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50 HUMAN SUBJECT REPEAT INSULT PATCH TEST SKIN IRRITATION/SENSITIZATION EVALUATION (OCCLUSIVE PATCH)

Date: September 12, 2017

CR Ref. No.: CSD.P0728-F.RS.O.50

Sponsor: C. Schmitz Drawing Salve

1.0 Objective:

Consumer products or raw materials designed for consistent reapplication to areas of the skin may, under proper conditions, prove to be contact sensitizers or irritants in certain individuals. It is the intention of a Repeat Insult Patch Test (RIPT) to provide a basis for evaluation of this irritation/ sensitization potential if such exists.

2.0 Reference:

The method is modified to test 50 panelists and not the 200 cited in the reference Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, published by The Association of Food and Drug Officials of The United States. The method also employs nine inductive patchings and not the ten cited in the reference under occlusive patch conditions.

3.0 Test Material:

3.1 Test Material Description:

On July 28, 2017, one test sample labeled C. Schmitz Drawing Salve without Peruvian Balsam was received from C. Schmitz Drawing Salve and assigned CR Lab No. P0728-F.

3.2 Test Material Handling:

Upon arrival at Cantor Research Laboratories, Inc., 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 test(s) requested. Samples are retained for a minimum period of three months beyond submission of final report unless otherwise specified by the sponsor. If the sample is known to be in support of governmental applications, samples are kept a minimum of two years beyond final report submission. Sample disposal is conducted in compliance with appropriate federal, state and local ordinances.

3.3 Test Material Evaluation Prerequisite:

Prior to induction of a human test panel, animal toxicology, microbiology and other in-vivo or in-vitro performance spectra may be required to assess the feasibility of commencement as dictated by an Institutional Review Board (IRB) described in Section 4.0.

Sponsor purports that prior to sample submission to Cantor Research Laboratories, Inc., the following tests were conducted with no adverse results and that the test data are on file on their premises and have not been made available to Cantor Research Laboratories, Inc., personnel:

- CTFA Preservative Efficacy Test or equivalent
- 90 Day Accelerated Stability and Container Compatibility Study

4.0 Institutional Review Board (IRB):

The annual IRB of Cantor Research Laboratories, Inc. consists of five or more individuals from diverse backgrounds. They are chosen from the local community to review and approve clinical study documents like protocols, SOPs, ICFs, AE/SAE procedures, reports, etc. that are presented to them. A few members from within the company are also present for technical expertise only to answer questions, if any and do not participate in the voting process. The outcome of the IRB, list of members etc. is kept on file at Cantor Research Laboratories, Inc. and is available for inspection during the hours of operation. Reference: CFR Title 21 Part 56, Subparts A, B, C, and D.

5.0 Panel Selection:

Healthy volunteers over eighteen years of age were recruited for this study. A trained technician performed a physical examination of the panelist's back to determine if study eligibility criteria were satisfied.

5.1 Standards for Inclusion in the Study:

- Individuals who are not currently under a doctor's care.
- Individuals free of any dermatological or systemic disorder which would have interfered with the results, at the discretion of the Investigator.
- Individuals free of any acute or chronic disease that may have interfered with or increased the risk of study participation.
- Individuals who have completed a preliminary medical history form mandated by Cantor Research Laboratories, Inc., and are in general good health.
- Individuals, who have read, understood and signed an informed consent document relating to the specific type of study they are subscribing.
- Individuals who were able to cooperate with the investigator and research staff, willing to have the test materials applied according to the protocol, and complete the full course of the study.
- Approximately 50% of the panelists inducted were self described as having sensitive skin.

5.2 Standards for Exclusion from the Study:

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

- Individuals who were currently taking any medication (topical or systemic) that may

have masked or interfered with the test results.
- Subjects with a history of any acute or chronic disease that may have interfered with or increased the risk of study participation.
- Individuals diagnosed with chronic skin allergies.
- Female volunteers who indicated that they were pregnant or nursing.

5.3 Recruitment:

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

5.4 Informed Consent and Medical History Forms:

Each panelist completed an extensive medical history form and was assigned a permanent identification number. An informed consent was obtained from each volunteer describing the 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. These forms are only available for inspection on the premises of Cantor Research Laboratories, Inc. Reference 21 CFR Ch. 1 Part 50, Subpart B.

5.5 Population Demographics:

Number of subjects enrolled		53
Number of subjects completed study		53
Number of subjects with Sensitive Skin		29
Age Range		18–70
Sex	Male	10
	Female	43
Race	Caucasian	32
	Hispanic	2
	Asian	3
	African American	16

6.0 Equipment:

- Patch Description: Parke-Davis Hypoallergenic Readi Bandages (20 x 20mm Webril affixed to the center of a 40 x 40mm adhesive bandage) or the equivalent.

