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Clinical Protocol

206827

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SUMMARY INFORMATION

Title:	A randomized, evaluator-blind, single-center and two-arm clinical study designed to evaluate the local tolerance and cosmetic efficacy of a topical skin care formulation in healthy female subjects with moderate to advanced photo-damaged facial skin who have undergone a 70% Glycolic Acid facial peel procedure.
Protocol Number:	206827
Sponsor:	GlaxoSmithKline (GSK) Rua Hungria, 1.240 - 4 ^o andar Jardim Europa - Sao Paulo - SP CEP: 01455-000, Brazil Tel: PPD
Product Name:	Physiogel Calming Relief Restoring Lipid Balm
Development Phase:	Not Applicable

Expert Advice Outside of Normal Working Hours:	Tel: PPD
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Key Protocol Authors:	
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Study Site Telephone Number:	PPD (business hours) or PP D (24 hours)

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PRINCIPAL INVESTIGATOR PROTOCOL AGREEMENT PAGE


- I confirm agreement to conduct the study in compliance with the protocol and any amendments and according to the current ICH GCP guidelines.
- I acknowledge that I am responsible for overall study conduct. I agree to personally conduct or supervise the described study.
- I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations. Mechanisms are in place to ensure site staff receives all appropriate information throughout the study.
- I agree to conduct this study in full conformance with the laws and regulations of the country in which the research is conducted and the Declaration of Helsinki.

Investigator Name:	
Investigator Qualifications:	
Investigator Signature:	PPD
Date of Signature/ Agreement:	DD/MMM/YYYY


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PROCESS FOR AMENDING THE PROTOCOL

Protocol modifications to ongoing studies which could potentially adversely affect the safety of subjects or which alter the scope of the investigation, the scientific quality of the study, the experimental design, dosages, duration of therapy, assessment variables, the number of subjects treated, or subject selection criteria are considered major/substantial amendments and must be made only after appropriate consultation between an appropriate representative of GSKCH and the investigator.

Details of amendments to the protocols should be recorded on the following page. Protocol modifications must be prepared by a representative of GSKCH. All changes must be justified in the Reason for Amendment section of the following Protocol Amendment Page. Approval of amendments will be made by the original protocol signatories or their appropriate designees.

All major/substantial protocol modifications must be reviewed and approved by the appropriate Independent Ethics Committee (IEC) in accordance with local requirements, before the revised edition can be implemented.

All non-substantial/ minor/ administrative amendments should be submitted to the IEC as per country specific requirements. In some countries pre-approval of a minor amendment is not required and will just be held on file by the sponsor and investigator.

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PROTOCOL AMENDMENT PAGE


Details of all amendments should be recorded in the table below. Affected sections should be listed in the table; the actual amendment/ change should be made in the relevant section of the main protocol.

To highlight the change, the following features will be used:


To **add** text: Use of **CAPITAL LETTERS, BOLD AND UNDERLINE**

To **delete** text: Use of Strikethrough e.g. ~~striketrough~~


Amendment No. & New Protocol Version No.	Type of Amendment	Reason for Amendment	Other Documents Requiring Amendment	Section(s) Amended	PI Amendment Agreement Signature & Date
Amendment No.: 1	Non-Substantial/Minor <input type="checkbox"/>	To increase the target number of randomised subjects from 80 to 100 in response to the first 10 subjects being incorrectly randomised into the study.	Informed Consent <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No Safety Statement <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No CRF <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	Protocol synopsis (page 23)	Signature: PPD
Protocol Version No.: 4	Substantial/ Major <input checked="" type="checkbox"/>			Section 3.3 (page 33) Section 9.1 (page 82)	Date: PPD
Amendment No.: 2	Non-Substantial/Minor <input checked="" type="checkbox"/>	To update the Data Manager details for the study.	Informed Consent <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No Safety Statement <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No CRF <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Summary information (page 3)	Signature: PPD
Protocol Version No.: 4	Substantial/ Major <input type="checkbox"/>				Date: PPD

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Amendment No.:	Non-Substantial/Minor <input type="checkbox"/>		Informed Consent <input type="checkbox"/> Yes <input type="checkbox"/> No Safety Statement <input type="checkbox"/> Yes <input type="checkbox"/> No CRF <input type="checkbox"/> Yes <input type="checkbox"/> No		Signature: PPD
Protocol Version No.:	Substantial/ Major <input type="checkbox"/>				Date: PPD
Amendment No.:	Non-Substantial/Minor <input type="checkbox"/>		Informed Consent <input type="checkbox"/> Yes <input type="checkbox"/> No Safety Statement <input type="checkbox"/> Yes <input type="checkbox"/> No CRF <input type="checkbox"/> Yes <input type="checkbox"/> No		Signature: PPD
Protocol Version No.:	Substantial/ Major <input type="checkbox"/>				Date: PPD


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SCHEDULE OF EVENTS

Procedure/ Assessment	Visit 1 Day 1	Visit 2 Day 2	Visit 3 ¹ Day 8	Visit 4 ¹ Day 9	Visit 5 ¹ Day 10	Visit 6 ¹ Day 11	Visit 7 ¹ Day 15	Visit 8 ¹ Day 22
	Screening/ Washout	1 Day After Visit 1	6 Days after Visit 2, Day of Procedure	1 Day after Visit 3	1 Day after Visit 4	1 Day after Visit 5	4 Days after Visit 6	7 Days after Visit 7
Informed Consent	X							
Demographics	X							
Medical History	X							
Current / Concomitant Medication	X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X
Continued Subject Eligibility		X	X	X	X	X	X	X
Compliance (Diary review) ²		X	X	X	X	X	X	X
Fitzpatrick Skin Type Assessment (Appendix 2)	X							
Glogau Photoaging Type Assessment (Appendix 3)	X							
In/Exclusion Criteria	X ³	X ⁴	X ⁴					
Subject Eligibility	X							
Study Material Sensitivity Test	X ⁵							
Subject Self-Assessment Sensitivity	X ⁶	X ⁷	X ⁸					
Dermatologist Assessment Sensitivity	X ⁶	X ⁷	X ⁸					
Exclusion Criteria 9	X	X	X					
Subject Eligibility	X	X	X					
Subject Randomisation			X					
Instrumental Measurements Pre-Procedure			X					
Image capture (VISIA) Pre-Procedure			X					
Subject Self-Assessment Pre-Procedure			X					
Dermatologist Assessment Pre-Procedure			X					
Dermatological Procedure (Facial Peel)			X ⁹					
Dermatologist Assessment Post-Procedure, Pre-Treatment (BASELINE)			X ¹⁰					
Instrumental Measurements Post-Procedure, Pre-Treatment (BASELINE)			X ¹⁰					
Image capture (VISIA) Post-Procedure, Pre-Treatment (BASELINE)			X ¹⁰					
Subject Self-Assessment Post-Procedure, Pre-Treatment (BASELINE)			X ¹⁰					
Washout Products and Washout Diary Dispensing	X							
Test Product and Test Diary Dispensing, Washout Diary return.			X ¹¹					
Supervised Test-Product Application Post-Procedure			X ¹²					
Instrumental Measurements Post-Procedure, Post-Treatment ¹³			X	X	X	X	X	X
Image capture (VISIA) Post-Procedure, Post-Treatment ¹⁴				X				X
Subject Self-Assessment Post-Procedure, Post-Treatment ¹⁵			X	X	X	X	X	X
Subject Global Self-Assessment								X
Dermatologist Assessment Post-Procedure, Post-Treatment ¹⁵			X	X	X	X	X	X
Dermatologist Global Assessment of Tolerance								X
Supervised Test-Product Application ¹⁶				X	X	X	X	
Supervised Sunscreen Application ¹⁷				X	X	X	X	
Products and Test Diary Return								X
Discharge from Study								X

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1. For Visits 3-8, subjects will be instructed to cleanse their face at home using the cleanser provided and must not use any other product on their face, including the test product (Group I only) and sunscreen. Subjects will be instructed to bring the dispensed cleanser, sunscreen and test product (Group I only) with them to all visits. Subjects will be invited to the site in the morning (prior to 9 am) to avoid exposure to strong sunlight.
2. The Investigator or designee will review the diary to monitor and encourage compliance. Additional or missed product applications will be recorded as deviations. The Evaluator must be blind to diary review.
3. Exclusion Criteria 9 will not be included for this assessment. Exclusion criteria 9 is evaluated based on the results from the sensitivity test.
4. To include a review of the inclusion/exclusion criteria specified in Appendix 4. Subjects must be considered compliant with these inclusion/exclusion criteria in order to remain eligible for the study.
5. Peel regimen (70% Glycolic Acid facial peel solution, Bicarbonate Neutralizing Solution and Sunmax Sensitive SPF 50) to be applied to the volar forearm of each subject by a qualified dermatologist.
6. Assessments to be taken 45±15 minutes after completion of the study material sensitivity test.
7. Assessments to be taken 24±4 hours after completion of the study material sensitivity test.
8. Assessments to be taken 7 days after completion of the study material sensitivity test.
9. 70% Glycolic Acid facial peel to be administered by a qualified dermatologist who must be blind to randomization. The Glycolic Acid treatment and neutralizing solution will be sourced commercially by the study site.
10. Assessments to be taken 60±15 minutes after completion of the facial peel procedure.
11. Only subjects randomised to Group I will be dispensed test product. Subjects in Group I and II will be dispensed different test diaries to reflect the difference in treatment allocation. The washout diary will be returned at the same time as test diary dispensing.
12. Test product application will occur immediately after the post-procedure, pre-treatment (Baseline) assessments are complete and under the supervision of the Investigator or designee to subjects in Group I, only. Subjects in Group II will not apply anything to their face. The Evaluator must be blind to test product application.
13. Measurements to be taken 180±15 minutes, 360±15 minutes, 24±4 hours, 48±4 hours, 72±4 hours, 168±4 hours and 336±4 hours after completion of the facial peel procedure. At Visit 3, there must be at least 30 minutes between test product application (Group I, only) and instrumental measurements.
14. Images to be captured 24±4 hours after completion of the facial peel procedure and at Visit 8 (Day 22).
15. Assessments to be taken 180±15 minutes, 24±4 hours, 48±4 hours, 72±4 hours, 168±4 hours and 336±4 hours after completion of the facial peel procedure.
16. Test product application will be conducted under the supervision of the Investigator or designee to subjects in Group I, only. Subjects in Group II will not apply the test product to their face.
17. Sunscreen application will be conducted under the supervision of the Investigator or designee to all subjects.

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PROTOCOL SYNOPSIS FOR STUDY 206827

Brief Summary

This is a randomized, evaluator-blind, single-center and two-arm clinical study designed to evaluate the local tolerance and cosmetic efficacy of a topical skin care formulation in healthy female subjects with moderate to advanced photo-damaged facial skin who have undergone a 70% Glycolic Acid facial peel procedure. It is hypothesized that the test product, which is specifically designed as a moisturizing cream for dry, sensitive skin, will present a favorable local tolerance profile in this population.

Objective(s) and Endpoint(s)

Objective(s)	Endpoint(s)
Primary	
Assessment of the local tolerance of the test product in subjects who have undergone a 70% Glycolic Acid facial peel	Evaluator (Dermatologist) global assessment of tolerance
Secondary	
Assessment of skin recovery (change from baseline) over a period of 14 days in subjects who have undergone a 70% Glycolic Acid facial peel	<p>Combined (sum of) Evaluator (Dermatologist) scores for signs/symptoms of erythema, edema, desquamation and dryness</p> <p>Individual Evaluator (Dermatologist) scores for erythema, edema, desquamation and dryness</p> <p>Combined (sum of) subject self-assessment scores for redness, pain, stinging/burning, itching, tightness and dryness</p> <p>Individual subject self-assessment scores for redness, pain, stinging/burning, itching, tightness and dryness</p> <p>Instrumental measurement of barrier function (Tewameter) and moisturisation (Corneometer)</p> <p>Subject global self-assessment</p>

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Assessment of skin recovery (change from baseline) between treatment groups.	All assessments and measurements listed above
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Study Design

Overall Design
<p>This is a randomized, evaluator-blind, single-center and two-arm clinical study designed to evaluate the local tolerance and cosmetic efficacy of a topical skin care formulation in healthy female subjects with moderate to advanced photo-damaged facial skin who have undergone a 70% Glycolic Acid facial peel procedure. It is hypothesized that the test product, which is specifically designed as a moisturizing cream for dry, sensitive skin, will present a favorable local tolerance profile in this population.</p>
Visit 1 / Day 1 (Screening / Washout)
<p>The following assessments will be conducted in the order written:</p> <ol style="list-style-type: none"> 1. Informed Consent 2. Demographics 3. Medical History 4. Current / Concomitant Medication 5. Fitzpatrick Skin Type Assessment (Appendix 2) 6. Glogau Photoaging Type Assessment (Appendix 3) 7. In/Exclusion Criteria (Not including Exclusion Criteria 9) 8. Subject Eligibility 9. Study Material Sensitivity Test 10. Subject Self-Assessment Sensitivity* 11. Dermatologist Assessment Sensitivity* 12. Exclusion Criteria 9 13. Subject Eligibility 14. Washout Products and Washout Diary Dispensing <p>* Assessments to be taken 45±15 minutes after completion of the study material sensitivity test</p>
Visit 2 / Day 2 (1 Day after Visit 1)
<p>The following assessments will be conducted in the order written:</p> <ol style="list-style-type: none"> 1. Current / Concomitant Medication 2. Adverse Events 3. Continued Subject Eligibility 4. Compliance (Diary review)

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5. Subject Self-Assessment Sensitivity*
6. Dermatologist Assessment Sensitivity*
7. Exclusion Criteria (Appendix 4)
8. Subject Eligibility

* Assessments to be taken 24±4 hours after completion of the study material sensitivity test

Visit 3 / Day 8 (6 Days after Visit 2 - Day of Procedure)

The following assessments will be conducted in the order written:

1. Current / Concomitant Medication
2. Adverse Events
3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Washout Diary Return
6. Subject Self-Assessment Sensitivity*
7. Dermatologist Assessment Sensitivity*
8. Exclusion Criteria (Appendix 4)
9. Subject Eligibility
10. Subject Randomisation
11. Instrumental Measurements Pre-Procedure
12. Image capture (VISIA) Pre-Procedure
13. Subject Self-Assessment Pre-Procedure
14. Dermatologist Assessment Pre-Procedure
15. Dermatological Procedure (Facial Peel)
16. Dermatologist Assessment Post-Procedure, Pre-Treatment (BASELINE)**
17. Instrumental Measurements Post-Procedure, Pre-Treatment (BASELINE)**
18. Image capture (VISIA) Post-Procedure, Pre-Treatment (BASELINE)**
19. Subject Self-Assessment Post-Procedure, Pre-Treatment (BASELINE)**
20. Test Product and Test Diary Dispensing
21. Supervised Test-Product Application Post-Procedure
22. Instrumental Measurements Post-Procedure, Post-Treatment***
23. Subject Self-Assessment Post-Procedure, Post-Treatment****
24. Dermatologist Assessment Post-Procedure, Post-Treatment*****

* Assessments to be taken 7 days after completion of the study material sensitivity test

** Assessments to be taken 60±15 minutes after completion of the facial peel procedure


*** Assessments to be taken 180±15 and 360±15 minutes after completion of the facial peel procedure.

**** Assessments to be taken 180±15 minutes after completion of the facial peel procedure.

Subjects should remain at the site until 5:00 PM to prevent exposure to intense sunlight.

