SKIN STUDY CENTER

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Final Report

to

AkPharma, Inc.

on

Dansyl Chloride Cell Renewal Study

KGL #5305A

January 20, 2004

Submitted by:

James J. Leyden, M.D. — *Date* 1/20/04

Gary L. Grove, Ph.D — *Date* 20 JAN 2004

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Quality Assurance Officer:

Patricia F. Alfano — *Date* 20 Jan 2004

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I. OBJECTIVE

The objective of this study was to evaluate the ability of a topically applied test formulation 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 to St. David's Human Research Review Board which was charged with reviewing and approving the study. This study was approved by the St. David's Human Research Review Board on October 23, 2003. This notification of the Board's approval along with a description by profession of the Board's composition has been provided to the Sponsor prior to the initiation of the study.

This study was conducted under the supervision of James Leyden, M.D. and Gary Grove, Ph.D., at the Skin Study Center in Broomall, Pennsylvania. A copy of Dr. Leyden 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 October 27, 2003 to December 22, 2003. A calendar of events outlining the schedule of treatments and evaluative procedures that were followed is attached as ***Appendix A****. The daily weather records covering this time as extracted from newspaper reports are included as* ***Appendix B****. A more detailed account issued by the US Weather Bureau can be provided upon the Sponsor's request.*

Briefly, this consisted of a three week treatment period during which time the product was applied twice daily including weekends to the test site, 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 formulation was 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 attached as ***Appendix C****. 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 D****.*

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 test product (Topical Calcium Glycerophosphate) was provided by the Sponsor in individual bottles and labeled with the subject #.

Product application to either the right or left upper inner arm followed the randomization schedule attached as ***Appendix E****. The design of this randomization allowed for each panelist to be assigned the test product and 1 non-treated site. This resulted in 20 sites for each product and non-treated control.*

The product was dispensed in individual bottles. Product was applied according to the Sponsor's instructions which are attached as ***Appendix F****. The panelists washed and partly dried (leaving the skin a little moist) the areas on their designated upper inner arms (approximately 5cm x 10cm). They mixed the bottle by shaking it several times up and down. The panelists applied 2 or 3 dabs (about the size of peas) of the cream directly onto the test site or onto their fingertips and gently rubbed the cream into the test site. After rubbing in the cream, the panelists wet their fingertips and shook off the excess water and rubbed their fingertips over the treatment site and let the site air dry or they could dab it dry with a towel. 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 G****.*

2. Stratum Corneum Turnover Time Determinations

After the three 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 Dr. Charles Zerweck.

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 prior to the Monday, Wednesday and Friday morning applications or more often if deemed necessary by the grader. A sample of the form used by Dr. Zerweck is attached as ***Appendix H****.*

Dr. Zerweck was not 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. A statistical analysis of the findings was made using the Paired T-Test provided within the Excel 7.0 environment to compare the treatment to the 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 20 panelists were recruited for this study, 17 of whom completed the entire study. Panelist (#2 G227) and panelist (#8 J004) withdrew for personal reasons unrelated to the study. Panelist (#16 F010) had an allergic reaction to the dansyl chloride and was discontinued. We have no reason to believe that the remaining panelists were not fully compliant with all provisions of this study. ***Appendix I*** *contains a listing of each panelist's age and sex.*

B. Stratum Corneum Turnover Time Determinations

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

Expert Grader Assessment Number of Days until Dye Disappearance									
No Rx			***Rx***			***p***	***Difference***		
Mean	***±***	***Std Dev***	***Mean***	***±***	***Std Dev***		***Mean***	***±***	***Std Dev***
23.2	*±*	*3.6*	*16.9*	*±*	*3.5*	*<0.0001*	*-6.4*	*±*	*2.7*

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. As anticipated, this group had a longer cell turnover time since they were selected based on being previously diagnosed with compromised epidermal cell renewal. 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 at least 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 6 days justifies it being rated as truly effective in this regard. In this case, epidermal cell renewal was enhanced approximately 27%.

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.

