SKIN STUDY CENTER

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Final Report

to

AkPharma Inc.

on

Dansyl Chloride Cell Renewal Study

KGL #5698

Submitted by:

James J. Leyden, M.D. — *Date* 1/20/05

The names of the Skin Study Center, Ivy Laboratories, KGL, Inc. any officer, employee or collaborating scientist are not to be used for any advertising, promotional or sales purposes without the written consent of the Skin Study Center, Ivy Laboratories or KGL, Inc.

Quality Assurance Officer:

Patricia F. Alfano — *Date* 20 Jan 2005

CONFIDENTIAL

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I. OBJECTIVE

The objective of this study was to evaluate the ability of two topically applied test formulations to enhance epidermal cell renewal.

II. BACKGROUND

The human epidermis represents a cell renewal system in which fully differentiated cells (corneocytes) are being continually shed from the skin surface. Since this system operates under steady-state conditions, this loss of desquamated cells must be balanced by new cell production in the germinative cell layers. One parameter that is especially important to measure in such a system is transit time - the time required for a cell to move through a compartment. Since cells move in unison as a layer through the stratum corneum, this means in this special case that the transit time is equivalent to turnover time - the time required for a compartment to completely renew itself.

Previous studies[1, 2, 3] have demonstrated that the turnover time of the stratum corneum can be measured non-intrusively by impregnating it with a fluorescent marker dye that binds avidly to the nonviable epidermal cells. Thus, the time required for the dye to disappear, which can be monitored by Wood's lamp examination, is an indication of the turnover time of the stratum corneum. Therefore, any differences in the time required for the dye to disappear from a treated and a non-treated site can be considered to be an expression of that product's ability to enhance epidermal renewal.

III. EXPERIMENTAL DESIGN

A. General Considerations

Prior to initiation of the study, the proposed protocol, the informed consent form and the product information was submitted by the Sponsor to St. David's Human Research Review Board, Inc. which was charged with reviewing and approving the study. This study was approved by the St. David's Human Research Review Board, Inc. on October 28, 2004. This notification of the Board's approval along with a description by profession of the Board's composition has been provided to the Investigator prior to the initiation of the study.

This study was conducted at the Skin Study Center in Broomall, Pennsylvania with James Leyden, M.D. serving as the Principal Investigator. Gary Grove, Ph.D. was the Sub-Investigator and was responsible for supervising the daily operations related to this study. A copy of Dr. Leyden's and Dr. Grove's curriculum vitae are on file with the Sponsor.

In conducting this study, we followed Good Clinical Practices (GCP) and Good Laboratory Practices (GLP) guidelines as well as the COLIPA Efficacy Testing Guidelines.

This study was conducted from November 1, 2004 to December 24, 2004. A calendar of events outlining the schedule of treatments and evaluative procedures that was followed is attached as ***Appendix A****. The daily weather records covering this time as extracted from newspaper reports are included as* ***Appendix B****.*

Briefly, this consisted of a two week treatment period during which time the products were applied twice daily including weekends to the test sites, a 2 day staining procedure during which time the treatments were suspended, followed by a 2 to 4 week period during which the twice daily applications of the formulations were restarted and continued. The intensity of the residual staining was monitored visually under Wood's lamp illumination by a trained observer just prior to treatment.

B. Panelist Selection

All volunteers were recruited from a pool of healthy suburban women who meet the inclusion/exclusion criteria. Briefly, they were within the range from 45 to 65 years of age and were previously diagnosed with compromised epidermal cell renewal and moderately severe dry skin.

Each candidate was interviewed to make certain that they have no medical problems and that they were not using concomitant medications that might interfere with the study results. They were also screened to make sure that they have no known sensitivities to cosmetics, moisturizers, adhesive dressings, etc. Women who were either pregnant or breast-feeding were also excluded from participating in this study.

All volunteers signed consent forms after being informed their obligations and risks that they might encounter as a participant in this study. A copy of the consent form used is attached as ***Appendix C****.*

Upon selection, each panelist was advised of the general nature and purpose of this study and instructed not to "tamper" with the test sites in any way. Panelists were also told that although the test sites may be washed during normal bathing, excessive scrubbing must be avoided. In addition, they were instructed not to go swimming and to take all baths/showers prior to their daily application.