Visit 4 / Day 9 (1 Day after Visit 3)

The following assessments will be conducted in the order written:

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1. Current / Concomitant Medication
2. Adverse Events
3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Instrumental Measurements Post-Procedure, Post-Treatment*
6. Image capture (VISIA) Post-Procedure, Post-Treatment*
7. Subject Self-Assessment Post-Procedure, Post-Treatment*
8. Dermatologist Assessment Post-Procedure, Post-Treatment*
9. Supervised Test-Product Application
10. Supervised Sunscreen Application

* Assessments to be taken 24±4 hours after completion of the facial peel procedure

Visit 5 / Day 10 (1 Day after Visit 4); Visit 6 / Day 11 (1 Day after Visit 5), Visit 7 / Day 15 (4 Days After Visit 6)

The following assessments will be conducted in the order written:


1. Current / Concomitant Medication
2. Adverse Events
3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Instrumental Measurements Post-Procedure, Post-Treatment*
6. Subject Self-Assessment Post-Procedure, Post-Treatment*
7. Dermatologist Assessment Post-Procedure, Post-Treatment*
8. Supervised Test-Product Application
9. Supervised Sunscreen Application

* Assessments to be taken 48±4 (Visit 5), 72±4 (Visit 6) and 168±4 (Visit 7) hours after completion of the facial peel procedure

Visit 8 / Day 22 (7 Days after Visit 7)

The following assessments will be conducted in the order written:

1. Current / Concomitant Medication
2. Adverse Events
3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Instrumental Measurements Post-Procedure, Post-Treatment*
6. Image capture (VISIA) Post-Procedure, Post-Treatment*
7. Subject Self-Assessment Post-Procedure, Post-Treatment*
8. Subject Global Self-Assessment
9. Dermatologist Assessment Post-Procedure, Post-Treatment*
10. Dermatologist Global Assessment of Tolerance
11. Products and Test Diary Return
12. Discharge from Study

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* Assessments to be taken 336±4 hours after completion of the facial peel procedure

Type and Planned Number of Subjects

Approximately ~~130~~ **178** healthy females within the ages of 30 and 60 years (inclusive) with Fitzpatrick Skin Classification II-IV and moderate to advanced photo-damaged skin will be screened to randomize ~~80~~ **100** subjects to ensure approximately ~~60~~ **80** subjects (~~30-40~~ subjects per group) successfully complete the study. ~~The sample size is based on clinical considerations and literature precedent [Narurkar, Schalka, Sulimovic, Kim]. With 30 subjects per treatment group, a change from baseline in Transepidermal Water Loss (TEWL) at least half the magnitude of the standard deviation (e.g. assume std=4 (ref. CCI), and 2.1 point mean change from baseline) can be detected at two-sided alpha=0.05 with 80% power.~~

Main Criteria for Inclusion

Healthy female subjects aged 30-60 years (inclusive) with a Fitzpatrick skin phototype II-IV and Glogau photoaging type II-III will be recruited for this study.


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Product Information

	Reference / Washout Cleanser	Test Product	Reference / Washout Sunscreen
Product Name	Simple Kind to Skin Moisturising Facial Wash	Physiogel Calming Relief Restoring Lipid Balm	Sunmax Sensitive SPF 50
Product Formulation Code	Not Applicable (Commercial, UK)	CCI	CCI (Commercial, Brazil)
Application Quantity	Approximately 0.6-1 grams (g)		
Route of Application	Topical		
Application Instructions	<p>Wet face with water. In your hands, work a small amount into a lather. Massage onto wet skin, rinse with water.</p> <p>Avoid contact with eyes. If contact occurs, rinse thoroughly with water.</p> <p>Use twice a day (morning and evening)</p>	<p>Dispense a pea-sized quantity of product onto the fingertips and apply to the full face.</p> <p>Avoid contact with eyes. If contact occurs rinse thoroughly with water.</p> <p>Apply twice a day (morning and evening)</p> <p>Do not apply in the morning if you are visiting the site on the same day.</p>	<p>Dispense a pea-sized quantity onto the fingertips and apply to the full face.</p> <p>Avoid contact with eyes. If contact occurs rinse thoroughly with water.</p> <p>Apply twice a day (morning and lunchtime)</p> <p>Do not apply in the morning if you are visiting the site on the same day.</p>

Statistical Methods

Descriptive statistics (N, %, 95% confidence intervals) will be used to summarize the global assessment of tolerance. Changes from baseline in the evaluator, subjective and instrumental endpoints will be tabulated by product group and summarized descriptively and assessed for significance (different from zero) using t-tests or Wilcoxon signed rank tests dependent upon the distribution of the data. Differences

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between product groups in the evaluator, subjective and instrumental endpoints will also be explored and the magnitude of product differences in the change from baseline for each will be estimated. Adverse events will be tabulated by product group.

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1. INTRODUCTION

A total of 11.7 million cosmetic procedures were performed in 2007 in the United States, and the majority (82%) of these were non-surgical in nature. Non-surgical techniques are aimed at reducing the signs of facial aging, such as hyperpigmentation, loss of elasticity, and wrinkles.

With all of these non-surgical procedures, there is an intentional generation of damage to the cutaneous barrier in order to promote the repair of the epidermis and increased cell renewal. By promoting damage to the stratum corneum or epidermis, some degree of irritation, which translates into erythema and/or edema, in addition to desquamation of greater or lesser intensity, is expected to occur clinically.

Facial chemical exfoliation is a well-established procedure in which the dermatologist uses some agent (usually acids) to insult the skin, with consequent damage to the cutaneous barrier. There are different types of chemical exfoliant (peels), used in dermatologic practice, with the most common being the use of retinoids and alpha-hydroxy acids (AHAs), including glycolic acid (GA). AHA peels have anti-inflammatory, keratolytic, and antioxidant effects and glycolic acid targets the corneosome by enhancing breakdown and decreasing cohesiveness, causing desquamation. The intensity of peel is determined by the concentration of the acid, the vehicle used to carry it, the amount of acid applied, and the technique used. 70% GA applied to skin for 1-3 minutes, followed by neutralization with a bicarbonate base is classified as a superficial facial peel procedure [Guerriero 2014].


Prior to and following facial resurfacing procedures, physicians often recommend that subjects use a range of topical skin care products.

Pre-procedure Regimen:

Pre-procedure, subjects may be instructed to use a gentle, nonirritating cleanser, an exfoliant, and creams containing a retinoid and hydroquinone. Such a regimen may help a subject's skin to be in optimal condition at the time of a procedure.

Post-procedure Regimen:

In the period immediately after the procedure, it is recommended that the dermatologist instruct the subject in the use of sunscreen and moisturizing agents that are able to provide a restorative action on the cutaneous barrier. This helps to relieve symptoms (such as burning, scaling, and erythema) and promotes the quick and


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efficient repair of the superficial structures of the epidermis, in particular the stratum corneum. Some post-procedure products, such as a 1% hydrocortisone cream, can help to manage the adverse effects of the procedure such as swelling and erythema. Others, like a sunscreen, help protect healing skin during recovery.

Physiogel Calming Relief Restoring Lipid Balm is a moisturising oil in water emulsion, formulated to be free of colourants and fragrances and is clinically proven to be suitable for use by subjects with dry, sensitive skin. It is therefore expected that this product will help relieve some of the adverse effects of cosmetic procedures, including glycolic acid facial peels, and will be of benefit to subjects.

Side-effects of the Procedure:

Proper selection of subjects, timing of peel, and neutralization on-time should ensure good results and minimize side effects [Sharad 2013]. The minor side effects reported are: erythema, desquamation, stinging sensation, sensation of pulling of facial skin, mild burning, and transient post-inflammatory hyperpigmentation. Unbuffered GA can cause erosive blisters and scarring. In rare cases, hypopigmentation, persistent erythema, and flare-up of pimples have been reported [Perić 2011].

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2. OBJECTIVE(S) AND ENDPOINT(S)


Objective(s)	Endpoint(s)
Primary	
Assessment of the local tolerance of the test product in subjects who have undergone a 70% Glycolic Acid facial peel	Evaluator (Dermatologist) global assessment of tolerance
Secondary	
Assessment of skin recovery (change from baseline) over a period of 14 days in subjects who have undergone a 70% Glycolic Acid facial peel	<p>Combined (sum of) Evaluator (Dermatologist) scores for signs/symptoms of erythema, edema, desquamation and dryness</p> <p>Individual Evaluator (Dermatologist) scores for erythema, edema, desquamation and dryness</p> <p>Combined (sum of) subject self-assessment scores for redness, pain, stinging/burning, itching, tightness and dryness</p> <p>Individual subject self-assessment scores for redness, pain, stinging/burning, itching, tightness and dryness</p> <p>Instrumental measurement of barrier function (Tewameter) and moisturisation (Corneometer)</p> <p>Subject global self-assessment</p>
Assessment of skin recovery (change from baseline) between treatment groups.	All assessments and measurements listed above

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3. STUDY PLAN

3.1. Study Design

Overall Design
<p>This is a randomized, evaluator-blind, single-center and two-arm clinical study designed to evaluate the local tolerance and cosmetic efficacy of a topical skin care formulation in healthy female subjects with moderate to advanced photo-damaged facial skin who have undergone a 70% Glycolic Acid facial peel procedure. It is hypothesized that the test product, which is specifically designed as a moisturizing cream for dry, sensitive skin, will present a favorable local tolerance profile in this population.</p>
Visit 1 / Day 1 (Screening / Washout)
<p>The following assessments will be conducted in the order written:</p> <ol style="list-style-type: none"> 1. Informed Consent 2. Demographics 3. Medical History 4. Current / Concomitant Medication 5. Fitzpatrick Skin Type Assessment (Appendix 2) 6. Glogau Photoaging Type Assessment (Appendix 3) 7. In/Exclusion Criteria (Not including Exclusion Criteria 9) 8. Subject Eligibility 9. Study Material Sensitivity Test 10. Subject Self-Assessment Sensitivity* 11. Dermatologist Assessment Sensitivity* 12. Exclusion Criteria 9 13. Subject Eligibility 14. Washout Products and Washout Diary Dispensing <p>* Assessments to be taken 45±15 minutes after completion of the study material sensitivity test</p>
Visit 2 / Day 2 (1 Day after Visit 1)
<p>The following assessments will be conducted in the order written:</p> <ol style="list-style-type: none"> 1. Current / Concomitant Medication 2. Adverse Events 3. Continued Subject Eligibility 4. Compliance (Diary review) 5. Subject Self-Assessment Sensitivity* 6. Dermatologist Assessment Sensitivity*

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<p>7. Exclusion Criteria (Appendix 4)</p> <p>8. Subject Eligibility</p> <p>* Assessments to be taken 24±4 hours after completion of the study material sensitivity test</p>
Visit 3 / Day 8 (6 Days after Visit 2 - Day of Procedure)
<p>The following assessments will be conducted in the order written:</p> <ol style="list-style-type: none"> 1. Current / Concomitant Medication 2. Adverse Events 3. Continued Subject Eligibility 4. Compliance (Diary review) 5. Washout Diary Return 6. Subject Self-Assessment Sensitivity* 7. Dermatologist Assessment Sensitivity* 8. Exclusion Criteria (Appendix 4) 9. Subject Eligibility 10. Subject Randomisation 11. Instrumental Measurements Pre-Procedure 12. Image capture (VISIA) Pre-Procedure 13. Subject Self-Assessment Pre-Procedure 14. Dermatologist Assessment Pre-Procedure 15. Dermatological Procedure (Facial Peel) 16. Dermatologist Assessment Post-Procedure, Pre-Treatment (BASELINE)** 17. Instrumental Measurements Post-Procedure, Pre-Treatment (BASELINE)** 18. Image capture (VISIA) Post-Procedure, Pre-Treatment (BASELINE)** 19. Subject Self-Assessment Post-Procedure, Pre-Treatment (BASELINE)** 20. Test Product and Test Diary Dispensing 21. Supervised Test-Product Application Post-Procedure 22. Instrumental Measurements Post-Procedure, Post-Treatment*** 23. Subject Self-Assessment Post-Procedure, Post-Treatment**** 24. Dermatologist Assessment Post-Procedure, Post-Treatment**** <p>* Assessments to be taken 7 days after completion of the study material sensitivity test</p> <p>** Assessments to be taken 60±15 minutes after completion of the facial peel procedure</p> <p>*** Assessments to be taken 180±15 and 360±15 minutes after completion of the facial peel procedure.</p> <p>**** Assessments to be taken 180±15 minutes after completion of the facial peel procedure.</p> <p>Subjects should remain at the site until 5:00 PM to prevent exposure to intense sunlight.</p>
Visit 4 / Day 9 (1 Day after Visit 3)
<p>The following assessments will be conducted in the order written:</p> <ol style="list-style-type: none"> 1. Current / Concomitant Medication 2. Adverse Events

