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COMEDOGENIC POTENTIAL ON HUMAN SUBJECTS

AMA Ref. No.: MS08.HCOM.L3214SO.DER

Date: November 7, 2008

Sponsor: Ego Pharmaceuticals Pty. Ltd.
21-31 Malcolm Road
Braeside, Victoria 3195, Australia

1.0 Objective:

This panel has been convened to determine the comedogenic potential of a group of cosmetic products when applied topically under semi-occlusion to the skin of human panelists.

2.0 Test Material:

2.1 Test Material Description:

On August 29, 2008 one test sample labeled KG/060/(B)G7951/000/025 was received from Dermatest Pty. Ltd. and assigned AMA Lab No. L-3214.

2.2 Controls:

Acetulan was used as the positive control.

2.3 Handling:

Upon arrival at AMA Laboratories, Inc., the test material is 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 are retained for a period of three months 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 retained samples are kept two years beyond final report submission.

Sample disposition is conducted in compliance with appropriate federal, state and local ordinances.

2.4 Test Material Evaluation Prerequisite:

Prior to induction of a human test panel, toxicology, microbiology 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 3.0.

Sponsor purports that prior to sample submission to AMA 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 AMA personnel:

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

3.0 Institutional Review Board:

Reference: CFR Title 21 Part 56, Subparts A, B, C, and D. The IRB of AMA Laboratories, Inc., consists of five or more individuals, chosen from within the company for technical expertise and from the local community for lay interaction. The list of IRB members is kept on file at AMA Laboratories, Inc., and is available for inspection during the hours of operation.

4.0 Panel Selection:

4.1 Standards For Inclusion In A Study:

1. Individuals eighteen years of age or older.

2. Individuals free of any dermatological or systemic disorder, which would interfere with the results, at the discretion of the Investigator.

3. Individuals who have completed a preliminary medical history mandated by AMA Laboratories, Inc.

4. Individuals who have read, understood and signed an informed consent document relating to the specific study to which they are subscribing. Consent forms are kept on file and are available for examination on the premises of AMA Laboratories, Inc., only.

5. Individuals displaying prominent follicular orifices on the medial region of the back (upper).

4.2 Standards for Exclusion from a Study:

1. Individuals who are under a doctor's care.

2. Individuals taking medication, which in the opinion of the Investigator would mask or interfere with the results.

3. Individuals with chronic skin allergies.

4. Females who are pregnant or lactating or have been pregnant or given birth within the six month period immediately preceding commencement.

5. Individuals exhibiting any clinically evident disease in the area of the back.

4.3 Recruitment:

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

4.4 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 sign and date 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 medical history form. These forms along with the signed consent forms, are available for inspection on the premises of AMA Laboratories, Inc. only. Reference 21 CFR Ch. 1 Part 50, Subpart B.

5.0 Population Demographics:

Number of subjects enrolled		6
Number of subjects completing study		6
Age Range		22 - 44
Sex	Male	2
	Female	4
Race	Caucasian	4
	Hispanic	2
	Asian	0

6.0 Procedure:

A total of 6 healthy males and/or females prescreened for prominent follicular orifices on the medial region of the upper back were selected. If necessary, follicular biopsy technique (Marks and Dawber, 1977) was used to further qualify the panelists for inclusion according to microscopic results.

Thrice weekly, 0.2 to 0.5 ml of the test material (enough to completely saturate the pad) was dispensed onto a 4x4 cm cotton cloth patch (i.e. Curity or Webril or the equivalent). The patches were then applied to the medial region of the panelist's back and closely secured to the skin by semi-occlusive hypoallergenic tape (i.e. Blenderm or Dermalite II or the equivalent) using an overlayer of adhesive taping if necessary (Scanpor or the equivalent).

On all test panelists an untreated "sham" control site was included in which the test site was occluded with the patching materials but no test material was applied.

This procedure was repeated every other day until three applications per week were accomplished for a total of 6 weeks. Patches were removed after 48 hour exposure (usually Wednesday and Friday) and once weekly after 72 hour exposure (usually Monday). On removal all sites were gently cleaned and evaluated for any overt signs of irritation prior to repatching.

A series of follicular biopsies were performed at induction and following the final patch removal at each test site. Prior to execution of the final series of follicular biopsies, all sites were cleaned, once with corn oil and once with alcohol, for the purpose of removing any waxy surface deposits that might interfere with biopsy. Sites were allowed to stand for 10-15 minutes prior to performing biopsies. Follicular biopsy was accomplished by means of a cyanoacrylate adhesive dispensed onto a glass slide and applied to the test area.

