Essex Testing Clinic, Inc.

ETC

FINAL REPORT

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

Progeneron DupurtyRx JH2-092-002

Sponsor

Progeneron
27402 Aliso Viejo Parkway
Aliso Viejo, CA

Sponsor Representative

Kai Hansen

Clinical Testing Facility

Essex Testing Clinic, Inc.
799 Bloomfield Avenue
Verona, NJ 07044

Sponsor Code: P145
ETC Panel No.: 20171
ETC Entry No.: 42068

Date of Final Report

6-23-20

ETC Panel No.: 20171
ETC Entry No.: 42068

SIGNATURE PAGE

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

Progeneron DupurtyRx JH2-092-002

John A. Erianne, MD
Board-Certified Dermatologist
Medical Investigator

6/17/20
Date

QUALITY ASSURANCE STATEMENT

This study (ETC Panel No.: 20171; ETC Entry No.: 42068) was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in 21 CFR Part 50 (Protection of Human Subjects – Informed Consent) and the Standard Operating Procedures of Essex Testing Clinic, Inc.

For purposes of this clinical study:

X	Informed Consent was obtained.
____	Informed Consent was not obtained.
X	An IRB review was not required.
____	An IRB review was conducted and approval to conduct the proposed clinical research was granted.

To assure compliance with the study protocol, the Quality Assurance Unit completed an audit of the applicable study records and report. This report is considered a true and accurate reflection of the testing methods and source data.

Sherri L. Sayles — 19 June 2020

Sherri L. Sayles, MS
Manager, Quality Assurance

Date

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CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

Progeneron DupurtyRx JH2-092-002

1.0 OBJECTIVE

The objective of this study was to determine the irritation and/or sensitization potential of the test article after repeated application under semi-occlusive patch test conditions to the skin of human subjects (non-exclusive panel).

2.0 SPONSOR

Progeneron
27402 Aliso Viejo Parkway
Aliso Viejo, CA

2.1 Sponsor Representative

Kai Hansen

3.0 CLINICAL TESTING FACILITY

The study was conducted by:

Essex Testing Clinic, Inc.
799 Bloomfield Avenue
Verona, NJ 07044

4.0 CLINICAL INVESTIGATORS

Study Director:	Annemarie E. Hollenback, BA
Principal Investigator:	Toni F. Miller, PhD, DABT, BCFE
Medical Investigator:	John A. Erianne, MD, Board-Certified Dermatologist

5.0 STUDY DATES

Study initiation: February 19, 2020

Final evaluation: June 5, 2020*

*Due to the COVID-19 pandemic the Testing Facility closed on March 21, 2020 as mandated by the State of New Jersey. The Challenge phase was conducted on June 3, 2020 through June 5, 2020 after reopening.

6.0 ETHICS

6.1 Ethical Conduct of the Study

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and/or Essex Testing Clinic (ETC) Standard Operating Procedures.

6.2 Subject Information and Consent

This study was conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed Consent was obtained from each subject in the study and documented in writing before participation in the study. A copy of the Informed Consent was provided to each subject.

7.0 TEST MATERIAL

The test article used in this study was provided by:

Beautiful Disruptions LLC
12015 Mora Drive
Unit 2
Santa Fe Springs, CA 90670

It was received on January 31, 2020 and identified as follows:

ETC Entry No.	Test Article ID	Description
42068	Progeneron DupurtyRx JH2-092-002	Taupe Lotion

8.0 TEST SUBJECTS

At least 50 male and female subjects ranging in age from 18 to 79 years, were to be empanelled for this test.

The subjects chosen were to be dependable and able to read and understand instructions. The subjects were not to exhibit any physical or dermatologic condition that would have precluded application of the test article or determination of potential effects of the test article.

9.0 TEST PROCEDURE

The 9 Repeated Insult (semi-occlusive) Patch Test (9-RIPT)[1] was conducted as follows:

9.1 Induction Phase

A sufficient amount of the test article (approximately 0.2 mL) was placed onto a 2 cm x 2 cm square of Webril® cotton fabric (approximately 0.05 mL/cm^2 of test material) affixed to Scanpor (Allerderm) semi-occlusive surgical tape. The patch was then applied to the back of each subject between the scapulae and waist, adjacent to the spinal mid-line. This procedure was performed by a trained technician/examiner and repeated every Monday, Wednesday and Friday until 9 applications of the test article had been made.

The subjects were instructed to remove the patch 24 hours after application. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. Subjects returned to the Testing Facility and the site was scored by a trained examiner just prior to the next patch application.

If a subject developed a positive reaction of a level 2 erythema or greater during the Induction phase or if, at the discretion of the Study Director, the skin response warranted a change in site, the patch was applied to a previously unpatched, adjacent site for the next application. If a level 2 reaction or greater occurred at the new site, no further applications were made. However, any reactive subjects were subsequently Challenge patch tested.