Appendix A

Calendar of Events

CALENDAR OF EVENTS
TOPICAL CALCIUM GLYCEROPHOSPHATE STUDY

	Oct 27	Nov. 3	Nov. 10	Nov. 17	Nov. 24	Nov. 25	Nov. 26	Nov. 28	Dec. 1	Dec. 3	Dec. 5	Dec. 8	Dec. 10	Dec. 12	Dec. 15	Dec. 17	Dec. 19	Dec. 22
DAY:	**-1 wk**	**1**	**8**	**15**	**22**	**23**	**24**	**26**	**29**	**31**	**33**	**36**	**38**	**40**	**43**	**45**	**47**	**50**
		Mon	**Mon**	**Mon**	**Mon**	**Tu**	**Wed**	**Fri**	**Mon**	**Wed**	**Fri**	**Mon**	**Wed**	**Fri**	**Mon**	**Wed**	**Fri**	**Mon**
Arms – Dansyl Day:						0	1	3	6	8	10	13	15	17	20	22	24	27
Consent	X																	
Screening	X																	
Inc/Exclusions	X	X																
Start Rx – Arms		X				X												
Stop Rx – Arms					X													X
ApplyDansyl – Arms(BID)					X													
Remove Dansyl patches						X												
UV Grade – Arms						X	X	X	X	X	X	X	X	X	X	X	X	X
Tolerance/Compliance			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Appendix B

Weather Information

2003 WEATHER INFORMATION

MONTH	DATE	DAY	HIGH TEMP °F	LOW TEMP °F	NOON TEMP °F	NOON HUMIDITY %	PRECIP. INCHES
OCTOBER	**27**	**MON**	65	52	64	96	1.35
	28	**TUE**	58	42	56	54	0.19
	29	**WED**	57	50	57	86	0.96
	30	**THU**	63	41	58	45	
	31	**FRI**	72	44	68	56	
NOVEMBER	**1**	**SAT**	78	48	71	62	
	2	**SUN**	74	53	70	70	
	3	**MON**	79	53	73	65	0.01
	4	**TUE**	72	58	66	86	0.01
	5	**WED**	66	58	63	100	0.24
	6	**THU**	64	57	61	89	0.22
	7	**FRI**	59	51	55	56	TRACE
	8	**SAT**	59	51	55	56	TRACE
	9	**SUN**	44	29	43	32	
	10	**MON**	47	28	44	29	
	11	**TUE**	56	34	54	43	TRACE
	12	**WED**	58	48	56	86	0.42
	13	**THU**	61	42	48	35	0.01
	14	**FRI**	48	37	45	36	
	15	**SAT**	54	43	51	45	
	16	**SUN**	55	38	52	58	TRACE
	17	**MON**	60	46	55	83	0.01
	18	**TUE**	57	42	53	89	
	19	**WED**	69	57	67	86	0.44
	20	**THU**	55	48	53	50	0.13
	21	**FRI**	67	40	60	53	
	22	**SAT**	62	42	60	64	
	23	**SUN**	61	42	56	77	
	24	**MON**	66	42	61	75	
	25	**TUE**	45	34	43	45	0.01
	26	**WED**	47	32	45	60	
	27	**THU**	55	38	53	46	

2003 WEATHER INFORMATION

MONTH	DATE	DAY	HIGH TEMP °F	LOW TEMP °F	NOON TEMP °F	NOON HUMIDITY %	PRECIP. INCHES
NOVEMBER	**28**	**FRI**	65	48	59	96	0.44
	29	**SAT**	45	37	44	45	TRACE
	30	**SUN**	51	37	48	42	
DECEMBER	**1**	**MON**	53	39	52	32	
	2	**TUE**	40	30	39	31	TRACE
	3	**WED**	35	21	33	34	
	4	**THU**	40	24	37	45	
	5	**FRI**	36	29	33	95	0.48
	6	**SAT**	30	26	29	85	0.10
	7	**SUN**	31	24	30	59	
	8	**MON**	34	21	32	53	
	9	**TUE**	38	25	35	58	
	10	**WED**	52	30	42	78	0.15
	11	**THU**	60	41	55	77	1.36
	12	**FRI**	42	33	40	48	
	13	**SAT**	35	27	33	43	
	14	**SUN**	44	29	33	95	0.88
	15	**MON**	42	32	41	50	TRACE
	16	**TUE**	48	28	41	57	
	17	**WED**	50	34	50	100	0.54
	18	**THU**	38	31	36	46	
	19	**FRI**	36	27	35	51	TRACE
	20	**SAT**	39	26	38	52	
	21	**SUN**	40	24	34	47	
	22	**MON**	51	33	47	40	