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3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Instrumental Measurements Post-Procedure, Post-Treatment*
6. Image capture (VISIA) Post-Procedure, Post-Treatment*
7. Subject Self-Assessment Post-Procedure, Post-Treatment*
8. Dermatologist Assessment Post-Procedure, Post-Treatment*
9. Supervised Test-Product Application
10. Supervised Sunscreen Application

* Assessments to be taken 24±4 hours after completion of the facial peel procedure

Visit 5 / Day 10 (1 Day after Visit 4); Visit 6 / Day 11 (1 Day after Visit 5), Visit 7 / Day 15 (4 Days After Visit 6)

The following assessments will be conducted in the order written:

1. Current / Concomitant Medication
2. Adverse Events
3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Instrumental Measurements Post-Procedure, Post-Treatment*
6. Subject Self-Assessment Post-Procedure, Post-Treatment*
7. Dermatologist Assessment Post-Procedure, Post-Treatment*
8. Supervised Test-Product Application
9. Supervised Sunscreen Application


* Assessments to be taken 48±4 (Visit 5), 72±4 (Visit 6) and 168±4 (Visit 7) hours after completion of the facial peel procedure

Visit 8 / Day 22 (7 Days after Visit 7)

The following assessments will be conducted in the order written:

1. Current / Concomitant Medication
2. Adverse Events
3. Continued Subject Eligibility
4. Compliance (Diary review)
5. Instrumental Measurements Post-Procedure, Post-Treatment*
6. Image capture (VISIA) Post-Procedure, Post-Treatment*
7. Subject Self-Assessment Post-Procedure, Post-Treatment*
8. Subject Global Self-Assessment
9. Dermatologist Assessment Post-Procedure, Post-Treatment*
10. Dermatologist Global Assessment of Tolerance
11. Products and Test Diary Return
12. Discharge from Study

* Assessments to be taken 336±4 hours after completion of the facial peel procedure

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3.2. Subject Restrictions

Lifestyle/ Dietary
<p>During the entire study (screening – Last-Subject, Last-Visit (LSLV));</p> <ol style="list-style-type: none"> 1. Not to participate in any other cosmetic or therapeutic study 2. Not to add any new cosmetic product to their current personal care regimen (e.g. shampoo, shower gel, hand soap) or switch brands of laundry products during the study
Medications and Treatments
<p>On the day of site visit;</p> <ol style="list-style-type: none"> 1. Not to apply any detergents (e.g. soaps, shampoos, bath and shower products) to their face other than the cleanser provided (Simple Kind to Skin Moisturising Facial Wash) 2. Not to apply any leave-on cosmetics (e.g. creams, lotions, oily cleansing products, mascara) including the test product (Physiogel Calming Relief Restoring Lipid Balm) and sunscreen (Sunmax Sensitive SPF 50) to their face or eyelashes 3. Not to consume any caffeine 4. Not to smoke (includes cigarettes, shisha, cigars) <p>During the entire study (screening – LSLV);</p> <ol style="list-style-type: none"> 1. Not to apply any detergents (e.g. soaps, shampoos, bath and shower products) to their face other than the cleanser provided (Simple Kind to Skin Moisturising Facial Wash) 2. Not to use any facial skin treatments or cosmetic products other than the products provided for this study. Subjects are permitted to wear their usual mascara during this study 3. Not to use any study prohibited medication as specified in the exclusion criteria, including anti-inflammatory, analgesic or photosensitizing treatments 4. To avoid direct exposure to sunlight by seeking the shade and to wear a sun hat and sunglasses when outside as far as practically possible 5. To avoid ultraviolet (UV) treatments and tanning salons 6. Female subjects of child-bearing potential must use effective contraception 7. Subjects must not change any hormonal treatment or contraception that they may be receiving and must have used the same contraception for 3 months prior to screening 8. Subjects must not undergo any aesthetic, cosmetic or dermatological treatment in the treatment area (face or eyes) 9. Use of facial scrubs, depilatory creams, waxing, bleaching, microdermabrasion, and laser hair removal

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3.3. Type and Planned Number of Subjects

Approximately ~~130~~ **178** Healthy females within the ages of 30 and 60 years (inclusive) with Fitzpatrick Skin Classification II-IV and moderate to advanced photo-damaged skin will be screened to randomize ~~80~~ **100** subjects to ensure approximately ~~60~~ **80** subjects (~~30-40~~ subjects per group) successfully complete the study. ~~The sample size is based on clinical considerations and literature precedent [Narurkar, Schalka, Sulimovic, Kim]. With 30 subjects per treatment group, a change from baseline in Transepidermal Water Loss (TEWL) at least half the magnitude of the standard deviation (e.g. assume std=4 (ref. CCI), and 2.1 point mean change from baseline) can be detected at two-sided alpha=0.05 with 80% power.~~


Subjects will be recruited from the site database and via local advertisement.

3.4. Study Design and Dose Justification

This study is a randomized, evaluator-blind, single-center and two-arm clinical study designed to evaluate the local tolerance and cosmetic efficacy of a topical skin care formulation in healthy female subjects with moderate to advanced photo-damaged facial skin who have undergone a 70% Glycolic Acid facial peel procedure. Glycolic acid is selected due to its widespread use and favourable tolerance profile. [Sharad]

The test product (Physiogel Calming Relief Restoring Lipid Balm) is designed for subjects with dry, irritated skin and there is favourable local tolerance clinical data to support its use for application to sensitive, post-procedure skin. In addition, the test product has been marketed in Brazil for many years and has a favourable benefit-risk profile based on post-marketing data. The test product will be applied twice daily, as consistent with the marketed instructions for use.

A 7 day washout phase is included to standardize subjects' skin care regimens. Subjects will be provided with a commercially available facial cleanser (Simple Kind to Skin Moisturising Facial Wash) and sunscreen (Sunmax Sensitive SPF 50) as standard of care. Subjects will be instructed to use the facial cleanser during the morning and evening, and to apply the sunscreen in the morning (after cleansing) and at lunchtime. Sunmax Sensitive SPF 50 is designed for subjects with sensitive skin and has favourable local tolerance clinical data to support its use for application to sensitive, post-procedure skin. Simple Kind to Skin Moisturising Facial Wash is also designed for subjects with sensitive skin.

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Within the washout phase, a study material sensitivity test is included to identify subjects who may be sensitive to the study materials in order to determine whether they are suitable to undergo the facial peel procedure. A qualified dermatologist will dispense a thin layer of the 70% glycolic acid peel solution to cover a demarcated 5 x 5 cm square area on the volar surface of the forearm and, within a period of 30-60 seconds, will neutralize the 70% glycolic acid peel solution with the bicarbonate neutralizing agent and then rinse the skin thoroughly with water and pat dry with a soft towel. Once dry, the dermatologist will apply a thin layer of the Sunmax Sensitive SPF50 Sunscreen to the 5 x 5 cm square area. Dermatologist and subject self-assessments will be used to evaluate local tolerance. If subject data for the study material sensitivity study contains a dermatologist or subject self-assessment score of “Severe” for any attribute, this subject will be deemed to be in violation of exclusion criteria 9 and must be discharged from the study.


Upon completion of the washout phase, subjects considered to be eligible for the test phase will be randomised to two groups (Group 1: Test product; Group 2: No-treatment) and a qualified dermatologist with experience administering facial peels will conduct the 70% Glycolic Acid procedure.

Subjects randomised to Group 1 will be instructed to apply the test product twice-daily (morning and evening) after cleansing, for a total of 14 consecutive days. All subjects will be instructed to continue using the facial cleanser twice-daily during the morning and evening, and to apply the sunscreen in the morning and at lunchtime. A summary of the subject’s post-randomization regimen is included below for clarity.

Randomized Group	Morning	Lunchtime*	Evening
Group 1	1. Cleansing 2. Test Product 3. Sunscreen	1. Sunscreen	1. Cleansing 2. Test Product
Group 2	1. Cleansing 2. Sunscreen	1. Sunscreen	1. Cleansing

*Lunchtime application must be at least 3 hours after previous sunscreen application

Subjects will not apply any sunscreen on the day of the facial peel procedure (Day 8), since they will remain at site until the evening (after 5 pm). On the morning of each visit, prior to arriving at the site, subjects will be instructed to cleanse their face and not to apply any test product or sunscreen until after all measurements and assessments have been completed. Before leaving the site, subjects will undergo

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supervised test product and/or sunscreen application. After leaving the site, subjects should apply the sunscreen a second time, but no sooner than 3 hours after the previous application.

Measurements of skin hydration (Corneometer) and transepidermal water loss (Tewameter), Dermatologist and Subject self-assessments and photographs (image capture) will be performed throughout the study on the scheduled days. Subjects will be instructed to complete a diary every day to encourage and record compliance. The diary will be reviewed by the Investigator or designee at each visit and any additional or missed product applications will be recorded as deviations. Dermatologists and other members of the study staff involved in the assessment of any study endpoints will be blind to randomization. All practical efforts will be made to ensure the same Dermatologist assesses the same subject throughout the study.

A comprehensive literature search of cosmetic procedures and skin care products claiming use post-cosmetic procedure was conducted to inform the development of this study. The literature search was limited to home-use topical products and aimed to identify all relevant clinical studies concerned with post-procedure cutaneous tolerability and efficacy. Sources used in the search included company websites, GNPd, e-commerce sites, Google Search (to identify products), Proquest, Pubmed, Scopus and Google Scholar. The search identified a total of 30 clinical studies primarily concerned with evaluating the local tolerance of cosmetic products for topical application following laser peel, photodynamic therapy and chemical peels.


In particular, Sulimovic (2002) studied the cosmetic benefits provided by topical application of a water treatment (Avene Extra Gentle Cleanser) compared to placebo (Petroleum) in a sample of 74 subjects who underwent CO₂ pulsed-laser treatment. 40 subjects were randomised to the cosmetic water group and 23 subjects to the placebo. Subjects were examined regularly over a total post-treatment period of 84 days. During the treatment course, the overall severity of erythema was less in the water group than in the control group, a difference shown to be statistically significant ($p \leq 0.04$) from day 14 until the end of treatment, except at day 28 ($p \leq 0.07$). Evolutions of the functional symptoms (pain, itching, stinging and tightening) in the two groups were all statistically significantly improved compared to the post-procedure baseline ($p \leq 0.05$) after 3-4 weeks of treatment, although inter-group significance was only observed for mean itching (Day 28), stinging (Days 14 and 21) and tightening (Days 12 and 21). Investigator-assessed global efficacy and subject self-assessed global tolerance at the end of the study was statistically significantly in favour of the water group compared to placebo ($p \leq 0.05$). Three treatment-related

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local side-effects were reported during the study. One subject experienced an allergic contact dermatitis of undetermined origin and was withdrawn from the study at the 28-day visit. One subject presented peri-labial pustules and was withdrawn at Day 7. A third subject presented cleanser-imputed contact allergy at the end of study. No systemic adverse effects that were considered possible or probably related to test treatment were recorded for either group.


Narurkar (2010) conducted a 14-week open-label study to evaluate the efficacy and safety of a topical cosmetic skin care regimen for minimizing localized Adverse Events (AEs) during two 6-week procedure cycles with fractionated laser or intense pulsed light. The skin care regimen consisted of a 2-week pre-procedure phase, a 1-week post-procedure phase and a 3-week maintenance phase. Investigators and subjects rated the presence and severity of erythema, itching, stinging/burning, edema, pain, pruritus, swelling, crusts/erosions and photo-damage. Two days after each procedure, most assessments were near baseline values and at 4 weeks all investigator scores were comparable to baseline. Two weeks post-procedure, mean subject ratings for most endpoints were 'none' to 'mild'. Fourteen subjects reported a total of 16 AE's. Of these, 4 subjects (15%) reported AE's considered possibly related to the non-ablative cosmetic procedure or the test product regimen. These AE's included acne and facial rash and were mild in intensity. Two subjects withdrew from the study due to an AE. One subject had a severe rash was considered probably related to the study treatment and one subject developed shingles, which was considered unrelated to treatment.

Schalka (2013) published the results of a clinical study which investigated the efficacy and safety of a novel cosmetic skin care product in subjects who underwent a 5% retinoic acid facial peel. This comparative, open-label clinical study randomized 52 subjects who were divided into two groups, with 26 subjects allocated to each group. One group was provided with a Sun Protection Factor (SPF) 30 cream (control) and the other group was provided with the test product and SPF 30 control. Regular clinical assessment and biophysical measurements were conducted for a period of 1 week post-procedure. Fifty subjects completed the study, with one subject withdrawing for personal reasons and the other discontinued from the study due to the occurrence of mild contact dermatitis in the test product plus sunscreen group. Statistically significant ($p \leq 0.05$) cosmetic benefits were observed for clinically-assessed desquamation (Days 4 to 7) and instrumental Corneometer measurements (Days 2 to 4) for the treatment group over the control group. Crucially, the magnitude of cosmetic assessments between groups was numerically largest between days 2 and 4, presumably because the skin's natural repair processes were continually reducing

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the cutaneous damage for both groups, making it more difficult to measure a cosmetic benefit over time. Barrier function was observed to gradually worsen over the duration of the study, with weak indications of improvement between days 4 and 7. There was no statistically significant barrier function benefit between groups at any time point.

Based on this literature review, subject visits have been included at 24-72 hours post-procedure, where differences between control and test groups are expected to be largest. While it is expected the skin's barrier function will return to normal 24 to 48 hours following the procedure, the total duration of the test phase is 14 days to enable sufficient time to monitor desquamation and erythema compared to the post-procedure, pre-treatment baseline.

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4. SELECTION OF STUDY POPULATION AND WITHDRAWAL CRITERIA


Specific information regarding warnings, precautions, contraindications, adverse events, and other pertinent information on the GSK investigational product or other study treatment that may impact subject eligibility is provided in the Product Label.

Deviations from inclusion and exclusion criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol is essential.