9.2 Challenge Phase

After a rest period of approximately 2 weeks (no applications of the test article), the Challenge patch was applied to a previously unpatched (virgin) test site. (Initiation of the Challenge phase was delayed due to Testing Facility closure during COVID-19 pandemic.) The site was scored 24 and 72 hours after application. All subjects were instructed to report any delayed skin reactivity that occurred after the final Challenge patch reading. When warranted, selected test subjects were called back to the Clinic for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

Dermal responses for both the Induction and Challenge phases of the study were scored according to the following 6-point scale:

0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

All other observed dermal sequelae (eg, edema, dryness, hypo- or hyperpigmentation) were appropriately recorded on the data sheet and described as mild, moderate or severe.

[1] Marzulli FN, Maibach HI. (1976) Contact allergy: predictive testing in man. *Contact Dermatitis*. 2, 1-17.

9.0 TEST PROCEDURE (CONT'D)

9.3 Data Interpretation

Edema, vesicles, papules and/or erythema that persist or increase in intensity either during the Induction and/or Challenge phase may be indicative of allergic contact dermatitis. Allergic responses normally do not resolve or improve markedly at 72-96 hours.

Exceptions to typical skin reactions may occur. These may include, but not be limited to, symptoms of allergic contact sensitivity early in the Induction period to one or more test products. When this occurs in one subject, such a reaction usually suggests either an idiosyncratic response or that the subject had a pre-exposure/sensitization to the test material or component(s) of the test material or a cross-reactivity with a similar product/component. Data for such reactions will be included in the study report but will not be included in the final study analysis/conclusion of sensitization.

10.0 RESULTS AND DISCUSSION

(See Table 1 for Individual Scores)

A total of 58 subjects (15 males and 43 females ranging in age from 18 to 74 years) were empanelled for the test procedure. Forty-three (43/58) subjects satisfactorily completed the test procedure on Test Article: Progeneron DupurtyRx JH2-092-002. Fifteen (15/58) subjects discontinued for personal reasons unrelated to the conduct of the study. Discontinued subject data are shown up to the point of discontinuation, but are not used in the Conclusions section of this final report.

Induction Phase Summary

Test Article	Induction Scores (Number of Responses)						Evidence of Irritation
	0.5	1	2	3	4	Other	
Progeneron DupurtyRx JH2-092-002	0	0	0	0	0	0	No

Challenge Phase Summary

Test Article	Challenge Scores (Number of Responses)						Evidence of Sensitization
	0.5	1	2	3	4	Other	
Progeneron DupurtyRx JH2-092-002	0	0	0	0	0	0	No

There was no skin reactivity observed at any time during the course of the study.

11.0 CONCLUSIONS

Under the conditions of a repeated insult (semi-occlusive) patch test procedure conducted in 43 subjects, Test Article: Progeneron DupurtyRx JH2-092-002 was "Dermatologist-Tested" and was not associated with skin irritation or allergic contact dermatitis in human subjects.

ETC Panel No.: 20171
ETC Entry No.: 42068

TABLE 1

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - SEMI-OCCLUSIVE

Test Article: Progeneron DupurtyRx JH2-092-002

Subj. No.	Induction Evaluation Number									Challenge Virgin Site	
	1	2	3	4	5	6	7	8	9	24hr	72hr
1	0	0	0	0	0	0	0	0	0	0	0
2	Discontinued										
3	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0
5	Discontinued										
6	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	Discontinued					
10	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	Discontinued	
14	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	Discontinued	
23	0	0	0	0	0	0	0	0	0	Discontinued	
24	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	Discontinued	
28	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	Discontinued	

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

TABLE 1 (CONT'D)

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - SEMI-OCCLUSIVE

Test Article: Progeneron DupurtyRx JH2-092-002

Subj. No.	Induction Evaluation Number									Challenge Virgin Site	
	1	2	3	4	5	6	7	8	9	24hr	72hr
31	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0
33	Discontinued										
34	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0
38	0	0	Discontinued								
39	0	0	Discontinued								
40	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0
52	Discontinued										
53	Discontinued										
54	0	0	0	0	0	0	0	0	0	Discontinued	
55	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	Discontinued							
57	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
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PROGENERON

Palmar Fibromatosis 180-Day Clinical Study Abstract

Progeneron Hand Cream is a specialized, topically applied product comprised of therapeutic ingredients with clinically published data. A recent IRB clinical safety trial followed product users with Palmar Fibromatosis for 180 days. Participants in the trial reported significant improvement in comfort, appearance and no symptom progression.

STUDY DESIGN

Participants with varying severity of Palmar Fibromatosis were enrolled in a 90-day IRB Safety Study Trial and instructed to apply PHC three times daily to both hands. The trial was extended an additional 90 days for a total of 180 days to collect data on participant outcomes. A physician examined and interviewed participants every four weeks throughout the trial. Each participant's disease state and relevant medical history were recorded.

TRIAL PARTICIPANTS

Of the 34 product users initially enrolled in the study, 29 completed the 90-day trial (12 weeks), and 19 agreed to conduct a follow-on 180-day trial (24 weeks). Of the 18 users completing the trial, 100% reported no disease progression.