C. Methods

1. Test Product and Treatment Schedule

The two test products utilized in this study were provided by the Sponsor and labeled with the designated (randomization) panelist number.

Product application to either the right or left upper inner arm followed the randomization schedule attached as ***Appendix D****. The design of this randomization allowed for each panelist to be assigned one of the 2 test materials and 1 non-treated site. This resulted in approximately 15 sites for each product and non-treated control pairing. The product was dispensed from a dropper bottle and the panelists rubbed in the product using their fingertip over the area (approximately 3" x 5") on their designated upper inner arm according to the Sponsor's instructions (****Appendix E****). A technician monitored each panelist's treatment on Monday, Wednesday and Friday mornings throughout the study.*

The panelists were provided with a diary form to record the time of their twice daily applications. A sample of this diary form is attached as ***Appendix F.***

2. Stratum Corneum Turnover Time Determinations

After the two week pretreatment, treatment was temporarily suspended and the test sites were stained using the following procedure: between 8:00 and 9:00 am, the first application of 0.1ml of a suspension of 5% Dansyl Chloride in white petrolatum was made under occlusion on each treatment site. Six hours later, a second application of the dye was made and the dressings renewed. After a twenty-four hour staining period, the occlusive dressings were removed and the test sites were thoroughly washed with soap and water. After being patted dry, each test site was examined under a Wood's lamp and the acceptability of staining determined by Charles Zerweck, Ph.D. with the assistance of Mr. John Chicchi.

Product application resumed on the evening the dye patches were removed and continued twice daily thereafter. The degree of residual staining in terms of brightness was determined by Dr. Zerweck or Mr. Chicchi prior to the Monday, Wednesday and Friday morning applications or more often if deemed necessary by the grader.

Neither Dr. Zerweck nor Mr. Chicchi was involved in any of the treatment aspects of the study, so that all assessments were made in a blind fashion. This routine of grading, followed by treatment, continued at the Skin Study Center, until all sites were no longer fluorescent under Wood's lamp illumination.

D. Statistical Evaluations

Dr. Grove was responsible for devising a sorting template based on Excel spreadsheet software and implemented on the IBM clone desktop computer. The sorted data was tabulated and arranged in order of panelist number for each point of evaluation. In creating these tables, column averages were computed, but only to give a preliminary look at the findings.

Dr. Grove was also responsible for statistical analysis of the stratum corneum turnover times using appropriate the statistics package provided within the Excel 2000 environment.

The approach used by Dr. Grove followed the general recommendations set forth by the International Federation of Society of Cosmetic Chemists in their Monograph on Principles of Product Evaluation: Objective Sensory Methods. In this approach, a Paired T-Test was employed to compare each treatment relative to its non-treated control.

For all analyses, a two tailed $p < 0.05$ was taken as the level of significance.

IV. RESULTS

A. Panelist Accountability

A total of 30 panelists were recruited for this study, 28 of whom completed the entire study. One panelist (#29 R092) withdrew for personal reasons unrelated to the study. One other panelist (#41 K128) was discontinued due to a dansyl reaction. ***Appendix G*** *contains a listing of each panelist's age and sex.*

There were no missed visits and we have no reason to believe that the remaining panelists were not fully compliant with all provisions of this study.

B. Stratum Corneum Turnover Time Determinations

*The data for the stratum corneum turnover time determinations is attached as **Appendix H**. Below is a summary of these data:*

Expert Grader Assessment Number of Days until Dye Disappearance								
No Rx			***Code C***			***No Rx vs. C***	***Difference***		
Mean	***±***	***Std Dev***	***Mean***	***±***	***Std Dev***	***P***	***Mean***	***±***	***Std Dev***
20.9	*±*	*2.7*	*17.3*	*±*	*2.7*	*0.0003*	*3.6*	*±*	*2.8*

Expert Grader Assessment Number of Days until Dye Disappearance								
No Rx			***Code R***			***No Rx vs. R***	***Difference***		
Mean	***±***	***Std Dev***	***Mean***	***±***	***Std Dev***	***P***	***Mean***	***±***	***Std Dev***
23.6	*±*	*3.9*	*18.4*	*±*	*3.8*	*<0.0001*	*5.2*	*±*	*2.9*

This shows quite clearly that both Code R and Code C are effective in enhancing stratum corneum renewal.