Upon curing, the slide was rapidly but accurately removed to protect the integrity of the biopsy. A total of five, 1-cm^2 area biopsies were taken, randomly selected from the 16 square centimeter grid comprising each test site. Slides were examined under a microscope and the numbers of follicles and microcomedones per square centimeter were counted. An optical micrometer was employed to measure the size of several microcomedones and follicles to provide a tangible reference for valuation. The mean numbers of follicles and microcomedones were then calculated for each test site.

7.0 Scoring:

Upon completion of the above-described counting procedure, scoring was conducted based on the following scale:

0 = no microcomedones or hyperkeratinization; normal follicular orifices.
1 = at least 25 percent of the follicles exhibiting microcomedones (small keratinatious cylinders inspissated within the lumina).
2 = at least 50 percent of the follicles exhibiting moderately sized microcomedones.
3 = at least 75 percent of the follicles displaying large, tightly compacted, globoid microcomedones.

8.0 Results:

The mean number of follicles and comedones per square centimeter and the comedogenic score (outlined in Section 7.0) for each subject have been calculated and are listed in Tables 2 thru 4. The ratio of follicles to comedones per square centimeter for each subject and for each treatment group have also been included in these tables to assess the degree of follicular involvement more extensively.

Table 1 lists the pre and post treatment mean ratios of follicles to comedones for each test material and positive and negative (untreated) controls. The data depicted in these tables represent the change in the test site expressed as a mean follicle to comedone ratio (i.e.: for Acetulan pre = 27.86 follicles for every 1 comedone; post = 18.31 follicles for every 1 comedone).
Therefore, to determine the amount of change in the comedone activity due to the test agent, a numeric value for the ratio was obtained (i.e.: 27.86:1 = 1/27.86 = 0.0359; 18.31:1 = 1/18.31 = 0.0546) and the values obtained can be used to determine the percent difference in comedone activity due to treatment.

A clinically significant increase in comedogenic scores was noted for the positive control test site, treated with Acetulan.

The results of panelists treated with the test material L-3214 exhibited difference of 5.51% in comedogenic activity relative to pre-treatment baseline. When compared to the untreated "sham" site, which showed a change in the comedogenic score of 2.16% and the positive control, Acetulan, which showed a change of 52.20%, the test material exhibited scores are considered non-comedogenic.

9.0 Observations:

Unremarkable.

10.0 Archiving:

All original samples, raw data sheets, technician's notebooks, correspondence files, and copies of final reports and remaining specimens are maintained on premises of AMA Laboratories in limited access storage files marked "Archive." A duplicate disk copy of final reports is separately archived in a bank safe deposit vault.

11.0 References:

A. Mills O.H., Kligman A.M.: A human model for assessing comedogenic substances. Archives of Dermatology 18:903-905, 1982.

B. Marks R., Dawber RPR: Skin surface biopsy: An improved technique for examination of the horny layer. British Journal of Dermatology 84: 117-123, 1971.

C. Ayres J.D., Mills O.H., Lyssikatos J., Kligman A.M., Groh D.G.: Assessment of a new method for determining the acnegenic potential of topically applied materials on human subjects. Presented at the IFSCC International Congress, Yokohama, Japan, October 13-16, 1992.

12.0 Conclusions:

Within the limits imposed by the conduct and population of the study described herein, the following test product (AMA Lab No.: L-3214, Client No.: KG/060/(B)G7951/000/025) may be considered **NON-COMEDOGENIC.**

Mayya Tatsene, M.D.
Study Director

Patrycja Bienias, M.S.
Technician

David R. Winne, B.S.
Technical Director

11/7/08
Date

Table 1

SUMMARY

DEGREE OF COMEDONE ACTIVITY

AMA LAB NOS.	RATIO OF FOLLICLES:COMEDONES PRE-TREATMENT	POST-TREATMENT	COMEDONE ACTIVITY VALUES *PRE TREATMENT	**POST TREATMENT	% DIFFERENCE
L-3214	30.31	28.72	0.0330	0.0348	5.51
ACETULAN	27.86	18.31	0.0359	0.0546	52.20
UNTREATED	30.25	29.61	0.0331	0.0338	2.16

$$* = \frac{1}{\text{Pre - treatment ratio of Follicles : Comedones}}$$

$$** = \frac{1}{\text{Post - treatment ratio of Follicles : Comedones}}$$

Table 2

PRE-TREATMENT SCORES

AMA Lab No.: L-3214
Client No.: KG/060/(B)G7951/000/025

Subject ID	Mean Follicles/ cm^2	Mean Comedones/ cm^2	Ratio of Follicles: Comedones	% of Foll. Showing Comedones	Comedogen. Score
58 3965	4.00	0.40	10.00	9.09	0.36
55 9599	14.60	0.60	24.33	3.95	0.16
28 0971	11.60	0.40	29.00	3.33	0.13
62 4500	16.20	0.40	40.50	2.41	0.10
54 4408	12.60	0.20	63.00	1.56	0.06
70 2436	9.00	0.60	15.00	6.25	0.25
MEAN:	11.33	0.43	30.31	4.43	0.18

