itle:	A Multi-Center Clinical Trial to Evaluate the Efficacy of Two Acne Treatments
Protocol number:	GLI.04.SPR.US10354
Study phase:	Phase IV
Sponsor name and address:	Galderma Laboratories, L.P. 14501 North Freeway Fort Worth, TX 76177 USA
Study products:	Product A Product B
Indication:	Not Applicable
Investigator agreement:	I have read the clinical study described herein, recognize its confidentiality, and agree to conduct the described study in compliance with Good Clinical Practices (GCP), the ethical principles contained within the Declaration of Helsinki, this protocol, and all applicable regulatory requirements.
Principal Investigator (Site 1):	 2/16/16 Signature Date
Name (Site 1):	Lily Jiang, PhD
Address (Site 1):	Thomas J. Stephens & Associates, Inc. Texas Research Center 1801 N. Glenville Drive, Suite 200 Richardson, TX 75081

Sub-Investigator/Study Physician (Site 1):

Signature 2/16/2016 Date

Name (Site 1): Peter D. Hino, MD, FAAD

Address (Site 1): Thomas J. Stephens & Associates, Inc.
Texas Research Center
1801 N. Glenville Drive, Suite 200
Richardson, TX 75081

Principal Investigator (Site 2):

Signature 2/16/2016 Date

Name (Site 2): Kun "Mark" Qian, MD, BRAMS

Address (Site 2): Thomas J. Stephens & Associates, Inc.
Colorado Research Center
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Colorado Springs, CO 80915

Sub-Investigator/Study Physician (Site 2):

Signature 2/16/16 Date

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Address (Site 2): Thomas J. Stephens & Associates, Inc.
Colorado Research Center
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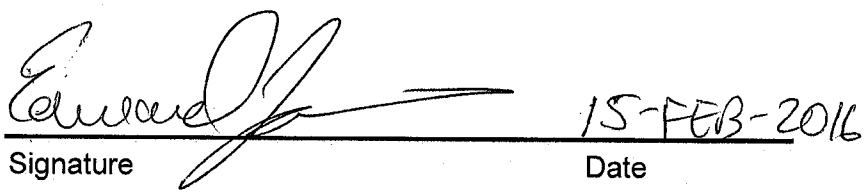
Colorado Springs, CO 80915

Investigator (Site 3):



Signature

15-FEB-2016

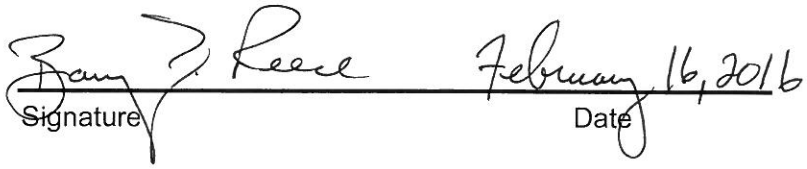
Date

Name (Site 3): Edward Lain, MD, MBA, FAAD

Address (Site 3):

Austin Institute for Clinical Research, Inc.
302 N. Heatherwilde Blvd, Suite 300
Pflugerville, TX 78660

Investigator (Site 4):



Signature Date

Name (Site 4): Barry Reece, MS, MBA

Address (Site 4):

RCTS, Inc.
3207 Esters Road
Irving, TX 75062

RETURN THE ORIGINAL SIGNED COPY TO GALDERMA LABORATORIES, L.P. AND KEEP A COPY AT YOUR SITE.

TITLE PAGE

Title:	A Multi-Center Clinical Trial to Evaluate the Efficacy of Two Acne Treatments
Short Title:	A Multi-Center Clinical Trial to Evaluate the Efficacy of Two Acne Treatments
Protocol number:	GLI.04.SPR.US10354
Study phase:	Phase IV
Sponsor:	Galderma Laboratories, L.P. 14501 North Freeway Fort Worth, TX 76177 USA Telephone: 1-817-961-5000

This study will be performed in compliance with applicable federal regulations and Good Clinical Practice (GCP). This Clinical Study Protocol follows guidelines outlined by the International Conference on Harmonization (ICH) and Galderma Laboratories, L.P. (GLLP).
All the data provided to the investigator and his/her staff and all data obtained through this GLLP protocol will be regarded as confidential and proprietary in nature and should not be disclosed to any third party without GLLP's written consent.

Effective Date: **11** February 2016

1. SYNOPSIS

Title: A Multi-Center Clinical Trial to Evaluate the Efficacy of Two Acne Treatments

Protocol Number: GLI.04.SPR.US10354

Study Period (Planned): Duration of subject participation is approximately 24 weeks (Screening/Baseline, Week 1, Week 2, Week 6, Week 12, Week 18, and Week 24)

Phase of Development: Phase IV

Objectives:

- To characterize the effectiveness of the acne treatment in lesion count at week 1, week 2, week 6, week 12, and week 24 as compared to baseline and compare between treatments
- To characterize the effectiveness of the acne treatment in Investigator's Global Improvement Assessment at week 1, week 2, week 6, week 12, and week 24 as compared to baseline and compare between treatments
- To characterize the effect of the acne treatment in clinical grading of efficacy parameters through digital images at week 6, week 12, and week 24 as compared to baseline and compare between treatments
- To characterize the effect of the acne treatment in subject self-assessment questionnaire responses at week 1, week 2, week 6, week 12, and week 24 as compared to baseline and compare between treatments

Overall Study Design:

This is a multicenter, double-blind, randomized, controlled clinical trial to be conducted in the United States at 4 testing facilities. The study will examine the effect of 2 acne treatments (Product A when used once daily and Product B when used 1-3x a day) for 24 weeks in adult men and women 21 to 45 years of age with mild to moderate facial acne, with at least 5 inflammatory lesions, and 10 – 100 non-inflammatory lesions at enrollment. Subjects meeting the inclusion/exclusion criteria are to be enrolled in the study. There will be up to 8 visits during the course of the study: Screening, Baseline, Week 1, Week 2, Week 6, Week 12, Week 18, and Week 24.

Number of Subjects Planned/Analyzed: Approximately 130 subjects will be enrolled to complete with 100 subjects (50 per cell). For the purposes of this protocol, enrolled is defined as a subject who has been consented, screened and eligibility has been verified.

Each site is to enroll no more than 40 subjects, with at least 100 subjects expected to complete when combined.

Main Inclusion Criteria: Men and women, 21 to 45 years of age with mild to moderate facial acne, at least 5 inflammatory lesions, and at least 10 – 100 non-inflammatory lesions.

Galderma Study Products:

Study product: Facial Cleanser

Form: Gel

Instructions for Use: massage a small amount onto wet skin. Rinse.

Mode of Administration: Topical

Duration of Use: 24 Weeks

Galderma Study Products:

Study product: Product A

Form: Gel

Instructions for Use: Dispense a nickel size amount of product and apply as a thin layer to the entire face or any other affected areas of the skin once daily, after washing gently with a mild soap-less cleanser and drying the area.

Mode of Administration: Topical

Duration of Use: 24 Weeks

Study product: Product B

Form: Gel

Instructions for Use: Clean the skin thoroughly before applying this product. Cover the entire affected area with a thin layer one to three times daily. Because excessive drying of the skin may occur, start with one application daily, then gradually increase to two or three daily if needed or as directed by a doctor. If bothersome dryness or peeling occurs, reduce application to once a day or every other day.

Mode of Administration: Topical

Duration of Use: 24 Weeks

Galderma Study Products:

Study product: Moisturizing Lotion

Form: Lotion

Instructions for Use: After applying the product, use moisturizer on the entire face. Apply as needed or as directed by a physician.

Mode of Administration: Topical

Duration of Use: 24 Weeks

Galderma Study Products:

Study product: Facial Moisturizer SPF 30

Form: Cream

Instructions for Use: Apply liberally 15 minutes before sun exposure. Use a water resistant sunscreen if swimming or sweating. Reapply at least every 2 hours

Mode of Administration: Topical

Duration of Use: 24 Weeks

Criteria for Evaluation:

All subjects who are enrolled and receive study products will be evaluable for safety analyses. All subjects who are enrolled, receive study products, and have at least one post treatment administration evaluation will be evaluable for intent-to-treat analyses.