V. CONCLUSIONS

On the basis of the data collected during previous studies, we know that cell turnover time as determined with this method is normally 18 - 22 days for a non-treated control. We also know from our studies of sham manipulated control sites that the effect of rubbing and massaging the sites normally causes a decrease in cell turnover time of 1 - 2 days. It has been our experience that in order to be considered a truly effective enhancer of epidermal cell renewal, a product should cause the turnover time to be approximately four days less than a non-treated, non-manipulated control site.

From the results obtained during the course of this study, we feel that it is reasonable to conclude that any test product that demonstrated a marked enhancement in cell turnover of at least 3 days justifies it being rated as truly effective in this regard. The following test products meet this criteria:

	Days Difference	***Degree of Enhancement expressed as a percentage***
Code C	*3.6*	*17.2%*
Code R	*5.2*	*22.0%*

One consequence of reduced cell renewal is that the corneocytes must reside at the skin surface for a longer period of time. Such surface cells are exposed to elements and do become more "weathered" than those that remain on the surface for shorter periods of time. We feel that if epidermal cell turnover is increased, through cosmetics intervention, these old weather beaten cells will be more rapidly replaced by fresh, new ones. In related studies, we have found that enhancing the quality of the surface corneocytes usually, but not always, results in an improvement in the appearance of the skin. One clear exception is with those substances that induce frank irritation which can dramatically elevate turnover rate by 50% or more but also lead to a red scaly appearance that clearly is not cosmetically acceptable.

VI. REFERENCES

1) Grove, G.L. and Kligman, A.M.: Age-associated changes in human epidermal cell renewal. J. Geron. 38:137-142, 1983.

2) Grove, G.L.: Microspectrophotometry and other nonradioactive methods for assessing proliferative activity in vivo. In: Cell Proliferation in Psoriasis. N.A. Wright and P. Camplejohn (eds.) Edinburgh: Churchill Livingstone, 1982, pp. 93-103.

3) Grove, G.L.: Age-associated changes in the replacement rate of exfoliated corneocytes in normal human skin. In: Cutaneous Aging. A. Kligman and Y. Takase (eds.) Tokyo: University of Tokyo Press, 1988, pp. 185-191.

VII. RECORD RETENTION

Please be advised that the records for this study will remain on file at KGL, Inc. (or a remote storage site) for a period of 1 year from the issue date of the final report and then destroyed unless we are notified otherwise by the Sponsor using the form accompanying this report. It is the responsibility of the Sponsor to ensure that the completed form is promptly returned to KGL.

Appendix A

Calendar of Events

CALENDAR OF EVENTS
DANSYL CHLORIDE CELL RENEWAL STUDY

WEEK OF	MON.	TUES.	WED.	THURS.	FRI.	SAT.	SUN.
Nov. 1, 2004	BEGIN WEAN Paperwork Day -7						
Nov. 8, 2004	START RX AT LAB	RX	RX	RX	RX	RX	RX
Nov. 15, 2004	RX AT LAB	RX	RX	RX	RX	RX	RX
Nov. 22, 2004	DANSYL APPLIED AM & PM OCCLUDED	PATCHES REMOVED SITES WASHED DAY 0	UV EXAM RX DAY 1	RX DAY 2	UV EXAM RX DAY 3	RX DAY 4	RX DAY 5
Nov. 29, 2004	UV EXAM RX DAY 6	RX DAY 7	UV EXAM RX DAY 8	RX DAY 9	UV EXAM RX DAY 10	RX DAY 11	RX DAY 12
Dec. 6, 2004	UV EXAM RX DAY 13	RX DAY 14	UV EXAM RX DAY 15	RX DAY 16	UV EXAM RX DAY 17	RX DAY 18	RX DAY 19
Dec. 13, 2004	UV EXAM RX DAY 20	RX DAY 21	UV EXAM RX DAY 22	RX DAY 23	UV EXAM RX DAY 24	RX DAY 25	RX DAY 26
Dec. 20, 2004	UV EXAM RX DAY 27	RX DAY 28	UV EXAM DAY 29				

