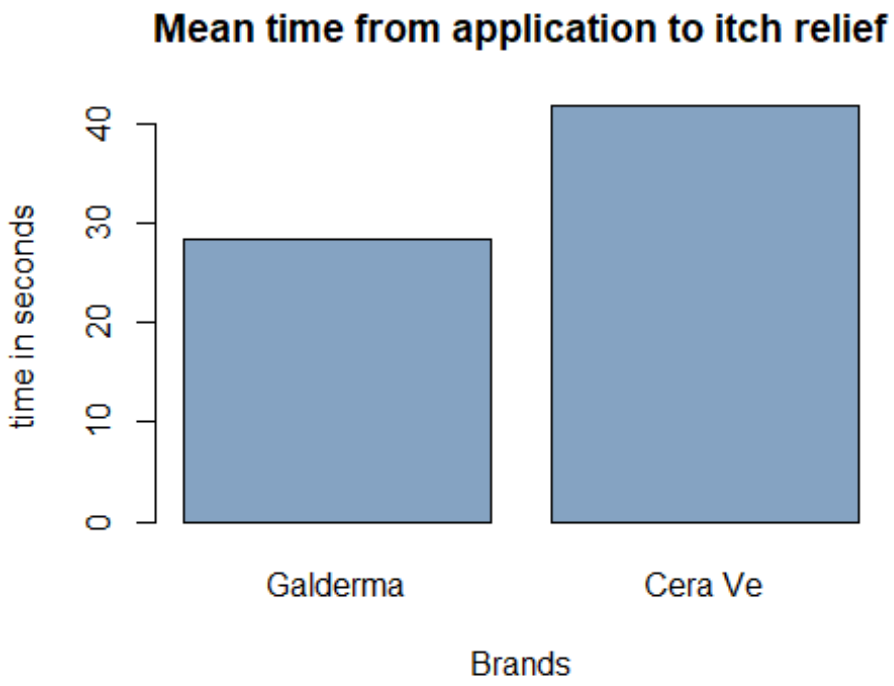
Table 14: Mean comparison for the Time to Itch Relief between Galderma and CeraVe

	Mean of the Difference (95% Confidence Interval)	P value
	-13.36 (-21.69, -5.02)	0.0026

Table 14 shows that p-value is less than 0.025. Also, confidence interval does not include zero which should not happen if means were equal. Based on the Time to Itch Relief results, we conclude that means for Galderma and CeraVe are not equal.

Mean Time from application to itch relief

Graph 2: Mean time from application to itch relief (in seconds)



Graph 2 shows that mean time from application to itch relief was lower for Galderma than CeraVe.

Summary of statistics for the time from application to itch relief (time in seconds)

	Galderma	Cera_Ve
n	33	33
Mean	28.48	41.84
sd	16.15	21.72
Median	30	37
Min.	5	7
Max.	66.56	108
10^{th} Percentile	9.2	20

The following values make up the 10^{th} percentile of the time from application to relief, as time is sorted in increasing order.

The lowest three recorded times for Galderma are: 5, 9, 9.2

The lowest three recorded times for CeraVe are: 7, 10, 20

Table 15: Summary of statistics for subjective tolerability on burning and stinging

Product	Statistic	Baseline	24 hours
Galderma	N	33	33
	Mean (SD)	1.55 (0.94)	0.79 (0.65)
	Median	1	1
	Min, Max	0, 3	0, 2
CeraVe	N	33	33
	Mean (SD)	1.52 (0.94)	1.18 (0.91)
	Median	1	1
	Min, Max	0, 3	0, 3

Table 16: Mean comparison for subjective tolerability on burning and stinging

Product	Mean of the Difference (95% Confidence Interval)	P value
Galderma	0.76 (0.49, 1.02)	1.98e-06
CeraVe	0.33 (0.1, 0.56)	0.0057

Table 16 shows that mean of the difference is inside the confidence interval for both products. Additionally, p-value is greater than 0.025 in both cases. Based on the results for subjective tolerability on burning and stinging, we conclude that the means between baseline and 24 hours are different for both products.

PROTOCOL SYNOPSIS

N° Protocol GL1899 SFRI

TITLE: EFFICACY AND TOLERABILITY OF AN ITCH RELIEF PRODUCT AND TO COMPARE WITH ITCH RELIEF PERFORMANCE Vs A COMPETITOR

SPONSOR: Galderma

INDICATION: Eczema or Atopic dermatitis (AD) prone

OBJECTIVES: EFFICACY AND TOLERABILITY OF AN ITCH RELIEF PRODUCT AND TO COMPARE WITH ITCH RELIEF PERFORMANCE Vs A COMPETITOR.

STUDY DESIGN: This will be a 24-hr randomized, blinded, split-body, intra-individual (left/right) comparison study. .

PLANNED TOTAL SAMPLE SIZE: 33 subjects

SUBJECT SELECTION CRITERIA: Subjects with AD prone or Eczema prone, with mild-to-moderate itch severity related to atopic condition on each side of the body, i.e., who do not require corticosteroid treatment

FORMULATIONS: Galderma Itch Relief Gel, formula number PP-980-4-2

CONCURRENT CONTROLS: CeraVe Itch Relief Moisturizing Cream

TEST DRUG DOSAGE: Galderma gel or CeraVe Cream will be applied once on the randomly assigned side of the body

ROUTE OF ADMINISTRATION: Topical application

MAIN PARAMETERS:

- **EFFICACY:** Itch severity will be graded separately on the left and right side of the body at baseline (pre-application), timing of itch relief, 8, 12, and 24 hours post-application. A subjective questionnaire will be used to evaluate Galderma Gel and CeraVe Cream
- **TOLERABILITY:** Objective tolerability will be assessed at baseline and 24 hours. All adverse events with relation to the test product will be reported

PROCEDURE: Included subjects with AD or eczema prone skin with mild-to-moderate itch severity related to atopic condition will apply at baseline Galderma Gel or CeraVe Cream on (including upper limbs) to opposite sides of the body as directed by pre-determined randomization. At baseline and 8 hrs, 12 hrs and 24 hrs, subjects will assess itch severity

based on 10-point scale on both sides of the body. Upon product application sequentially, timing will be recorded until subjects inform itch relief. The assessment of itch severity, onset of itch will be performed on one pre-established location on both sides of the body and subjective questionnaire. Adverse events will reported during the whole course of the study.

STATISTICAL CONSIDERATIONS: Paired T-test

1. BACKGROUND AND RATIONALE

Atopic dermatitis (AD) is a skin disease of unknown etiology with a genetic predisposition, associating chronic inflammation of the skin and xerosis. The ceramide-based emollient is known to have been shown to be beneficial in reducing itch, especially on AD or eczema prone subjects.

The aim of this study is to know if these pharmacological results can be reproduced in AD subjects using Galderma Gel.

2. OBJECTIVES OF THE STUDY

To evaluate in subjects suffering from AD or Eczema prone

- The efficacy of the Galderma Gel (GG) when used as an itch relief gel
- The tolerance of the product
- Comparison with CeraVe Itch Relief Moisturizing Cream

3. EXPERIMENTAL DESIGN

3.1 Overall design

This will be a 24-hr randomized, blinded, split-body, intra-individual (left/right) comparison study.

