THE INSTITUTE FOR SKIN RESEARCH

Consumer Product Evaluation

Prof. Sarah Brenner, Director
Specialist in Dermatology

February 11, 2007

DETERMINATION OF SENSITIZING PROPERTIES OF ONE (1) PRODUCT BY DRAIZE REPEATED INSULT PATCH TEST (RIPT) IN HUMAN VOLUNTEERS

Report Number: 443

Product:

Lederman Natural Multi Purpose Cosmetic Ointment

Galenic form: /

Sponsor: Lederman Consulting

Protocol date: 11.2.2007

Test completion date: 11.2.2007

Report date: 11.2.2007

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STATEMENT OF QUALITY ASSURANCE

Number of the clinical study: 443

Starting date of trial: 7.1.2007

Completion date of trial: 11.2.2007

The above study was carried out in accordance with the Good Clinical Practice and Standards established by the International Standardization Organization (ISO), and the standard operating procedures of the Institute for Skin Research (ISR).

The Quality Assurance Auditor testifies to the adherence to the rules, standards and procedures, and to the control of raw and final data emanating from this study.

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AIM

The aim of the study was to determine the sensitizing properties of the test article using Draize Repeated Insult Patch Test in human volunteers.

METHOD

2-1 Schedule of the trial
Order from: Lederman Consulting

Tested product received 1.1.07
Innocuousness certificate receipt: /
Subject recruited 4.1.07
Trial period: 6 weeks
Data analysis: 11.2.2007
Data fax: /
Final report: 11.2.2007

2-2 Experimental plan

Randomized with reference

2-3 Assessment criteria

2-3-1 Studied criteria

The sensitizing properties of the test article

2-3-2 Instrumentation

The sensitizing properties were evaluated by a patch preparation consisting of an occlusive application of the product by Finn Chamber/Hill Top Chamber/Leukotest or any other similar chamber on the volunteers. Each patch contained the test material.

2-3-3 Principle

The method employed in carrying out the test is similar to that described in "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" by J.H. Draize and published by the Association of Food and Drug Officials of the United States.

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2-4 Performance of the trial

2-4-1 Method of operation and trial schedule

2-4-1-1 Test Panel

The test involved the application of the test article on the intrascapular region of the back, or the arm of a group of 50 volunteer panelists. The panelists ranged from 18 to 65 years of age. These panelists were determined to be in good general health and free of any visible skin disease or anomaly in the area to be patched. Each panelist was required to read, understand and sign an informed consent statement.

2-4-1-2 Patch preparation

The test article was tested as supplied or diluted according to the product; soaps were diluted 10-20 times. When dilution was necessary, for example 20 times, 2.0 grams of the material and 38.0 grams of D.I. water (Total weight 40.0 grams) were stirred with magnetic rod or on a stirring plate until the solution was homogeneous. The final concentration of the product was 5.0% (w:w). 0.07-0.1 ml or gr. of the test material was applied in a patch test.
For tests of wipes, the test is conducted on a mixture of the wipe fabric and the material with which the wipe is impregnated.

2-4-1-3 Schedule of the trial

Volunteers were visited at home. They read the information sheet and signed the consent form.

Induction Phase: The patch was applied to its designated contact site and remained in place for 24 hours. At the end of this period the patch was removed and the site was examined for any dermal response. The panelists rested for 24 hours, after which the skin site was examined again. A patch was then applied to the same site as previously used. The second application was identical to the first and remained in place 24 hours. This procedure was repeated on Mondays, Wednesdays and Fridays or Sundays, Tuesdays and Thursdays until a series of nine applications were made. The panelists examined the site for any dermal response and reported their observations prior to the next application. The same site was used throughout the study. Each application was put on and removed by the staff of the Institute. A quality control person monitored the adherence to study protocol.

Challenge Phase: Following the 9th application, a rest period of 2 weeks elapsed after which a challenge application was applied in the same manner and to the same site described above. The challenge application was removed after 24 hours and the site was examined and graded for signs of irritation or sensitization. A follow-up examination was conducted at 48 hours after the challenge application (24 hours after patch removal), as well as at 48 and 72 hours after removal.

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2-4-2 Grading scale

0 No visible reaction

? Doubtful reaction: faint, minimal erythema, no infiltration

1 Weak positive reaction: erythema, infiltration, discrete papules

2 Strong positive reaction: erythema, infiltration, papules, discrete vesicles

3 Extra positive reaction: intense erythema, infiltration, coalescing vesicles / bullous reaction

IR Irritation reaction: discrete erythema without infiltration / patchy follicular erythema / hemorrhagic and follicular pustules

NT Not tested

2-4-3 Critical events

Definition: An adverse event was any clinical or biological alteration to the initial condition of the subject (including Intercurrent diseases), regardless of whether it was related to the tested product.

