In February 2013, GlaxoSmithKline (GSK) announced a commitment to further clinical transparency through the public disclosure of GSK Clinical Study Reports (CSRs) on the GSK Clinical Study Register.

The following guiding principles have been applied to the disclosure:

- *Information will be excluded in order to protect the privacy of patients and all named persons associated with the study*
- *Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information, please see the Patient Level Data section of the* ***GSK Clinical Study Register****.*
- *Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

Synopsis Report Study Number	207235
Study Title	A Human Subject 24 Hour Patch Test to Assess the Irritation Potential of Four Skin Serum Products
Test Products	Experimental Daily Defence Serum CCI Experimental Daily Defence Serum CCI Experimental Daily Defence Serum CCI Experimental Daily Defence Serum CCI
Indication	Dermatology
Phase	N/A
Authors:	
Clinical Research	PPD , MSc.
Biostatistics	PPD , MSc., Pharm.D
Medical Writing Support	MMS Holdings Inc.
Approvers:	
Clinical Operations	PPD , Pharm.D
Biostatistics	PPD , MSc.
Head of Clinical Development, Toxicology and Pre-Clinical Medicine	PPD , PhD

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Study 207235 Synopsis Report

Name of Company:	**GlaxoSmithKline Consumer Healthcare**
Name of Finished Product:	**Experimental Daily Defence Serum**
Name of Active Ingredient:	**N/A**
Title of Study:	**A Human Subject 24 Hour Patch Test to Assess the Irritation Potential of Four Skin Serum Products**
Investigator:	**Dr. Regina M. Doi**
Study Center:	**Azidus Brasil Pesquisa Científica e Desenvolvimento Ltda.** **Rua: General Osório, n° 507** **Bairro: Vila Martina – Valinhos – Sao Paulo – Brazil** PPD
Publication (Reference):	**N/A**
Study Period:	**First Enrollment: 22 May 2017** **Last Completed: 26 May 2017**
Clinical Phase:	**N/A**

Objectives:

Primary Objective

To assess the irritation potential of 4 prototype daily defence serum formulations after 24 (± 2) hours under semi-occlusive patch application to the skin of healthy volunteers.

Secondary Objective

To evaluate the general safety of 4 prototype daily defence serum formulations.

Design/Methodology:

This was an evaluator blind, single site, test site randomized and intra-subject comparison patch test study to evaluate the cutaneous irritation potential of 5 overall treatments (4 experimental daily defence serum formulations and a saline solution as a negative control), under maximized conditions with dermatologist supervision.

At the screening visit (Visit 1), informed consent, demographics, and medical history and concomitant medication information were collected. Visit 2 (Day 1) may have been combined with Visit 1 (screening) but no later than 7 days following Visit 1. All test products were applied via semi-occlusive patches (CCI onto the dorsum (scapular region) skin of healthy subjects for a 24-hour period (Visit 2, Day 1). Subjects left the patches in place until they returned to the site where the patches were removed and the skin assessed for any signs of irritation. Visual evaluations of dermal irritancy were performed by (wherever possible) the same trained assessor 15 to 30 minutes after patch removal (Visit 3, Day 2), and again at 24 (± 2) (Visit 4, Day 3) and 48 (± 2) hours (Visit 5, Day 4) after patch removal. Scores were analyzed to establish the irritation potential of each test product. At all study visits, subjects were asked by a trained technician if there

were any feelings of discomfort since the last visit (for potential adverse event [AE] collection), and also if any medications were taken during that period.

Number of Subjects (Planned and Analyzed):

The subject disposition is summarized in Table 14.1.1. Approximately 40 subjects were planned to be randomized to ensure at least 30 evaluable subjects completed the study. In total, 46 subjects were screened and 40 subjects were randomized. Out of the 6 subjects not randomized, 3 subjects did not meet study criteria and 3 subjects withdrew consent. Thirty-nine (39) subjects completed the study. One (1) subject was lost to follow-up and did not complete the study. All 40 subjects were in the safety population, and 39 subjects were in the intent-to-treat (ITT) population. The ITT population included all subjects who were randomized into the study and had post-baseline skin irritation scores from at least 1 of the test sites available. A by-subject listing of the randomization details for all randomized subjects is provided in Listing 16.1.7. There was 1 protocol deviation reported for the study. Subject PPD appeared outside the window of ± 2 hours for Visit 3 (Listing 16.2.2). This protocol deviation was not deemed to affect the primary endpoint this study.