Visit (24hrs 12)

Baseline

24hrs 12

Treatment

3.2 Number of subjects

Minimum 30 evaluable subjects.

4. SUBJECT SELECTION CRITERIA

4.1 *Inclusion criteria*

- Male or female subjects (majority females) of at least 18-year-old.
- Inclusive mix of Fitzpatrick skin types I-VI and ethnicities, minimum 5 subjects of racial minorities (African American, Asian, Latino, etc.).
- Male and Female subjects with AD or Eczema prone
- Subjects who are willing to undergo 3-day washout period.
- Subjects with mild-to-moderate itch severity at baseline (score 3-6 based on a 10-point scale; where 0 = none, 1-3 = mild, 4-6 = moderate, 7-9 = severe), on each side of the body, with no more than 1-point difference between both sides.
- Subjects who are free of any dermatological or systemic disorder (other than eczema/atopic dermatitis), which would interfere with the results, at the discretion of the Investigator.
- Subjects in good general health.
- Subjects who complete a preliminary medical history.
- Subjects who will read, understand, and sign an informed consent document and has received a copy.
- Subjects who understand the language used in the research center; subject without intellectual/mental inability or incapacitation
- Subjects willing to comply with protocol requirements, following the study rules and a fixed schedule.
- Subjects who will be able to cooperate with the Investigator and research staff, have the test product applied according to the protocol and complete the full course of the study.
- Subjects who have not participated in any clinical study involving the same test sites in the past 7 days.
- Subjects who will agree to discontinue use of their current body personal care products (e.g., cleansers, lotions, sunscreen) for the duration of the study and to not introduce any new products, with the exception of the test products.
- Subjects who will agree to refrain from shower or bathe during the duration of the study (from baseline to 24-hour visit)
- Subjects who agree not to sunbathe/tan and agree to avoid sun (UV) exposure as much as possible for the duration of the study.

4.2 *Exclusion criteria*

- Subjects with uncontrolled Eczema
- Subjects who have had a history of acute or chronic disease that could interfere with the study
- Subjects with no symmetrical itch severity related to AD or Eczema
- History of cancer or other serious/progressive disease/personal history of skin cancer or family history of melanoma that could have an impact on the evaluated area, per the discretion of the Investigator.
- Subjects who have a medical treatment or will be vaccinated or expecting to be vaccinated during the study, that makes the subject ineligible or place him/her at undue risk or negatively impacts the outcome of the study per the discretion of investigator.
- Individuals with planned hospitalization during the study period.
- Individuals who indicate that they are pregnant, planning a pregnancy or nursing.
- Individuals who have been medically diagnosed with Type I Diabetes.
- Individuals who have a known history of hypersensitivity to any cosmetics, personal care

products, and/or fragrances.

- Subjects who have been treated with topical corticosteroids or antiseptics within 3 days prior to entry into the study.
- Subjects who have been treated with oral or topical antibiotics within 1 week prior to entry into the study.
- Subjects who began or changed any systemic treatment for concomitant diseases within 1 week prior to entry into the study.

4.3 Informed consent from subjects

The investigator will obtain written informed consent from each subject, after adequate explanation to the aims, methods, anticipated benefits, and potential hazards of the study. The investigator will explain that the subjects are completely free to refuse to enter the study or to withdraw from it at any time for any reason, Appendix I.

5. TRIAL PRODUCTS

5.1 Assignment of the trial products

Subjects will apply a single application of Galderma Gel or CeraVe Cream to opposite sides of the body as directed by pre-determined randomization. The application of Galderma or CeraVe product to each side are to be assigned sequentially in the order in which the subjects are enrolled. The investigator will enter the randomization number in the appropriate place on each subject's case report form.

5.2 Test products

The ingredient list for the test product is provided as Appendix II.

- Test product: Galderma Itch Relief Gel
  Formula number: PP-980-4-2
- Comparative product: CeraVe Itch Relief Cream
  Formula number: N/A

5.3 Dosage and administration

No test products or any product should be applied on the test areas 3 days prior to day of the visit.

Subjects will be instructed on how to apply each test product by the site technician at baseline, prior to the study start.

- Galderma Itch Relief Gel: squeeze a small amount, using the roller applicator to apply the product to the assigned are until fully absorbed.
- CeraVe Itch Relief Cream: using fingers to apply an appropriate amount to the assigned area until fully absorbed.

Under observation of the site technician, Galderma Gel and CeraVe Cream will be applied by the subjects on the randomly assigned side of the body.

Each subject will receive a copy of written instructions which details the proper method of assessment of itch relief of the test products (Appendix III).

6. PROCEDURE

1. Subjects will report to the facility a minimum of three (3) days prior to the start of the study.
2. Prior to beginning any study related activities, subjects will be given an informed consent form, HIPAA form, Code of Conduct form, and sponsor provided authorization and release form to read.
3. Once subject has completed reading, they will be interviewed to ensure their understanding of the aforementioned forms and be given the opportunity to ask any study related questions.
4. Subjects who agree to sign the aforementioned forms will be asked to complete a medical history form. Subjects declining to sign any of the forms will be dismissed from the study.
5. Subjects will be screened on the basis of the subject selection criteria. Subjects failing to meet criteria will be dismissed from the study.
6. Subjects will be instructed to discontinue using their current personal care products (e.g., lotions, cleansers, sunscreen) on their body for the duration of the study and to not introduce any new products, with the exception of the test product provided by the study site.
7. Enrolled subjects will begin the washout period. They will be provided with a neutral soap (Neutrogena) to be used for cleansing body for the washout period.
8. Following the three-day washout period, subjects will return to the testing facility. Subjects will be instructed to wear clothing that does not cover their test areas on their body on evaluation day.

Day 0 (baseline)

1. Subjects will be instructed on how to assess itch severity based on a visual analog scale (10- point)
2. Subjects will then identify the area on both symmetrical sides of the body that experiences itchiness. Subjects must meet itch severity criteria of mild-to-moderate (score 3-6) at each symmetrical side of the body to continue on the study, with no more than 1-point difference between both sides. Otherwise, subjects will be missed from the study participation.
3. Subjective tolerability assessment will be performed at baseline.
4. Subjects will be assigned the test products and the side of the body each should be used based on a computer-generated randomization.
5. Subjects will be instructed by the site technician on how to use and apply each test product appropriately.
6. Under the observation of site technician or supervisor, subjects will first apply one test product to the assigned side of the body. Upon first product application, the technician will start the stopwatch until the subjects announce that their itch is relieved. Timing for itch relief on this side will be recorded. Subjects will then fill out the questionnaire for this side of the body.
7. Subjects and site technician will repeat step 14 on the other side of the body, accordingly.
8. Subjects will be informed not to apply any product to the test areas for the remaining of the study. Subjects will be informed not to take any medical treatment or cosmetical product including shower or bathe until the study completion. They will be provided with diary to assess itch severity at 8 hours and 12 hours at home, a questionnaire to be completed at 8 hours and 12 hours at home. Subjects will be instructed to return the completed diary and questionnaire at their 24-hour visit.
9. Subjects will be dismissed form the testing site and informed to return after 24 hours.