Appendix C

Inclusion/Exclusion Criteria

INCLUSION/EXCLUSION CHECKLIST

#_____ CODE _____ NAME _____ KGL#5305

INCLUSIONS (Answer must be "yes"):		
YES	*NO*	
		1. Informed Consent obtained.
		2. Female, 45-65 years of age previously diagnosed with compromised epidermal cell renewal and moderately severe dry skin
		3. Ambulatory: defined as not depending exclusively on a wheelchair for mobility
		4. Able to remain on stable doses of concomitant medications from the Screening Visit (V1) through the Final Visit (V18) of the study
EXCLUSIONS (Answer must be "no"):		
YES	*NO*	
		1. Pregnant or breast-feeding.
		2. Major psychiatric disorder within the past two years not controlled by a stable dose of medication for the last 6 months.
		3. Alcohol or substance abuse within the past two years.
		4. Participation in any clinical trial within the past 3 months.
		5. Known allergy or hypersensitivity to calcium supplements.

_____ _____

Interviewer *Date*

Appendix D

Sample Consent Form

INFORMED CONSENT FORM

TITLE: A SINGLE-BLIND, RANDOMIZED, CONTROLLED STUDY WITH TOPICAL CALCIUM GLYCEROPHOSPHATE 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
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Broomall, PA 19008
610-544-1715
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)

The purpose of this study is to evaluate if this non-prescription skin treatment reduces your symptoms associated with moderately severe dry skin with compromised epidermal cell renewal. Non-invasive measurements of the skin, expert assessments, logs and questionnaires will be used to determine this.

You will be one of approximately 20 females age 45 – 65 involved in this research project at KGL Laboratories, Skin Study Center. Your participation will last for approximately 8 weeks and will require 19 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 6 months.

- Alcohol or substance abuse within the past two years.
- Participation in any clinical trial within the past 3 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. You will also complete a questionnaire to determine how you feel about your skin condition. 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 two treatment groups:

(1)Topical CGP applied twice daily to the LEFT arm and leg as instructed – OR -
(2) Topical CGP applied twice daily to the RIGHT arm and leg 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 either treatment group 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.

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

You will be instructed not to apply any products, other than those provided, nor to tamper with your arms and legs 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 be instructed to not shave your legs within 30 hours prior to each evaluative study visit.

You will be asked to complete a self-assessment questionnaire about your skin condition with the help of a study staff member. You will also be asked about any changes in medication or any problems you may have experienced since the last visit. An expert skin grader will assess the condition of your skin and non-

invasive measurements of the leg test sites will be taken.

You will be given a one week supply of study treatment. You will also be given a "Patient's Application Log" to record the time of your twice daily applications to be completed and returned at your next visit.

VISITS THREE & FOUR

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 complete a self-assessment questionnaire about your skin condition and inform the study staff of medication changes and/or problems that may have occurred since your last visit. An expert skin grader will assess the condition of your skin and non-invasive measurements of the leg test sites will be taken. You will bring your completed "Patient's Application Log" to these visits along with your remaining study treatment. You will be given a new one week supply of study treatment and a "Patient's Application Log" to take home with you.

VISITS FIVE, SIX & SEVEN

You will return to the office for Visit Five one week after Visit Four. You will bring your completed "Patient's Application Log" to these visits along with your remaining study treatment. At Visit Five 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 one week supply of study treatment and a "Patient's Application Log" to take home with you.

Visit Six will be six hours after Visit Five. At Visit 6, a second application of the dye will be made and the dressings renewed.

Visit Seven will be scheduled ~~two~~ one days after Visit Six. At Visit Seven, 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 EIGHT & NINE

You will return to the office for Visit Eight one day after Visit Seven, then again two days after Visit Eight for Visit Nine. 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 remaining study treatment.

VISIT TEN

You will return to the office for Visit 10 Three days after Visit Nine. At Visit 10 treatment to the leg test sites will end. You will be asked to complete a self-assessment questionnaire about your skin condition and inform the study staff of medication changes and/or problems that may have occurred since your last visit. An expert skin grader will assess the condition of your skin and non-invasive measurements of the leg test sites will be taken. 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 one week supply of study treatment and a "Patient's Application Log" to take home with you.