PANEL: 30 FEMALE PANELISTS, AGES 45-65

PRODUCT: 2 PRODUCT TO BE SUPPLIED BY SPONSOR WITH DOSAGE & USE INSTRUCTIONS

RANDOMIZATION: RIGHT ARM VS. LEFT ARM
- TREATED CODE "C" VS. NON-TREATED
- TREATED CODE "R" VS. NON-TREATED

TEST SITES: UPPER INNER ARMS; ONE SITE ON EACH ARM
EACH SITE APPROXIMATELY 5 cm X 10 cm

UV EXAM: VISUAL EXAMINATION UNDER WOOD'S LIGHT TO DETERMINE DANSYL APPEARANCE/DISAPPEARANCE

Appendix B

Weather Information

2004 WEATHER INFORMATION

MONTH	DATE	DAY	HIGH TEMP °F	LOW TEMP °F	PRECIP. INCHES
NOVEMBER	1	MON	64	50	
	2	TUE	67	47	
	3	WED	64	54	
	4	THU	49	39	0.52
	5	FRI	55	48	
	6	SAT	60	39	
	7	SUN	69	42	
	8	MON	58	45	
	9	TUE	44	34	
	10	WED	47	29	
	11	THU	58	40	
	12	FRI	48	41	0.66
	13	SAT	47	37	0.20
	14	SUN	50	28	
	15	MON	60	30	
	16	TUE	60	35	
	17	WED	59	37	
	18	THU	58	45	
	19	FRI	62	43	
	20	SAT	57	50	0.02
	21	SUN	54	49	
	22	MON	55	43	
	23	TUE	52	48	
	24	WED	59	51	0.07
	25	THU	65	49	0.03
	26	FRI	47	30	
	27	SAT	55	35	
	28	SUN	60	53	1.30
	29	MON	49	36	
	30	TUE	50	36	

2004 WEATHER INFORMATION

MONTH	DATE	DAY	HIGH TEMP °F	LOW TEMP °F	PRECIP. INCHES
DECEMBER	1	WED	59	45	0.87
	2	THU	47	32	
	3	FRI	49	29	
	4	SAT	46	26	
	5	SUN	55	37	
	6	MON	45	36	0.01
	7	TUE	48	39	0.56
	8	WED	61	50	0.22
	9	THU	48	37	0.03
	10	FRI	51	48	0.22
	11	SAT	50	49	0.01
	12	SUN	46	38	
	13	MON	47	42	0.02
	14	TUE	40	32	
	15	WED	36	22	
	16	THU	43	23	
	17	FRI	47	33	
	18	SAT	47	26	
	19	SUN	41	30	0.03
	20	MON	20	10	
	21	TUE	39	14	
	22	WED	54	27	
	23	THU	60	42	0.22
	24	FRI	37	31	

Appendix C

Sample Consent Form

INFORMED CONSENT FORM

TITLE: A COMPARATIVE,DOUBLE-BLIND RANDOMIZED, CONTROLLED STUDY OF TOPICAL CALCIUM GLYCEROPHOSPHATE VS. UNTREATED SKIN VS. REGENERIST® IN PATIENTS WITH COMPROMISED EPIDERMAL CELL RENEWAL AND MODERATELY SEVERE DRY SKIN

SPONSOR: AkPharma, Inc

PRINCIPAL INVESTIGATOR: James J. Leyden, M.D.
KGL Laboratories - Skin Study Center
505 Parkway
Broomall, PA 19008
610-544-1715 (Daytime)
After hours: Dr. Grove: 610-358-2381
Dr. Leyden: 610-251-9775

INTRODUCTION

You are being invited to participate in this research study of a non-prescription skin treatment at KGL Laboratories - Skin Study Center. This study is sponsored by AkPharma Inc. You are being invited to take part because you have moderately severe dry skin with compromised epidermal cell renewal. The active ingredient of this non-prescription skin treatment is calcium glycerophosphate (CGP). This treatment will be compared to untreated skin and to Regenerist®, a non-prescription skin treatment that is available in stores as an over-the-counter product.