Day 1 (24 hours)

10. Subjects will then assess itch severity at their test site on both sides of the body, followed by filling out the questionnaire at 24 hours.

Subjective tolerability assessment will be performed at day 1. Once completed, subjects will be dismissed from the study.

7. CONCOMITANT MEDICATIONS AND TREATMENTS DURING THE STUDY

Any medical treatment or cosmetical product is not allowed during 24-hour duration of the study. This includes, but not limited to, oral or topical antibiotics, oral antihistamines, oral or topical anti-inflammatories, UV-treatments, topical cortisteroid, cosmetic emollients or moisturizer, etc.

If one of these medications or cosmetical products is necessary during the course of the study, the subject will be withdrawn from the study.

8. STUDY DESIGN SUMMARY

BASELINE TREATMENT

□----------□

DAY	3-Day Washout Prior to Day 0	Day 0	8 hrs	12 hrs	Day 1 □ 0.5
Selection of subjects	X	X			
Subject identification	X	X			
Signed informed consent	X				
Medical and treatment history	X				
Subject Assessment of Itch (Severity)		X	X	X	X
Timing of each relief post-application		X			
Safety study parameters		X			X
Subject instructions		X			
Product dispensing		X			
Local tolerance		X			
Adverse events		X	-----	-----	X
Concomitant diseases and medications		X			X
Product application		X			
Self-assessment questionnaire		X	X	X	X
Compliance					

9. STUDY PARAMETERS

No product of any kind should be applied on the test areas the day of the visit. The conditions of assessment (light, temperature, etc.), should be identical at each study visit.

9.1 Primary efficacy and tolerability parameters

The rating of itch and onset of itch will be performed by subjects. The assessment will be made on each of the pre-established site of application as follows:

Itch severity will be assessed using a 10-point visual analog scale (VAS, where 0-3=mild, 4- 6=moderate, 7-9=severe) at baseline (pre-product application), 8 hours, 12 hrs, and 24 hrs post- application. Half-point scores may be used as necessary to more accurately describe the skin condition. Timing till itch relief upon product application will be capture on each side of the test side, respectively.

Tolerability will be performed by subjects at baseline and day 1 (24 hours). Subjects will report the degree of irritation parameters: burning and stinging, based on a 4-point scale (where 0=none, 1=mild, 2=moderate, 3=severe). Half-point scores may be used as necessary to more accurately describe the clinical condition.

9.2 Self-assessment questionnaire

Each subject will be instructed to complete a self-assessment questionnaire pertaining to each test side of the body assigned to each test product, provided by the Sponsor (Appendix IV), once itch is relieved post-application, after 8, 12, and 24 hours.

10. STATISTICAL ANALYSIS

For the evaluations over the 24-hour test periods, paired-t tests will be used to compare individual scores at each post-baseline time point relative to their respective baseline scores for both efficacy and tolerability scores. Additionally for comparisons between the treatment cells were made using the null hypothesis that the mean change from baseline was equal between the 2 treatment cells at post-baseline time points. For timing till itch relief, data will be calculated as average and statistical analysis be performed between the 2 treatment groups. For questionnaires, the onset of itch response frequencies will be compared between the 2 treatments. The test null hypothesis will be that the proportion of the combined designated favorable responses (Agree Strongly and Agree Somewhat) was equal between the 2 treatment cells. An alpha of 0.05 will be used for all analyses.

11. SAFETY

As with the introduction of any new topical product, burning, stinging, itching, redness, or irritation may occur at the test sites. There also may be risks and discomforts, which are not yet known.

Adverse Events

Definitions

Adverse events (AE)

An adverse event (AE) is defined as any untoward medical occurrence in a subject taking part in the clinical study, and which does not necessarily require a causal relationship with the investigational product and/or a clinical trial procedure.

An AE can be any unfavourable and unintended sign (including an abnormal laboratory value), symptom, or disease temporally associated with the use of the investigational product, whether or not related to this product.

When an AE has a likely or very likely causal relationship with the investigational product and/or a clinical trial procedure, it is named undesirable effect or related AE (see Section 3).

11.1 *Local tolerability signs and symptoms (only applicable for cosmetic safety studies)*

In cosmetic studies, local skin tolerability includes some expected functional and/or physical signs on the application area, observed by the Investigator or reported by the subjects (see Appendix). Those signs are collected in the final report based on scales or a diary. If the severity of a local skin tolerability sign or symptom, is such that the product application is permanently discontinued and/or a corrective concomitant treatment (except moisturizer or emollient) is prescribed, it is recorded as an undesirable effect (related AE).

11.2 *Serious Adverse Events (SAE) and serious undesirable effect/related SAE*

A Serious Adverse Event (SAE) is any adverse event which results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Notes:

The term “immediate vital risk” refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event that hypothetically might have caused death if it was more severe.

Inpatient hospitalization is considered to have occurred if the subject has had to stay for a night at the hospital. Hospitalization solely for the purpose of a diagnostic test (even if related to an AE), elective hospitalization for an intervention that was already planned before subject enrolment in the clinical trial, admission to a day-care facility, social admission (e.g., if the subject has no place to sleep), or administrative admission (e.g., for a yearly examination) should not be considered as a SAE.

A serious undesirable effect/related SAE is defined as any SAE which the Investigator classifies as having a reasonable possibility for a causal relationship with the investigational product and/or the clinical trial procedure.

11.4. *Severity assessment*

For all AEs occurring during the clinical trial, the Investigator is to classify and report the intensity of AEs using the following definitions as a guideline:

- Mild: awareness of signs and symptoms, but easily tolerated
- Moderate: discomfort, enough to cause interference with usual activity
- Severe: incapacitating, with inability to work or perform usual activity.

11.5. *Causality assessment*

The Investigator is to assess the causal relationship (causality) between an adverse event and the investigational product and/or the clinical trial procedure according to the following definitions (Decision

of 25 November 2013 on Guideline on Annex I to Regulation (EC) No 1223/2009 (2013/674/EU) - Causality assessment of undesirable effect caused by cosmetic products):

- Very likely
- Likely
- Not clearly attributable
- Unlikely
- Excluded

Medical judgment should be used to determine the relationship, considering all relevant factors including the pattern of reaction, temporal relationships, positive de-challenge or re-challenge, relevant medical history, and confounding factors such as co-medication or concurrent diseases.

11.6. *Collection, management and reporting procedures for adverse events/undesirable* effects and serious adverse events/effects

The period of collection of adverse events starts from the time of signature of the Informed Consent Form (ICF) by the subject *(and/or, for subjects who are minor, by the parents/legal representatives)* until the end of the subject's participation in the clinical study.

If a Serious Adverse Event (SAE) is on-going at the final clinical trial visit, it should be followed by the Investigator until it has resolved or has reached a stable condition.

After the subject completes the clinical study, the Investigator should also inform the Sponsor (see Sponsor's contact details below) if he/she becomes aware of an SAE involving a subject who has participated in the clinical study.

At each post-enrollment visit, the Investigator will question the subject about AEs using an open non-persuasive question to elicit reporting of AEs, for example "*Have you noticed any change in your health since the last visit?*" Direct questioning and examination will be performed when appropriate.