4.1. Inclusion Criteria

A subject will be eligible for inclusion in this study only if all of the following criteria apply:

1. CONSENT
Demonstrates understanding of the study procedures, restrictions and willingness to participate as evidenced by voluntary written informed consent and has received a signed and dated copy of the informed consent form.
2. AGE
Aged between 30 and 60 years inclusive.
3. GENDER
Female.
4. GENERAL HEALTH
Good general and mental health with, in the opinion of the investigator or medically qualified designee no clinically significant and relevant abnormalities in medical history or upon physical examination.
5. COMPLIANCE
Willingness to actively participate in the study and to attend all scheduled visits.
6. SKIN TYPE
A) Fitzpatrick phototype II-IV (Appendix 2). B) Subjects with Glogau photoaging type II-III (Appendix 3).

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7. CONTRACEPTION

Females of childbearing potential who are, in the opinion of the investigator, practising a reliable method of contraception. Adequate contraception is defined as abstinence, oral contraceptive, either combined or progestogen alone OR injectable progestogen OR implants of levonorgestrel OR estrogenic vaginal ring OR percutaneous contraceptive patches OR intrauterine device or intrauterine system OR double barrier method (condom or occlusive cap [diaphragm or cervical vault caps] plus spermicidal agent [foam, gel, film, cream, suppository]) OR male partner sterilization prior to the female subject's entry into the study, and this male is the sole partner for that subject.

4.2. Exclusion Criteria

A subject will not be eligible for inclusion in this study if any of the following criteria apply:

1. PREGNANCY


Women who are known to be pregnant or who are intending to become pregnant over the duration of the study.

2. BREAST-FEEDING

Women who are breast-feeding.

3. CONCURRENT MEDICATION/ MEDICAL HISTORY

- A. Active skin disease or open wound in the test area.
- B. Medical history of using a medicated acne treatment (e.g. Benzoyl Peroxide, Clindamycin, isotretinoin) within the last 24 months.
- C. Medical history of dysplastic nevi or melanoma.
- D. Preexisting inflammatory dermatoses such as psoriasis, atopic dermatitis
- E. Moles, tattoos, scars, irritated skin, hairs, etc. at the test area that could, in the opinion of the investigator, influence the investigation.
- F. Systemic therapy with immuno-suppressive drugs (e.g. corticosteroids) and/or antihistamines within 7 days prior to screening and/or throughout the entire course of the study.
- G. Systemic use of over-the-counter (OTC) analgesics or anti-inflammatory drugs 24 hours prior to screening.
- H. Systemic use of any photosensitizing medication 2 weeks prior to screening.
- I. Intense sun exposure, UV-treatments or tanning salon visit within two weeks prior to screening.
- J. One of the following illnesses that might require regular systemic medication: Insulin-dependent diabetes, cancer.

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- K. One of the following illnesses if not medicated: Asthma, hypertension
- L. Medical history of abnormal response to sunlight.
- M. Subjects with a history of mental illness.
- N. Ocular surgery within the last 12 months.
- O. Ocular trauma, infection or inflammation within the last 3 months.
- P. Active blepharitis, conjunctivitis, uveitis.
- Q. Any ocular pathology requiring topical ocular treatment within the last 1 month.
- R. Ocular laser within the last 3 months.
- S. Aesthetic, cosmetic or dermatological treatment in the treatment area (face), including the use of skin tone lightening products, within the last 3 months.
- T. Use of facial scrubs, depilatory creams, waxing and/or bleaching within the last 2 weeks prior to screening.
- U. Microdermabrasion and/or laser hair removal within the last 4 weeks prior to screening.
- V. Medical history of Herpes Simplex (Cold Sores).

4. ALLERGY/ INTOLERANCE


- A. Known or suspected intolerance or hypersensitivity to the study materials (or closely related compounds) or any of their stated ingredients.
- B. Documented allergies to cosmetic products or study ingredients.

5. CLINICAL STUDY/ EXPERIMENTAL PRODUCT

- A. Participation in another clinical study (including cosmetic studies) or receipt of an investigational drug within 30 days of the screening visit.
- B. Previous participation in this study.

6. SUBSTANCE ABUSE

Recent history (within the last 5 years) of alcohol or other substance abuse.

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7. PERSONNEL

An employee of the sponsor or the study site or members of their immediate family.

8. LIFESTYLE

- A. Required to work outside during daylight hours over the duration of the study.
- B. Required or otherwise intending to spend prolonged periods of time outside during daylight hours over the duration of the study (e.g. holiday, sunbathing, and gardening).

9. STUDY MATERIAL SENSITIVITY TEST

A score of “Severe” for any Dermatologist or Subject Self-Assessed endpoint at any time for the study material sensitivity test.

4.3. Screening/ Baseline Failures

Screen failures are defined as subjects who consent to participate in the study but are never subsequently randomized. In order to ensure transparent reporting of screen failure subjects, a minimal set of screen failure information is required including Demography, Screen Failure details, Eligibility Criteria, and any Serious Adverse Events (SAEs). Re-screening of subjects will not be allowed in this study.


4.4. Withdrawal/ Stopping Criteria

A subject may withdraw from the study at any time at his/her own request, or may be withdrawn at any time at the discretion of the investigator for safety, behavioural or administrative reasons.

If the reason for removal of a subject from the study is an AE or an abnormal laboratory test result, the principal specific event or test will be recorded on the electronic Case Report Form (eCRF). If a subject is withdrawn from the study because of a product limiting AE, thorough efforts should be clearly made to document the outcome. Any AEs ongoing at the final visit will be followed up until resolved, the condition stabilizes, is otherwise explained, or the subject is lost to follow-up.

The following actions must be taken in relation to a subject who fails to attend the clinic for a required study visit:

- The site must attempt to contact the subject and re-schedule the missed visit as soon as possible.

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- The site must counsel the subject on the importance of maintaining the assigned visit schedule and ascertain whether or not the subject wishes to and/or should continue in the study.
- In cases where the subject is deemed ‘lost to follow up’, the investigator or designee must make every effort to regain contact with the subject (where possible, at least 2 telephone calls). The contact attempt should be documented in the subject’s record.
- Should the subject continue to be unreachable, only then will he/she be considered to have withdrawn from the study with a primary reason of “Lost to Follow-up”.

4.5. Subject Replacement

Subjects who withdraw from the study post-randomization will not be replaced.

4.6. Subject and Study Completion

A completed subject is one who has completed all phases of the study.

The end of the study is defined as the date of the last subject’s last visit.


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5. PRODUCT INFORMATION

5.1. Study Product

The following study products will be supplied by the Clinical Supplies Department, GSKCH:

	Reference / Washout Cleanser	Test Product	Reference / Washout Sunscreen
Product Name	Simpli Kind to Skin Moisturising Facial Wash	Physiogel Calming Relief Restoring Lipid Balm	Sunmax Sensitive SPF 50
Product Formulation Code	N/A (Commercial, UK)	CCI	CCI
Application Quantity	Approximately 0.6-1 g		
Route of Application	Topical		
Application Instructions	<p>In your hands, work a small amount into a lather. Massage onto wet skin, rinse with water.</p> <p>Avoid contact with eyes. If contact occurs, rinse thoroughly with water.</p> <p>Apply twice a day (morning and evening)</p>	<p>Dispense a pea-sized quantity onto the fingertips and apply to the full face.</p> <p>Avoid contact with eyes. If contact occurs rinse thoroughly with water.</p> <p>Apply twice a day (morning and evening)</p> <p>Do not apply in the morning if you are visiting the site on the same day.</p>	<p>Dispense a pea-sized quantity onto the fingertips and apply to the full face.</p> <p>Avoid contact with eyes. If contact occurs rinse thoroughly with water.</p> <p>Apply twice a day (morning and lunchtime)</p> <p>Do not apply in the morning if you are visiting the site on the same day.</p>

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Other items to be supplied by the Clinical Supplies Department, GSKCH:

Name of Item	Purpose
Not Applicable	Not Applicable


Other items to be supplied by the Site:

Name of Item	Purpose
70% Glycolic Acid Treatment - SM Emprendimentos Farmacêuticos (Fagron) from MagisPharma	Glycolic acid solution with which to execute the facial peel procedure
Sodium Bicarbonate Neutralizing Solution - Labsynth Produtos para Laboratórios (Synth) from MagisPharma	Neutralizing agent used in the final step of the facial peel procedure

5.2. Application Schedule

A 7 day washout phase is included to standardize subjects' skin care regimens. Subjects will be provided with a commercially available facial cleanser (Simple Kind to Skin Moisturising Facial Wash) and sunscreen (Sunmax Sensitive SPF 50) as standard of care. Subjects will be instructed to use the facial cleanser during the morning and evening, and to apply the sunscreen in the morning (after cleansing) and at lunchtime. Sunmax Sensitive SPF 50 is designed for subjects with sensitive skin and has favourable local tolerance clinical data to support its use for application to sensitive, post-procedure skin. Simple Kind to Skin Moisturising Facial Wash is also designed for subjects with sensitive skin.

Within the washout phase, a study material sensitivity test is included to identify subjects who may be sensitive to the study materials in order to determine whether they are suitable to undergo the facial peel procedure. A qualified dermatologist will dispense a thin layer of the 70% glycolic acid peel solution to cover a demarcated 5 x 5 cm square area on the volar surface of the forearm and, within a period of 30-60 seconds, will neutralize the 70% glycolic acid peel solution with the bicarbonate neutralizing agent and then rinse the skin thoroughly with water and pat dry with a soft towel. Once dry, the dermatologist will apply a thin layer of the Sunmax Sensitive SPF50 sunscreen to the 5 x 5 cm square area. Dermatologist and subject self-assessments will be used to evaluate local tolerance. If subject data for the study material sensitivity study contains a dermatologist or subject self-assessment score of "Severe" for any attribute, this subject will be deemed to be in violation of exclusion criteria 9 and must be discharged from the study.

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Upon completion of the washout phase, subjects considered to be eligible for the test phase will be randomised to two groups (Group 1: Test product; Group 2: No-treatment) and a qualified dermatologist with experience administering facial peels will conduct the 70% Glycolic Acid procedure.

Subjects randomised to Group 1 will be instructed to apply the test product twice-daily (morning and evening) after cleansing, for a total of 14 consecutive days. All subjects will be instructed to continue using the facial cleanser twice-daily during the morning and evening, and to apply the sunscreen in the morning and at lunchtime. A summary of the subject's post-randomization regimen is included below for clarity.

Randomized Group	Morning	Lunchtime*	Evening
Group 1	1. Cleansing 2. Test Product 3. Sunscreen	2. Sunscreen	1. Cleansing 2. Test Product
Group 2	1. Cleansing 2. Sunscreen	2. Sunscreen	2. Cleansing

*Lunchtime application must be at least 3 hours after previous sunscreen application


Subjects will not apply any sunscreen on the day of the facial peel procedure (Day 8), since they will remain at site until the evening (after 5 pm). On the morning of each visit, prior to arriving at the test site, subjects will be instructed to cleanse their face and not to apply any test product or sunscreen until after all measurements and assessments have been completed. Before leaving the site, subjects will undergo test product and/or sunscreen application under supervision. After leaving the site, subjects should apply the sunscreen a second time, but no sooner than 3 hours after the previous application.

5.3. Application Modification

No modification of product application is permitted in this study.

5.4. Product Compliance

A daily diary will be used to monitor and promote compliance. Subjects will not be excluded due to missed applications, but will be reminded to use the products as per the instructions provided and to complete the diary card on a daily basis to encourage compliance. Missed or additional product applications will be recorded by the

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Investigator or designee as deviations. Subjects will be asked to bring their washout and test products to each site visit.

To be considered compliant and part of the per-protocol (PP) population, a subject must have used the test product and/or sunscreen at least 80% of the instructed number of applications following completion of the facial peel procedure.

5.5. Precautions

No special precautions are required providing the study is carried out in accordance with this protocol.

5.6. Overdose

An overdose is a deliberate or inadvertent administration of a product at a dose higher than specified in the protocol.

Overdose is not likely to occur in this study. Limited quantities of the product will be supplied, and closely monitored by the site for each subject.

Overdose per se is not an AE. However, any clinical sequelae of an overdose should be reported as an AE (and serious adverse event (SAE), if appropriate). For reporting, follow the AE and SAE reporting instructions.

5.7. Rescue Therapy

No rescue therapy is required in this study.

5.8. Product Assignment

Subjects will be assigned to study product in accordance with the randomization schedule generated by the Biostatistics Department, GSKCH, prior to the start of the study, using validated internal software.

5.8.1 Randomization

A unique screening number will identify each subject screened for study participation. Screening numbers will be assigned in ascending numerical order as each subject signs their consent form. Subjects who meet all inclusion and exclusion criteria will be randomized according to the randomization schedule. Randomization numbers will be assigned in ascending numerical order as each subject is determined to be fully eligible.

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5.8.2 Blinding

This is an evaluator-blind clinical study. Therefore, all personnel and evaluators who may influence study outcomes are blinded to the product allocation of subjects and their diaries. The Investigator or their designees who are not involved in procedures or processes which may influence study outcomes are not required to be blinded to the product allocation of subjects and will have visibility of the subject diary.

5.8.3 Code Breaks

The blind must only be broken in an emergency where it is essential to know which product a subject received in order to give the appropriate medical care. Wherever possible the Investigator (or designee) must contact the Sponsor prior to breaking the blind. The investigator must document the reason for breaking the code and sign and date the appropriate document.

The study blind must be returned to GSKCH at the end of the study.

5.9. Packaging and Labelling

The Washout/ Reference products (Simple Kind to Skin Moisturising Facial Wash and Sunmax Sensitive SPF 50) and Test Product (Physiogel Calming Relief Restoring Lipid Balm) will be over-wrapped in opaque vinyl and any branding on the commercial products will be obscured.


A new label will be created by the Clinical Supplies Department, GSKCH and applied to each product. The contents of the label will be in accordance with all applicable regulatory requirements and will be the responsibility of the Clinical Supplies Department, GSKCH. Each study label will contain, but not be limited to, protocol number, product code letter for Test Product only and directions for storage.

Care should be taken with the supplied products and their labels so that they are maintained in good condition. It is important that all labels remain intact and legible for the duration of the study. Subjects should be instructed to not remove or deface any part of the study label.

5.9.1. Accountability of Product

All products supplied are for use only in this clinical study and should not be used for any other purpose.