The purpose of this study is to evaluate if these non-prescription skin treatments reduce symptoms associated with moderately severe dry skin with compromised epidermal cell renewal. Non-invasive measurements of the skin will be used to determine this.

You will be one of approximately 30 females age 45 – 65 involved in this research project at KGL Laboratories, Skin Study Center. Your participation will last for approximately 7 weeks and will require 18 office visits.

HOW THE STUDY WORKS

VISIT ONE

If you agree to participate in the study and sign this consent form, a member of the study staff will assess your medical history.

You cannot participate in this study if any of the following apply to you:

- Pregnant or breast feeding.
- Major psychiatric disorder within the past two years not controlled by a stable dose of medication for the last six months.

- Alcohol or substance abuse within the past two years.
- Participation in any clinical trial within the past three months.
- Known allergy or hypersensitivity to calcium supplements.
- Known allergy or hypersensitivity to dansyl chloride

An expert skin grader will assess the condition of your skin. We will ask you what medication(s), both prescription and over-the-counter, you are now taking. If there are any changes in your medications, or you become pregnant, during the study, you are to tell us immediately. Your study doctor will determine your continuing status in the study.

If the doctor determines you are an appropriate candidate for the study, you will be required to discontinue the use of all "skin care" products on any parts of your body (face is exempt) through study completion.

VISIT TWO

After a one week "weaning" period from whatever skin care products you previously used, you will return for an office visit, at which your suitability for continuation in the study will be determined by Charles Zerweck, Ph.D.

If you continue in the study, you will be "randomized" into one of four treatment groups.

(1)Topical CGP applied twice daily to the LEFT arm as instructed – OR -
(2)Topical CGP applied twice daily to the RIGHT arm as instructed - OR
(3)Topical OTC applied twice daily to the LEFT arm as instructed – OR -
(4)Topical OTC applied twice daily to the RIGHT arm as instructed.

Being randomized means that you are put into a group by a chance process, like flipping a coin. Your chance of being assigned to any of the four treatment groups is equal. Please do not disclose this information. The doctors who assess your skin condition throughout the study won't know which group you are in, until the study is over.

The disclosure mentioned above refers to the subject not disclosing Left or Right side as "treated" or "untreated" skin to the Expert Grader, who will be examining both the untreated skin and the treated skin under an ultraviolet Woods Lamp.

Both the investigator site and the subject will be blinded as to which topical product the subject receives. Subjects will subsequently be evaluated at each clinic visit.

You will be provided with application instructions. You will be instructed to apply your assigned study product to the appropriate (LEFT or RIGHT) arm according to the instructions provided.

You will be instructed not to apply any products, other than those provided, nor to tamper with your arms in any way during the remaining study period. You will be instructed to allow the study product to be absorbed by the skin before covering again with any clothing. You will be instructed not to bathe or shower on the day of your study visits until after your evaluations have been completed by the Skin Study Center.

You will also be asked about any changes in medication or any problems you may have experienced since the last visit. Non-invasive measurements of the arm test sites will be taken.

You will be given enough study treatment product to last you until completion of the study. You will also be given a "Patient's Application Log" to record the time of your twicedaily applications to be completed and returned at your next visit.

VISIT THREE

You will return to the office for Visit Three one week after Visit Two; then one week after Visit Three for Visit Four. At Visit Three and at Visit Four you will be asked to inform the study staff of medication changes and/or problems that may have occurred since your last visit. You will bring your completed "Patient's Application Log" to these visits along with your remaining study treatment. You will be given a new "Patient's Application Log" to take home with you.

VISITS FOUR, FIVE & SIX

You will return to the office for Visit Four one week after Visit Three. You will bring your completed "Patient's Application Log" to these visits along with your remaining study treatment. At Visit Four treatment to the arm test sites will be temporarily suspended. The arm test sites will be stained using a suspension of 5% Dansyl Chloride in white petrolatum and covered with a dressing. You will be given a new "Patient's Application Log" to take home with you.

Visit Five will be six hours after Visit Four. At Visit Five, a second application of the dye will be made and the dressings renewed.