The Investigator will obtain and maintain in the subject's files all pertinent medical records, and (if applicable) information and medical judgment from colleagues who assisted in the treatment and follow-up of the subject. If necessary, the Investigator will contact the subject's personal physician or hospital staff to obtain further details.

As a minimum, Investigators are requested to report in the Case Report Form (CRF) and in the report all related adverse events (i.e., undesirable effects) and all Serious Adverse Events, whether related or not.

11.7 *Management and reporting procedures for Serious Adverse Events*

The Investigator is to take the following steps:

1. Take prompt and appropriate medical action, if necessary. The safety of clinical trial subjects is the first priority
2. Ensure the AE is classified as an SAE. Immediately inform the Sponsor's representative of the event by email or fax (see contact details below) and discuss further actions to be taken:

   E-mail: pharmacovigilance@galderma.com
3. Complete the Serious Adverse Event (SAE) form provided by the Sponsor's representative **Within 24 hours**, fax or send by e-mail **to the Sponsor's representative** the completed SAE form, accompanied any other relevant information (e.g., test results or medical records).
4. Monitor, record and send to Sponsor's representative the progress of the event until it resolves or reaches a stable outcome, with or without sequelae (send the updated SAE

form with follow-up information and any other relevant information to Sponsor's representative).

5. Obtain and maintain in the subject's file all pertinent medical records, information, and medical judgments from colleagues who assisted in the treatment and follow-up of the subject. If necessary, contact the subject's personal physician or hospital staff to obtain further details.

6. If applicable, comply with the regulatory requirement(s) related to the reporting of SAEs to the Institutional Review Board (IRB) / Independent Ethics Committee (IEC).

11.9. Pregnancy

Pregnancy itself is not to be considered as an adverse event. If a pregnancy occurs during the clinical trial, **the product application should be stopped immediately**, the subject should be withdrawn from the clinical study and Sponsor's representative (see Sponsor's contact details above) should be informed **within 24 hours.**

Pregnancy must be recorded as a reason for discontinuation in the exit form of the CRF.

No specific follow-up of pregnancy is required, except if it is a regulatory requirement in the country(ies) where the clinical trial is conducted.

11.10. Process for suspected allergic reactions

In case of a positive reaction (suspicion of allergy) in the clinical study, the Investigator will inform the Sponsor if the reaction occurs with the Sponsor's company product(s) following the procedure below. The Investigator will also inform if products other than the Sponsor's product(s) were concomitantly tested in the clinical trial, and if there were positive reaction(s) for these other products.

- *Stop the investigational product.*
- Take a picture of the affected area and the surrounding skin.
- Report the event by email **within 24 hours** to the Sponsor's representative (see Sponsor's contact details above). The Sponsor will then contact you to explain the general procedure to be followed.
- Follow the procedure detailed below:

1. After all signs and symptoms of the event have resolved and after a minimum of at least two weeks from last dose application perform a re-challenge test with the assigned study product.
2. Ensure the subject has not been under any treatment with corticosteroids or antihistaminics within the week before testing.
3. Ensure that the skin on the back has not been irradiated by the sun or artificial ultraviolet sources within the week before testing.
4. Apply an appropriate quantity of the study product to fill in the cupule of the test chamber and then to the upper part of the back skin (or the inner forearm if more appropriate) either at right or left from the central line. If no test chamber is available on site, patch test units will be provided by the Sponsor. The use of semi-occlusive conditions can be preferred depending on the irritant potential of the study product and the intensity of the reaction which was reported. The method to be used should be discussed with the Sponsor.

Choose a skin site that was not previously involved in the inflammatory skin reaction. Cover it for 48 hours with a hypoallergenic tape

5. Subject should be informed about avoiding exercise, showers, etc. to keep the test system dry
6. After 48 hours, remove the tests and evaluate the site reactions:

- 30 minutes after patch test removal (1st reading),
- 48 hours after patch removal (2nd reading).
- 72 or 96 hours after patch removal (3rd reading).

Pictures of the tested areas will be taken systematically at each reading and properly documented

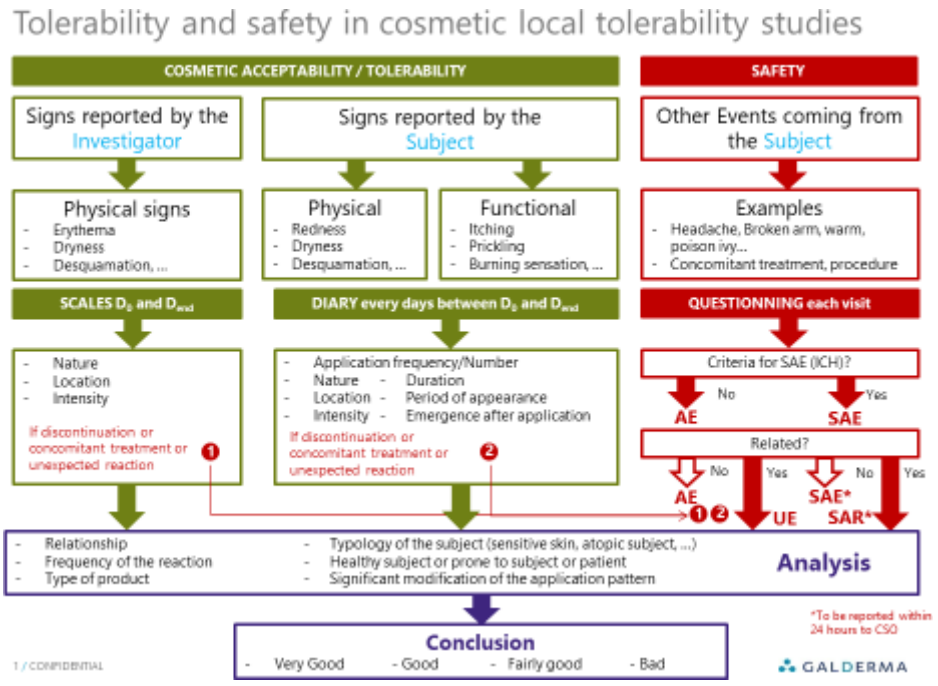
7. Use the following scoring system (International Contact Dermatitis Research Group) at each reading:

Score	**Morphology**	**Interpretation**
-	No reaction	Negative
?	Erythema only, no infiltration	Doubtful reaction
+	Erythema, infiltration, possibly discrete papules	Weak positive reaction
++	Erythema, infiltration, papules, vesicles	Strong positive reaction
+++	Erythema, infiltration, confluent vesicles, bullae	Extreme positive reaction
ir	Inflammation sharply limited to the exposed area, lack of infiltrate, small petechiae, pustules, and efflorescences other than papules and vesicles	Irritant reaction
Nt		Not tested

8. At last reading, the investigator will provide an assessment regarding a possible sensitization reaction using the following scale:

Sensitization Reaction	
0	Negative (absence of reaction or might be irritative reaction)
1	Equivocal
2	Positive

2. Report the results from the re-challenge test as directed by the Sponsor and document with photographs.
3. In case of absence of reaction after quotation with the ICDRG scale, the subject may resume product application, if appropriate.
4. After quotation with the ICDRG scale, if the re-challenge is positive, equivocal or in favour of an irritation, notify the Sponsor immediately. Except specific situations, a new series of patch test will be initiated as directed by the Sponsor (with individual ingredients at different concentrations and possibly negative and positive controls) after a minimum of additional two weeks (but not later than 6 months) and after all signs and symptoms have resolved. The patch tests will be placed on a back skin site (or the inner forearm if more appropriate) distant from the site of re-challenge test (e.g., at the left upper back skin if the re-challenge test was done on the right). Follow the same procedure for the patch test as for the re-challenge.