The investigator or designee will maintain a full record of study product accountability. A Product Dispensing Log must be kept current and will contain the following information:

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1. The identification of the subject to whom the study product was dispensed.
2. The date(s) and quantity of the study product dispensed to the subject.
3. The date(s) and quantity of the study product returned by the subject (if applicable).

The inventory must be available for inspection by the study monitor during the study. At the end of the study, study product supplies will be verified by the monitor. Study product supplies will then be either collected by the study monitor or returned by the investigator or designee to the GSKCH Clinical Supplies Department or designated vendor.

5.9.2. Storage of Product

Study product supplies must be stored in compliance with the label requirements in a secure place with limited or controlled access.

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6. STUDY ASSESSMENTS AND PROCEDURES

This section lists the procedures and parameters of each planned study assessment. The exact timing of each assessment at each scheduled visit is listed in the Schedule of Events section.

Adherence to the study design requirements, including all assessments and procedures are essential and required for study conduct.

6.1. Visit 1 – Screening / Washout Visit

6.1.1. Informed Consent


The investigator, or designee, must obtain written (signed and dated by the subject) informed consent from each subject participating in this study after adequate explanation of the aims, methods, objectives, and potential hazards of the study.

The investigator, or designee, must also explain to the subjects that they are completely free to refuse to enter the study or to withdraw from it at any time. Appropriate forms for documenting a written consent will be provided by the investigator or by GSKCH. The investigator, or designee, should sign and date the consent form to confirm that the consent process was completed correctly. The subject will be provided with a copy of their signed and dated informed consent form (ICF) and any other written information which they should be instructed to retain.

A list of the chemical entities present in all formulations will be provided to subjects so that they may evaluate the list for any known sensitivity or intolerance to the study materials. It will be made clear on the ICF that subjects who have a known sensitivity or intolerance to the study materials should not provide their consent to continue.

If, during a subject's participation in the study, any new information becomes available that may affect the subject's willingness to participate in the study, each ongoing subject should receive a copy of this new information and be re-consented into the study. Subjects should be provided with a copy of the signed and dated amended consent form. The date of consent will be recorded on the eCRF.

Photographs (Image Capture – VISIA) are to be captured for both clinical assessment and potential commercial exploitation. Subjects will be requested to provide their consent on the ICF. Subjects who do not provide consent for the potential commercial exploitation of their photographic data will still be considered eligible for the study. All subjects will have their photographs taken at the scheduled time points to enable

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the Evaluator to make an accurate assessment of global tolerance and cosmetic efficacy.

6.1.2. Demographics

The following demographic parameters will be captured by the Investigator or designee and recorded on the eCRF: year of birth, race and gender.

6.1.3. Medical History and Concomitant Medication

Medical history will be assessed as related to the inclusion/exclusion criteria by the Investigator or designee. Details of any relevant medical or surgical history within the last year, including allergies or drug sensitivity, will be recorded on the eCRF. Any concomitant therapy taken in the 30 days prior to the Screening Visit and throughout the study will also be recorded.


6.1.4. Fitzpatrick Skin Type Assessment

Fitzpatrick skin type assessment will be conducted by a trained, qualified technician and recorded on the eCRF using the scale below.

Type	Description
I	Always burns, never tans
II	usually burns, tans minimally
III	sometimes mild burn, tans uniformly (cream white; fair with any hair or eye color)
IV	burns minimally, always tans well (moderate brown)
V	very rarely burns, tans very easily (dark brown)
VI	Never burns, never tans (deeply pigmented dark brown to darkest brown)

6.1.5. Glogau Photoaging Type Assessment

Glogau photoaging type assessment will be confirmed by a trained, qualified technician and recorded on the eCRF using the scale below.

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Group	Classification	Skin Characteristics
I	Mild	Early Photoaging: mild pigment changes, no keratosis, minimal wrinkles, minimal or no makeup
II	Moderate	Early to Moderate Photoaging: Early brown spots visible, keratosis palpable but not visible, parallel smile lines begin to appear, wears some foundation
III	Advanced	Advanced Photoaging: Obvious discolorations, visible capillaries (telangiectasias), visible keratosis, wears heavier foundation always
IV	Severe	Severe Photoaging: Yellow-gray skin color, prior skin malignancies, wrinkles throughout - no normal skin, cannot wear makeup because it cakes and cracks

6.1.6. Inclusion / Exclusion Criteria


Inclusion/exclusion criteria will be assessed by the Investigator or medically qualified designee and recorded on the eCRF. Exclusion 3P will be assessed by a qualified ophthalmologist. At this point, exclusion criteria 9 will not be evaluated until after completion of the study material sensitivity test and corresponding Dermatologist and Subject self-assessment data.

6.1.7. Subject Eligibility

Subjects meeting the inclusion and exclusion criteria, whom provide their informed consent and who are also considered eligible for enrollment in the study by the Investigator or medically qualified designee will be enrolled into the study. Confirmation of whether a subject was enrolled, or not, will be recorded on the eCRF.

6.1.8. Study Material Sensitivity Test

This procedure is included to determine whether each subject is overly sensitive to the washout products and glycolic acid peel regimen. A qualified dermatologist will dispense a thin layer of the 70% glycolic acid peel solution (approximately 0.5 ml) to cover a demarcated 5 x 5 cm square area on the volar surface of the forearm and, within a period of approximately 30-60 seconds, will neutralize the 70% glycolic acid peel solution with the bicarbonate neutralizing agent then rinse the skin thoroughly with water and pat dry with a soft towel. Once dry, the dermatologist will apply a thin layer of the Sunmax Sensitive SPF50 sunscreen to the forearm. Successful completion of this procedure will be recorded on the eCRF.

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6.1.9. Subject Self-Assessment of Sensitivity

The following assessments will be conducted by test subjects reflective of their skin condition at the 5 x 5 cm square area on the volar surface of the forearm at the time of evaluation and recorded on the eCRF.

Score	Pain	Stinging/ Burning	Itching	Tightness	Redness	Dryness
0	None	None	None	None	None	None
1	Mild	Mild	Mild	Mild	Mild	Mild
2	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
3	Severe	Severe	Severe	Severe	Severe	Severe

6.1.10. Dermatologist Assessment of Sensitivity

The following assessments will be conducted by a dermatologist reflective of the subject's skin condition at the 5 x 5 cm square area on the volar surface of the forearm at the time of the evaluation and recorded on the eCRF. Whenever possible, it is preferable for the same dermatologist to evaluate the same subject through the entire study.

Erythema

Score	Description
0	None - No evidence of erythema present
1	Mild – Slight red coloration
2	Moderate - Definite redness
3	Severe - Marked erythema, bright red to dusky dark red in color

Dryness

Score	Description
0	None - No dryness
1	Mild - Barely perceptible, fine scales or flakes present to limited areas of the test site
2	Moderate - Fine scales or flakes generalized to all areas of the test site
3	Severe - Scaling and peeling of skin over all areas of the test site

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Desquamation

Score	Description
0	None - No evidence of desquamation/peeling
1	Mild - Barely perceptible scaling; evident only on scratching
2	Moderate - Minimal scaling, adherent to the skin
3	Severe - Moderate scaling, loosely adherent to the skin and easily removable

Edema

Score	Description
0	None - No edema present
1	Mild - Barely perceptible edema present
2	Moderate - Definite edema present
3	Severe - Marked/pronounced edema present

6.1.11. Exclusion Criteria 9

Dermatologist and Subject self-assessment data will be evaluated by the Investigator or designee. Any subject with a score of “Severe” for any of the Dermatologist (Erythema, Dryness, Desquamation, Edema) or Subject self-assessed (Pain, Stinging/Burning, Itching, Tightness, Redness, Dryness) parameters will be considered to be in violation of exclusion criteria 9 and will be discharged from the study. All other subjects will be considered eligible to continue in the study.


Any Dermatologist or Subject self-assessed score of “severe” will also be considered an adverse event and reported as per the procedures outlined in Section 7. Dermatologist or Subject self-assessed scores of “none”, “mild” and “moderate” will not be considered adverse events.

6.1.12. Subject Eligibility

See 6.1.7.

6.1.13. Washout Products and Washout Diary Dispensing

Dispensing of washout products and washout diary to subjects to standardize skin care regimen and usage instructions will be recorded on the eCRF.

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6.2. Visit 2 – 1 day after Visit 1

6.2.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.

6.2.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.

As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

6.2.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

6.2.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout products more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will be recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

6.2.5. Subject Self-Assessment of Sensitivity

Assessments to be taken as per 6.1.9, 24±4 hours after completion of the study material sensitivity test.

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6.2.6. Dermatologist Assessment of Sensitivity

Assessments to be taken as per 6.1.10, 24±4 hours after completion of the study material sensitivity test.

6.2.7. Exclusion Criteria

The exclusion criteria described in Appendix 4 will be confirmed by the Investigator or medically qualified designee and recorded on the eCRF.

Any subject with a score of “Severe” for any of the Dermatologist (Erythema, Dryness, Desquamation, Edema) or Subject self-assessed (Pain, Stinging/Burning, Itching, Tightness, Redness, Dryness) parameters will be considered to be in violation of exclusion criteria 9 and will be discharged from the study. All other subjects will be considered eligible to continue in the study.

Any Dermatologist or Subject self-assessed score of “severe” will also be considered an adverse event and reported as per the procedures outlined in Section 7. Dermatologist or Subject self-assessed scores of “none”, “mild” and “moderate” will not be considered adverse events.

6.2.8. Subject Eligibility

See 6.1.7.

6.3. Visit 3 – Day of Procedure - 6 days after Visit 2


6.3.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.

6.3.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.

As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

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6.3.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

6.3.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout product more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

6.3.5. Subject Self-Assessment of Sensitivity

Assessments to be taken as per 6.1.9, 7 days after completion of the study material sensitivity test.

6.3.6. Dermatologist Assessment of Sensitivity


Assessments to be taken as per 6.1.10, 7 days after completion of the study material sensitivity test.

6.3.7. Exclusion Criteria

Exclusion criteria detailed in Appendix 4 will be assessed by the Investigator or medically qualified designee to confirm subject eligibility and recorded on the eCRF. Subjects who trigger any of the exclusion criteria will be discharged from the study.

Any subject with a score of “Severe” for any of the Dermatologist (Erythema, Dryness, Desquamation, Edema) or Subject self-assessed (Pain, Stinging/Burning, Itching, Tightness, Redness, Dryness) parameters will be considered to be in violation of exclusion criteria 9 and will be discharged from the study. All other subjects will be considered eligible to continue in the study.

Any Dermatologist or Subject self-assessed score of “severe” will also be considered an adverse event and reported as per the procedures outlined in Section 7. Dermatologist or Subject self-assessed scores of “none”, “mild” and “moderate” will not be considered adverse events.

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6.3.8. Subject Eligibility

See 6.1.7. Note, to be considered compliant eligible to continue in the study, a subject must not have missed more than 5 applications of either the washout cleanser or sunscreen. Subjects failing to meet this criterion will be considered to have deviated from the protocol and will be discharged from the study.

6.3.9. Subject Randomisation

Subject randomisation will be conducted as per the process detailed in Section 5.8.1 and documented on the eCRF.

6.3.10. Instrumental Measurements Pre-Procedure

Instrumental measurements of Transepidermal Water Loss and skin hydration will be conducted by the Investigator or designee and recorded on the eCRF. Subjects will acclimatize to the controlled room temperature (21 ± 1 °C) and humidity ($50 \pm 10\%$) for at least 30 minutes prior to instrumental assessment.

Instrumental Measurement of Transepidermal Water Loss


TEWL measurement will be performed by evaporimetry with a Tewameter TM 300 (Courage & Khazaka, Cologne, Germany) following the European Expert Group on Efficacy Measurement of Cosmetics and Other Topical Products (EEMCO) Guidance for the Assessment of Transepidermal Water Loss in Cosmetic Sciences. [Rogiers] Measurements will be taken in triplicate on the left cheek (below the cheekbone, between the nose and ear and not overlapping with the site previously used for TEWL measurements) with units of $\text{g/m}^2/\text{hr}$. TEWL measurements will be taken with the subject lying horizontally, on their back, so that the chimney of the Tewameter probe is aligned vertically.

Instrumental Measurement of Moisturisation

Measurement of stratum corneum hydration will be performed by the electrical capacitance method with a Corneometer CM 865 (Courage & Khazaka, Cologne, Germany) following the EEMCO Guidance for the Assessment of Stratum Corneum Hydration. [Berardesca] Corneometer measurements will be taken in triplicate at the left cheek (below the cheekbone, between the nose and ear) with the subject lying horizontally, on their back. Instrumental data will be reported in Corneometer Units

6.3.11. Image Capture (VISIA) Pre-Procedure

VISIA CR[®] high resolution photographs of the front, left and right sides of subject's faces will be taken using polarised and non-polarised lighting and documented on the

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eCRF. Jewelry will be removed and hair loosely tied back and covered with a black veil so that it does not interfere with the photograph. Subjects will be asked to maintain a relaxed, neutral expression with their eyes closed. Photographic images of subjects are considered personal identifiable information (PII) and will be transferred securely from the site to GSK. Subjects who did not provide consent for the commercial exploitation of their photographic data will not have their photographs taken.

6.3.12. Subject Self-Assessment Pre-Procedure

The following assessments will be conducted by test subjects reflective of their facial skin condition at the time of evaluation and recorded on the eCRF.

Score	Pain	Stinging/ Burning	Itching	Tightness	Redness	Dryness
0	None	None	None	None	None	None
1	Mild	Mild	Mild	Mild	Mild	Mild
2	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
3	Severe	Severe	Severe	Severe	Severe	Severe

6.3.13. Dermatologist Assessment Pre-Procedure

The following assessments will be conducted by a dermatologist reflective of the subject's facial skin condition at the time of the evaluation and recorded on the eCRF. Whenever possible, it is preferable for the same dermatologist to evaluate the same subject through the entire study.