General instructions:

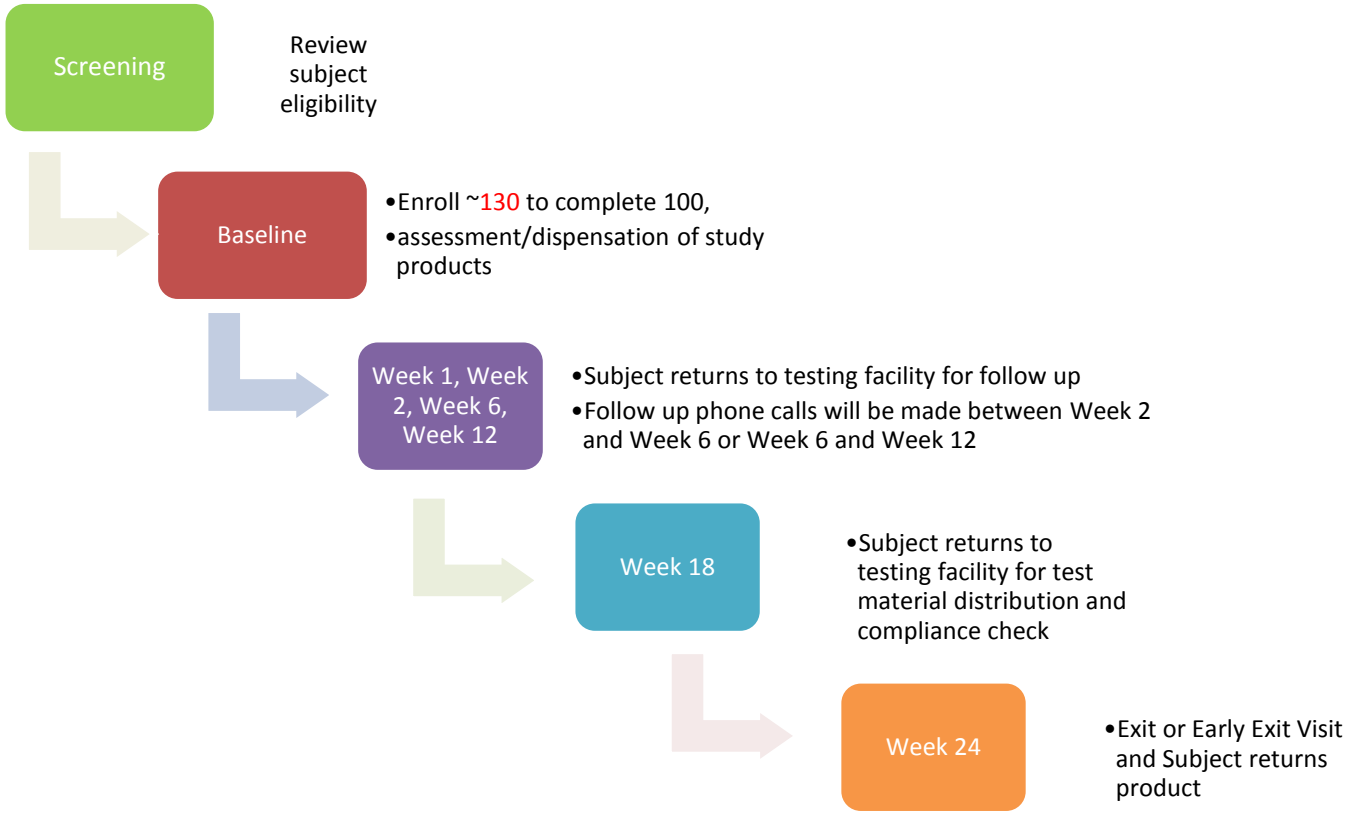
Use all products as directed. Cleanser, test material, and moisturizer should be used as a regimen.

Avoid extended periods of sun exposure, all use of tanning beds, and sunless tanning products for the duration of the study. Extra care should be taken to wear protective clothing, including sunglasses, and avoid sun exposure from 10 AM to 4 PM.

Continue use of all regular brands of color cosmetics, makeup remover, and use the assigned test material for the duration of the study. Individuals must refrain from using any acne products and beginning the use of any new facial products other than the assigned test material. Use of moisturizing foundation will be acceptable as long as the subject has a history of safe usage of the foundation.

Assessment	Measure
• Lesion count	Investigator or designee will count the inflammatory and non-inflammatory lesions on each subject's face
• Investigator's Global Assessment (IGA)	Investigator or designee will assess acne severity on each subject's face using FDA's Investigator's Global Assessment scale on acne severity
Clinical Grading of Efficacy Parameters via digital images (will be performed by Stephens expert graders at the end of the study): • Skin texture • Skin tone evenness • Clarity • Overall skin complexion	Investigator or designee will assess efficacy through digital images using a modified Griffith's 10-point scale
Clinical Grading of Tolerance Parameters: • Erythema • Dryness • Scaling • Stinging/Burning	Investigator or designee will assess tolerance using a 4-point scale.
• Self-Assessment Questionnaires	6 to 25 item questionnaire
• Digital Images	Digital photography using VISIA on the left, right, and center views under standard lightings: 1, 2, cross-polarized, parallel polarized, UV-fluorescence lighting. Beauty shots (no head band/headrest/chinrest) will also be taken of the center view under visible light (Site 1 and 2 only)
• Safety	Number of adverse events

1.1 Study Schematic



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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse Event
CRF	Case Report Form
eCRF	Electronic Case Report Form
etc.	et cetera
e.g.	for example (Latin; exempla gratia)
FDA	The Food and Drug Administration
GCP	Good Clinical Practice
GLLP	Galderma Laboratories, L.P.
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IPL	Intesnse Pulse Light
IRB	Institutional Review Board
LOCF	Last Observation Carried Forward
N or n	Number
OTC	Over-the-Counter
%	Percent
P	Probability (as in significance level)
Rx	Prescription
SAE	Serious Adverse Event
SAP	Statistical Analyses Plan
SD	Standard deviation
SOP	Standard Operating Procedure
i.e.	that is (Latin: id est)
USV	Unscheduled Visit

2. BACKROUND AND RATIONALE

Acne is an inflammatory disease of the sebaceous gland that occurs during adolescence and persists into adulthood. Non-inflammatory acne lesions form when the opening of the follicle becomes blocked by the presence of dense keratin and sebum. Inflammatory acne lesions develop when the orifice of the follicle becomes completely occluded and bacteria replicate and excrete substances that induce an inflammatory reaction.
Treatment with acne medications has been shown to help dissolve keratin plugs and help prevent the proliferation of bacteria in the sebaceous gland. This results in a reduction in the numbers of non-inflammatory and inflammatory acne lesions.[1,2]

3. STUDY OBJECTIVES AND HYPOTHESIS

3.1.1. Overall Purpose

The purpose of this study is to evaluate the efficacy of 2 acne treatments for 24 weeks of use in adult men and women with mild to moderate facial acne, at least 5 inflammatory lesions, and at least 10 – 100 non-inflammatory lesions.

3.1.2. Hypothesis

After 24 weeks of 1 to 3 times per day use:

- Subjects will demonstrate an improvement in acne lesion counts (inflammatory and non-inflammatory) as assessed by a trained grader when compared to baseline.
- Subjects will demonstrate an improvement in global assessment (IGA) as assessed by a trained grader over the course of the study, when compared to baseline.
- Subjects will demonstrate an improvement in facial skin condition as assessed by a trained grader, through digital images, when compared to baseline.
- Subjects will report high satisfaction with the acne treatment as measured through self-assessment questionnaires.

4. SELECTION AND DISPOSITION OF STUDY POPULATION

4.1 INCLUSION CRITERIA

1. Men and women age 21 to 45 years at the time of enrollment.
2. Individuals with mild to moderate acne (score of 2-3 on FDA Investigator's Global Assessment Scale[1]) on the face.
3. Individuals with at least 5 inflammatory lesions.
4. Individuals with 10 – 100 non-inflammatory lesions.
5. Individuals willing to use the test products as instructed for 24 weeks.
6. Fitzpatrick skin type I-VI (refer to Appendix I: Fitzpatrick Skin Type).
7. Individuals willing and able to comply with all of the time commitments and procedural requirements of the clinical trial protocol.
8. Individuals willing to provide written informed consent including photo release, Health Insurance Portability and Accountability Act (HIPAA), and are able to read, speak, write, understand English and are willing to share personal information and data, as verified by signing a written authorization at the screening.
9. Willing to withhold all facial treatments during the course of the study including botulinum toxin, injectable fillers, microdermabrasion, IPL, peels, facials, laser treatments and tightening treatments. Waxing and threading is allowed but not facial

laser hair removal.

10. Males who are regular shavers and willing to shave on the day of the study visits (prior to clinic visits).

11. Women of child bearing potential who are willing to take a urine pregnancy test prior to study enrollment, at week 24, and when deemed appropriate by the Investigator and/or Sponsor.
12. Individuals of child bearing potential who use an acceptable method of contraception throughout the study. Acceptable methods of birth control include:

    - Oral and other system contraceptives. Individuals must be on a stable use for 3 months prior to study enrollment. Individuals on oral contraceptives must not alter their use, including dose or regimen for the duration of the study
    - Double barrier
    - Bilateral tubal ligation
    - Partner vasectomy
    - Abstinence

13. Individuals willing to follow study requirements and report any changes in health status or medications, adverse event symptoms, or reactions immediately.
14. Subjects must be stable on any medication they are taking for at least 30 days

4.2 EXCLUSION CRITERIA

1. Individuals diagnosed with allergies to topical acne products.
2. Individuals having a condition and/or disease of the skin that the Investigator deems inappropriate for participation.
3. Women who are nursing, pregnant, or planning to become pregnant during the study.
4. Individuals who have pre-existing or dormant dermatologic conditions on the face (e.g., psoriasis, rosacea, eczema, seborrheic dermatitis, severe excoriations etc.) which in the opinion of the Investigator could interfere with the outcome of the study.
5. Individuals with a history of immunosuppression/immune deficiency disorders (including (HIV infection or AIDS) or currently using immunosuppressive medications (e.g., azathioprine, belimumab, cyclophosphamide, Enbrel, Imuran, Humira, mycophenolate mofetil, methotrexate, prednisone, Remicade, Stelara.).
6. Individuals with an uncontrolled disease such as asthma, diabetes, hypertension, hyperthyroidism, or hypothyroidism. Individuals having multiple health conditions may be excluded from participation even if the conditions are controlled by diet, medication, etc. at the Investigator's discretion.
7. Individuals who are currently participating in another facial usage study or have participated in a clinical trial within 4 weeks prior to inclusion into the study.
8. Individuals with a history of skin cancer on the face within the past 5 years.
9. Individuals with any planned surgeries and/or invasive medical procedures during the course of the study.
10. Individuals who started hormone replacement therapies (HRT) or hormones for birth control less than 3 months prior to study entry or who plan on starting, stopping, or changing doses of HRT or hormones for birth control during the study.
11. Individuals with facial sunburn or excessive tanned facial skin or that are not willing to avoid daily sun exposure on the face and the use of tanning beds or sunless tanning products for the duration of the study.
12. Individuals with severe acne, acne conglobata, multiple nodules or cysts (more than 2).