5. REFERENCES

1. Matthew J. Zirwas MD FAAD• and Sylvia Barkovic BNAnti-Pruritic Efficacy of Itch Relief Lotion and Cream in Patients With Atopic History: Comparison With Hydrocortisone Cream; J Drugs Dermatol. 2017;16(3):243-247.

PART 2

1. *STUDY DOCUMENTATION, CASE REPORT FORMS AND* RECORD KEEPING

1.1 Investigator files / Retention of documents

The investigator must maintain adequate records to enable the conduct of the study, and to enable the study to be fully documented. Copies of protocols, case report forms, originals of test result reports, product dispensing logs, correspondence, records of informed consent and other documents pertaining to the conduct of the study must be kept on file by the investigator for a period of time specified by the local law for the preservation of subject documents. No study document should be destroyed without prior written agreement between the sponsor and the investigator. Should the investigator wish to assign the study records to another party, or move them to another location, the Galderma clinical trial monitor must be notified first.

APPENDIX I

INFORMED CONSENT FOR PARTICIPATION OF THE GALDERMA STUDY (PROTOCOL N° GL1899 SFRI)

By my signature on the last page, I..... acknowledge that

I have freely and voluntarily agreed to participate in a research study of an investigational product. I give my consent after being informed of the nature of the products involved and the known risks and adverse effects that may result from their use.

I understand that the research study for which I am volunteering to participate will evaluate an investigational treatment for my skin condition.

1. PROCEDURES: I understand that the study will last 24 hrs. At the initial visit, I will be screened by my research Investigator to determine whether or not I might qualify for this research program. A brief history will be performed. If I do qualify for the program, I will take the test product as directed and follow the subject instructions as follows: I will apply Itch Gel or Itch Cream to opposite sides of the body as directed as instructed by the research staff. I will complete a questionnaire at baseline, 8 hrs, 12hrs and 24 hrs after application of the product.

At the termination visit, I agree to return the questionnaire. A final history and evaluation will then be completed by my Investigator.

I understand that 3 days before the study, I must not use any skincare product including moisturizer, besides the Neutrogena bar soap provided for 3-day washout period. I understand that during the study, I must refrain from any medication or cosmetic treatment including shower or bathe. I understand that the use of my usual products is not permitted during this trial, but that I must report to my Investigator on the following visit if I used any.

(If female): I acknowledge that I am not pregnant and that I do not intend to become pregnant during the study.

2. BENEFITS: A potential benefit of participation in the study is that I will be treated with products which may improve my skin itch. An additional benefit is the knowledge that this research may help develop better anti itch product. I understand that the medication, evaluations, and professional care required for completion of this study are provided at no cost.

I agree that a financial compensation of $200 will be available for participation in and completing this study. If I terminate the study, I will receive a prorated compensation.

3. RISKS AND SIDE EFFECTS: I recognize that taking any product has potential risks. A specific risk is that the product provided in this study will be ineffective in improving my skin condition or my quality of life. I acknowledge that no guarantees, have been made to me as to the results or improvements which may be obtained from my participation in the study. The reasonably foreseeable risks and discomforts include failure to improve my skin condition possible worsening of my skin condition, possible development of skin irritation or allergy. My Investigator will have the option of removing from this study if I develop serious problems.

4. ALTERNATIVE THERAPY: If I choose not to participate in this study, many alternative therapies and products are currently available for the treatment of my skin itch condition. These treatments can be explained by my Investigator, with the possible benefits and risks of each.

5. COMPENSATION FOR INJURY: Payment for the treatment of research-related physical injury or hospitalization will be the responsibility of sponsor if these expenses are not covered by other resources. I agree that no financial compensation will be voluntarily provided, either by sponsor or by my research Investigator, for any such injury or damage. This agreement to provide free medical treatment does not include treatment for any complication of my previous illnesses or for any other illnesses I might experience in the course of this study, if the complications are not the result of the research activities.

6. WHO TO CONTACT IN CASE QUESTIONS ARISE: If an adverse reaction or injury as a result of this study occurs, or requires more information, I may contact my Investigator

7. ADDITIONAL INSTRUCTIONS: In giving my consent, I acknowledge that my participation in this study is voluntary and that I am free to withdraw my consent and to stop my participation (or the participation of my child) in the study at any time, without loss of benefits to which I am otherwise entitled. This participation may also be terminated without my consent if my Investigator feels that it is my best interest, or in the best interest of the research project, or if I fail to cooperate or follow the subject instructions upon request, I will have all the final clinical evaluations.

I understand, and agree to follow, the instructions fully and carefully, and to promptly report to my research Investigator any information relevant to the study. I have been informed of the purpose of this study, the nature of the test products involved, and any adverse effects that may result from its use. I have been given an opportunity, to ask freely, questions about this study, and all my questions have been explained and answered to my satisfaction and plain understanding. My Investigator and I have discussed the known risks involved in my participation, and all my additional questions have been answered.

I certify that I have read and fully understand this information and that I voluntarily and willingly sign this consent form. Therefore, I freely agree to participate (or make my child participate) in this research study program.

I have received a copy of this form.

.....	.....	.....
Subject’s Signature	Date	Subject's Name (Print)

.....	.....	.....
Investigator's Signature	Date	Investigator's Name (Print)

Authorization and Release Form

I hereby for good and valuable consideration grant to SF Research Institute Inc., the study sponsor and their respective affiliates, agencies, agents, employees, and assigns (collectively, "Authorized Entities"), the unrestricted, royalty free, irrevocable and perpetual right and permission to reproduce, distribute, broadcast and/or otherwise use for advertising and other commercial/noncommercial purposes: (i) my name, likeness, image, video, and any other biographical or personal information ("Personal Content"); and (ii) any statement or endorsement, or any portions thereof ("Testimonial(s)"), made by me relating to the study sponsor's products ("Products"), in any and all media now known or later developed, worldwide in perpetuity, without further compensation or approval by me.

I hereby assign to the Authorized Entities all of my world-wide right, title, and interest, including my copyright interests and all renewals, reissues, and extensions thereof, in and to the Personal Content and Testimonial(s), including without limitation, any photographic portraits, sound recordings and video performances of and/or by me in connection with the Personal Content and/or Testimonial(s).

I am at least 18 years of age, and competent to contract in my own name. I have read and understand this Authorization and Release.