Adverse events: Serious adverse events included:

Hospitalization
Life-threatening
Death
Sequellae or partial or permanent invalidism

2-4-4 Drop-out

Conditions for exit from the test were in accordance with the Helsinki/Tokyo/Venice declaration and Israeli law concerning the protection of subjects in biomedical research. Subjects had the right to leave the study at any time and for any reason.

The investigator was authorized to terminate observation of the subject at any time if there was an intercurrent disease or an untoward event.

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The company could demand a subject be excluded from the test for violation of the protocol, for administrative reasons, or for any reason whatsoever.

Early exit from the study was avoided in order to avoid premature removal of a high proportion of subjects which would jeopardize the test results and render the study meaningless.

All premature exits due to intercurrent disease or untoward events were fully documented, entered in the case report form, and assigned to one of the following categories:

patient lost to follow-up
major violation of the protocol
withdrawal of consent
intercurrent disease
untoward event
administrative or other reason

2-4-5 Conditions for replacement of subjects

A subject removed from the trial during the study could be replaced. All replacements were discussed previously with the trial manager.

2-4-6 Collection and validation of data

The Study Technician enters data on case report forms and in a computerized database.

The Study Director validates the data.

2-4-7 Quality Assurance

The test report was written by the Study Technician and monitored by the Study Director and by a person authorized to perform the quality control of the study.
The test report was then sent to the Sponsor.

2-5 Selection of subjects

2-5-1 Pre-Inclusion criteria

None

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2-5-2 Inclusion criteria

2-5-2-1 General criteria

Subjects were aware of the test procedure and signed the consent form. They had to be cooperative, and fully cognizant of the necessity and the duration of the study controls and the importance of strict adherence to the protocol as determined by the ISR.

2-5-2-2 Specific criteria

Gender: male or female.

Age: between 18 and 65 years.

2-5-3 Non- Inclusion criteria

2-5-3-1 Population

Pregnant or nursing women.

2-5-3-2 Associated pathology

Cutaneous pathology on the treated zone.

Subjects suffering from serious or progressive diseases.

2-5-3-3 Previous or current treatment

Subjects using a treatment (retinoids, anti-inflammatory substances such as steroids) and modifiers of the cutaneous hydration.

2-5-3-4 Personal hygiene and habits

Unstable weight.

Excessive use of alcohol or tobacco.

2-5-4 Evaluation of compliance

If a subject deviated from the protocol, and the deviation was minor, the technician responsible cautioned the subject about the importance of adhering to the prescribed protocol. If the subject persisted or the deviation was major, the subject was declared non-compliant and removed from the test for the reason of non-compliance.

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2-5-5 Associated treatment during the study

No water was applied to the test site during application of the patch.

No systemic or topical treatment likely to modify the skin was permissible.

No use of dermopharmaceutical or cosmetic products, including cleansing products, was permissible on the zones being evaluated.

2-6 Number of subjects

The study was carried out on 50 volunteers as requested by the Sponsor.

2-7 Tested product

2-7-1 Treatment confidentiality

The product supplied by the Sponsor was encoded and applied to the subjects by the Study Technician.

2-7-2 Dosage

Standard quantity: 0.07-0.1 ml or gr.

2-7-3 Packaging

The product was labeled as follows:

The Institute for Skin Research
12 Tosefta Street
Tel Aviv 62917 Israel
Test number: 443
Product:

Lederman Natural Multi Purpose Cosmetic Ointment
This product is to be used only
under strict medical supervision

2-7-4 References

Product reference:
Standard: The method employed in carrying out this test was similar to that described in "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" by Draize and published by the Association of Food and Drug Officials of the United States.

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2-7-5 Form

Ointment

2-7-6 Storage

The product was maintained at room temperature in a dedicated air-conditioned room which was locked and access controlled.

2-7-7 Product Issue

The product was not distributed.

2-7-8 Application method

The product was applied by the Study Technician into the Finn Chamber/Hill Top Chamber/Leukotest or any other similar chamber, which was then applied on the intrascapular region of the back, or the arm.

TEST FOLLOW UP

The study was carried out on 50 volunteers, 12 male and 38 female subjects, aged 18 to 65 years.

50 subjects finished the study.

