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50 SUBJECT HUMAN REPEAT INSULT PATCH TEST FOR SKIN IRRITATION AND SKIN SENSITIZATION EVALUATION

Claims:

✓Clinically Tested ✓Non-Irritation ✓Non-Allergenic ✓Non-Skin Sensitizing

Date: December 19, 2012

BCS Study No.: 12/124A

Sponsor: Terrain Pharmaceuticals
200 South Virginia Street –
8th Floor, Reno NV 89501

1.0 Objective:

To determine the irritation and sensitization (contact allergy) potential of a test material after repeated application to the skin of human subjects.

2.0 Test Material

2.1 Test Material Desription

Date Received: 10/26/2012
Number of Test Samples Received: 2
Label On Test Samples: Pain Cream with 4 Active Ingredients, Formula # PA-200-171G Accession No.: 778392

2.2 Handling:

Upon arrival at BioScreen Clinical Services (BCS) the test material was assigned a unique laboratory code number and entered into a daily log identifying the lot number, sample description, sponsor, date received and tests requested. Samples will be retained for a period of thirty (30) days beyond submission of final report unless otherwise specified by the sponsor or, if sample is known to be in support of governmental applications, in which case representative retained samples are kept two (2) years beyond final report submission.
Sample disposition will be conducted in compliance with appropriate federal, state and local ordinances.

2.3 Test Material Evaluation Prerequisite:

Prior to induction of a human test panel, animal toxicology, microbiology and other in-vivo or in-vivo or in-vitro performance data were required to assess the feasibility of commencement.

3.0 Panel Selection:

3.1 Standards for Inclusion in a Study:

- Individuals who were not currently under a doctor's care
- Individuals who were free of any dermatological or systemic disorder that would interfere with the results, at the discretion of the Investigator.
- Individuals who were free of any acute or chronic disease that would interfere with or increase the risk of study participation
- Individuals who completed a preliminary medical history form mandated by BCS and were in general good health.
- Individuals who read, understood and signed an informed consent document relating to the specific type of study.
- Individuals who were able to cooperate with the Investigator and research staff, and were willing to have test materials applied according to the protocol, and compete the full course of the study.

3.2 Standards for Exclusion from a Study:

- Individuals who were under 18 years of age.
- Individuals who were currently under a doctor's care.

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- Individuals who were currently taking any medication (topical or systemic) that might mask or interfere with the test results.
- Individuals who had a history of any acute or chronic disease that might interfere with or increase the risk associated with study participation.
- Individuals who were diagnosed with chronic skin allergies.
- Female volunteers who indicated that they were pregnant or nursing.

3.3 Recruitment:

Panel selection was accomplished by advertisements in local periodicals, community bulletin boards, phone solicitation, electronic media or any combination thereof.

3.4 Informed Consent and Medical History Forms:

An informed consent was obtained from each volunteer prior to initiating the study describing reasons for the study, possible adverse effects, associated risks and potential benefits of the treatment and their limits of liability, Panelists signed and dated the informed consent document to indicate their authorization to proceed and acknowledge their understanding of the contents. Each subject was assigned a permanent identification number and completed an extensive medication history form. These forms along with the signed consent forms are available for inspection on the premises of BCS only. [Reference 21 CFR Ch. 1 Part 50, Subpart B] The parties agree to comply with applicable state and federal privacy laws for the use and disclosure of a subject's personal health information by taking reasonable steps to protect the confidentiality of this information. This obligation shall survive the termination or expiration of this Agreement.