_____

Printed Name of Adult Study Subject

_____

Signature of Adult Study Subject Date

_____

Printed Name of Person Explaining Release Form

_____

Signature of Person Explaining Release Form Date

Copy of consent form given to subject on _____(date) by _____(initials)

APPENDIX II

INGREDIENT LIST

Itch Relief Gel
Formula No: PP-980-4-2

Active Ingredient:

COLLOIDAL OATMEAL 0.5%

Inactive Ingredient:

ARGININE BUTYLENE
GLYCOL C13-15
ALKANE CARBOMER
CERAMIDE NP
ETHYLHEXYLGLYCERIN GLYCERIN
HYDROXYPHENYL PROPAMIDOBENZOIC ACID LAURYL
LACTATE
MALTODEXTRIN
OPHIOPOGON JAPONICUS ROOT EXTRACT PENTYLENE
GLYCOL
PHENOXYETHANOL
PROPANEDIOL SODIUM
GLUCONATE SODIUM
HYDROXIDE SODIUM
PCA
TOCOPHEROL (VITAMIN E) WATER
XANTHAN GUM

APPENDIX III

INFORMATION FOR SUBJECTS

Protocol number: GL1899 SFRI

Information about the test products

Your Investigator gave you 2 kinds of products: An Itch Relief Gel and an Itch Relief Moisturizing Cream.

How to use the test products during the study:

The Anti-Itch Gel will be applied (using the attached roller applicator) on the randomly assigned side of the body. The Anti-Itch Moisturizing Cream will be applied (with the fingers) one time only on the randomly assigned side of the body.

No other moisturizer is permitted during the study.

Do not forget:

* During the study period, not apply any other medication or product including shower or bathe.

* You will see your research Investigator on day 1 and 24 hrs after.
  At the last visit, you will return all completed questionnaire

Assessment of Degree of Itch Severity

Itch intensity assessment based on 10-point scale, it will be performed at baseline (pre- product application), 8 hours, 12 hrs, and 24 hrs post-application. Itch relief will be assessed by the subjects upon product application on each side of the body, to capture time duration for itch relief.

Itch severity will be assessed using a 10-point visual analog scale (VAS, where 0-3=mild, 4-6=moderate, 7-9=severe). Half-point scores may be used as necessary to more accurately describe the skin condition.

You will be required to have at least mild-to-moderate itch severity related to atopic condition on each side of the body to qualify with no more than a 1-point difference between sides.

COMMENTS:

Thank you for joining this study.

APPENDIX IV

SELF-ASSESSMENT QUESTIONNAIRE

Once timer stops for left side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The product quickly soothed my itchy skin					
My skin felt an instant cooling sensation upon application					
The product immediately helped calm my eczema-prone skin					
This product delivers a great application experience with its unique packaging					
I like the product texture					
I had the most pleasant experience using the product					

Once timer stops for right side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The product quickly soothed my itchy skin					
My skin felt an instant cooling sensation upon application					
The product immediately helped calm my eczema-prone skin					
This product delivers a great application experience with its unique packaging					
I like the product texture					
I had the most pleasant experience using the product					

Once finished with both left and right questionnaire	Left	Right	No preference
Which product provides better immediate relief?			

After 8 Hours for left side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The product continuously relieves my itch					
My skin does not feel irritated since the product application					
The product helps soothe my eczema-prone skin					
My skin still feels comfortable					

After 8 Hours for right side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The product continuously relieves my itch					
My skin does not feel irritated since the product application					
The product helps soothe my eczema-prone skin					
My skin still feels comfortable					

After 12 Hours for left side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The product continuously soothes my eczema-prone skin					
This product consistently keeps my skin comfortable					
My itchiness is still much relieved					

After 12 Hours for right side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
The product continuously soothes my eczema-prone skin					
This product consistently keeps my skin comfortable					
My itchiness is still much relieved					

After 24 Hours for left side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
This is the best product to relieve itch					
I have not noticed an urge to scratch my skin					
My skin comfort is completely maintained					
The product is a game changer for my itchy skin					
The product keeps my irritated skin at ease throughout the day					

After 24 Hours for right side	Strongly Agree	Agree	Neither Agree nor Disagree	Disagree	Strongly Disagree
This is the best product to relieve itch					
I have not noticed an urge to scratch my skin					
My skin comfort is completely maintained					
The product is a game changer for my itchy skin					
The product keeps my irritated skin at ease throughout the day					

	Left	Right	No preference
Of the 2 samples, which one do you prefer overall?			
Which one would you recommend?			
Which one would you purchase?			
Which product delivered more than your itch relief expectations?			

APPENDIX V

RAW DATA

1.1 Self-Assessment Questionnaire at 0 Hr

Galderma

CCID	0 HR					
	Q1	Q2	Q3	Q4	Q5	Q6
1	2	2	2	2	2	2
2	2	2	2	2	2	2
3	2	2	2	2	2	2
4	1	1	1	1	1	1
5	1	1	1	2	2	1
6	2	2	2	2	2	2
7	1	1	0	1	1	1
8	1	0	1	1	1	1
9	1	0	1	0	1	1
10	2	2	2	2	2	2
11	2	2	2	1	0	2
12	2	2	2	2	1	1
13	2	2	2	2	0	0
14	1	2	2	1	1	1
15	2	2	2	2	2	2
16	1	1	0	0	1	1
17	2	1	2	1	1	1
18	1	2	1	2	1	1
19	1	1	1	1	1	1
20	2	2	2	2	2	2
21	2	2	1	2	1	2
22	2	2	2	2	2	2
23	2	2	2	2	2	2
24	2	2	2	2	2	2
25	0	2	2	2	2	2
26	1	1	1	1	1	0
27	2	2	2	2	1	2
28	2	2	2	2	2	2
29	-1	1	-1	1	0	0
30	1	1	1	0	0	0
31	2	1	2	2	1	2
32	2	2	1	1	0	0
33	-2	1	-1	0	-1	-2

CeraVe

CCID#	0 HR					
	Q1	Q2	Q3	Q4	Q5	Q6
1	1	2	2	2	2	2
2	2	2	1	2	2	2
3	2	2	2	2	2	2
4	1	2	1	1	1	1
5	2	2	2	2	2	2
6	2	2	2	1	2	2
7	1	1	1	1	1	1
8	1	2	1	1	1	1
9	1	1	1	1	1	1
10	1	1	1	1	1	1
11	0	1	1	2	2	2
12	2	2	2	2	2	2
13	2	0	0	-1	2	2
14	1	1	0	1	1	0
15	-1	1	1	-2	0	0
16	0	0	0	1	1	1
17	1	2	1	1	1	1
18	1	1	1	-1	0	0
19	2	2	2	2	2	2
20	1	1	1	0	0	0
21	1	1	1	2	1	1
22	1	0	1	0	1	0
23	1	1	1	1	1	1
24	1	1	1	1	1	1
25	0	2	2	2	0	2
26	2	2	2	2	2	2
27	2	1	2	0	1	1
28	1	1	1	1	1	1
29	1	1	1	0	1	0
30	1	1	1	2	1	2
31	2	2	2	2	2	2
32	0	1	1	1	0	0
33	0	0	1	-1	0	-1