13. Individuals currently taking a natural or prescription testosterone blocker (e.g. saw palmetto, blask cohosh, chaste tree, chasteberry, spironolactone, drospirenone, progestins).
14. Individuals currently on a testosterone booster or prescription testosterone (e.g. DHEA, tribulus, testosterone cypionate, testosterone enanthate, Sustanon, testosterone propionate, testosterone phenylpropriate, Omnadren etc.).
15. Individuals that are currently taking or have taken within the last 30 days oral or topical prescription medications for acne such as Doxycycline, Minocycline, Clindamycin, Bactrim, Tetracycline, Erythromycin, Vibramycin and topical tretinoin.(Retin A Renova, Adapalene, Tazarotene), Azelaic acid, benzoyl peroxide, Dapsone, Sodium sulfacetamide, Differin, Epiduo.
16. Individuals that have used oral isotretinoin (Accutane) within the past 6-months.
17. Individuals routinely using (3x a week or more) topical OTC acne product (e.g. benzoyl peroxide, salicylic acid, alpha hydroxyl, beta hydroxyl and/or poly-hydroxy products or medicated cleansers, wipes, masks, scrubs, gels and creams) within 14 days of the study entry.
18. Individuals using or who have used any systemic medication considered to affect the course of acne, specifically, but not exclusively antibiotics or steroids within the last 30 days prior to entry into the study.
19. Individuals with excessive facial hair, including beard, mustache or goatee, or scars, which could interfere with evaluations by Investigator or designee.

4.3 CONCOMITANT THERAPIES

4.3.1. Authorized Therapies

Product A used once daily or Product B used 1 to 3 times daily in AM/PM are required for this study. Subject Product Kit will include: study drug, cleanser, moisturizing lotion, and moisturizer SPF.
Unless listed under the exclusion criteria (Section 4.2) or in Prohibited Therapies (Section 4.3.2), other therapies to treat ongoing conditions are authorized.

4.3.2. Prohibited Therapies

The prohibited treatments are provided in the exclusion criteria in section 4.2.
The decision to administer a prohibited medication/treatment should be made with the safety of the subject being the primary consideration. Whenever possible, GLLP should be notified before the prohibited medication/treatment is administered to discuss possible alternatives.
If a subject receives prohibited therapy during the study, the subject may be allowed (at the discretion of the investigator / GLLP) to continue in the study for safety evaluation purposes, only. Galderma must be immediately notified in all instances of administration of prohibited meds.

5. STUDY PROCEDURES

5.1 Protocol Waivers/Exemptions

Neither ICH nor the Food and Drug Administration (FDA) have defined the terms 'Protocol Violations' and 'Protocol Deviations'. **No "waivers" or "approvals" will be granted for protocol deviations or inclusion/exclusion criteria violations.**
Sites are instructed to report protocol deviations to Stephens and Associates which will report the deviations to the Independent Ethics Committee/Institutional Review Board (IEC/IRB) per their

IEC/IRB's guidelines.
Protocol non-compliance including lost to follow-up subjects should be reported to the site monitor as well as study management as soon as it is identified.

5.2 Informed Consent Procedures

An IEC/IRB approved informed consent template containing the required elements of an informed consent will be reviewed and approved by GLLP. Any changes made to these templates must be approved by GLLP prior to submission to the IEC/IRB for site approval. After approval by GLLP, the informed consent form must be submitted to and approved by the IEC/IRB.
It is the responsibility of the investigator to inform each subject, prior to the screening evaluation, of the purpose of the study, including possible risks and benefits, and to document the informed consent process in the subject's research chart (and medical record, if applicable). Prior to entry into the study or initiation of any study related procedures, the subject must read, sign, and date the current IEC/IRB approved version of the consent form in accordance with local legal requirements and IEC/IRB requirements. The original informed consent form is to be retained at the study site, and a copy is to be given to the subject.

5.3 Screening Procedures

Screening will not be allowed at the site until the site has obtained all applicable IEC/IRB approvals and a fully executed Clinical Study Agreement (CSA). The sponsor will notify the site once screening may begin.
Subjects must be consented using the IEC/IRB approved informed consent(s) prior to all study assessments and discontinuation of medication(s). Date and time of consent, as well as a summary of the consent discussion should be documented in the source.

Each screened subject will be assigned a unique subject number. The subject numbers will be assigned by site, with the first digit will be used to indicate which site the subject was enrolled at and with an additional 2 numbers at the end being the subject number (3 digits total).

- Site 1 (Stephens Texas) examples: 101, 102, 103, etc.
- Site 2 (Stephens Colorado) examples: 201, 202, 203, etc.
- Site 3 (Austin Institute for Clinical Research, Inc.) examples: 301, 302, 303, etc.
- Site 4 (RCTS, Inc.) examples: 401, 402, 403, etc.

5.3.1. Demographics

The following demographic parameters will be captured at the screening visit:

- Age
- Gender
- Ethnicity and Race (subject self-identified)
- Fitzpatrick Skin Type Classification

****Fitzpatrick Skin Type Classification** *(Please select one)*:

I – Always burns; never tans

II – Burns easily; tans minimally

III – Burns moderately; tans gradually to light brown

IV – Burns minimally; tans well to moderate brown

V – Rarely burns; tans profusely to dark brown

VI – Never burns; tans profusely to black

5.3.2. Medical History

The investigator or designee should complete a thorough review of the subject's medical history for missing information. Medical conditions obtained at screening prior to enrollment should be captured and recorded in the subject's baseline medical history. All **relevant "lifetime"** medical conditions are to be included. Items to include are:

- All ongoing medical diseases/condition, including chronic, intermittent, or recurrent disease.
- Any condition that requires ongoing therapy.
- All disease/conditions resolved in the past 30 days.
- Any condition that, in the opinion of the investigator, is clinically relevant including diseases for which the subject required surgery.
- Subjects with conditions that, in the opinion of the investigator, may put the subject at risk, may confound study results, or may interfere with participation in the study must be excluded from the study.

Contact GLLP Medical Lead if further clarifications are needed.

Name/Title	Affiliation/Tel./Fax
Marie-Jose Rueda, MD Rx Medical Director	Galderma Laboratories, L.P. Tel : (817) 961-5227

5.3.3. Medication and Non-Drug Treatment History

Previous drug and non-drug therapies should be assessed as related to the eligibility criteria listed in the protocol. Information on previous therapies (including herbal products) that have been stopped within 6 months prior to visit screening should be recorded on the CRF.

Other medications to treat concurrent medical conditions ARE permitted provided the dose is stable for at least 30 days prior to screening and throughout the study.

Any therapy used by the subject during the study will be considered a concomitant medication/non-drug treatment. Concomitant medications and non-drug treatments obtained at screening and baseline prior to enrollment should be captured and recorded in the subject's baseline medication and non-drug treatment history. Every attempt should be made to keep all concomitant medication/therapy dosing and regimens constant during the study. Any change to this therapy should be noted on the CRFs. If applicable, an Adverse Event CRF/eCRF should be completed for any subject starting new concomitant medications, unless the therapy is used for prophylaxis.

Concomitant medications and non-drug therapies during the course of the study are defined as:

Any new therapy received by the subject after subject enrollment, including:

- Drug therapies, such as Rx medications, OTC products (excluding OTC personal hygiene products), birth control medication, homeopathic preparations, vitamins, sunscreens, etc.

- Non-drug therapies, such as medical/surgical procedures.
- Any changes to existing therapies, such as changes in dose or formulation.

The concomitant therapies are to be recorded at each visit on the appropriate CRF/eCRF.

5.3.4. Screen Failures

If a consented subject fails to meet all of the requirements to participate in the study, or decides not to participate up to the point of enrollment at visit 1 (baseline), the subject will be considered a screen failure. The reason for screen failure should be documented appropriately in the source document and the CRF/eCRF.

5.3.5. Visit Windows

Visit windows as outlined below are allowed during the study:

- Screening (up to 14 days prior to baseline visit)
- Baseline
- Week 1 ±2 days from Baseline Visit
- Week 2 ± 2 days from Baseline Visit
- Week 6 ± 3 days from Baseline Visit
- Week 12 ± 3 days from Baseline Visit
- Week 18 ± 3 days from Baseline Visit
- Week 24 ± 3 days from Baseline Visit

5.3.6. Adverse Weather Provision

Study visits may be delayed if adverse weather conditions present a risk to the safety of persons traveling to the investigative site. Visits will be resumed immediately with the earliest acceptable improvement of travel conditions and staff availability. GLLP will be notified of changes in scheduled visit dates.