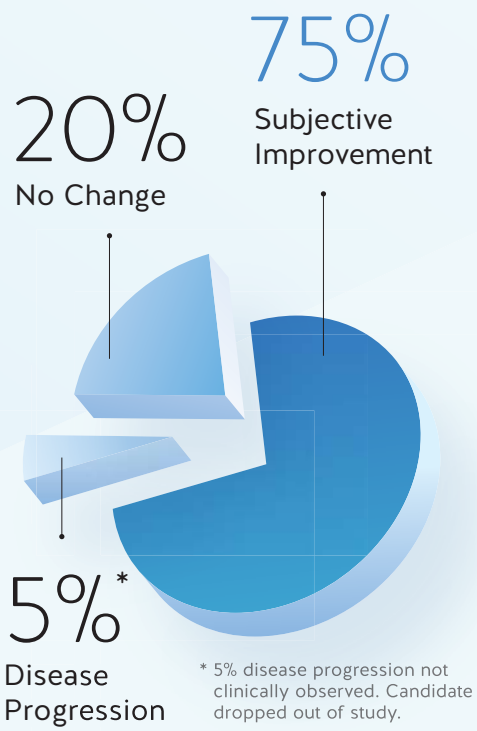
In a 24-week clinical evaluation using Progeneron Hand Cream:

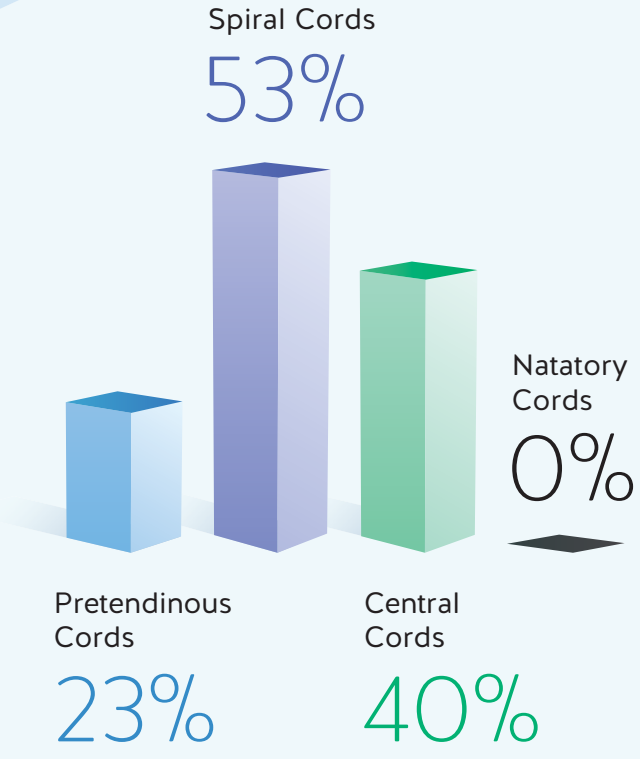
95%
of participants reported no disease progression

100%
of participants who completed the trial reported no disease progression

75%
of participants reported softer hands and improved mobility in their hands

2/3
of participants with a medical history of trigger finger reported more flexibility in their hands





DETAILS

While the clinical trial results were promising in many respects, participants with prior surgical intervention fared particularly well after using Progeneron Hand Cream: **100% of trial participants with previous surgical interventions for Dupuytren's complications reported a subjective improvement of symptoms.**

In addition to subjective self-reporting, a physician evaluated trial participants every four weeks, counting and characterizing cords and nodules throughout the study. On average, participants demonstrated significant improvement in cord progression, with over 50% reduction in spiral cord prevalence after 90 days of using PHC. Natatory cords were the only cord type that did not experience a reduction, and they were the smallest group at n=6 cords observed in participants at study onset.

eresina For complete study details, please contact **Eresina, LLC**:

info@progeneron.net +1 833-513-4020 27402 Aliso Viejo Pkwy, Aliso Viejo, CA 92656

CareOne Research
Redefining Site Management

Date: 10SEP2021

Eresina LLC - 0724.1, A Study of the Safety of Progeneron Hand Cream in Subjects with Palmar Fibromatosis

Principal Investigator: Raymond Raven, MD

Data Analysis:

The percent of subjects with adverse events and serious adverse events will be reported. ***Results: 0 % (There were no reported adverse events or serious adverse events that were reported during the study)***

The adverse and serious adverse events will be characterized by their type, location, and severity. ***Results: None* (*Characterization by type, location, and severity of adverse events cannot be assessed as there are no adverse events that were reported)***

Adverse and serious adverse events will be analyzed and reported by demographic characteristics (eg, the % of patients younger than 65 with and adverse event vs. the % of patient greater/equal 65. ***Results: None* (*Characterization of adverse events cannot be assessed as there are no adverse events that were reported)***

Raymond Raven, MD
Principal Investigator

09/14/2021
Date