SUBJECT CHARACTERISTICS

Table 1: summarizes the characteristics of the subjects.

PRODUCT	SEX	AVERAGE AGE	MEDICAL HISTORY LIKELY TO INFLUENCE THE STUDY
1	F	40.6	None
1	M	40.8	None

The study of the product was carried out on 50 healthy volunteers aged 18 to 65 years.

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Lederman Natural Multi Purpose Cosmetic Ointment
Test No. 443

RESULTS

Table 2 presents the results of the product tested on the 50 volunteers

					RESULTS ACCORDING TO THE GRADING SCALE									
NO	SUBJECT	PRODUCT	SEX	AGE	1	2	3	4	5	6	7	8	9	10
1	M.R.	1	F	35	0	0	0	0	0	0	0	0	0	0
2	M.S.	1	F	61	0	0	0	0	0	0	0	0	0	0
3	V.B.	1	F	30	0	0	0	0	0	0	0	0	0	0
4	S.L.	1	F	35	0	0	0	0	0	0	0	0	0	0
5	Z.M.	1	F	30	0	0	0	0	0	0	0	0	0	0
6	G.S.	1	M	27	0	0	0	0	0	0	0	0	0	0
7	I.I.	1	M	43	0	0	0	0	0	0	0	0	0	0
8	I.V.	1	F	38	0	0	0	0	0	0	0	0	0	0
9	B.S.	1	F	39	0	0	0	0	0	0	0	0	0	0
10	M.L.	1	F	36	0	0	0	0	0	0	0	0	0	0
11	I.R.	1	F	38	0	0	0	0	0	0	0	0	0	0
12	B.R.	1	F	27	0	0	0	0	0	0	0	0	0	0
13	M.L.	1	F	34	0	0	0	0	0	0	0	0	0	0
14	A.M.	1	M	35	0	0	0	0	0	0	0	0	0	0
15	G.K.	1	F	46	0	0	0	0	0	0	0	0	0	0
16	R.O.	1	F	36	0	0	0	0	0	0	0	0	0	0
17	C.H.	1	F	49	0	0	0	0	0	0	0	0	0	0
18	G.R.	1	M	35	0	0	0	0	0	0	0	0	0	0
19	G.A.	1	F	34	0	0	0	0	0	0	0	0	0	0
20	T.Z.	1	F	37	0	0	0	0	0	0	0	0	0	0
21	H.E.	1	M	58	0	0	0	0	0	0	0	0	0	0
22	L.M.	1	M	42	0	0	0	0	0	0	0	0	0	0
23	D.O.	1	F	47	0	0	0	0	0	0	0	0	0	0
24	B.O.	1	F	38	0	0	0	0	0	0	0	0	0	0
25	S.O.	1	F	37	0	0	0	0	0	0	0	0	0	0
26	L.T.	1	F	41	0	0	0	0	0	0	0	0	0	0
27	M.I.	1	F	52	0	0	0	0	0	0	0	0	0	0
28	B.M.	1	F	48	0	0	0	0	0	0	0	0	0	0
29	B.E.	1	F	53	0	0	0	0	0	0	0	0	0	0
30	P.N.	1	M	31	0	0	0	0	0	0	0	0	0	0
31	M.R.	1	F	53	0	0	0	0	0	0	0	0	0	0
32	M.H.	1	M	52	0	0	0	0	0	0	0	0	0	0
33	G.O.	1	M	59	0	0	0	0	0	0	0	0	0	0
34	L.Y.	1	M	54	0	0	0	0	0	0	0	0	0	0
35	G.I.	1	F	59	0	0	0	0	0	0	0	0	0	0
36	L.S.	1	M	20	0	0	0	0	0	0	0	0	0	0
37	K.H.	1	F	29	0	0	0	0	0	0	0	0	0	0
38	K.B.	1	F	43	0	0	0	0	0	0	0	0	0	0
39	S.N.	1	F	32	0	0	0	0	0	0	0	0	0	0
40	V.V.	1	F	23	0	0	0	0	0	0	0	0	0	0
41	G.A.	1	F	59	0	0	0	0	0	0	0	0	0	0
42	B.R.	1	F	45	0	0	0	0	0	0	0	0	0	0
43	T.M.	1	F	34	0	0	0	0	0	0	0	0	0	0
44	H.H.	1	M	34	0	0	0	0	0	0	0	0	0	0
45	V.O.	1	F	35	0	0	0	0	0	0	0	0	0	0
46	L.R.	1	F	32	0	0	0	0	0	0	0	0	0	0
47	H.E.	1	F	54	0	0	0	0	0	0	0	0	0	0
48	A.S.	1	F	46	0	0	0	0	0	0	0	0	0	0
49	N.L.	1	F	49	0	0	0	0	0	0	0	0	0	0
50	H.S.	1	F	27	0	0	0	0	0	0	0	0	0	0

This table shows the results of the test on 50 volunteers.