7.0 Procedure:

- Subjects are requested to bathe or wash as usual before arrival at the facility.
- The test material was applied neat, with no dilution.
- 0.2g of the test material was placed onto the occlusive, hypoallergenic patch.
- The patch was then applied directly to the skin of the infrascapular regions of the back, to the right or left of the midline and the subject was dismissed with instructions not to wet or expose the test area to direct sunlight.
- After 24 hours the patch was removed by the panelist at home.
- This procedure was repeated until a series of nine consecutive 24 hour exposures have been made for every Monday, Wednesday and Friday for three consecutive weeks.

- In the event of an adverse reaction, the area of erythema and edema is measured. The edema is estimated by the evaluation of the skin with respect to the contour of the unaffected normal skin. Reactions are scored just before applications two through nine and the next test date following application nine. Clients are notified immediately in the case of adverse reaction and determination is made as to treatment program if necessary.
- Subjects were then given a 10 - 14 day rest period after which a challenge or retest dose was applied once to a previously unexposed test site. The retest dose is equivalent to any one of the original nine exposures. Reactions are scored 24 and 48 hours after application.
- Comparison was made between the nine inductive responses and the retest dose.

8.0 Adverse Reactions:

Panelists were instructed to promptly report adverse effects to the investigator. The investigator would then determine the need for an interim examination and, if warranted, termination from the study. Any adverse effect(s), spontaneously expressed by the panelist or observed by the investigator or research staff, during or after the study were recorded on an Adverse Effect(s)/Intercurrent Event(s) Report.

9.0 Observations:

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

10.0 Results:

Please refer to attached Table.

11.0 Archiving and Confidentiality:

Hard copies of records such as raw data sheets, correspondence between the sponsor and Cantor Research Laboratories, Inc., executed ICFs, IRB approvals, AEs/SAEs associated with the study, etc. are maintained on the premises of Cantor Research Laboratories, Inc. in limited access storage files marked "Archive" for at least five years or more when specified by appropriate regulatory requirements. Electronic backups of reports are done on a secured server and a copy kept in an offsite secure location. Other study related information and documents such as forms, subject database, etc. are stored in a secure place at the lab.

The Principle Investigator (PI) & employees of Cantor Research Laboratories, Inc. will keep the test product, test related information, and the sponsor's identity confidential.

12.0 Conclusions:

The test material [CR Lab No.: P0728-F; Client No.: C. Schmitz Drawing Salve without Peruvian Balsam] when tested under occlusive conditions, as described herein, on a panel consisting of fifty three, of which twenty nine subjects were self-described as having sensitive skin, may be considered as a **NON-PRIMARY IRRITANT** and a **NON-PRIMARY SENSITIZER** to the skin according to the reference.

Shyla Cantor, Ph.D.
Principle Investigator

Mary Stroud, M.S.
Sub-Investigator

Maryann Muzzillo
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Quality Assurance Supervisor

9/12/17
Date

50 HUMAN SUBJECT REPEAT INSULT PATCH TEST SKIN IRRITATION / SENSITIZATION EVALUATION (OCCLUSIVE PATCH)

TABLE: SUMMARY OF RESULTS

Sponsor : C. Schmitz Drawing Salve
CR Lab No. : P0728-F
Client No. : C. Schmitz Drawing Salve without Peruvian Balsam

No.	*	Subject ID	Age	Sex	Race	Evaluation Response										
						Induction Phase									Challenge	
						1	2	3	4	5	6	7	8	9	24 Hour	48 Hour
1	*	03 7116	34	F	H	0	0	0	0	0	0	0	0	0	0	0
2	*	03 6100	35	F	C	0	0	0	0	0	0	0	0	0	0	0
3		03 8266	57	F	C	0	0	0	0	0	0	0	0	0	0	0
4	*	03 9147	64	F	AA	0	0	0	0	0	0	0	0	0	0	0
5		03 8973	63	F	C	0	0	0	0	0	0	0	0	0	0	0
6		03 9200	41	M	C	0	0	0	0	0	0	0	0	0	0	0
7	*	03 6805	54	M	A	0	0	0	0	0	0	0	0	0	0	0
8		03 7183	65	F	C	0	0	0	0	0	0	0	0	0	0	0
9		03 9103	58	M	AA	0	0	0	0	0	0	0	0	0	0	0
10	*	03 8241	46	F	AA	0	0	0	0	0	0	0	0	0	0	0
11		03 8268	46	M	AA	0	0	0	0	0	0	0	0	0	0	0
12		03 9104	64	M	C	0	0	0	0	0	0	0	0	0	0	0
13	*	03 7617	57	F	C	0	0	0	0	0	0	0	0	0	0	0
14		03 8874	56	F	C	0	0	0	0	0	0	0	0	0	0	0
15	*	03 8908	57	F	C	0	0	0	0	0	0	0	0	0	0	0
16	*	03 8957	52	F	C	0	0	0	0	0	0	0	0	0	0	0
17	*	03 9231	65	F	A	0	0	0	0	0	0	0	0	0	0	0
18	*	03 7391	40	F	AA	0	0	0	0	0	0	0	0	0	0	0
19		03 9196	38	F	C	0	0	0	0	0	0	0	0	0	0	0
20	*	03 6643	61	F	C	0	0	0	0	0	0	0	0	0	0	0
21	*	03 9174	70	F	C	0	0	0	0	0	0	0	0	0	0	0
22	*	03 8318	46	F	C	0	0	0	0	0	0	0	0	0	0	0
23	*	03 8972	52	F	C	0	0	0	0	0	0	0	0	0	0	0
24		03 8905	45	F	C	0	0	0	0	0	0	0	0	0	0	0
25		03 8444	36	F	C	0	0	0	0	0	0	0	0	0	0	0
26	*	03 9033	26	F	C	0	0	0	0	0	0	0	0	0	0	0
27		03 9233	34	F	AA	0	0	0	0	0	0	0	0	0	0	0
28		03 9059	30	F	AA	0	0	0	0	0	0	0	0	0	0	0