Self-Assessment Questionnaire at 8 Hr

Galderma

CCID	8 HR			
	Q1	Q2	Q3	Q4
1	0	0	1	0
2	2	1	2	2
3	1	2	2	2
4	2	2	2	2
5	2	2	2	2
6	1	2	2	2
7	0	0	0	0
8	0	1	1	1
9	1	0	0	1
10	2	2	2	2
11	1	2	2	2
12	-2	-2	-2	-2
13	2	2	2	2
14	1	2	1	1
15	2	2	2	2
16	1	2	0	0
17	2	2	2	2
18	1	1	2	1
19	1	1	1	1
20	1	2	2	2
21	1	1	1	1
22	1	1	1	1
23	1	1	1	1
24	2	2	2	2
25	2	2	2	2
26	2	2	2	2
27	0	2	0	0
28	2	2	2	2

29	0	1	1	1
30	1	1	0	1
31	2	2	1	2
32	2	2	2	2
33	-1	-1	-2	-1

Cera-Ve

CCID#			8 HR	
	Q1	Q2	Q3	Q4
1	2	2	2	2
2	1	2	2	2
3	-1	-1	2	2
4	1	1	1	1
5	2	2	2	2
6	1	2	2	2
7	1	1	1	1
8	0	0	1	0
9	1	1	1	1
10	1	1	1	1
11	2	2	2	2
12	2	2	2	2
13	-2	-2	-2	-2
14	0	0	0	1
15	1	1	1	1
16	0	2	0	2
17	1	1	1	2
18	-1	0	0	0
19	1	1	1	1
20	1	1	0	0
21	1	1	1	1
22	0	0	0	0
23	1	0	0	0
24	2	2	2	2
25	2	2	2	2

26	1	1	1	1
27	1	2	1	2
28	2	2	2	2
29	0	0	-1	-1
30	1	1	1	1
31	2	2	2	2
32	2	2	2	2
33	0	-2	-1	-1

Self-Assessment Questionnaire at 12 Hr

Galderma

CCID	12 HR		
	Q1	Q2	Q3
1	2	2	2
2	1	1	1
3	1	1	1
4	2	2	2
5	2	2	2
6	2	2	2
7	0	0	0
8	1	1	0
9	0	1	1
10	2	2	2
11	2	2	0
12	-2	-2	-2
13	-2	-2	-2
14	1	1	0
15	2	2	2
16	0	0	1
17	0	0	1
18	1	1	1
19	0	0	0
20	1	1	1

21	1	1	0
22	1	1	1
23	0	0	0
24	2	2	2
25	2	2	2
26	2	2	2
27	0	0	0
28	2	2	2
29	0	1	0
30	1	1	1
31	2	1	2
32	2	2	2
33	0	0	1

Cera-Ve

CCID#	12 HR		
	Q1	Q2	Q3
1	2	2	2
2	2	2	2
3	2	1	2
4	1	1	1
5	2	2	2
6	2	2	2
7	1	1	1
8	-1	0	0
9	1	1	1
10	1	1	1
11	2	2	2
12	2	2	2
13	2	2	2
14	0	0	1
15	1	1	1
16	0	1	0
17	0	0	1

18	1	1	-1
19	0	0	0
20	1	0	0
21	1	1	0
22	0	0	0
23	-1	-1	-1
24	2	2	2
25	2	2	2
26	1	1	1
27	0	2	1
28	1	1	1
29	-1	0	0
30	1	1	1
31	2	1	2
32	2	2	2
33	-2	-2	-2

Self-Assessment Questionnaire at 24 Hr

Galderma

CCID	24 HR				
	Q1	Q2	Q3	Q4	Q5
1	2	2	2	2	2
2	2	2	2	2	2
3	0	1	1	1	1
4	2	1	1	1	1
5	2	2	2	2	2
6	2	1	2	2	2
7	0	0	0	0	0
8	1	1	1	1	1
9	0	0	1	0	1
10	2	2	2	2	2
11	0	0	1	1	0
12	0	0	0	0	0

13	-2	-2	-2	-2	-2
14	0	1	0	0	2
15	2	2	2	2	0
16	2	-1	1	2	2
17	0	1	0	0	0
18	1	2	1	1	1
19	0	0	0	0	0
20	2	2	2	2	2
21	1	0	1	1	1
22	1	1	1	1	1
23	1	1	1	1	1
24	2	2	2	2	2
25	2	2	2	2	2
26	2	2	2	2	2
27	0	-1	0	0	0
28	2	2	2	2	2
29	0	1	1	1	0
30	0	1	0	1	1
31	2	1	2	1	2
32	2	1	2	2	2
33	-2	-2	-2	-2	-2

Cera-Ve

CCID#			24 HR		
	Q1	Q2	Q3	Q4	Q5
1	2	2	2	2	2
2	2	1	2	2	2
3	0	1	1	0	0
4	1	2	2	1	2
5	2	2	2	2	2
6	2	1	2	2	2
7	1	1	1	1	1
8	0	0	1	0	0
9	1	1	0	1	1

10	1	1	1	1	1
11	1	1	1	1	1
12	2	2	2	2	2
13	2	2	2	2	2
14	0	1	0	0	1
15	1	1	1	1	0
16	0	0	2	0	0
17	0	0	0	0	0
18	-1	-1	0	-1	-1
19	0	0	0	0	0
20	0	0	0	0	0
21	1	0	1	1	1
22	0	0	0	0	0
23	0	0	0	0	0
24	2	2	2	2	2
25	2	2	2	2	2
26	1	1	1	1	1
27	1	2	1	0	1
28	2	1	2	1	2
29	-1	-1	-1	-1	0
30	0	1	1	1	1
31	2	2	1	2	1
32	2	2	2	2	2
33	1	0	1	-1	1

1.2 ITCH SEVERITY

CCID#	Baseline GALDERMA	CERAVE	8 HRS GALDERMA	CERAVE	12 HRS GALDERMA	CERAVE	24 HRS GALDERMA	CERAVE
1	5	5	0	0	0	0	0	0
2	6	6	0	2	0	0	0	0
3	3	3	0	3	2	4	3	2
4	6	6	0	1	0	0	0	0
5	5	5	0	1	0	0	0	1
6	4	4	1	1	1	1	2	2
7	4	4	0	0	4	3	0	2
8	5	5	1	6	2	2	6	2
9	4	4	2	3	2	3	3	2
10	5	5	3	2	3	2	0	2
11	5	5	3	5	3	5	2	3
12	5	5	0	0	0	0	0	0
13	6	6	4	6	4	7	3	5
14	4	4	3	4	3	3	3	4
15	3	3	5	5	3	3	3	3
16	3	3	0	4	4	0	3	2
17	3	3	3	4	6	7	6	7
18	4	4	0	4	0	4	4	2
19	6	6	4	3	5	5	4	5
20	4	4	0	0	0	0	0	3
21	4	4	0	0	0	0	1	1
22	3	3	2	0	0	3	3	0
23	4	4	0	4	4	4	4	4
24	4	4	3	3	3	3	2	3
25	5	5	0	0	0	0	0	0
26	4	4	0	7	0	2	2	0
27	3	3	0	1	2	0	1	3
28	6	6	0	4	0	0	2	2
29	3	3	1	3	0	0	0	0
30	5	5	1	0	0	7	0	6
31	4	4	3	4	4	4	2	4
32	5	5	0	0	3	0	0	2
33	4	4	7	5	5	7	4	6