5.4 Visits and Examinations

5.4.1. Screening (up to 14 days prior to baseline or may be combined)

1. Review and explain the purpose and nature of the study to the subject.
2. Obtain Subject Informed Consent.
    - Have the subject read, sign and date an IEC/IRB approved informed consent including photo and video release, HIPAA authorization, and applicable state Bill of Rights.
    - Document the informed consent process in the source documents and CRF/.
    - Give a signed copy of the informed consent form to subject.
3. Assign the subject a unique screening number. Update screening and enrollment log.
4. Have subjects acclimate for at least 15 minutes in ambient temperature and humidity - conditions (68-75ºF and 35-65% humidity)
5. Confirm subject meets inclusion/exclusion criteria including mild to moderate facial acne (score of 2-3 on FDA Investigator's Global Assessment Scale), at least 5 inflammatory lesions, and 10 -100 non-inflammatory lesions and have this recorded by the Investigator or designee.
6. Have the Investigator or designee complete the tolerance grading.

7. Obtain demographic information and medical history, including information on all medications/therapies used within the last 6 months. Inform the subject as to the allowed and prohibited concomitant medications (see Section 4.2 and 4.3.2). If the candidate subject qualifies and is female of child-bearing potential, conduct a urine pregnancy test. Candidate female subjects with negative results, females of non-child-bearing potential, or candidate males that qualify will proceed to the next step.
8. Candidate subject's eligibility will be overseen by a dermatologist or MD physician. The dermatologist will confirm that the subject is suitable for the test materials. Those that qualify will be asked to return for the baseline visit.
9. Record any AEs that occur after the subject has signed the informed consent form.

Note: Subject screening and baseline visits may occur on the same day if site logistics permit.

5.4.2. Baseline (Screening and Baseline may be combined)

1. Obtain information on any changes in medical health and/or the use of concomitant medications/therapies to ensure the subject's eligibility in the study.
2. Record any AEs that are observed or reported, including those of changes in concomitant medication dosing/therapies.
3. Confirm subject still meet inclusion/exclusion criteria including mild to moderate facial acne (score of 2-3 on FDA Investigator's Global Assessment Scale), at least 5 inflammatory lesions, and 10 -100 non-inflammatory lesions and have this recorded by the Investigator or designee.
4. Subject's eligibility and health will be re-reviewed. Those that still pass eligibility requirements will be enrolled into the study and assigned a subject number.
5. Have the Investigator or designee complete the tolerance grading.
6. Subjects will participate in digital images procedures.
7. Subject will be randomly assigned to receive Product A or Product B as determined by a randomization schedule provided by Stephens. Study products will be dispensed and subjects will be provided instructions on how to properly use the study products.
8. Subjects will be provided with a daily diary to record product application.
9. Emphasize the importance of compliance with the instructions and application requirements.
10. Instruct the subject to bring back the dispensed study products at the next visit

5.4.3. Week 1 ± 2 days from Baseline Visit and Week 2 ± 2 days from Baseline Visit

1. Obtain information on any changes in medical health and/or the use of concomitant medications/therapies to ensure the subject's eligibility in the study.
2. Record any AEs that are observed or reported, including those of changes in concomitant medication dosing/therapies.
3. Have the subject acclimate for at least 15 minutes in ambient temperature and humidity condition (68-75ºF and 35-65% humidity).
4. Have the investigator or designee complete the lesion count (inflammatory and non-inflammatory).
5. Have the Investigator or designee complete the Investigator Global Assessments (IGA) on acne severity.
6. Have the Investigator or designee complete the tolerance grading.
7. Have the subject complete the self-assessment questionnaire.
8. Emphasize the importance of compliance with the instructions and application requirements.

9. Daily diaries will be collected, reviewed for compliance of the study product application. The diaries will be returned to the subjects at week 1. At week 2, diaries will be retained by the testing facility and new diaries will be distributed to the subjects.
10. Collect, weigh, and re-dispense study product.
11. Instruct the subject to bring back the dispensed study products at the next visit.

5.4.4. Week 6 ± 3 days from Baseline Visit and Week 12 ± 3 days from Baseline Visit

1. Obtain information on any changes in medical health and/or the use of concomitant medications/therapies to ensure the subject's eligibility in the study.
2. Record any AEs that are observed or reported, including those of changes in concomitant medication dosing/therapies.
3. Have the subject acclimate for at least 15 minutes in ambient temperature and humidity condition (68-75ºF and 35-65% humidity). '
4. Have the investigator or designee complete the lesion count (inflammatory and non-inflammatory).
5. Have the Investigator or designee complete the Investigator Global Assessments (IGA) on acne severity.
6. Have the Investigator or designee complete the tolerance grading.
7. Have subjects participate in digital images procedures.
8. Have the subject complete the self-assessment questionnaire.
9. Emphasize the importance of compliance with the instructions and application requirements.
10. Daily diaries will be collected, reviewed for compliance of the study product application, and retained by the testing facility. New diaries will be distributed to the subjects.
11. Collect, weigh, and re-dispense study product. Products will be retained and new products will be dispensed as necessary.
12. Instruct the subject to bring back the dispensed study products at the next visit.

Follow-up phone calls will be made between Week 6 and Week 12 to inquire how subjects are progressing and if subjects have enough study product to use until the next visit.

5.4.5. Week 18 ± 3 days from Baseline Visit

1. Obtain information on any changes in medical health and/or the use of concomitant medications/therapies to ensure the subject's eligibility in the study.
2. Record any AEs that are observed or reported, including those of changes in concomitant medication dosing/therapies.
3. Emphasize the importance of compliance with the instructions and application requirements.
4. Daily diaries will be collected, reviewed for compliance of the study product application, and retained by the testing facility. New diaries will be distributed to the subjects.
5. Collect, weigh, and re-dispense study product.
6. Instruct the subject to bring back the dispensed study products at the next visit.

5.4.6. Week 24/Early Exit ± 3 days from Baseline Visit

1. Obtain information on any changes in medical health and/or the use of concomitant medications/therapies to ensure the subject's eligibility in the study.
2. Record any AEs that are observed or reported, including those of changes in concomitant medication dosing/therapies.

3. Conduct a urine pregnancy test on women of child-beraing potential.
4. Have the subject acclimate for at least 15 minutes in ambient temperature and humidity condition (68-75ºF and 35-65% humidity).
5. Have the investigator or designee complete the lesion count (inflammatory and non-inflammatory).
6. Have the Investigator or designee complete the Investigator Global Assessments (IGA) on acne severity.
7. Have the Investigator or designee complete the tolerance grading.
8. Have subjects participate in digital images procedures.
9. Have the subject complete the self-assessment questionnaire.
10. Daily diaries will be collected, reviewed for compliance of the study product application, and retained by the testing facility.
11. Collect and weigh study product.
12. Complete the Exit Form CRF/eCRF.

After study completion, a trained grader from Stephens will evaluate the digital images taken at baseline, week 6, week 12, and week 24 for clinical grading of efficacy parameters.

5.4.7. Unscheduled Visits

Any visit that occurs between the regularly scheduled visits must be documented in the Unscheduled Visit (USV) pages of the CRF/eCRF. During all USVs, the following procedures will be conducted:

1. Obtain information on any changes in medical health and/or the use of concomitant medications/therapies to ensure the subject's eligibility in the study.
2. Record any AEs that are observed or reported, including those of changes in concomitant medication dosing/therapies.
3. Daily diaries will be collected and reviewed for compliance of the study product application.
4. Have the investigator or designee complete the lesion count (inflammatory and non-inflammatory).
5. Have the Investigator or designee complete the Investigator Global Assessments (IGA) on acne severity.
6. Have the Investigator or designee complete the tolerance grading.
7. Have the subject acclimate for at least 15 minutes in ambient temperature and humidity condition. Upon acclimation, have subjects participate in digital images procedures.
8. Have the subject complete the self-assessment questionnaire.
9. Emphasize the importance of compliance with the instructions and application requirements.
10. Collect and weigh study products.

These procedures are required at USVs; however at the investigator discretion additional assessments may be performed and recorded on the USV CRF/eCRF. If a subject is discontinued at an USV, refer to Section 5.5 for guidance.

5.4.8. Non-Clinic Days

Instruct subjects to use Product A once daily or Product B 1-3 times a day following the same instructions discussed during the clinic visit. Subjects will be instructed to cleanse their face and remove any make-up (if applicable) 30 minites prior to each clinic visits.