VISITS ELEVEN & TWELVE

You will return to the office for Visit 11 two days after Visit 10, then again two days after Visit 11 for Visit 12. At these visits you will be asked to complete a self-assessment questionnaire about your skin condition and inform the study staff of medication changes and/or problems that may have occurred since your last visit. An expert skin grader will assess the condition of your skin and non-invasive measurements of the leg test sites will be taken. 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 THIRTEEN

You will return to the office for Visit 13 three days after Visit 12. At Visit 13 you will be asked to complete a self-assessment questionnaire about your skin condition and inform the study staff of medication changes and/or problems that may have occurred since your last visit. An expert skin grader will assess the condition of your skin and non-invasive measurements of the leg test sites will be taken. 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 one week supply of study treatment and a "Patient's Application Log" to take home with you.

VISITS FOURTEEN & FIFTEEN

You will return to the office for Visit 14 two days after Visit 13, then again two days after Visit 14 for Visit 15. 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 SIXTEEN

You will return to the office for Visit 16 three days after Visit 15. At Visit 16 you will be asked to complete a self-assessment questionnaire about your skin condition and 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 one week supply of study treatment and a "Patient's Application Log" to take home with you.

VISITS SEVENTEEN & EIGHTEEN

You will return to the office for Visit 17 two days after Visit 16, then again two days after Visit 17 for Visit 18. 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 NINETEEN

You will return to the office for Visit 19 three days after Visit 18 for your final study visit. At Visit 19 you will be asked to complete a self-assessment questionnaire about your skin condition and 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 product being studied is a non-prescription treatment, not a drug. At this time, there are no known side effects of using this non-prescription treatment. It is possible that you may experience some skin irritation from the treatment 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 three hundred dollars ($300.00) 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:

$5.00 Complete Visit 1 but not accepted into study
$25.00 per visit completed for Visits 2-5
$5.00 for completing Visit 6
$10.00 per visit completed for Visits 7-9
$25.00 per visit completed for Visits 10-13
$10.00 per visit completed for Visits 14-19

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 877-398-5012 (toll-free)

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

Appendix E

Randomization Schedule

Randomization Schedule KGL #5305

#	Code	Right	Left
1	R157	No Rx	Rx
2	G227	Rx	No Rx
3	C340	Rx	No Rx
4	M025	No Rx	Rx
5	M691	No Rx	Rx
6	T042	Rx	No Rx
7	G114	Rx	No Rx
8	J004	No Rx	Rx
9	K048	Rx	No Rx
10	D017	No Rx	Rx
11	N076	No Rx	Rx
12	C294	Rx	No Rx
13	H176	Rx	No Rx
14	S279	No Rx	Rx
15	E009	Rx	No Rx
16	F010	No Rx	Rx
17	D283	No Rx	Rx
18	P108	Rx	No Rx
19	W028	Rx	No Rx
20	C219	No Rx	Rx

Appendix F

Panelist Instructions

Instructions for Application of Topical CGP to Skin

1- Have portions of skin to be treated freshly washed and dried. Ideally, skin can be "still a little moist" from the washing.

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

3- Apply 2 or 3 small dabs (about the size of peas) of the cream, directly to the skin. -OR- If direct application is not feasible apply product to your fingertips and apply from fingertips to the leg and arm areas as instructed.

4- Using the fingertips of one hand, rub the cream thoroughly into the skin, using up and down, as well as circular motions. The cream will 'disappear' into the skin and the moisture will evaporate in such a way that the rubbing becomes dry.

5- The amount of cream used should be sufficient so that when dry, there is no more than a very thin coat of dry white residue remaining over the treated area; if needed, apply slightly more, and use a larger dab next time. If too much remaining, apply slightly less next time.

6- Hold your fingertips under tap water and wet them slightly; shake off all excess moisture so that the fingertips are barely wet. Again, rub the fingertips on the same area you just coated with the cream. This will provide a slight bit of additional moisture to assure adequate absorption of the remaining white residue. Let treated skin air dry -OR- if necessary, you can DAB DRY with a towel – DO NOT RUB .

7- When the skin dries after Step 6, there should be little or no whitish residue seen.