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Table 3
Observation Sheets

No	Subject	Sex	Age	20 MINUTES AFTER REMOVAL OF THE 10TH APPLICATION DATE: 9.2.07	24 HOURS AFTER REMOVAL OF THE 10TH APPLICATION DATE 10.2.07	48HOURS AFTER REMOVAL OF THE 10TH APPLICATION DATE: 11.2.07
1	M.R.	F	35	0	0	0
2	M.S.	F	61	0	0	0
3	V.B.	F	30	0	0	0
4	S.L.	F	35	0	0	0
5	Z.M.	F	30	0	0	0
6	G.S.	M	27	0	0	0
7	I.I.	M	43	0	0	0
8	I.V.	F	38	0	0	0
9	B.S.	F	39	0	0	0
10	M.L.	F	36	0	0	0
11	I.R.	F	38	0	0	0
12	B.R.	F	27	0	0	0
13	M.L.	F	34	0	0	0
14	A.M.	M	35	0	0	0
15	G.K.	F	46	0	0	0
16	R.O.	F	36	0	0	0
17	C.H.	F	49	0	0	0
18	G.R.	M	35	0	0	0
19	G.A.	F	34	0	0	0
20	T.Z.	F	37	0	0	0
21	H.E.	M	58	0	0	0
22	L.M.	M	42	0	0	0
23	D.O.	F	47	0	0	0
24	B.O.	F	38	0	0	0
25	S.O.	F	37	0	0	0
26	L.T.	F	41	0	0	0
27	M.I.	F	52	0	0	0
28	B.M.	F	48	0	0	0
29	B.E.	F	53	0	0	0
30	P.N.	M	31	0	0	0
31	M.R.	F	53	0	0	0
32	M.H.	M	52	0	0	0
33	G.O.	M	59	0	0	0
34	L.Y.	M	54	0	0	0
35	G.I.	F	59	0	0	0
36	L.S.	M	20	0	0	0
37	K.H.	F	29	0	0	0
38	K.B.	F	43	0	0	0
39	S.N.	F	32	0	0	0
40	V.V.	F	23	0	0	0
41	G.A.	F	59	0	0	0
42	B.R.	F	45	0	0	0
43	T.M.	F	34	0	0	0
44	H.H.	M	34	0	0	0
45	V.O.	F	35	0	0	0
46	L.R.	F	32	0	0	0
47	H.E.	F	54	0	0	0
48	A.S.	F	46	0	0	0
49	N.L.	F	49	0	0	0
50	H.S.	F	27	0	0	0

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Summary: No subjects discontinued or missed any of applications or readings

SUMMARY OF THE RESULTS

These Case Report Forms are an integral part of the Final Report. The data are listed and summarized in Table I and Table II.

A total of 50 subjects, 12 male and 38 female, completed the test. Subjects range in age from 18 to 65 years: 20 subjects are 18 to 35, 13 subjects are 36 to 45, and 17 subjects are 46 to 65.

Results during the Induction Phase

The original patch sites exhibited no reactions during the Induction Phase, the Rest Period or the Challenge Phase.

No other reactions were exhibited.

At the Challenge Phase (the 10th application), no reaction was observed in any of the volunteers.

CONCLUSION

In this RIPT Study performed according to the aforementioned Experimental Design, after repeated applications, test material **Lederman Natural Multi Purpose Cosmetic Ointment**

did not induce in the 10th application (Challenge Phase) a contact dermal irritation and/or sensitization in human subjects.

This is to certify that the product was tested by the Institute for Skin Research according to the Draize Method on a panel of 50 volunteers, aged 18-65 years.

BIBLIOGRAPHY

"Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics" by J.H. Draize and published by the Association of Food and Drug Officials of the United States.

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Quality control was assured.

ISR
Avigail Vainer
Quality Assurance Auditor

Signature: _____ Date: 11.2.2007

Avigail Vainer
Quality Assurance Auditor

ISR
Ornit Almog
Study Director

Signature: _____ Date: 11.2.2007

Ornit Almog
Study Director

I.S.R
Sarah Brenner, M.D.
Director, Institute for Skin Research
Professor of Dermatology

Signature: _____ Date: 11.2.2007

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