Erythema

Score	Description
0	None - No evidence of erythema present
1	Mild – Slight red coloration
2	Moderate - Definite redness
3	Severe - Marked erythema, bright red to dusky dark red in color

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Dryness

Score	Description
0	None - No dryness
1	Mild - Barely perceptible, fine scales or flakes present to limited areas of the face
2	Moderate - Fine scales or flakes generalized to all areas of the face
3	Severe - Scaling and peeling of skin over all areas of the face

Desquamation

Score	Description
0	None - No evidence of desquamation/peeling
1	Mild - Barely perceptible scaling; evident only on scratching
2	Moderate - Minimal scaling, adherent to the skin
3	Severe - Moderate scaling, loosely adherent to the skin and easily removable

Edema

Score	Description
0	None - No edema present
1	Mild - Barely perceptible edema present
2	Moderate - Definite edema present
3	Severe - Marked/pronounced edema present

6.3.14. Dermatological Procedure (Facial Peel)

The 70% Glycolic Acid facial peel procedure will be conducted by a medically qualified professional with hands-on experience administering peels of this nature. The site will source 70% Glycolic Acid treatment (SM Empreendimento Farmacêuticos (Fagron)) and Sodium Bicarbonate neutralizing solution (Labsynth Produtos para Laboratórios (Synth)) from MagisPharma and will retain a copy of the purchase order and certificate of analysis, which will be stored in the Trial Master File (TMF).

Prior to the Glycolic Acid treatment, the subject's skin will be degreased by wiping with a gauze soaked in an alcohol solution (70% (w/w) in water). A fresh gauze will

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then be soaked in the 70% Glycolic Acid solution, which will be applied evenly over the entire face (excluding eyelids) starting in the center and moving to the periphery of the face. The Glycolic Acid solution will remain in contact with the skin for a minimum of 1 minute and a maximum of 3 minutes. The dermatologist will determine the exact treatment time on a subject by subject basis by monitoring their individual response to treatment. The dermatologist may determine that it is in the interests of the subject to terminate the treatment phase sooner than 1 minute after initial application. This will be considered a protocol deviation and recorded on the Deviations Log. Similarly, a treatment phase of longer than 3 minutes will be reported as a deviation. Subjects who do not receive at least 1 minute or who receive more than 3 minutes of Glycolic Acid treatment will still be considered eligible to continue the study unless the dermatologist believes them otherwise unsuitable to continue (e.g. for safety reasons).

Once the Glycolic Acid treatment period is complete, a fresh gauze will be soaked with the sodium bicarbonate solution, which will be applied evenly over the entire face (excluding eyelids) starting in the center and moving to the periphery of the face. This process will be repeated until the dermatologist considers the Glycolic Acid solution to be successfully neutralized. The dermatologist will then rinse the subject's face thoroughly with water.

Subjects will be instructed to contact the study site (in person or by phone) in case of discomfort between visits. A medically qualified dermatologist will evaluate the subject's reports of discomfort and determine an appropriate course of action, including whether to discontinue a subject's involvement in the study. Adverse events will be reported as per the procedures in Section 7.

6.3.15. Dermatologist Assessment Post-Procedure, Pre-Treatment (BASELINE)


Assessments to be taken and recorded as per 6.3.14, 60±15 minutes after completion of the facial peel procedure.

6.3.16. Instrumental Measurements Post-Procedure, Pre-Treatment (BASELINE)

Assessments to be taken and recorded as per 6.3.10, 60±15 minutes after completion of the facial peel procedure.

6.3.17. Image Capture (VISIA) Post-Procedure, Pre-Treatment (BASELINE)

Assessments to be taken and recorded as per 6.3.11, 60±15 minutes after completion of the facial peel procedure.

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6.3.18. Subject Self-Assessment Post-Procedure, Pre-Treatment (BASELINE)

Assessments to be taken and recorded as per 6.3.12, 60±15 minutes after completion of the facial peel procedure.

6.3.19. Test Product and Test Diary Dispensing. Washout Diary Collection.

The time and date of test product dispensing will be documented on the eCRF. Test product diary will be dispensed and washout diary collected. Subjects randomised to test product will be dispensed a different diary than subjects who are not randomised to test product. The Investigator or designee involved in test product and test diary dispensing must not be involved in any assessments in order to protect the blind.

6.3.20. Supervised Test Product Application Post-Procedure

Subjects randomized to test product (Group I) will be instructed to apply the test product as per the labelled usage instructions immediately after the post-procedure, pre-treatment (baseline) assessments are complete. The Investigator or designee will oversee this initial product application. Group II will not apply any test product. Product application will be recorded on the eCRF and subject diary and must happen at least 30 minutes prior to any further instrumental measurements. The Investigator or designee involved in this step must not be involved in any assessments in order to protect the blind.

6.3.21. Instrumental Measurements Post-Procedure, Post-Treatment


Measurements to be taken and recorded as per 6.3.10, 180±15 and 360±15 minutes after completion of the facial peel procedure.

6.3.22. Subject Self-Assessment Post-Procedure, Post-Treatment

Assessments to be taken and recorded as per 6.3.12, 180±15 minutes after completion of the facial peel procedure.

6.3.23. Evaluator (Dermatologist) Assessment Post-Procedure, Post-Treatment

Assessments to be taken and recorded as per 6.3.13, 180±15 minutes after completion of the facial peel procedure.

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Subjects will remain at site until at least 5:00 PM to prevent exposure to intense sunlight.

6.4. Visit 4 – 1 day after Visit 3

Subjects will be instructed to arrive at the site prior to 9:00 AM to minimize exposure to intense sunlight.

6.4.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.

6.4.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.


As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

6.4.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

6.4.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout products (All subjects) and test product (Group I, only) more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

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6.4.5. Instrumental Measurements Post-Procedure, Post-Treatment (24±4 hours after Facial Peel)

Measurements to be taken and recorded as per 6.3.10, 24±4 hours after completion of the facial peel procedure.

6.4.6. Image Capture (VISIA) Post-Procedure, Post-Treatment (24±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.11, 24±4 hours after completion of the facial peel procedure.

6.4.7. Subject Self-Assessment Post-Procedure, Post-Treatment (24±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.12, 24±4 hours after completion of the facial peel procedure.

6.4.8. Dermatologist Assessment Post-Procedure, Post-Treatment (24±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.13, 24±4 hours after completion of the facial peel procedure.

6.4.9. Supervised Test Product Application

Only subjects in Group I will undergo supervised test product application. The Investigator or designee will oversee application of the test product. Product application will be recorded on the eCRF and subject diary. The Investigator or designee involved in this step must not be involved in any assessments in order to protect the blind.

6.4.10. Supervised Sunscreen Application

All subjects will undergo supervised sunscreen application. The Investigator or designee will oversee application of the SPF 50 sunscreen. Product application will be recorded on the eCRF and subject diary.

6.5. Visit 5 – 1 day after Visit 4

Subjects will be instructed to arrive at the site prior to 9:00 AM to minimize exposure to intense sunlight.

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6.5.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.

6.5.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.

As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

6.5.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

6.5.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout products (All subjects) and test product (Group I, only) more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

6.5.5. Instrumental Measurements Post-Procedure, Post-Treatment (48±4 hours after Facial Peel)

Measurements to be taken and recorded as per 6.3.10, 48±4 hours after completion of the facial peel procedure.

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6.5.6. Subject Self-Assessment Post-Procedure, Post-Treatment (48±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.12, 48±4 hours after completion of the facial peel procedure.

6.5.7. Dermatologist Assessment Post-Procedure, Post-Treatment (48±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.13, 48±4 hours after completion of the facial peel procedure.

6.5.8. Supervised Test Product Application

Only subjects in Group I will undergo supervised test product application. The Investigator or designee will oversee application of the test product. Product application will be recorded on the eCRF and subject diary. The Investigator or designee involved in this step must not be involved in any assessments in order to protect the blind.

6.5.9. Supervised Sunscreen Application

All subjects will undergo supervised sunscreen application. The Investigator or designee will oversee application of the SPF 50 sunscreen. Product application will be recorded on the eCRF and subject diary.

6.6. Visit 6 – 1 day after Visit 5

Subjects will be instructed to arrive at the site prior to 9:00 AM to minimize exposure to intense sunlight.


6.6.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.

6.6.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.

As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s

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condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

6.6.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

6.6.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout products (All subjects) and test product (Group I, only) more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

6.6.5. Instrumental Measurements Post-Procedure, Post-Treatment (72±4 hours after Facial Peel)

Measurements to be taken and recorded as per 6.3.10, 72±4 hours after completion of the facial peel procedure.

6.6.6. Subject Self-Assessment Post-Procedure, Post-Treatment (72±4 hours after Facial Peel)


Assessments to be taken and recorded as per 6.3.12, 72±4 hours after completion of the facial peel procedure.

6.6.7. Dermatologist Assessment Post-Procedure, Post-Treatment (72±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.13, 72±4 hours after completion of the facial peel procedure.

6.6.8. Supervised Test Product Application

Only subjects in Group I will undergo supervised test product application. The Investigator or designee will oversee application of the test product. Product

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application will be recorded on the eCRF and subject diary. The Investigator or designee involved in this step must not be involved in any assessments in order to protect the blind.

6.6.9. Supervised Sunscreen Application

All subjects will undergo supervised sunscreen application. The Investigator or designee will oversee application of the SPF 50 sunscreen. Product application will be recorded on the eCRF and subject diary.

6.7. Visit 7 – 4 days after Visit 6

Subjects will be instructed to arrive at the site prior to 9:00 AM to minimize exposure to intense sunlight.

6.7.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.


6.7.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.

As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

6.7.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

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6.7.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout products (All subjects) and test product (Group I, only) more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will be recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

6.7.5. Instrumental Measurements Post-Procedure, Post-Treatment (168±4 hours after Facial Peel)

Measurements to be taken and recorded as per 6.3.10, 168±4 hours after completion of the facial peel procedure.

6.7.6. Subject Self-Assessment Post-Procedure, Post-Treatment (168±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.12, 168±4 hours after completion of the facial peel procedure.

6.7.7. Dermatologist Assessment Post-Procedure, Post-Treatment (168±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.13, 168±4 hours after completion of the facial peel procedure.

6.7.8. Supervised Test Product Application

Only subjects in Group I will undergo supervised test product application. The Investigator or designee will oversee application of the test product. Product application will be recorded on the eCRF and subject diary. The Investigator or designee involved in this step must not be involved in any assessments in order to protect the blind.

6.7.9. Supervised Sunscreen Application

All subjects will undergo supervised sunscreen application. The Investigator or designee will oversee application of the SPF 50 sunscreen. Product application will be recorded on the eCRF and subject diary.

6.8. Visit 8 – 7 days after Visit 7

Subjects will be instructed to arrive at the site prior to 9:00 AM to minimize exposure to intense sunlight.

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6.8.1. Current / Concomitant Medication

Any concomitant therapy taken since the last visit and throughout the study will be recorded on the eCRF by the Investigator or designee.

6.8.2. Adverse Events

Adverse events will be assessed by the Investigator or designee and recorded on the eCRF, as per the process detailed in Section 7.

As per Section 7.1, the following does not meet the definition of an adverse event: “Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject’s condition.” Therefore, the Dermatologist (erythema, edema, dryness, and desquamation) and Subject-self assessment (pain, stinging/burning, itching, tightness, redness, and dryness) grades will only be considered adverse events if they are scored as “Severe”, or if the investigator judges them to be more severe than expected in context of the Glycolic Acid treatment procedure.

6.8.3. Continued Subject Eligibility

The Investigator or designee will ascertain whether there have been any deviations from the protocol since the last visit, whether the subject has adhered to the lifestyle restrictions since the last visit and whether, in their opinion, the subject is eligible to continue in the study. Subject Continued Subject Eligibility will be recorded on the eCRF.

6.8.4. Compliance (Diary Review)

Subject diaries will be reviewed by the Investigator or their designee. Subjects who apply the washout products (All subjects) and test product (Group I, only) more or less frequently than twice a day will be considered to have deviated from the protocol and additional/missed applications will be recorded on the Deviations Log. The total number of product applications and total number of missed product applications will be recorded on the eCRF.

6.8.5. Instrumental Measurements Post-Procedure, Post-Treatment (336±4 hours after Facial Peel)

Measurements to be taken and recorded as per 6.3.10, 336±4 hours after completion of the facial peel procedure.

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6.8.6. Image Capture (VISIA) Post-Procedure, Post-Treatment (336±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.11, 336±4 hours after completion of the facial peel procedure.

6.8.7. Subject Self-Assessment Post-Procedure, Post-Treatment (336±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.12, 336±4 hours after completion of the facial peel procedure.

6.8.8. Subject Global Self-Assessment

Test subjects will rate the level of satisfaction with the post-procedure skin care regimen to which they were randomized using scale below. These data will be recorded on the eCRF.


Score	Description
0	Very Satisfied
1	Satisfied
2	Poorly Satisfied
3	Not at all Satisfied

6.8.9. Dermatologist Assessment Post-Procedure, Post-Treatment (336±4 hours after Facial Peel)

Assessments to be taken and recorded as per 6.3.13, 336±4 hours after completion of the facial peel procedure.

6.8.10. Dermatologist Global Assessment

The Dermatologist will assess the local tolerance of the post-procedure skin care regimen in context of the expected effects of the procedure for each subject using the scale below and document the score on the eCRF. To make this assessment, the Dermatologist will draw on the total set of clinical and subject self-assessment data for each subject. The Dermatologist must be unaware of whether a subject was randomized to test product to protect the blind.

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Rating	Description
0 - Product Regimen was Well Tolerated	No clinically significant worsening of the expected signs/symptoms of the procedure. No new signs/symptoms manifest during product use.
1 - Product Regimen was Not Well Tolerated	Clear, clinically relevant worsening of the severity or frequency of expected signs/symptoms of the procedure and/or any occurrence of new, unexpected signs/symptoms during product use.


6.8.11. Products and Test Diary Return

Washout products, test product and test diary will be returned to the Investigator or designee and documented on the eCRF.

6.8.12. Discharge from Study

Subjects will be evaluated to determine if they completed all study procedures or if they were discontinued from the study early. If the subject discontinued at any point during the study, the primary reason for withdrawal should be recorded on the Study Conclusion page of the eCRF by selecting one of the options below.