Visit Six will be scheduled one day after Visit Five. At Visit Six, the dressings will be removed and the test sites will be thoroughly washed with soap and water. After being patted dry, each arm test site will be examined under a Wood's lamp and the acceptability of staining determined by Dr. Charles Zerweck. If Dr. Zerweck determines that the UV staining is not acceptable then the dansyl patches will be reapplied and you will be required to return to the office six hours later that day for acceptability. Study product application will resume on the evening the dressings are removed and will continue twice daily thereafter.

VISITS SEVEN & EIGHT

You will return to the office for Visit Seven one day after Visit Six, then again two days after Visit Seven for Visit Eight. At these visits you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. An expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your study treatment product.

VISIT NINE

You will return to the office for Visit Nine three days after Visit Eight. You will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment. You will be given a new "Patient's Application Log" to take home with you.

VISITS TEN & ELEVEN

You will return to the office for Visit Ten two days after Visit Nine, then again two days after Visit Ten for Visit 11. At these visits you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment.

VISIT TWELVE

You will return to the office for Visit 12 three days after Visit 11. At Visit 12 you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment. You will be given a new "Patient's Application Log" to take home with you.

VISITS THIRTEEN & FOURTEEN

You will return to the office for Visit 13 two days after Visit 12, then again two days after Visit 13 for Visit 14. At these visits you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment.

VISIT FIFTEEN

You will return to the office for Visit 15 three days after Visit 14. At Visit 15 you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment. You will be given a new "Patient's Application Log" to take home with you.

VISITS SIXTEEN & SEVENTEEN

You will return to the office for Visit 16 two days after Visit 15, then again two days after Visit 16 for Visit 17. At these visits you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment.

VISIT EIGHTEEN

You will return to the office for Visit 18 three days after Visit 17 for your final study visit. At Visit 18 you will inform the study staff of medication changes and/or problems that may have occurred since your last visit. The expert grader will assess the condition of your arm skin test sites using a Wood's lamp. You will bring your completed "Patient's Application Log" to these visits along with your supply of study treatment.

RISKS

The products being studied are non-prescription treatments, not drugs. At this time, there are no known side effects of using these non-prescription treatments. It is possible that you may experience some skin irritation

from the treatments or the dressings.

BENEFITS
You may or may not benefit from your participation in this study. The treatment may or may not improve your dry skin symptoms. The information gained from this study may benefit others with problematic skin symptoms.

ALTERNATIVE TREATMENTS
You do not have to participate in this research study to receive treatment. There are standard therapies available, which the study staff will discuss with you.

COST TO PARTICIPATE
There will be no costs to you for participating in this research study.

PAYMENT FOR PARTICIPATION

You will be compensated for your participation in this research study in the amount of one hundred fifty dollars ($150.00) to defray transportation expenses. You will be paid in full at the completion of your participation in the study. If you do not successfully complete the entire study, you will be paid based on the following pro-rated basis:

$8.33 per visit completed, Visit 1 through 18.

All payments will be by check, within two weeks of your study participation termination.

COMPENSATION FOR INJURY
In the event you are injured as a result of your participation in this study, KGL Laboratories – Skin Study Center will provide or arrange for medical treatment as needed. In the event that you develop an adverse reaction, side effect, or complication as a result of your participation in this study, emergency medical treatment will be provided by physician at KGL, Inc. at no cost to you. No additional compensation is available. You will not lose any of your legal rights by signing this consent form.

WITHDRAWAL
Your participation in this study is completely voluntary. You should feel under no pressure to be in the study. If you decide not to be in the study, it will not in any way harm your relations with your doctors or with KGL Laboratories – Skin Study Center. You are free to stop participating in the study if you change your mind at any time. This will not harm your relations with your doctors or with KGL Laboratories – Skin Study Center. Should you decide against participation, you will not be denied access to other available treatments for your skin condition.

You will be notified of significant new findings that may affect your treatment or your willingness to continue in this study. Your participation may also be ended without your consent if the study doctor feels that it is in your best interest, if you do not follow the study procedures or if AkPharma, Inc. cancels the study. If the study doctor ends your participation, or if you decide not to continue, you will be asked to come to the office to complete the procedures that would normally be done at the final study visit.