4.0 Population Demographics:

Number of subjects enrolled	**51**
Number of subjects completing study	**51**
Age Range	**18-60**
Sex	
Male	**1**
Female	**50**
Fitzpatrick Skin Type*	
1 – always burn, does not tan	**0**
2 – burn easily, tan slightly	**8**
3 – burn moderately, tan progressively	**41**
4 – burn a little, always tan	**2**
5 – rarely burn, tan intensely	**0**
6 – never burn, tan very intensely	**0**

*[Agache P., Hubert P.. Measuring the skin. (p. 473, table 48.1) Springer-Verlag Berlin Heidelberg, 2004, (p. 473, table 48.1)]

5.0 Equipment:

Test materials to be tests under occlusive conditions were placed on an 8-millimeter aluminum chamber (Finn Chamber, Epitest Ltd Oy, Tuussula, Finland) supported on a sheet of Scanpore® (occlusive) tape (Norgesplaster A/S, Kristiansand, Norway) or a 7mm IQ-ULTRA® closed cell system which is made of additive-free polyethylene plastic foam with a filter paper incorporated (It is supplied in units of 10 chambers on a hypoallergenic non-woven adhesive tape; the width of the tape is 52mm and the length is 118mm) or other equivalents.

6.0 Procedure:

- Subjects were requested to bathe or wash as usual before arrival at the facility.
- Patches containing the test material were then affixed directly to the skin of the intrascapular regions of the back, to the right or left of the midline and subjects were dismissed with instructions not to wet or expose the test area to direct sunlight.

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- Subjects were instructed to remove the patches approximately 48 hours after the first application and 24 hours thereafter for the remainder of the study.
- This procedure was repeated until a series of nine (9) consecutive, 24-hour exposures had been made three (3) times a week for three (3) consecutive weeks.
- Prior to each reapplication, the test sites were evaluated by trained laboratory personnel.
- Following a 10-14 day rest period a retest/challenge dose was applied once to a previously unexposed test site. Test sites were evaluated by trained laboratory personnel 48 to 96 hours after application.
- In the event of an adverse reaction, the area of erythema and edema were measured. Edema is estimated by the evaluation of the skin with respect to the contour of the unaffected normal skin.
- Subjects were instructed to report any delayed reactions that might occur after the final reading.
- Clients will be notified immediately in the case of an adverse reaction and a determination is made as to treatment program if necessary.

7.0 Scoring:

Scoring scale and definition of symbols shown below are based on the scoring scheme according to the International Contact Dermatitis Research Group scoring scale [Rietschel, R.L., Fowler, J.F., Ed., Fisher's Contact Dermatitis (fourth ed.). Baltimore, Williams & Wilkins, 1995] listed below:

0 no reaction (negative)
1 erythema throughout at least ¾ of patch area
2 erythema and induration throughout at least ¾ of patch area
3 erythema, induration and vesicles
4 erythema, induration and bullae
D Site discontinued
Dc Subject discontinued

NOTE: Clinical evaluations are performed by a BCS investigator or designee trained in the clinical evaluation of the skin. Whenever feasible, the same individual will do the scoring of all the subjects throughout the study and will be blinded to the treatment assignments and any previous scores.

8.0 Results:

Accession No.: 778392
Test Material Description: Pain Cream with 4 Active Ingredients, Formula # PA-200-171G
Patch Description: Open

Subject Information				Skin	Induction									Challenge	
No.	ID	Sex	Age	Type	1	2	3	4	5	6	7	8	9	1	2
1	1625587	F	48	3	0	0	0	0	0	0	0	0	0	0	0
2	1673579	F	47	3	0	0	0	0	0	0	0	0	0	0	0
3	1780184	F	42	2	0	0	0	0	0	0	0	0	0	0	0
4	1889481	F	38	3	0	0	0	0	0	0	0	0	0	0	0
5	1890981	F	40	3	0	0	0	0	0	0	0	0	0	0	0
6	3195696	F	60	2	0	0	0	0	0	0	0	0	0	0	0
7	3227559	F	54	3	0	0	0	0	0	0	0	0	0	0	0
8	3234827	F	52	3	0	0	0	0	0	0	0	0	0	0	0
9	3235149	F	52	3	0	0	0	0	0	0	0	0	0	0	0
10	3235707	F	54	3	0	0	0	0	0	0	0	0	0	0	0
11	3239139	F	52	3	0	0	0	0	0	0	0	0	0	0	0