5.5 DISCONTINUED SUBJECTS

Any subject is free to discontinue his/her participation in this study at any time and for whatever reason, specified or unspecified, and without prejudice.
Subjects who discontinue the study prematurely should be fully evaluated, whenever possible. The procedures designated for the early exit visit (Section 5.4.7) should be completed for all prematurely discontinued subjects and the appropriate CRFs should be completed.
All subjects who prematurely discontinue the study should have the reason carefully documented by the investigator on the exit CRF/eCRF, and, if applicable, on the adverse event CRF/eCRF. In no case, shall a subject who prematurely discontinues (who has been included and has had a subject identification number assigned), be replaced by another subject. In the case of premature discontinuation due to an AE, the investigator should ensure that the subject receives appropriate follow-up and therapy for their condition. All data gathered on the subject related to AE resolution will be made available to the Sponsor and/or regulatory authorities.
An investigator may decide to discontinue a subject from the study for safety reasons or when it is in the best interest of the subject. GLLP may also decide to prematurely terminate or suspend the study or the participation of a subject in the study. All data gathered on the subject prior to termination should be made available to GLLP.
The Exit Form must be completed and one of the following reasons for discontinuation must be identified:

- Adverse Event
- Subject Request
- Protocol Violation
- Lost to Follow-up
- Other

If reason for discontinuation is “other”, the subject will be questioned to definitively rule out the possibility of an AE.

5.6 STUDY DURATION AND TERMINATION

Study duration for each subject is approximately 24 weeks. It is estimated a maximum of 10 months will elapse between first subject first visit and last subject last visit.
The investigator may terminate the study at his/her study site at any time with appropriate notification to GLLP. Likewise, GLLP may terminate prematurely the participation of a particular study site (e.g., for non-enrollment or non-compliance with protocol, regulation or Good Clinical Practice) or terminate prematurely the entire study (e.g., for safety, quality of study product, regulatory, efficacy or logistics reasons) at any time with appropriate notification.

6. TREATMENT ADMINISTERED

At baseline, qualified subjects will be enrolled and randomized to receive Product A or Product B. Throughout the study, the investigator will be responsible for the accounting of the study product and will ensure that the study product is not used in any unauthorized manner.

6.1 PRODUCT IDENTIFICATION AND USE

Study Product: Product A	
Form	Gel

Instructions for use	Dispense a nickel size amount of product and apply as a thin layer to the entire face or any other affected areas of the skin once daily, after washing gently with a mild soap-less cleanser and drying the area.
Mode of Administration:	Topical
Duration of Use:	24 Weeks
Quantity:	1
How supplied:	Kit
Storage and Handling	Product to be stored at USP Controlled Room Temperature conditions: 68°F – 77°F (20°C – 25°C) with excursions permitted between 59°F – 86°F (15°C – 30°C)
Study Product: Product B	
Form	Gel
Instructions for use	Clean the skin thoroughly before applying this product. Cover the entire affected area with a thin layer one to three times daily. Because excessive drying of the skin may occur, start with one application daily, then gradually increase to two or three daily if needed or as directed by a doctor. If bothersome dryness or peeling occurs, reduce application to once a day or every other day.
Mode of Administration:	Topical
Duration of Use:	24 Weeks
Quantity:	2
How supplied:	Kit
Storage and Handling	Product to be stored at Room Temperature conditions: 68°F – 77°F (20°C – 25°C). Keep product away from excess heat and moisture.

Facial Cleanser	
Form	Gel
Instructions for use	Massage a small amount onto wet skin. Rinse
Mode of Administration:	Topical
Duration of Use:	24 Weeks
Quantity:	1
How supplied:	Kit
Storage and Handling	Fragile, handle with care. Keep from freezing and extreme heat.
Moisturizing Lotion	
Form	Lotion
Instructions for use	After applying the product, use moisturizer on the entire face. Apply daily to dry skin as needed or as directed by physician.
Mode of Administration:	Topical
Duration of Use:	24 Weeks
Quantity:	1
How supplied:	Kit

Storage and Handling	Fragile, handle with care. Store at controlled room temperateure; 68°F – 77°F (20°C – 25°C) with excusrsions permitted between 59°F -86°F (15°C – 30°C).
Facial Moisturizer SPF 30	
Form	Cream
Instructions for use	Apply lilberally 15 minutes before sun exposure. Use a water resistant sunscreen if swimming or sweating. Reapply at least every 2 hours.
Mode of Administration:	Topical
Duration of Use:	24 Weeks
Quantity:	1
How supplied:	Kit
Storage and Handling	Fragile, handle with care. Keep from freezing and extreme heat.

General instructions:

Use all products as instructed. Cleanser, test material, and moisturizer should be used as a regimen.

Avoid extended periods of sun exposure, all use of tanning beds, and sunless tanning products for the duration of the study. Extra care should be taken to wear protective clothing, including sunglasses, and avoid sun exposure from 10 AM to 4 PM.

Continue use of all regular brands of color cosmetics, makeup remover, and use the assigned test material for the duration of the study. Individuals must refrain from using any acne products and beginning the use of any new facial products other than the assigned test material. Use of moisturizing foundation and waterproof SPF will be acceptable as long as the subject has a history of safe usage of the foundation and waterproof SPF.

Subjects will be instructed to use Product A once daily or Product B 1-3x a day.

6.2 ACCOUNTABILITY

Upon receipt of the study products, the investigator or designee will conduct an inventory. In accordance with federal regulations, the investigator must agree to keep all study products in a secure location with restricted access. Designated study personnel will provide the study products to the subjects in accordance with the protocol. A daily temperature log will be maintained documenting appropriate study product storage conditions.

During the study, the investigator must maintain records of study treatment dispensation for each subject. This record must be made available to the study monitor for the purposes of verifying the accounting of clinical supplies. Any discrepancies and/or deficiencies between the observed disposition and the written account must be recorded along with an explanation.
Compliance will be assessed by study staff at each visit. Subjects will be considered compliant with the treatment product if they use at least 80% of the expected applications for each of the test product during participation in the study. Subjects will be considered non-compliant if usage is over 120%.

Subjects will complete a daily diary recording test material applications and comments during the course of the study. Diaries will be reviewed and test materials will be visually inspected at

each post-baseline study visit to evaluate treatment compliance. Additionally, test material units will be weighed prior to distribution and at week 1, week 2, week 6, week 12, week 18, and week 24.

If subjects do not return their diary or test materials during an interim visit, a verbal confirmation will be obtained for usage compliance and will be documented as a note to file. The subject will be reminded to return their diary and test materials at the next study visit.

6.3 METHOD OF TREATMENT ASSIGNMENT

Prior to the start of the study, Stephens will generate a randomization list to establish treatment assignment to 1 of the treatment cells (Cell 1 and Cell 2), which will be balanced between sites. Stephens will provide the product label coding according to the provided randomization.

7. ADVERSE EVENTS

Throughout the course of the study, all adverse events will be monitored and reported on an adverse event CRF/eCRF without omitting any requested and known information. When AEs occur, the main concern is the safety of the study subjects. At the time of the informed consent signature, each subject must be given the name and phone number of study site personnel for reporting AEs and medical emergencies.This information is included in the Informed Consent.
At each visit, after the subject has had the opportunity to spontaneously mention any problems, the investigator or designee should inquire about AEs by asking the standard questions (e.g):

"Have you had any health problems since your last study visit?"

"Have there been any changes in the medicines you take since your last study visit?"

AEs should be reported as a result of an untoward (unfavorable and unintended) change from baseline in a subject's medical health following signature of the Informed Consent.
Changes from baseline in any protocol-specific parameter evaluated during the study are to be reviewed by the investigator. In addition, the subject's responses to any questionnaire utilized during the study are to be reviewed by the investigator. Any untoward (unfavorable and unintended) change from baseline in a protocol-specific parameter or questionnaire response is to be reported as an AE. These clinically relevant changes will be reported regardless of causality.

7.1 DEFINITIONS

7.1.1. Adverse Events (AE)

Adverse event means any untoward medical occurrence associated with the use of a study product in humans, whether or not considered study product related.
An *adverse event* (also referred to as an adverse experience) can be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of a study product, and does not imply any judgment about causality. An adverse event can arise with any use of the study product (e.g., off-label use, use in combination with another study product) and with any route of administration, formulation, or dose, including an overdose.
Thus any new sign, symptom or disease, or clinically significant increase in the intensity of an existing sign, or symptom should be considered as an adverse event.
Notes:
Any new clinically relevant sign or symptom suffered by the subject, which appears after the study procedures should also be reported as an adverse event.

7.1.2. Suspected Adverse Reaction (SAR)

Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the study product caused the adverse event. 'Reasonable possibility' means there is evidence to suggest a causal relationship between the study product and the adverse event.
Any adverse event, whether or not it is related to the study product, will be reported on the AE CRF along with the date of onset, the severity, the relationship with the study product and the outcome.
If the subject discontinues due to an AE, the AE CRF and exit CRF must be completed.

7.1.3. Serious Adverse Events (SAE)

An adverse event or suspected adverse reaction is considered "serious" if in a view of either the investigator or sponsor, it results in any of the following outcomes:

- death,
- life-threatening adverse event (the event places the subject at immediate risk of death),
- inpatient hospitalization or prolongation of existing hospitalization,
- a persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions, or
- a congenital anomaly/birth defect

Additionally:

Important medical events that are based on appropriate medical judgment may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

Note: The term "life-threatening" refers to an adverse event or suspected adverse reaction if, in the view of either the investigator or sponsor, its occurrence places the subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death.
Hospitalization solely for the purpose of diagnostic tests, even if related to an AE, elective hospitalization for an intervention which was already planned before the inclusion of the subject in the study, and admission to a day-care facility may not themselves constitute sufficient grounds to be considered as a serious adverse event. Hospitalization is defined as admission to a hospital for greater than 24 hours.