1. Subject did not meet study criteria
2. Adverse Event
3. Lost to Follow Up
4. Protocol Violation
5. Withdrawal of Consent
6. Other

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7. SAFETY ASSESSMENTS

7.1. Definitions of an Adverse Event and Serious Adverse Event

7.1.1. Adverse Events

The investigator or site staff will be responsible for detecting, documenting and reporting events that meet the definition of an AE or SAE.

Adverse Event Definition:


1. An AE is any untoward medical occurrence in a subject or clinical investigation subject, temporally associated with the use of an investigational or washout product, whether or not considered related to the investigational or washout product.
2. NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of an investigational or washout product.

Events meeting AE definition include:

1. Any abnormal laboratory test results (if applicable) or other safety assessments, including those that worsen from baseline, and felt to be clinically significant in the medical and scientific judgment of the investigator.
2. Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
3. New condition(s) detected or diagnosed after study product administration even though it may have been present prior to the start of the study.
4. Signs, symptoms, or the clinical sequelae of a suspected interaction.
5. Signs, symptoms, or the clinical sequelae of a suspected overdose of either study product or a concomitant medication (overdose per se will not be reported as an AE/SAE).

Events NOT meeting definition of an AE include:


1. Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the subject's condition.
2. The disease/disorder/ condition being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the subject's condition..
3. Medical or surgical procedure (e.g., endoscopy, appendectomy): the condition that leads to the procedure is an AE.

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4. Situations where an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
5. Anticipated day-to-day fluctuations of pre-existing disease(s) or condition(s) present or detected at the start of the study that do not worsen.

7.1.2. Serious Adverse Events

Serious Adverse Event is defined as any untoward medical occurrence that, at any dose:
A. Results in death
B. Is life-threatening NOTE: The term 'life-threatening' in the definition of 'serious' refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.
C. Requires hospitalization or prolongation of existing hospitalization NOTE: In general, hospitalization signifies that the subject has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or out-subject setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.
D. Results in disability/incapacity NOTE: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g. sprained ankle) which may interfere or prevent everyday life functions but do not constitute a substantial disruption.
E. Is a congenital anomaly/birth defect
F. Other Situations <ol style="list-style-type: none"> 1. Medical or scientific judgment should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be

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considered serious.

2. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization or development of drug dependency or drug abuse or reports of spontaneous abortion.

7.2. Recording Adverse Events and Serious Adverse Events

Recording of adverse events and serious adverse events:


1. The investigator or site staff will be responsible for detecting, documenting and reporting events that meet the definition of an AE or SAE.
2. The investigator or site staff will then record all relevant information regarding an AE/SAE in the eCRF.
3. There may be instances when copies of medical records for certain cases are requested by GSK. In this instance, all subject identifiers, with the exception of the subject number, will be blinded on the copies of the medical records prior to submission to GSK.
4. The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. In such cases, the diagnosis will be documented as the AE/SAE and not the individual signs/symptoms. Clinical AEs will be described by diagnosis and not by symptoms when possible (e.g., upper respiratory tract infection, seasonal allergy, etc. instead of runny nose).
5. AEs will be collected from the start of the study material sensitivity test at Visit 1 and until 5 days following last administration of the study product.
6. SAEs will be collected over the same time period as stated above for AEs. However, any SAEs assessed as **related** to study participation (e.g., investigational product, protocol mandated procedures, invasive tests, or change in existing therapy) or related to a GSK concomitant medication will be recorded from the time a subject consents to participate in the study up to and including any follow-up contact.
7. Medical conditions reported prior to the time period for reporting AEs/SAEs should be recorded as part of the subject's medical history.

7.3. Evaluating Adverse Events and Serious Adverse Events

Assessment of Intensity:

The investigator or designee will make an assessment of intensity for each AE and SAE reported during the study and will assign it to one of the following categories:

1. Mild: An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2. Moderate: An event that is sufficiently discomforting to interfere with normal

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everyday activities

3. Severe: An event that prevents normal everyday activities. - an AE that is assessed as severe will not be confused with an SAE. Severity is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

Note: An event is defined as 'serious' when it meets at least one of the pre-defined outcomes as described in the definition of an SAE.


Assessment of Causality:

1. The investigator is obligated to assess the relationship between study product and the occurrence of each AE/SAE.
2. A "reasonable possibility" is meant to convey that there are facts/evidence or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
3. The investigator will use clinical judgment to determine the relationship.
4. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the study product will be considered and investigated.
5. The investigator will also consult the Product Information, for marketed products, in the determination of his/her assessment.
6. For each AE/SAE the investigator **must** document in the medical notes (source document) or eCRF that he/she has reviewed the AE/SAE and has provided an assessment of causality.
7. There may be situations when an SAE has occurred and the investigator has minimal information to include in the initial report to GSK. **However, it is very important that the investigator always make an assessment of causality for every event prior to the initial transmission of the SAE data to GSK.**
8. The investigator may change his/her opinion of causality in light of follow-up information, amending the SAE data collection tool accordingly.
9. The causality assessment is one of the criteria used when determining regulatory reporting requirements.

7.4. Reporting Adverse Events and Serious Adverse Events

AE Reporting to GSKCH:

1. AEs will be recorded in the AE section of the eCRF.
2. Medical conditions recorded by the subject on a diary card or similar document that meet the definition of an AE must also be recorded in the AE section of the eCRF, if not previously well-characterized by the investigator in the subject's medical history.
3. AEs elicited by the investigator in a standard manner at the study visits should also be recorded in the AE section of the eCRF. The investigator or designee must ask the subject the following question during each visit including any

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follow-up visits: ***“Have you felt unwell, experienced any symptoms or taken any medication (since your last visit) (today) (since your last dose) (since the last session)?”***

4. The medically qualified investigator should review adverse events in a timely manner; this review should be documented in writing in the source document or in the eCRF.
5. After the study is completed at a given site, and the site has received their study data on Compact Discs (CDs), the electronic data collection tool will be removed from the internet to prevent the entry of new data or changes to existing data.

SAE Reporting to GSKCH:

A paper copy of the SAE form provided in the investigator study master file should be completed as fully as possible.

It is essential to enter the following information:

1. Protocol and subject identifiers
2. Subject's demography
3. Description of events, with diagnosis if available
4. Investigator opinion of relationship to study product (see section 7.3)
5. Criterion for seriousness.

The following are desirable and are of particular relevance for investigator and GSKCH assessment of the SAE report:

1. Date of onset of AE
2. Date AE stopped, if relevant
3. Study product start date
4. Study product end date if relevant
5. Action taken on study product
6. Outcome if known


The SAE form, completed as fully as possible, and SAE fax cover sheet must be faxed or e-mailed to the appropriate GSKCH Study Manager as soon as possible, **but not later than 24 hours** after study site personnel learn of the event. The GSKCH Study Manager should be notified of the situation by telephone or email.

Fax Serious Adverse Events to:

US: PPD

The GSKCH SAE Coordinator will be responsible for forwarding the SAE form to the Case Management Group, Global Clinical Safety and Pharmacovigilance, the Medical Director responsible for the study and other GSKCH personnel as appropriate via email.

Brazil SAE Coordinator (PPD):

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Tel: PPD
 E-mail: PPD
Brazil backup contact (PPD):
 Tel: PPD

The initial report will be followed up with more information as relevant, or as requested by the GSKCH study manager.

7.5. Follow-up of Adverse Events and Serious Adverse Events

Follow-up of AEs and SAEs:

1. After the initial report, the investigator is required to proactively follow up with each subject and provide further information on the subject's condition.
2. All AEs/SAEs will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the subject is lost to follow-up.
3. The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as may be indicated or as requested by GSK to elucidate as fully as possible the nature and/or causality of the AE or SAE.
4. Investigators are not obliged to actively seek AEs or SAEs in former subjects. However, if the investigator learns of any SAE, including the death, at any time after a subject has been discharged from the study, and considers the event reasonably related to the investigational product or study participation, the investigator will promptly notify GSKCH.
5. The investigator will submit any updated SAE data to GSK within the designated reporting time frames.

Regulatory and ethics reporting requirements for SAEs:

1. The investigator will promptly report all SAEs to GSKCH within the designated reporting timeframes (within 24 hours of learning of the event). GSKCH has a legal responsibility to notify, as appropriate, the local regulatory authority and other regulatory authorities about the safety of a product under clinical investigation. Prompt notification of SAEs by the investigator to GSKCH is essential so that legal obligations and ethical responsibilities towards the safety of subjects are met.
2. GSKCH will comply with country specific regulatory requirements relating to safety reporting to the regulatory authority, IEC and investigators.
3. Investigator safety reports are prepared according to GSKCH policy and are forwarded to investigators as necessary. An investigator safety report is prepared for a SAE(s) that is both attributable to investigational product and unexpected. The purpose of the report is to fulfill specific regulatory and GCP requirements, regarding the product under investigation.
4. An investigator who receives an investigator safety report describing a SAE(s) or other specific safety information (e.g., summary of listing of SAEs) from

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GSKCH will file it with the Investigator Brochure (or safety statement) and will notify the IEC, if appropriate according to local requirements.

7.6. Collection of Pregnancy Information

7.6.1. Time Period for Collecting of Pregnancy Information


Collection of Pregnancy Information:

1. Pregnancy information will be collected on all pregnancies reported following administration of any washout product. Information on pregnancy identified during the screening phase and prior to investigational (test product) and washout products administration does not need to be collected.

7.6.2. Action to be Taken if Pregnancy Occurs

Action to be Taken:

1. The investigator will collect pregnancy information on any subject who becomes pregnant while participating in the study after administration of the washout product. The investigator will record pregnancy information on the appropriate form and submit it to GSKCH within 2 weeks of learning of the subject becoming pregnant. The subject will be followed to determine the outcome of the pregnancy. Information on the status of the mother and infant / neonate (including concomitant medications taken by the mother during the pregnancy) will be forwarded to GSKCH. Generally, follow-up will be no longer than 6 to 8 weeks following the estimated delivery date. Any termination of the pregnancy will be reported.
2. While pregnancy itself is not considered to be an AE, any pregnancy complication or elective termination for medical reasons will be recorded as an AE or SAE.
3. A spontaneous abortion is always considered to be an SAE and will be reported as such. An SAE occurring in association with a pregnancy, brought to the investigator's attention after the subject completed the study and considered by the investigator as possibly related to the investigational product, must be promptly forwarded to GSK.
4. While the investigator is not obliged to actively seek this information in former study participants, he or she may learn of an SAE through spontaneous reporting.
5. If the subject becomes pregnant during the study they should be withdrawn from the study and this should be recorded in the appropriate section of the eCRF.

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8. DATA MANAGEMENT

For this study subject data will be entered into an electronic case report form, using a GSKCH validated data system.

8.1. Source Documents/ Data

The source documents (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, at the laboratory and at the medico-technical departments involved in the clinical study) which contain the source of data recorded in the eCRF should be specified in the Source Document Designation Form. In some cases the eCRF can be used as a source document.

Each subject will be assigned and identified by a unique Screening Number. Any reference made to an individual subject within the study must be done using the unique Screening Number.

8.2. Electronic Case Report Form

An eCRF is an electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

For each subject who has given informed consent/assent and has been screened, eCRFs must be completed and signed by the Principal Investigator (or authorized designee) to certify that the data are complete and correct.

Management of clinical data will be performed in accordance with applicable GSKCH standards and data cleaning procedures to ensure the integrity of the data e.g. removing errors and inconsistencies in the data.

In order to protect the privacy of subjects, no Personally Identifiable Information (including the subject's name or initials or birth date) is to be recorded in the eCRF or as part of the query text. Photographs will be collected of subject's who provide their consent to do so. These photographs are considered PII and will be transferred securely to GSK. All photographs will be anonymized.

Adverse events and concomitant medications terms (if applicable) will be coded using MedDRA (Medical Dictionary for Regulatory Activities) and an internal validated medication dictionary, GSKDrug.

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Subject data will be entered into GSKCH defined eCRFs and transmitted electronically to GSKCH in a validated (21 CFR Part 11 compliant) web-based electronic data capture system (InForm™).

All eCRF pages should be completed during a subject self-assessment when the eCRF has been designated as the source. Data that is sourced elsewhere should be entered into the eCRF in an agreed upon timeframe between the Investigator and Sponsor.

The eCRFs (including queries, query responses and audit trails) will be retained by GSKCH. Site data archived compact discs (CD(s)) prepared by a third party will be sent to the investigator to maintain as the investigator copy following the decommissioning of the study.

8.3. Data Handling

Documentation of all data management activities should allow step-by-step retrospective assessment of data quality and study performance. Any changes or corrections to data will be performed in the Electronic Data Capture (EDC) System, and it will include rationale for changes. The EDC system has an audit trail, which will provide a complete record of the changes and corrections endorsed by the Investigator.


8.3.1. Data Queries

Programmed edit checks will be generated automatically, as the data is being entered into the system. Data Management will also run reports and listings on the eCRF data, in addition to the queries already programmed and generated by the system, to raise manual queries as needed for site clarification or correction. The Clinical Dictionary Development and Management Group will raise queries as needed on safety data to code the terms (Adverse Events and Drugs) are reported appropriately.

The study monitor at the study site will review the eCRFs in accordance with the monitoring plan, and any queries will be generated in the EDC System to the Investigator or designee, enabling the errors to be addressed in parallel with Data Management review. Monitor can also run reports and listings on the eCRFs, to raise manual queries as needed for site clarification or correction


8.4. External Data

External Data are subject data obtained externally to the eCRF. These data are generated from laboratory instruments, computers, photographic cameras or other sources and then transcribed into a file and format agreed upon by GSKCH to identify the subject and time point referenced in the eCRF and/or protocol. In this study, VISEA photographs are considered external data.

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An agreed upon quality control process is performed against the transcribed data to the source to ensure the accuracy of the transcription. The transcribed data is transmitted in an agreed upon format to GSKCH via secured web portal or CD via mail carrier with tracking capabilities.

Proper reconciliation will be performed between the transcribed data and the clinical database to ensure subject and time point referenced in the Clinical Database match before Clinical Database Freeze (locking of the database) can occur.