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12	3253226	F	50	3	0	0	0	0	0	0	0	0	0	0	0
13	3260795	F	49	3	0	0	0	0	0	0	0	0	0	0	0
14	3262876	F	49	3	0	0	0	0	0	0	0	0	0	0	0
15	3283686	F	46	2	0	0	0	0	0	0	0	0	0	0	0
16	3313052	F	42	3	0	0	0	0	0	0	0	0	0	0	0
17	3315085	F	41	3	0	0	0	0	0	0	0	0	0	0	0
18	3322907	F	39	3	0	0	0	0	0	0	0	0	0	0	0
19	3341786	F	36	3	0	0	0	0	0	0	0	0	0	0	0
20	3387036	F	34	3	0	0	0	0	0	0	0	0	0	0	0
21	3387165	F	29	3	0	0	0	0	0	0	0	0	0	0	0
22	3394536	F	28	3	0	0	0	0	0	0	0	0	0	0	0
23	3408603	F	23	2	0	0	0	0	0	0	0	0	0	0	0
24	3421023	F	25	2	0	0	0	0	0	0	0	0	0	0	0
25	3426103	F	24	3	0	0	0	0	0	0	0	0	0	0	0
26	3434139	F	23	3	0	0	0	0	0	0	0	0	0	0	0
27	3435135	F	23	3	0	0	0	0	0	0	0	0	0	0	0
28	3439501	M	23	2	0	0	0	0	0	0	0	0	0	0	0
29	3458507	F	20	3	0	0	0	0	0	0	0	0	0	0	0
30	3458880	F	20	3	0	0	0	0	0	0	0	0	0	0	0
31	3465309	F	20	3	0	0	0	0	0	0	0	0	0	0	0
32	3467931	F	19	3	0	0	0	0	0	0	0	0	0	0	0
33	3480894	F	18	3	0	0	0	0	0	0	0	0	0	0	0
34	7055108	F	57	3	0	0	0	0	0	0	0	0	0	0	0
35	7059667	F	55	3	0	0	0	0	0	0	0	0	0	0	0
36	7136242	F	35	4	0	0	0	0	0	0	0	0	0	0	0
37	9094694	F	42	3	0	0	0	0	0	0	0	0	0	0	0
38	11010431	F	34	3	0	0	0	0	0	0	0	0	0	0	0
39	11076087	F	32	3	0	0	0	0	0	0	0	0	0	0	0
40	11281007	F	26	3	0	0	0	0	0	0	0	0	0	0	0
41	11312610	F	25	2	0	0	0	0	0	0	0	0	0	0	0
42	110020327	F	34	2	0	0	0	0	0	0	0	0	0	0	0
43	11290565	F	27	3	0	0	0	0	0	0	0	0	0	0	0
44	113060552	F	25	3	0	0	0	0	0	0	0	0	0	0	0
45	113280213	F	25	3	0	0	0	0	0	0	0	0	0	0	0
46	113650501	F	24	3	0	0	0	0	0	0	0	0	0	0	0
47	304600039	F	20	3	0	0	0	0	0	0	0	0	0	0	0
48	700920285	F	43	3	0	0	0	0	0	0	0	0	0	0	0
49	155801100906	F	19	3	0	0	0	0	0	0	0	0	0	0	0
50	155806279236	F	45	4	0	0	0	0	0	0	0	0	0	0	0
51	155810462307	F	27	3	0	0	0	0	0	0	0	0	0	0	0

9.0 Evaluation Period:

The study was conducted from November 5, 2012 to December 14, 2012.

10.0 Observations:

No adverse reactions of any kind were reports during the course of this study.

11.0 Study Archives:

All original samples, raw data sheets, technician's notebooks, correspondence files and copies of final reports and remaining specimens will be maintained on premises of BCS in limited access storage files marked "Archive".

12.0 Conclusions:

Under conditions of the study, there were no identifiable signs or symptoms of primary irritation or sensitization (contact allergy) noted for Pain Cream with 4 Active Ingredients, Formula # PA-200-171G Accession No. 778392

Study conducted by BioScreen Testing, Inc. www.BioScreen.com