7.1.4. Severity

Severity is a clinical determination of the intensity of an adverse event.
The severity assessment for an AE is to be completed using the following definitions as a guideline for all AEs occurring during clinical trials conducted or sponsored by Galderma, Laboratories, L.P.:

Mild:	Awareness of sign or symptom, but easily tolerated
Moderate:	Discomfort, enough to cause interference with usual activity
Severe:	Incapacitating with inability to work or perform usual activity

7.1.5. Relationship to Study Products

The relationship assessment for an AE is to be completed using the following definitions as a guideline for all AEs occurring during clinical trials conducted or sponsored by Galderma Laboratories, L.P.:

7.1.6. Causality assessment

The Investigator is to determine whether there is a reasonable causal relationship between the trial/test products(s) and/or procedures and the event. Medical judgment should be used to determine the relationship, considering all relevant factors including the pattern of event, temporal relationships, positive de-challenge or re-challenge, relevant medical history, and confounding factors such as co-medication or concurrent diseases.

The relationship assessment for an event is to be completed using the following definitions:

- *Reasonable possibility*: According to the reporting Investigator, there is a reasonable possibility (i.e., suggestive evidence or arguments) that there is a causal relationship irrespective of the dose administered between the trial/test product and/or procedures and the event,
- *No Reasonable Possibility*: No suggestive evidence or arguments can be identified regarding a causal relationship between the trial/test product and/or procedures and the event.

The expression "reasonable causal relationship" is meant to convey in general that there are facts or arguments to suggest a causal relationship.

Assessment of casualty must be completed by the investigator.

7.2 REPORTING PROCEDURES

7.2.1. Procedures for Reporting Adverse Events

The collection of AEs will begin when a subject signs the informed consent up to the final visit. At each visit, the investigator or designee will question the subject about AEs using questions taking care not to influence the subject's answer (e.g. "Have you noticed any change in your health?"). Directed questioning and examination will then be done when appropriate.
Any AE, whether or not it is related to the study product, will be reported on the AE CRF/eCRF along with the date of onset, the severity, the relationship with the study product and the outcome without omitting any requested and known information. Additional information may be requested under certain circumstances to ensure accurate reporting.
Every time a concomitant medications/therapy is administered or prescribed during the study, an AE CRF/eCRF will be completed if appropriate and the reason for the treatment noted.
When an AE persists after a subject exits the study, the investigator will ensure an appropriate follow-up of the subject until the investigator/GLLP agrees the event is satisfactorily resolved or has reached a stable clinical endpoint.

Sites 2, 3, and 4 will report AEs to Site 1 by e-mail to areaka@stephens-associates.com. Site 1 will report AEs to GLLP.

7.2.2. Procedure for Reporting a Serious Adverse Event

For any SAE, occurring during the study, whether or not related to the study product, expected or not, the investigator is to take the following steps:

1. Take prompt and appropriate medical action, if necessary. The safety of study subjects is the first priority.
2. Inform GLLP of the event by fax (682-831-9197) and email at pharmacovigilanceUS@galderma.com within 24 hours, and discuss further steps to be taken. Galderma representatives and their contact information are provided in the

communication plan that accompanies this protocol. Also inform Stephens & Associates by e-mail at areaka@stephens-associates.com, the same as GLLP.

3. Complete the AE CRF/eCRF with as much information as possible.
4. Complete the SAE Form. Fax the completed form accompanied by the demography CRF/eCRF, the Medical History CRF/eCRF, the Previous and Concomitant Medication/TherapiesCRF/eCRF, the AE CRF/eCRF, and any other relevant information (e.g. test results) immediately to GLLP at 682-831-9197.
5. Monitor and record the progress of the event until it resolves or reaches a clinically stable outcome, with or without sequel. Every effort should be made to obtain further safety details and follow-up information from the subject and his/her doctors within limits described by local laws and regulations.
6. Obtain and maintain in his/her files all pertinent medical records, information, and medical judgments from who may have assisted in the treatment and follow-up of the subject. If necessary, contact the subject's personal physician or hospital to obtain further information.
7. Inform GLLP of the ongoing progress and final outcome of the event. Send a revised or updated SAE Form, if appropriate to the above fax number.
8. Comply with the applicable regulatory requirement(s) related to the reporting of serious adverse events to the regulatory authority (ies) and the IRB.

8. STATISTICAL METHODS PLANNED

8.1 STATISTICAL AND ANALYTICAL PLANS

A separate document, named the Statistical Analysis Plan (SAP), will be developed by Stephens during the conduct of the study and approved by GLLP prior to database lock. It will contain a more detailed and technical description of specific data conventions, calculations and of statistical procedures for executing the analyses that are specified in the sections of the protocol below.
Any changes to the statistical analyses planned in the protocol will be justified and documented in the SAP if they were decided before database lock. Any change made to the SAP after the database lock will be documented in the final clinical study report as deviations from the planned analysis.

8.1.1. Variables to be analyzed

The following variables will be analyzed or summarized:

8.1.1.1. Primary Variables

- Percent Change in Total Lesions at Week 12

8.1.1.2. Secondary Variables

- Change in lesion count from baseline.
- Change in Investigator's Global Assessment (IGA)
- Change in clinical grading of efficacy parameters through digital images from baseline.
- Subject self-assessment questionnaire at Weeks 1, 2, 6, 12, and 24.
- Change in tolerance grading from baseline.

8.1.1.3. Safety Variables

- Incidence of adverse events

8.1.1.4. Data Transformations

No data transformations are planned.

8.1.2. Populations Analyzed, Evaluability and Limitation / Evaluation of Bias

Statistical analyses will be performed based on the following subject populations.

8.1.2.1. Intent-to-Treat (ITT) Population

The ITT population is defined as all subjects who are randomized and have at least one post-treatment administration evaluation. This is the primary population for efficacy analyses. All primary efficacy variables and secondary efficacy variables will be analyzed based on the ITT population. LOCF (Last Observation Carried Forward) will be used to impute missing efficacy data for this population.

8.1.2.2. Safety Population

The safety population is defined as all subjects who are enrolled and receive at least one dose of study product. In practice, only the subjects who return their study product unopened will be excluded from the safety population. Safety variables will be analyzed based on the safety population.

8.1.3. Data Presentation and Graphics

The subject disposition, demographics, baseline characteristics, compliance (number of missed applications, total number of applications, etc.), visit dates including informed consent date, inclusion/exclusion criteria, previous therapies and concomitant therapies by treatment will be listed or summarized. All primary and safety variables listed will be summarized at each visit. The categorical variables will be summarized by frequency and percentage for each response category (N, %). The continuous variables will be summarized using means, medians, minimum, maximum, and standard deviations (SD) for each visit.

Additional summary tables will be provided for AEs that are considered serious (SAEs), related to the study product, and AEs leading to discontinuation. All AE summary tables are based on the number of subjects in safety population who have experienced AE(s). For a given AE, a subject will be counted once, even if he or she has experienced multiple episodes for that particular AE.

8.2 SAMPLE SIZE DETERMINATION

Sample size is determined according to Sponsor’s recommendation.

9. STUDY CONDUCT CONDISERATIONS

9.1 CLINICAL MONITORING

The conduct of the study will be closely monitored by representatives of GLLP following GCP, ICH guidelines, applicable SOPs, regulatory guidelines and all local regulations. The clinical investigation will be monitored to ensure that: the rights and well-being of the subjects are protected; the reported data are accurate, complete and verifiable from applicable source documents; and the study is conducted in accordance with the currently approved protocol and any other study agreements, GCP, and all applicable regulatory requirements. The investigator

will allow the GLLP representatives to have access to all study records, CRF, corresponding subject medical records, and any other documents considered source documentation. The investigator also agrees to assist the representatives, if required, which can include AE reporting.

DATA COLLECTION

Investigators must keep accurate records of all subjects' visits and all procedures done, being sure to include all pertinent study related information from which CRF/eCRF data will be recorded. Data for this study may be recorded in the subject's chart (e.g. source documents / electronic records) or if approved by the GLLP directly into CRF. If electronic records are maintained, the method of verification must be determined in advance of starting the study. A statement should be made indicating that the subjects have been enrolled in protocol GLI.04.SPR.US10329 and have been provided with a copy of the signed informed consent. The process of administering the informed consent must also be documented. Any and all side effects and AEs with the concomitant therapies associated must be thoroughly documented. Results of any diagnostic tests conducted during the study should be included in the source documentation. Pertinent telephone conversations with the subjects and/or GLLP concerning the study will be documented and kept on file.
It is required that the author of an entry in the source documents be identifiable. Direct access to all source documentation (medical records) must be allowed for the purpose of verifying that the data recorded in the CRF/eCRF are consistent with the original source.
Only designated individuals may complete the CRF. The principal investigator will review the reported data and certify that the CRF are accurate and complete.
After monitoring has occurred at the clinical site(s) and the CRF have been reviewed, additional data clarifications and/or additions may be needed including AE reporting. Data clarifications and/or additions are documented and are part of each subject’s CRF.