1.3 TIME TO ITCH RELIEF

CCID	Galderma Time	Cera-ve Time
1	32	42.3
2	10.2	33
3	33.1	20
4	42	67
5	39	36.67
6	15	20.1
7	9.42	83
8	30	23
9	39	67
10	10.5	21
11	48	55
12	9.2	10
13	45	47
14	20	32
15	10	30
16	42	33
17	20	55
18	20	30
19	31	51.25
20	32	29
21	30	70
22	5	7
23	12	37
24	41	37
25	9	50
26	20	25.8
27	47	38.14
28	26	108
29	65	28.33
30	12.82	37
31	29.2	28
32	39	64.2
33	66.56	65

1.4TOLERABILITY

CCID	Baseline		24 hrs	
	Galderma	Cera-Ve	Galderma	Cera-Ve
1	1	1	1	1
2	2	2	1	1
3	3	3	1	2
4	1	1	0	1
5	1	1	0	1
6	2	2	1	1
7	3	3	1	2
8	1	1	1	0
9	0	0	0	0
10	2	2	1	1
11	1	1	1	1
12	2	2	1	1
13	3	3	1	2
14	2	2	1	1
15	1	1	0	1
16	0	0	0	0
17	1	1	1	2
18	1	1	0	1
19	2	1	1	1
20	2	2	0	1
21	2	1	1	1
22	3	3	1	2
23	2	0	1	1
24	1	1	0	1
25	0	1	0	0
26	1	1	1	1
27	2	2	2	2
28	3	3	2	2
29	0	1	0	1
30	1	1	2	2
31	1	2	1	1
32	1	1	0	1
33	3	3	2	3

1.5 Product Preference Questionnaire

	0 HR		24 HR		
CCID	Q1	Q2	Q3	Q4	Q5
1	N	G	G	G	G
2	G	G	C	G	G
3	N	G	N	G	G
4	G	C	C	C	C
5	C	G	G	G	G
6	G	G	G	G	G
7	C	C	C	C	C
8	C	C	C	C	C
9	C	C	C	C	C
10	G	G	G	G	G
11	C	C	C	C	C
12	C	C	C	C	C
13	C	C	C	C	C
14	G	N	N	N	N
15	G	G	G	G	G
16	G	N	N	N	N
17	G	G	G	G	G
18	N	G	G	N	G
19	G	G	G	G	N
20	G	G	G	G	G
21	N	N	N	N	N
22	G	G	G	G	G
23	G	G	G	G	G
24	G	G	G	G	G
25	G	G	G	G	G
26	G	G	G	G	G
27	N	C	C	N	C
28	G	G	G	N	G
29	C	G	G	G	G
30	C	C	C	C	C
31	N	C	C	C	C
32	G	G	N	N	C
33	C	N	N	N	N

1.6 BODY AREA FOR PRODUCT APPLICATION

CCID#	Bilateral Eczema Location
1	Arms
2	Legs
3	Hands
4	arms
5	Hands
6	Arms
7	Legs
8	Arms
9	Hands
10	Wrists
11	Arms
12	Arms
13	Arms
14	Arms
15	Hands
16	Legs
17	thighs
18	Legs
19	Hands
20	Legs
21	Hands
22	Hands
23	Arms
24	Arms
25	Legs
26	Arms
27	Ankles
28	Ankles
29	Legs
30	Neck
31	arms
32	Elbows
33	hands

APPENDIX VI

SOURCE DOCUMENT

Name:	ID:	Phone:	Email:	DOB:

Did the subject complete the 3-day washout period	Yes/ No
Demographics	Race: Age: Gender:
Did the subject sign informed consent?	Yes/No Date:
Review of Inclusion criteria	
Review of Exclusion criteria	
Eczema prone areas of the body	
Symmetrical side of the body with Eczema	
Randomization code	
Itch severity	Before application: At 8 Hrs: At 12 Hrs: At 24 Hrs:
Tolerability	Before application: At 24 Hrs:
Application of Galderma anti-itch gel	Time applied: Time of itch relief:

Application of Cera Ve cream	Time applied: Time of itch relief:
Did the subject experience any Adverse Events?	
List all Concomitant medications	
List Medical history	

Comments:

Staff Name:	Sign:	Date:

APPENDIX VII

RANDOMIZATION CODE

CCID#	CERA VE	Galderma Anti-itch gel site
1	L	R
2	R	L
3	L	R
4	L	R
5	L	R
6	R	L
7	L	R
8	R	L
9	L	R
10	R	L
11	L	R
12	R	L
13	L	R
14	R	L
15	L	R
16	R	L
17	L	R
18	R	L
19	L	R
20	R	L
21	L	R
22	R	L
23	L	R
24	R	L
25	L	R
26	R	L
27	L	R
28	R	L
29	L	R
30	R	L
31	L	R
32	R	L
33	L	R

APPENDIX VIII

SUBJECT TESTIMONIALS

CCID #	CERAVE	Galderma Anti-itch gel site	COMMENTS
1	L	R	I preferred the gel because it stayed dry and soft
2	R	L	The left product made my skin feel clean and invigorating and cool. The right product was also nice soothing and creamy on skin
3	L	R	Left side was under the sun while driving and it made it itchy with the cream.
4	L	R	
5	L	R	I really enjoyed the roller product, mainly the idea of the roller is great for the product. The amount of itch was not felt at all with the roller. The cream side was noticeable during the day but not the rolling product. The cerave is very moisturizing.
6	R	L	The left product was easy to apply with roller and was thin enough to absorb in the skin quickly
7	L	R	I liked the cream because I felt something soft and refreshing on my skin. I didn't feel the burning or itch.
8	R	L	
9	L	R	
10	R	L	Instant relief upon application of product gel
11	L	R	The left side felt better than the right side, the whole 24 hrs
12	R	L	The gel has a cool feeling but is to watery. The cream is very good
13	L	R	
14	R	L	Although both gave relief, left side actually helped with redness and a previous light swelling
15	L	R	I felt an itch on another part of my left hand, 4 hours after application
16	R	L	
17	L	R	
18	R	L	Loved the gel applicator, cool to the touch. And non-greasy, did not need hand washing
19	L	R	
20	R	L	The product used on the left had a better absorbing feel compared to the right side. It was instant relief to the touch, didn't feel greasy. However, I feel I would like to apply more throughout the day
21	L	R	I Did not feel much on my skin
22	R	L	Gel was a nice sensation. The cream was just regular lotion to me
23	L	R	I Preferred the texture of the right side. It was less greasy. I also preferred the roller with right side
24	R	L	
25	L	R	
26	R	L	
27	L	R	I Like the applicator of the new product but it did not feel as effective in reducing the itchiness
28	R	L	The cool touch applicator is easier to apply, more cool upon application so faster relief. Lighter texture finger application took longer for cooling effect, thicker texture, not as sanitary since dipping fingers. But both are good and would use both.
29	L	R	The right side felt cool and a little itchy at first but later on it made my skin soft and not dry and itchy .
30	R	L	Liked the cooling sensation on right side, think it would help relief eczema
31	L	R	I liked everything about it. I would recommend everyone to use it, really helps
32	R	L	I Liked the right product better but left one is better packaged which will help it store properly
33	L	R	