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TABLE: SUMMARY OF RESULTS *(Cont'd)*

CR Lab No. : P0728-F
Client No. : C. Schmitz Drawing Salve without Peruvian Balsam

No.	*	Subject ID	Age	Sex	Race	Evaluation Response										
						Induction Phase									Challenge	
						1	2	3	4	5	6	7	8	9	24 Hour	48 Hour
29	*	03 9181	42	F	H	0	0	0	0	0	0	0	0	0	0	0
30		03 8369	47	F	AA	0	0	0	0	0	0	0	0	0	0	0
31	*	03 7511	37	F	C	0	0	0	0	0	0	0	0	0	0	0
32		03 9086	54	F	C	0	0	0	0	0	0	0	0	0	0	0
33		03 9154	22	F	C	0	0	0	0	0	0	0	0	0	0	0
34	*	03 8873	59	F	C	0	0	0	0	0	0	0	0	0	0	0
35	*	03 9130	56	M	AA	0	0	0	0	0	0	0	0	0	0	0
36	*	03 8176	51	F	AA	0	0	0	0	0	0	0	0	0	0	0
37	*	03 7390	32	F	C	0	0	0	0	0	0	0	0	0	0	0
38	*	03 7460	41	F	C	0	0	0	0	0	0	0	0	0	0	0
39	*	03 8996	20	F	AA	0	0	0	0	0	0	0	0	0	0	0
40		03 9247	18	F	A	0	0	0	0	0	0	0	0	0	0	0
41		03 9131	40	F	C	0	0	0	0	0	0	0	0	0	0	0
42	*	03 9152	40	M	C	0	0	0	0	0	0	0	0	0	0	0
43		03 7750	44	F	AA	0	0	0	0	0	0	0	0	0	0	0
44	*	03 6509	59	F	AA	0	0	0	0	0	0	0	0	0	0	0
45		03 8910	56	F	AA	0	0	0	0	0	0	0	0	0	0	0
46		03 8952	58	M	C	0	0	0	0	0	0	0	0	0	0	0
47		03 9054	57	F	C	0	0	0	0	0	0	0	0	0	0	0
48	*	03 9161	18	M	C	0	0	0	0	0	0	0	0	0	0	0
49		03 6770	47	F	C	0	0	0	0	0	0	0	0	0	0	0
50	*	03 8281	52	F	C	0	0	0	0	0	0	0	0	0	0	0
51	*	03 9039	56	F	C	0	0	0	0	0	0	0	0	0	0	0
52	*	03 8635	58	F	AA	0	0	0	0	0	0	0	0	0	0	0
53		03 8636	27	M	AA	0	0	0	0	0	0	0	0	0	0	0

** Panelist self-described as having sensitive skin*

Evaluation Period: This study was conducted from August 2, 2017 through September 8, 2017.

Definition of Symbols Shown in Table:

0 - No evidence of any effect

? - (Barely perceptible) minimal faint (light pink) uniform or spotty erythema

1 - (Mild) pink uniform erythema covering most of contact site

2 - (Moderate) pink\red erythema visibly uniform in entire contact area

3 - (Marked) bright red erythema with accompanying edema, petechiae or papules

4 - (Severe) deep red erythema with vesiculation or weeping with or without edema

D - Patch eliminated due to reaction

Dc - Discontinued due to absence of subject on application date

M - Patch applied to an adjacent site after strong test reaction

S - Skin stained from pigment in product

T - Tan