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9. STATISTICAL CONSIDERATIONS AND DATA ANALYSES

9.1 Sample Size Determination

Approximately ~~130~~ **178** healthy females within the ages of 30 and 60 years with Fitzpatrick Skin Classification II-IV and moderate to advanced photo-damaged skin will be screened to randomize ~~80~~ **100** subjects to ensure approximately ~~60~~ **80** subjects (~~30~~ **40** subjects per group) successfully complete the study. The sample size is based on clinical considerations and literature precedent [Narurkar, Schalka, Sulimovic, Kim].

~~With 30 subjects per treatment group, a change from baseline in TEWL at least half the magnitude of the standard deviation (e.g. assume std=4 (ref. CCI [REDACTED]), and 2.1 point mean change from baseline) can be detected at two-sided alpha=0.05 with 80% power.~~


THE FIRST 10 SUBJECTS WERE MIS-ALLOCATED TREATMENT. TO PROTECT THE STATISTICAL POWER OF THE STUDY FOR THE SECONDARY TEWL ENDPOINT, 20 ADDITIONAL SUBJECTS WILL BE RECRUITED INTO THE STUDY. WITH 100 SUBJECTS RANDOMISED, 80 SUBJECTS (40 SUBJECTS PER GROUP) ARE EXPECTED TO COMPLETE THE STUDY.

WITH 40 SUBJECTS PER TREATMENT GROUP WITH 5 SUBJECTS PER GROUP RECEIVING THE INCORRECT TREATMENT DUE TO MIS-ALLOCATION, A WITHIN CHANGE FROM BASELINE IN TEWL OF 1.83 CAN BE DETECTED AT TWO-SIDED ALPHA=0.05 WITH AN SD=4.053 AND 80% POWER.

9.2. General Considerations

9.2.1. Definition of Analysis Populations

All randomized subjects will be included in the intent-to-treat (ITT) population. All subjects with at least one application of product in the test phase (i.e. test product for subjects in Group I or sunscreen for subjects in Group II) will be included in the Safety population.

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Subjects will be considered eligible for a Per Protocol (PP) population if they were randomized, received at least one application of test product, had at least one post-procedure, post-treatment assessment available and were compliant with both test and washout products post-procedure. Other considerations for eligibility for the PP population including but not limited to use of concomitant medications will be detailed in the Statistical Analysis Plan prior to database unblinding.

9.2.2. Exclusion of Data from Analysis

No data will be excluded from any analyses.

9.2.3. Criteria for Evaluation

The primary evaluation of tolerance will be based on the Dermatologist global assessment. The trial will be considered a success if the majority (i.e. more than 50%) of subjects in the test product group have a favorable Dermatologist global assessment score.

9.2.4. Criteria for Assessing Efficacy

Efficacy measurements in this study will be based on changes from baseline in TEWL and Corneometer values at each visit. The baseline for these measurements will be defined as the measurements made 60±15 minutes after the facial peel procedure, before any test product application. Differences between product groups will also be explored.

9.2.5. Criteria for Assessing Local Tolerance

Secondary assessments of local tolerance will be based on Dermatologist and Subject self-assessment scores at each visit and reported adverse events. The baseline for these assessments will be defined as the assessments made 60±15 minutes after the facial peel procedure, before any test product application.

9.2.6. Handling of Dropouts and Missing Data

Missing data will not be imputed. All data available for dropouts will be considered in analyses.

9.3. Statistical Methods and Analytical Plan

Additional details of the proposed statistical analysis will be documented in the statistical analysis plan (SAP), which will be written following finalization of the protocol and prior to study unblinding / analysis (as appropriate).

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9.3.1. Demographic and Baseline Characteristics

Age will be summarized descriptively for each product group using means, medians and standard deviations. Race, gender, Fitzpatrick phototype and Glogau photoaging type will be summarized by product group using frequency counts and percentages.

9.3.2. Primary Analysis(es)

Descriptive statistics (N, %, 95% confidence intervals) will be used to summarize the proportion of subjects in each product group with a favorable Evaluator global assessment of tolerance. The proportions may also be compared between product groups using Chi-square test, and difference in proportion and 95% confidence interval.

9.3.3. Secondary Analysis(es)

Changes from baseline in the Evaluator, Subject self-assessment and instrumental endpoints will be tabulated by product group and summarized descriptively using means, standard deviations and 95% confidence intervals and assessed for significance (different from zero) using t-tests or Wilcoxon signed rank tests dependent upon the distribution of the data.

Differences between product groups in the mean changes from baseline in Evaluator, Subject self-assessment and instrumental endpoints will also be explored using t-tests or Wilcoxon rank sum tests and summarised using 95% confidence intervals.

9.3.4. Safety Analysis(es)

Adverse events will be tabulated by product group and listed for inspection.

10. STUDY GOVERNANCE CONSIDERATIONS

10.1. Posting of Information on Publicly Available Clinical Trials Registers

Study information from this protocol will be posted on publicly available clinical trial registers before enrollment of subjects begins.

10.2. Regulatory and Ethical Considerations, Including the Informed Consent

The study will be conducted in accordance with all applicable regulatory requirements, and with GSK policy.

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The study will also be conducted in accordance with ICH Good Clinical Practice (GCP), all applicable subject privacy requirements, and the guiding principles of the current version of the Declaration of Helsinki. This includes, but is not limited to, the following:

- Before initiating a trial, the investigator/institution should have written and dated approval/favorable opinion from the IEC for the trial protocol (including amendments), written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), investigator brochure/ safety statement (including any updates) and any other written information to be provided to subjects. A letter or certificate of approval will be sent by the investigator to the sponsor prior to initiation of the study, and also when subsequent amendments to the protocol are made.
- Signed informed consent to be obtained for each subject before participation in the study (and for amendments as applicable)
- Investigator reporting requirements (e.g. reporting of AEs/SAEs/protocol deviations to IEC)
- GSK will provide full details of the above procedures, either verbally, in writing, or both.

10.3. Quality Control (Study Monitoring)


In accordance with applicable regulations including GCP, and GSK procedures, GSK or designee (i.e. third party vendor) monitors will contact the site prior to the start of the study to review with the site staff the protocol, study requirements, and their responsibilities to satisfy regulatory, ethical, and GSK requirements.

When reviewing data collection procedures, the discussion will include identification, agreement and documentation of data items for which the eCRF will serve as the source document.

GSK or designee will monitor the study and site activity to verify that the:

- Data are authentic, accurate, and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol and any other study agreements, GCP, and all applicable regulatory requirements.

The extent and nature of monitoring will be described in a written monitoring plan on file at GSKCH. The investigator (or designee) agrees to allow the monitor direct access to all relevant documents and agrees to co-operate with the monitor to ensure that any problems detected in the course of these monitoring visits are resolved.

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10.4. Quality Assurance

To ensure compliance with GCP and all applicable regulatory requirements, GSK may conduct a quality assurance assessment and/or audit of the site records, and the regulatory agencies may conduct a regulatory inspection at any time during or after completion of the study.

In the event of an assessment, audit or inspection, the investigator (and institution) must agree to grant the advisor(s), auditor(s) and inspector(s) direct access to all relevant documents and to allocate their time and the time of their staff to discuss the conduct of the study, any findings/relevant issues and to implement any corrective and/or preventative actions to address any findings/issues identified.

The sponsor will be available to help investigators prepare for an inspection.

10.5. Conditions for Terminating the Study


Upon completion or premature discontinuation of the study, the GSKCH monitor will conduct site closure activities with the investigator or site staff, as appropriate, in accordance with applicable regulations including GCP, and GSKCH Standard Operating Procedures.

Both GSKCH and the Investigator reserve the right to temporarily suspend or prematurely discontinue this study at any time for reasons including, but not limited to, safety or ethical issues or severe non-compliance. For multicenter studies (if applicable), this can occur at one or more or at all sites.

If the trial is prematurely terminated or suspended for any reason, the investigator site should promptly inform the trial subjects and should assure appropriate therapy/follow-up for the subjects. Where required by the applicable regulatory requirements, GSKCH should inform the regulatory authority(ies).

In addition:

1. If the investigator terminates or suspends a trial without prior agreement of GSKCH, the investigator site should promptly inform the sponsor and the IEC, and should provide the sponsor and the IEC a detailed written explanation of the termination or suspension.
2. If the GSKCH terminates or suspends a trial, the investigator should promptly inform the IEC and provide the IEC a detailed written explanation of the termination or suspension.
3. If the IEC terminates or suspends its approval/favorable opinion of a trial, the investigator should promptly notify the GSKCH and provide GSKCH with a detailed written explanation of the termination or suspension.

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10.6. Records Retention

Following closure of the study, the investigator must maintain all site study records (except for those required by local regulations to be maintained elsewhere), in a safe and secure location.

The records (study/ site master file) must be maintained to allow easy and timely retrieval, when needed (e.g., for a GSK audit or regulatory inspection) and must be available for review in conjunction with assessment of the facility, supporting systems, and relevant site staff.


Where permitted by local laws/regulations or institutional policy, some or all of these records can be maintained in a format other than hard copy (e.g., microfiche, scanned, electronic); however, caution needs to be exercised before such action is taken.

The investigator must ensure that all reproductions are legible and are a true and accurate copy of the original and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the investigator must ensure there is an acceptable back-up of these reproductions and that an acceptable quality control process exists for making these reproductions.

The investigator must assure that the subject's anonymity will be maintained. On eCRFs or other documents submitted to GSKCH, subjects should not be identified by their names or initials, but by an identification code. The investigator should keep a separate log of subjects' codes, names and addresses. Documents not for submission to GSKCH, e.g. subjects' written consent forms, should be maintained by the investigator in strict confidence.

GSK will inform the investigator of the time period for retaining these records to comply with all applicable regulatory requirements (GSKCH recommends that documents be kept for 10 years). The investigator is also required to keep subject identification codes on file for at least 15 years after completion or discontinuation of the study. The minimum retention time will meet the strictest standard applicable to that site for the study, as dictated by any institutional requirements or local laws or regulations, GSK standards/procedures, and/or institutional requirements.

No study document should be destroyed without a prior written agreement between GSKCH and the investigator. The investigator must notify GSK of any changes in the archival arrangements, including, but not limited to, archival at an off-site facility or transfer of ownership of the records in the event the investigator is no longer associated with the site.

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10.7. Provision of Study Results to Investigators, posting of Information on Publicly Available Clinical Trials Registers and Publication

Where required by applicable regulatory requirements, an investigator signatory will be identified for the approval of the clinical study report. The investigator will be provided reasonable access to statistical tables, figures, and relevant reports and will have the opportunity to review the complete study results at a GSK site or other mutually-agreeable location.

GSK will also provide the investigator with the full summary of the study results. The investigator is encouraged to share the summary results with the study subjects, as appropriate.

The procedures and timing for public disclosure of the results summary and for development of a manuscript for publication will be in accordance with GSK Policy.

A manuscript will be progressed for publication in the scientific literature if the results provide important scientific or medical knowledge.

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12. APPENDICES


12.1. Appendix 1 - Abbreviations and Trademarks

Abbreviations

AE	Adverse Event
AHA	Alpha Hydroxy Acid
ANVISA	Agência Nacional de Vigilância Sanitária
CD	Compact Disc
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EEMCO	Efficacy Measurement of Cosmetics and Other Topical Products
g	Grams
GA	Glycolic Acid
GCP	Good Clinical Practice
GSKCH	GlaxoSmithKline Consumer Healthcare
h	Hours
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICF	Informed Consent Form
IEC	Independent Ethics Committee
ITT	Intention to Treat
LSLV	Last-Subject, Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
min	Minutes
OTC	Over the Counter
PII	Personally Identifiable Information
PP	Per Protocol
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SPF	Sun Protection Factor
TEWL	Transepidermal Water Loss
TMF	Trial Master File
UV	Ultraviolet

Trademark Information

Trademarks of the GlaxoSmithKline group of companies:
Physiogel
SunMax

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Trademarks not owned by the GlaxoSmithKline group of companies:

Simple

12.2. Appendix 2 - Fitzpatrick Skin Type

Type	Description
I	Always burns, never tans
II	usually burns, tans minimally
III	sometimes mild burn, tans uniformly (cream white; fair with any hair or eye color)
IV	burns minimally, always tans well (moderate brown)
V	very rarely burns, tans very easily (dark brown)
VI	Never burns, never tans (deeply pigmented dark brown to darkest brown)

12.3. Appendix 3 - Glogau Photoaging Scale

Group	Classification	Skin Characteristics
I	Mild	Early Photoaging: mild pigment changes, no keratosis, minimal wrinkles, minimal or no makeup
II	Moderate	Early to Moderate Photoaging: Early brown spots visible, keratosis palpable but not visible, parallel smile lines begin to appear, wears some foundation
III	Advanced	Advanced Photoaging: Obvious discolorations, visible capillaries (telangiectasias), visible keratosis, wears heavier foundation always
IV	Severe	Severe Photoaging: Yellow-gray skin color, prior skin malignancies, wrinkles throughout - no normal skin, cannot wear makeup because it cakes and cracks

12.4. Appendix 4 - Exclusion Criteria for Review at Visit 2 and 3


1. PREGNANCY

Women who are known to be pregnant or who are intending to become pregnant over the duration of the study.

2. BREAST-FEEDING

Women who are breast-feeding.

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3. CONCURRENT MEDICATION/ MEDICAL HISTORY

- A. Active skin disease or open wound in the test area.
- E. Moles, tattoos, scars, irritated skin, hairs, etc. at the test area that could influence the investigation.

9. STUDY MATERIAL SENSITIVITY TEST

A score of “Severe” for any Dermatologist or Subject Self-Assessed endpoint at any time for the study material sensitivity test.

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SIGNATURE PAGE

Protocol 206827 CCI.doc

Date	Signed By
13-Sep-2017 12:38:35	PPD
Justification	Clinical Operations Approval

Date	Signed By
14-Sep-2017 03:52:05	PPD
Justification	Biostatistics Approval

Date	Signed By
15-Sep-2017 09:27:10	PPD
Justification	Approved

Date	Signed By
Justification	

Date	Signed By
Justification	

Date	Signed By
Justification	