CONFIDENTIALITY

The records of this study will be kept confidential, except as required by law. In any sort of report we might publish, we will not include any information that will make it possible to identify you. Your record for this study may, however, be reviewed by AkPharma, Inc., KGL Laboratories - Skin Study Center, representatives of the Food and Drug Administration (FDA), or other governmental agencies, or by the St. Davids Human Research Review Board, an Institutional Review Board. An Institutional Review Board is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's safety and welfare in mind.

QUESTIONS

If you have questions relating to this research study, or to report a research related injury, you may contact:

Dr. James J. Leyden or Dr. Gary L. Grove
KGL Laboratories – Skin Study Center
505 Parkway
Broomall, PA 19008
Daytime telephone: 610-544-1715
After hours telephone: 610-251-9775 – Dr. Leyden
610-358-2381 – Dr. Grove

If you have questions about your rights as a research subject, you may call:

St. Davids Human Research Review Board at 610-975-5212

CONSENT

I have read the above consent form. I have asked any questions I had and those questions have been answered. I agree to be in this study. Dr. Leyden or his staff will give me a signed copy of this form.

_____
Patient's Printed Name

_____ _____
Patient's Signature Date

_____ _____
Signature of Person Obtaining Consent Date

_____ _____
Investigator's Signature Date

ST. DAVIDS
HUMAN RESEARCH REVIEW BOARD
APPROVED OCT 28 2004

Appendix D

Randomization Schedule

KGL #5698

RANDOMIZATION SCHEDULE

#	Code	Right	Left
21	L057	No Rx	C
22	N076	No Rx	R
23	L012	C	No Rx
24	S171	R	No Rx
25	C294	No Rx	C
26	R157	R	No Rx
27	C010	C	No Rx
28	D093	No Rx	C
29	R092	No Rx	R
30	S035	R	No Rx
31	M389	C	No Rx
32	C187	No Rx	R
33	B262	No Rx	R
34	D338	No Rx	C
35	W019	No Rx	C
36	L163	R	No Rx
37	I020	C	No Rx
38	E009	C	No Rx
39	K166	R	No Rx
40	C383	No Rx	R
41	K128	C	No Rx
42	L174	No Rx	R
43	M025	No Rx	C
44	C248	No Rx	C
45	G199	R	No Rx
46	H223	No Rx	R
47	T042	C	No Rx
48	T035	No Rx	R
49	C024	C	No Rx
50	W028	R	No Rx

Appendix E

Application Instructions

Instructions for Application of Topical Test Product to Skin

1- Have portion of skin to be treated freshly washed and dried.

2- **Thoroughly mix contents of bottle by shaking** several times in a direction from top to bottom.

3- Apply 2 dabs (about the size of peas) of the cream, directly to the center of your upper inner arm (bicep) -OR- If direct application is not feasible apply product to your fingertip and apply from fingertip to center of your upper inner arm (bicep) as instructed. Use enough cream to cover a 3" high x 5" long area. Refer to "Example of Area Size to be Covered" card enclosed with these instructions.

4- Using the fingertip of one hand, rub the cream thoroughly into the skin, using up and down, as well as circular motions, starting in the center of the arm moving outward. The cream will 'disappear' into the skin and the moisture will evaporate. Let treated skin air dry – DO NOT OVER RUB.

5- Do not wash off until the new application time. Follow the rest of the printed directions given below:

Your ID Number is : **021**

You are assigned to apply this study product to:

LEFT arm (upper-inner, inside of bicep) as instructed above.