9.2 QUALITY ASSURANCE / AUDIT / INSPECTION

To ensure compliance with GCP and all applicable regulatory requirements, GLLP may conduct a quality assurance audit of the site records, and the regulatory agencies may conduct a regulatory inspection at any time during or after completion of the study. The investigator must agree to grant the auditor(s) and inspector(s) direct access to all relevant documents and to allocate their time and the time of their staff to discuss any findings/relevant issues.

9.3 RECORD RETENTION

The investigator is required to maintain up-to-date, complete regulatory documentation as indicated by GLLP and the investigator’s files will be reviewed as part of the ongoing study monitoring. The records must be easily accessible when needed (e.g., for a Galderma Laboratories L.P.’s audit or regulatory inspection) and must be available for review in conjunction with assessment of the facility, supporting systems, and relevant site personnel. Financial information is not subject to regulatory inspection and should be kept separately.
GLLP will inform the investigator of the time period for retaining the site records in order to comply with all applicable regulatory requirements. The minimum retention time will meet the strictest standard applicable to a particular site, as dictated by local laws/regulations, GLLP SOPs, and/or institutional requirements.
The investigator should take measures to prevent accidental or premature destruction of these documents. If the investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. GLLP must be notified in writing of the name and address of the new custodian.

9.4 CHANGES IN STUDY CONDUCT / AMENDMENTS

No amendment will be done for modification(s) due to change in logistical or administrative aspect of the study (e.g., change in monitors, change of telephone numbers). In such a case, the appropriate institution(s) and/or person(s) will be notified of the changes.
Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by GLLP and must be approved by the IEC/IRB prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions.
Amendments may necessitate that the informed consent and other study-related material be revised. If the consent form is revised, all patients/subjects currently enrolled in the study may be required by the IRB/IEC to sign the approved, revised informed consent form.

10. ETHICS

This study will be conducted in accordance with the HELSINKI Declaration (1964) and it's TOKYO (1975), VENICE (1983), HONG-KONG (1989), SOMERSET WEST (1996) and EDINBURGH (2000), Washington (2002). Tokyo (2004), Seoul (2008), and Brazil (2013) amendments, the ICH Good Clinical Practice (GCP) guidelines, FDA Code of Federal Regulations (CFR), Health Insurance Portability and Accountability Act (HIPAA) and local regulatory requirements. The investigator and all clinical study staff will conduct the clinical study in compliance with the protocol. The investigator will ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience.
Before clinical study initiation, this protocol, the informed consent form with any other written information given to subjects, and any advertisements planned for subject recruitment must be approved by an IEC/IRB. The investigator must provide documentation of the IEC/IRB approval to GLLP. The approval must be dated and must identify the applicable protocol, amendments (if any), informed consent form, all applicable recruiting materials, written information for subject, and subject compensation programs. The IEC/IRB will be provided with any periodic safety updates, and all other information required by local regulation and/or the IEC/IRB. At the end of the study, the investigator will notify the IEC/IRB about the study's completion. The IEC/IRB also will be notified if the study is terminated prematurely. Finally, the investigator will report to the IEC/IRB on the progress of the study at intervals stipulated by the IEC/IRB.
Voluntary informed consent will be obtained from every subject prior to the initiation of any screening or other study-related procedures. The investigator must have a defined process for obtaining consent. Specifically, the investigator, or designee, will explain the clinical study to each potential subject and the subject must indicate voluntary consent by signing and dating the approved informed consent form. The subject must be provided an opportunity to ask questions of the investigator, and if required by local regulation, other qualified personnel. The investigator must provide the subject with a copy of the consent form written in a language the subject understands. The consent document must meet all applicable local laws and will provide subjects with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits of the study product, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Subjects will be told about the voluntary nature of participation in the study and will be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The subject also will be told that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The investigator must keep the original, signed copy of the consent and must provide a duplicate copy to each subject.

11. STUDY FLOW CHART

11.1 Study flow chart

PROCEDURES	Study Visits								
	Visit 1 Screening [a]	**Visit 2 Baseline [a]**	**Visit 3 Week 1 (±2 Days) /Early Exit**	**Visit 4 Week 2 (±2 Days) /Early Exit**	**Visit 5 Week 6 (±3 Days) /Early Exit**	**Visit 6 Week 12 (±3 Days)/Early Exit**	**Visit 7 Week 18 (±3 Days)/Early Exit**	**Visit 8 Week 24 (±3 Days)/Early Exit**	**Unscheduled Visit (USV)[c]**
Informed Consent	X								
Inclusion/Exclusion Criteria	X	X							
Demographics	X								
Previous Therapies & Procedures	X								
Medical History	X								
Urine pregnancy test	X							X	X
Diaries Dispensed/Collected		X		X	X	X	X	X	X
Concomitant therapies & procedures	X	X	X	X	X	X	X	X	X
Lesion count	X	X	X	X	X	X		X	X
IGA	X	X	X	X	X	X		X	X
Clinical Grading of Efficacy Parameters through digital images		X			X	X		X	X
Clinical Grading of Tolerance Parameters	X	X	X	X	X	X		X	X
Imaging procedures		X			X	X		X	X
Self-Assessment Questionnaire			X	X	X	X		X	X
Test Products dispensing		X			X	X	X	X	X
Adverse Events [b]		X	X	X	X	X	X	X	X
Exit Form								X	X

[a] Screening and Baseline visit may be combined.
[b] Adverse events are to be collected starting from the signing of the Informed Consent Form.
[c] If a subject is discontinued at Week 1, Week 2, Week 6, Week 12, Week 18 or USV, Week 24/Exit or Early Exit Procedures are to be completed

12. REFERENCES

1. U.S. Food and Drug Administration. Guidance for industry: acne vulgaris: developing drugs for treatment. September 2005. http://www.fda.gov.
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3. Rizer, RL, Mills, OH, Trookman, NS. The assessment of acne: a re-evaluation of grading strategies. Scientific Poster, Annual Meeting of the Am. Acad. Dermatol (2001).
4. Griffiths CE, Wang TS, Hamilton TA, Voorhees JJ, Ellis CN. A photonumeric scale for the assessment of cutaneous photodamage. Arch Dermatol. 1992 Mar;128(3):347-351.

13. ATTACHMENTS

Attachment 12.1 – Elements of Informed Consent
Attachment 12.2 – Assessment Scale and Descriptions

13.1 ELEMENTS OF INFORMED CONSENT

The following information must be provided to each subject in obtaining informed consent. If written consent is being obtained, the subject (or subject's legal representative) should be provided with a copy of the signed written informed consent.

1. State that the study involves RESEARCH.
    a. Explain the PURPOSES of the research
    b. State the expected DURATION of the subject's participation
    c. Explain the trial treatments
    d. Describe the PROCEDURES to be followed
    e. Identify any EXPERIMENTAL procedures
    f. Explain the subject's responsibilities
2. Describe any reasonably foreseeable RISKS OR DISCOMFORTS to the subject (skin irritation)
3. Describe any BENEFITS to the subject or to others which may reasonably be expected from research
4. Note appropriate ALTERNATIVE procedures or courses of treatment, if any that might be advantageous to the subject.
5. Describe the extent, if any, to which CONFIDENTIALITY of records identifying the subject will be maintained. Note that the monitors, the auditors, the IRB and the Food and Drug Administration (FDA) will be granted access to the subject's original medical records for verification of clinical trial procedures and/or data without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that by signing a written informed consent form, the subject or the subject's legally acceptable representative is authorizing such access.
6. Describe the anticipated prorated payment, if any, to the subject for participating in the trial.
7. For research involving more than minimal risk, explain if any COMPENSATION or medical treatments are available should injury occur. If so, explain (a) what they consist of, OR (b) where further information may be obtained.
8. Tell whom to contact for ANSWERS to pertinent questions about (a) the research and (b) research subject's rights.

9. State that:
    a. participation is VOLUNTARY
    b. refusal to participate will involve NO PENALTY or loss of benefits to which the subject is otherwise entitled, and
    c. the subject MAY DISCONTINUE participation at any time without penalty or loss of benefits to which the subject is otherwise entitled

Additional Elements of Informed Consent

When appropriate, one or more of the following elements of information shall also be provided to each subject.

1. A statement that the particular treatment or procedure may involve risks to the subject which are currently unforeseeable.
2. Any additional costs to the subject that may result from participation in the research.
3. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
4. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject or the subject's legally acceptable representative in a timely manner.
5. The approximate number of subjects involved in the study.
6. A statement that a description and/or summary of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. The subject may review the information posted in this web site at any time. The web site will not include information that can identify the subject.

References:

21 CFR Part 50.25 – Protection of Human Subjects, Basic Elements of Informed Consent
International Conference on Harmonization Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance, 4.8 Informed Consent of Trial Subjects (April 1996)
The informed consent requirements in these regulations are not intended to pre-empt any applicable federal, state, or local laws.

13.2 Assessment Scales and Descriptions

13.2.1. Lesion Count

Clinic Day Assessments: Screening/Baseline, Week 1, Week 2, Week 6, Week 12, Week 24
A trained grader will count and record the number of open comedones, closed comedones papules, and pustules on each subject's face. Note that papules and pustules are classified as inflammatory acne lesions while open and closed comedones are classified as non-inflammatory lesions.