POST-TREATMENT SCORES

AMA Lab No.: L-3214
Client No.: KG/060/(B)G7951/000/025

Subject ID	Mean Follicles/ cm^2	Mean Comedones/ cm^2	Ratio of Follicles: Comedones	% of Foll. Showing Comedones	Comedogen. Score
58 3965	5.20	0.40	13.00	7.14	0.29
55 9599	11.80	0.60	19.67	4.84	0.19
28 0971	11.80	0.60	19.67	4.84	0.19
62 4500	12.20	0.20	61.00	1.61	0.06
54 4408	9.00	0.20	45.00	2.17	0.09
70 2436	8.40	0.60	14.00	6.67	0.27
MEAN:	9.73	0.43	28.72	4.55	0.18

Table 3

PRE-TREATMENT SCORES

AMA Lab No.: Acetulan

Subject ID	Mean Follicles/ cm^2	Mean Comedones/ cm^2	Ratio of Follicles: Comedones	% of Foll. Showing Comedones	Comedogen. Score
58 3965	4.60	0.20	23.00	4.17	0.17
55 9599	14.00	0.40	35.00	2.78	0.11
28 0971	6.40	0.20	32.00	3.03	0.12
62 4500	13.60	0.60	22.67	4.23	0.17
54 4408	7.60	0.20	38.00	2.56	0.10
70 2436	6.60	0.40	16.50	5.71	0.23
MEAN:	8.80	0.33	27.86	3.75	0.15

POST-TREATMENT SCORES

AMA Lab No.: Acetulan

Subject ID	Mean Follicles/ cm^2	Mean Comedones/ cm^2	Ratio of Follicles: Comedones	% of Foll. Showing Comedones	Comedogen. Score
58 3965	4.00	0.40	10.00	9.09	0.36
55 9599	11.00	0.60	18.33	5.17	0.21
28 0971	6.00	0.80	7.50	11.76	0.47
62 4500	11.20	0.40	28.00	3.45	0.14
54 4408	7.40	0.20	37.00	2.63	0.11
70 2436	5.40	0.60	9.00	10.00	0.40
MEAN:	7.50	0.50	18.31	7.02	0.28

Table 4

PRE-TREATMENT SCORES

AMA Lab No.: Untreated

Subject ID	Mean Follicles/ cm^2	Mean Comedones/ cm^2	Ratio of Follicles: Comedones	% of Foll. Showing Comedones	Comedogen. Score
58 3965	6.80	0.20	34.00	2.86	0.11
55 9599	12.00	0.40	30.00	3.23	0.13
28 0971	6.80	0.20	34.00	2.86	0.11
62 4500	13.80	0.40	34.50	2.82	0.11
54 4408	14.80	0.40	37.00	2.63	0.11
70 2436	7.20	0.60	12.00	7.69	0.31
MEAN:	10.23	0.37	30.25	3.68	0.15

POST-TREATMENT SCORES

AMA Lab No.: Untreated

Subject ID	Mean Follicles/ cm^2	Mean Comedones/ cm^2	Ratio of Follicles: Comedones	% of Foll. Showing Comedones	Comedogen. Score
58 3965	5.20	0.20	26.00	3.70	0.15
55 9599	11.80	0.40	29.50	3.28	0.13
28 0971	6.00	0.20	30.00	3.23	0.13
62 4500	10.40	0.20	52.00	1.89	0.08
54 4408	11.80	0.40	29.50	3.28	0.13
70 2436	6.40	0.60	10.67	8.57	0.34
MEAN:	8.60	0.33	29.61	3.99	0.16

13.0 Quality Assurance Statement:

This study was inspected in accordance with the Standard Operating Procedures of AMA Laboratories, Inc. To assure compliance with the study protocol, the Quality Assurance Unit completed an audit of the study records and report.

Report reviewed by:

Kamil Wojtowicz, M.S.
Quality Assurance Supervisor

11/7/08
Date