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

Your ID Number is : **0XX**

You are assigned to apply this study product to:

L –or- R leg (calf area - ankle to knee) and **L – or- R** arm (upper-inner, inside of bicep) as instructed.

Appendix G

Sample Diary Form

PRODUCT USE DIARY *KGL #5305 #1*

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 3, 2003 [visit 2]	_____	_____	Fri.	Nov 14, 2003	_____	_____
		May shave AFTER visit					
Tue.	Nov 4, 2003	_____	_____	Sat.	Nov 15, 2003	_____	_____
						MUST SHAVE	
Wed.	Nov 5, 2003	_____	_____	Sun.	Nov 16, 2003	_____	_____
						Don't shave	
Thu.	Nov 6, 2003	_____	_____	Mon.	Nov 17, 2003 [visit 4]	_____	_____
						May shave AFTER visit	
Fri.	Nov 7, 2003	_____	_____	Tue.	Nov 18, 2003	_____	_____
Sat.	Nov 8, 2003	_____	_____	Wed.	Nov 19, 2003	_____	_____
		MUST SHAVE					
Sun.	Nov 9, 2003	_____	_____	Thu.	Nov 20, 2003	_____	_____
		Don't shave					
Mon.	Nov 10, 2003 [visit 3]	_____	_____	Fri.	Nov 21, 2003	_____	_____
		May shave AFTER visit					
Tue.	Nov 11, 2003	_____	_____	Sat.	Nov 22, 2003	_____	_____
						MUST SHAVE	
Wed.	Nov 12, 2003	_____	_____	Sun.	Nov 23, 2003	_____	_____
						Don't shave	
Thu.	Nov 13, 2003	_____	_____				

Please do not apply your product when you come to the lab.
PLEASE BRING PRODUCTS WITH YOU TO EACH VISIT

VISIT 3 – Monday, Nov 10 at _____for Grades and Instruments.

VISIT 4 – Monday, Nov 17 at _____for Grades and Instruments.

VISIT 5 – Monday, Nov 24 at _____for Grades and Instruments and patches applied.
VISIT 6 – Return Monday afternoon at _____to have patches renewed.

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 H

Sample Expert Grader Form

Dye Appearance KGL #5305

Date: _____ Expert Grader: Charles Zerweck

#	CODE	Dye Appearance	
		Right Arm	Left Arm
1	R157		
2	G227		
3	C340		
4	M025		
5	M691		
6	T042		
7	G114		
8	J004		
9	K048		
10	D017		
11	N076		
12	C294		
13	H176		
14	S279		
15	E009		
16	F010		
17	D283		
18	P108		
19	W028		
20	C219		

Appendix I

Demographic Data

DEMOGRAPHIC DATA

#	I D	AGE	SEX	INITIALS
1	R157	47	F	KDR
2	G227	65	F	P-G
3	C340	62	F	G-C
4	M025	51	F	VLM
5	M691	64	F	MMM
6	T042	51	F	JMT
7	G114	48	F	G-G
8	J004	61	F	R-J
9	K048	48	F	D-K
10	D017	51	F	DAD
11	N076	56	F	JMN
12	C294	54	F	KJC
13	H176	50	F	DAH
14	S279	53	F	JMS
15	E009	48	F	SME
16	F010	63	F	SAF
17	D283	62	F	STD
18	P108	65	F	CWP
19	W028	59	F	BMW
20	C219	65	F	HDC

Appendix J

Stratum Corneum Turnover Time Determinations Data

EXPERT GRADER ASSESSMENT
NUMBER OF DAYS UNTIL DYE DISAPPEARANCE

#	Code	No Rx	Rx	Difference
1	R157	23	20	-3
2	G227			
3	C340	21	16	-5
4	M025	22	13	-9
5	M691	23	18	-5
6	T042	24	16	-8
7	G114	24	15	-9
8	J004			
9	K048	22	17	-5
10	D017	16	14	-2
11	N076	29	26	-3
12	C294	23	15	-8
13	H176	31	22	-9
14	S279	26	20	-6
15	E009	21	12	-9
16	F010			
17	D283	20	17	-3
18	P108	20	15	-5
19	W028	22	14	-8
20	C219	28	17	-11
Mean		***23.2***	***16.9***	***-6.4***
Std Dev		***3.6***	***3.5***	***2.7***
Paired T-Test		***0.0000***		