Acne lesion counts will be assessed globally on the face for each of the following facial locations/quadrants: forehead, left cheek, chin (including the area above the upper lip), and right cheek. Lesions on the nose, under the jaw line or along the hairline (including eye brows) will not be included in the counts.[3]

13.2.2. Investigator's Global Assessment (IGA)

Clinic Day Assessments: Screening/Baseline, Week 1, Week 2, Week 6, Week 12, and Week 24
A trained grader will evaluate each subject's global face for Investigator's Global Improvement Assessment.

FDA Investigator's Global Assessment of Acne Severity scale

0	Clear	No inflammatory or non-inflammatory lesions
1	Almost Clear	Rare non-inflammatory lesions with no more than one small inflammatory lesion
2	Mild	Greater than Grade 1, some non-inflammatory lesions with no more than a few inflammatory lesion (papules/pustules only, no nodular lesions)
3	Moderate	Greater than Grade 2, up to many non-inflammatory lesions and may have some inflammatory lesions, but no more than one small nodular lesion
4	Severe	Greater than Grade 3, up to many non-inflammatory and inflammatory lesions, but no more than a few nodular lesions

13.2.3. Clinical Grading of Efficacy Parameters through digital images

Clinic Day Assessments: Baseline, Week 6, Week 12, and Week 24
Stephen's trained grader will evaluate each digital images for clinical grading of efficacy parameters. The efficacy parameters will be assessed globally on each subject's face using a modified Griffiths' 10-point scale[4] according to the following numerical definitions (half-point scores may be used as necessary to more accurately describe the skin condition):

0 = none (best possible condition)
1 to 3 = mild
4 to 6 = moderate
7 to 9 = severe (worst possible condition)

The following parameters will be evaluated using the indicated scale anchors:

Parameter	0 =	9 =
Skin texture	Smooth, even looking skin	Rough, uneven looking skin

Parameter	0 =	9 =
	texture	texture
Skin tone evenness	Even skin tone	Severely uneven skin tone
Clarity	Translucent skin appearance	Dull/flat matte skin appearance
Overall skin complexion	Excellent	Poor

13.2.4. Clinical Grading of Tolerability Parameters

Tolerability evaluations will be performed at screening, baseline, and weeks 1, 2, 6, 12, and 24. Local cutaneous tolerability will be evaluated by assessing the signs and symptoms of erythema, dryness, and scaling, and by subject reporting of the degree of stinging/burning on the global face (treatment area).

For subject assessments of subjective irritation, subjects will report the degree of any parameters that they typically experience when using a product similar to the test material(s) at the baseline visit. At post-baseline time points, subjects will report the degree of any of these symptoms they have experienced since the previous time point.

The following static (without reference to any prior visits) scales and definitions will be used for tolerability evaluations (with half-point scores used as necessary to better describe the clinical condition):

Objective Irritation Parameters

Erythema	
0 = None	No erythema of the treatment area
1 = Mild	Slight, but definite redness of the treatment area
2 = Moderate	Definite redness of the treatment area
3 = Severe	Marked redness of the treatment area

Dryness	
0 = None	No dryness of the treatment area
1 = Mild	Slight, but definite dryness of the treatment area
2 = Moderate	Definite dryness of the treatment area
3 = Severe	Marked dryness of the treatment area

Scaling	
0 = None	No scaling of the treatment area
1 = Mild	Barely perceptible, fine scales in limited areas of the treatment area
2 = Moderate	Fine scaling generalized to all areas of the treatment area
3 = Severe	Scaling and peeling of skin over all areas of the treatment area

Subjective Irritation Parameters

Burning/stinging	
0 = None	No burning/stinging of the treatment area
1 = Mild	Slight burning/stinging sensation of the treatment area; not really bothersome
2 = Moderate	Definite warm, burning/stinging of the treatment area that is somewhat bothersome
3 = Severe	Hot burning/marked stinging sensation of the treatment area that causes definite discomfort and may interrupt daily activities and/or sleep

13.2.5. Digital images

Clinic Day Assessments: Baseline, Week 6, Week 12, and Week 24
Prior to photography procedures, clinic personnel will ensure that subjects have a clean face with no makeup as described in the study procedures. Subjects will remove any jewelry from the area(s) to be photographed and equilibrate for at least 15 minutes to ambient conditions (68-75ºF and 35-65% humidity) within the clinic before any photographs are taken.

VISIA Imaging:
Subjects will be provided with a black or gray matte headband to keep hair away from the face and instructed on proper headband placement. Subjects will be provided with a black matte shirt or a black or gray matte cloth will be draped over the subjects' clothing. Subjects will be instructed to adopt neutral, non-smiling expressions with their eyes gently closed. Subjects will be carefully positioned for each photograph, for the center, right, and left side views.

Full-face digital images will be taken of each subject (right side, left side, and center views) using the VISIA CR photo-station (Canfield Imaging Systems, Fairfield, New Jersey) with a Canon Mark II 5D or 6D digital SLR camera (Canon Incorporated, Tokyo, Japan) under the following lighting conditions:

Standard lighting 1
Standard lighting 2
Cross-polarized
Parallel polarized
UV fluorescence

Visible Light Imaging (Beauty shot)
For subjects completing at sites 1 and 2 (Stephens' Texas and Colorado locations), digital images will be taken of each subject's face using visible light. Full-face images will be taken of each subject's center view. Subjects will not be wearing any headband or using any headrest/chinrest. Subjects will be instructed to adopt neutral, non-smiling expressions with their eyes open.

13.2.6. Self-Assessment Questionnaires

Clinic Day Assessments: Week 1, Week 2, Week 6, Week 12, and Week 24
Subjects will be asked to complete a self-assessment questionnaire. This questionnaire has a 5-point Likert Response Scale (1=Strongly Agree; 5=Strongly Disagree). Responses for each item will be transformed into percent agreement (percentage of subjects with a score of 1 or 2) and presented descriptively. The individual items will be asked at the indicated time points:

Questions	Visit 2: Week 1	Visit 3: Week 2	Visit 4: Week 6	Visit 5: Week 12	Visit 7: Week 24
I experienced noticeable improvement in my skin tone				X	X
I experienced noticeable improvement in my skin texture				X	X
I experienced noticeable improvement in my skin radiance				X	X
My skin has a more youthful appearance				X	X
My skin is clearer skin using this treatment		X	X	X	X

I feel my skin is now clear			X	X	X
This treatment works faster than my previous acne treatment.	X	X			
This treatment is strong enough to give me clear, acne free skin.				X	X
The treatment helped to reduce redness and inflammation caused by my acne.			X	X	X
I feel that this treatment deep cleans and unblocks my pores.	X	X	X		
This treatment visually minimized my pore size.			X	X	X
I noticed an improvement in my acne. Strongly agree to Strongly disagree	X	X			X
This treatment reduces my acne without leaving behind dry, flakey skin.			X	X	X
I have noticed I had fewer breakouts than my previous treatments.	X	X	X	X	X
My skin looks better than before			X	X	X
This treatment breaks my cycle of acne and keeps my skin clear				X	X
I saw improvement in the overall health of my skin since starting the regimen	X		X	X	X
My skin looks noticeably smoother and healthier			X	X	
The areas of my skin where I used to have acne is now clear and radiant after daily treatment.		X	X	X	X
I feel better about my skin since I've started the treatment regimen			X	X	X
I feel more confident since I've started the treatment			X	X	X
Has your quality of life improved now that you have started using this product?				X	X
I would continue using this treatment beyond 24 weeks as a regular part of my skincare routine.					X
What is your overall satisfaction with the regimen?			X	X	X
I have noticed a positive difference in the appearance of my skin with this regimen.			X	X	X
This once a day regimen is easy to use every day.	X		X		
I liked the feel of this product.	X				
I would recommend this product to others.				X	X
My acne is as clear as if I went to a doctor or received a prescription.				X	X

I don’t feel the need for a prescription after using this product.				X	X
Total:	7	6	16	24	25

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APPROVAL SIGNATURE PAGE

2/15/16

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Galderma Laboratories, L.P.

15 Feb 2016

Medical Lead – Matthew Meckfessel, PhD — Date
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Medical Director Rx – Marie-Jose Rueda, MD — Date
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Feb 15, 2016

Director, Regulatory Affairs – Sean Griffin, MBA — Date
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2/15/16

Associate General Counsel – Nishan Patel — Date
Galderma Laboratories, L.P.

APPENDIX I: FITZPATRICK SKIN TYPE

The Fitzpatrick skin classification is based on the skin's unprotected response to the first 30 to 45 minutes of sun exposure after a winter season without sun exposure. The categories of skin types are as follows:

I	White; very fair; red or blonde hair; blue eyes; freckles	Always burns easily; never tans
II	White; fair; red or blonde hair; blue, hazel, or green eyes	Always burns easily; tans minimally
III	Cream white; fair with any eye or hair color; very common	Burns moderately; tans gradually
IV	Brown; typical Mediterranean white skin	Burns minimally; always tans well
V	Dark Brown; mid-eastern skin types, black hair, olive skin	Rarely burns; tans profusely
VI	Black; black hair, black eyes, black skin	Never burns; deeply pigmented