Appendix F

Sample Diary Form

PRODUCT USE DIARY

S# _____ *CODE:* ___ ___ ___ ___ *NAME* _____

IF YOU HAVE ANY QUESTIONS ABOUT THE PRODUCT
OR PRODUCT USAGE PLEASE CALL 610-544-1715
PLEASE KEEP THIS WITH YOUR PRODUCT AND FILL IN THE TIMES THAT IT WAS USED.
(USE A PEN - NOT A PENCIL - TO COMPLETE THIS FORM)
REMEMBER YOU MAY NOT GET TAN DURING THE STUDY OR YOU WILL BE DROPPED

DAY	DATE	TIME OF PRODUCT APPLICATIONS AM	PM	DAY	DATE	TIME OF PRODUCT APPLICATIONS AM	PM
Mon.	Nov. 8, 2004	_____ AM AT LAB	_____	Mon.	Nov. 15, 2004	_____ AM AT LAB	_____
Tue.	Nov. 9, 2004	_____	_____	Tues.	Nov. 16, 2004	_____	_____
Wed.	Nov. 10, 2004	_____	_____	Wed.	Nov. 17, 2004	_____	_____
Thu.	Nov. 11, 2004	_____	_____	Thu.	Nov. 18, 2004	_____	_____
Fri.	Nov. 12, 2004	_____	_____	Fri.	Nov. 19, 2004	_____	_____
Sat.	Nov. 13, 2004	_____	_____	Sat.	Nov. 20, 2004	_____	_____
Sun.	Nov. 14, 2004	_____	_____	Sun.	Nov. 21, 2004	_____	_____

Please do not apply your product when you come to the lab.

Your next appointment will be Mon, Nov. 15, 2004 at _____for Tolerance/Compliance (~10 mins.)

Your next appointment will be Mon. Nov. 22, 2004 at _____for Patches on (~10 mins.)
PLEASE DO NOT APPLY PRODUCT BEFORE COMING TO THE LAB ON THIS DAY

Return at _____for Patches off/Patches on (~10 mins.)

EMERGENCY #'s: *Dr. James Leyden* *610-251-9775*
Dr. Gary Grove *610-358-2381*
Dr. Kays Kaidbey *215-238-1225*

PLEASE RETURN ALL PRODUCTS TO THE SKIN STUDY CENTER
I CERTIFY THAT I HAVE COMPLETED THE TREATMENTS AS REQUIRED.

_____ _____
SIGNATURE OF PANELIST *DATE*

Appendix G

Demographic Data

DEMOGRAPHIC DATA

#	CODE	AGE	SEX
21	L057	46	F
22	N076	57	F
23	L012	47	F
24	S171	63	F
25	C294	55	F
26	R157	48	F
27	C010	59	F
28	D093	53	F
30	S035	51	F
31	M389	47	F
32	C187	51	F
33	B262	48	F
34	D338	58	F
35	W019	56	F
36	L163	54	F
37	I020	51	F
38	E009	48	F
39	K166	46	F
40	C383	46	F
41	K128	51	F
42	L174	49	F
43	M025	52	F
44	C248	48	F
45	G199	50	F
46	H223	62	F
47	T042	51	F
48	T035	47	F
49	C024	53	F
50	W028	59	F

Appendix H

Stratum Corneum Turnover Time Determinations Data

SORTED DATA KGL #5698

EXPERT GRADER ASSESSMENT

NUMBER OF DAYS UNTIL DYE DISAPPEARANCE

#	Code	No Rx	C	Difference	#	Code	No Rx	R	Difference
21	L057	22	22	0	22	N076	31	24	7
23	L012	23	21	2	24	S171	22	17	5
25	C294	18	18	0	26	R157	22	12	10
27	C010	22	19	3	29	R092			
28	D093	26	17	9	30	S035	23	15	8
31	M389	18	13	5	32	C187	31	24	7
34	D338	18	15	3	33	B262	22	17	5
35	W019	16	13	3	36	L163	25	23	2
37	I020	20	19	1	39	K166	27	20	7
38	E009	22	18	4	40	C383	21	16	5
41	K128				42	L174	23	14	9
43	M025	22	15	7	45	G199	19	19	0
44	C248	22	18	4	46	H223	25	22	3
47	T042	24	16	8	48	T035	22	19	3
49	C024	20	18	2	50	W028	18	16	2
Mean		***20.9***	***17.3***	***3.6***	***Mean***		***23.6***	***18.4***	***5.2***
Std Dev		***2.7***	***2.7***	***2.8***	***Std Dev***		***3.9***	***3.8***	***2.9***
Paired T-Test		***0.0003***			***Paired T-Test***		***0.0000***		