Main Criteria for Inclusion:

Healthy male and female subjects aged 18 to 65 years, with Fitzpatrick phototype I to IV, intact skin (no dermatological disorders) on the proposed application site (dorsum, scapular region) and no known or suspected intolerance or hypersensitivity to cosmetic products were enrolled in the study.

Test Product, Dose and Mode of Administration:

- Experimental Daily Defence Serum A (Product Formulation Code [MFC]: CCI)
- Experimental Daily Defence Serum C (CCI)
- Experimental Daily Defence Serum G (CCI)
- Experimental Daily Defence Serum N (CCI)

Subjects underwent 1 application of a semi-occlusive patch (adhesive tape) measuring 65 cm^2, containing 6 paper discs of 1.2 cm^2 onto which 0.02 ml/cm^2 each of the 4 experimental daily defence serum formulations and negative control were applied by trained personnel, once, according to the randomization schedule, for 24 (± 2) hours on the dorsum (scapular) region. Only 5 of the 6 discs were used for this study.

Reference Therapy, Dose and Mode of Administration:

Saline solution (Sodium Chloride [$NaCl_{(aq)}$: 0.9%]) was applied to 1 of the patch discs in the patch system.

Duration of Treatment:

Subjects were exposed to a single 24 (± 2) hour dermal application of the 4 experimental daily defence serum formulations and negative control.

Subjects were instructed to keep the patches dry and in place for 24 (± 2) hours. The subjects were asked to return to the study site where the patches were removed and discarded.

Criteria for Evaluation:

The success criteria for this study was defined as no irritation was observed which was attributable to the test products at any time point, or if any observed irritation for the test products, it was not clinically differentiable from the saline solution.

Safety:

The criteria for evaluating safety were AEs and their relation with the study treatment.

Statistical Methods:

The primary evaluation analyses were based on the ITT population (39 subjects). All safety analyses were performed using the safety population (40 subjects). The ITT population was reported as per randomized product whereas the safety population was reported by treatment received. Descriptive statistics (number of subjects, mean, standard deviation [SD], median, minimum and maximum for continuous variables, and frequency and percentage for categorical variables) were provided for demographic and baseline data. All analyses were conducted using Statistical Analysis System® (SAS) Version 9.4. No formal statistical inference was performed.

Primary Analysis:

The primary analysis was based on the irritation scores assessed using the dermal scale described in Table 1-1. Summary statistics were presented by product group for skin irritation scores at 15 to 30 minutes, 24 and 48 hours after patch removal. The number and percentage of subjects recording each category of skin irritation scores were presented. Mean, median, minimum and maximum irritation scores were also presented.

Table 1-1 Skin Irritation Scoring System – Dermal Response

Score	Skin Appearance
0	No evidence of irritation
1	Minimal erythema, barely perceptible
2	Definite erythema, readily visible, or minimal edema, or minimal popular response
3	Erythema and papules
4	Definite edema
5	Erythema, edema, and papules
6	Vesicular eruption
7	Strong reaction spreading beyond test site

Source: Protocol, Appendix 1.1.

Secondary Analysis:

The secondary analysis included effect on superficial layers of the skin as defined in Table 1-2. A combined dermal response and other effect score was derived as the sum of "Dermal Response Score" plus numerical equivalent for the "Other Effect" lettered score. This combined score was also summarized descriptively as the number and percent of subjects reporting/developing each category of score. The "Other Effect" score was summarized descriptively as the number and percent of subjects reporting each category of score.

Table 1-2 Skin Irritation Scoring System – Other Effects

Score (Numeric Equivalent)	Observation
A (0)	Slight glazed appearance
B (1)	Marked glazed appearance
C (2)	Glazing with peeling and cracking
F (3)	Glazing with fissures
G (3)	Film of dried serous exudate covering all or portion of the patch site
H (3)	Small petechial erosions and/or scabs

Source: Protocol, Appendix 1.1.

Safety Analysis:

All AEs were summarized by primary system organ class (SOC) and preferred term (PT).

Treatment-emergent AEs (TEAEs), defined as the AEs reported after study product application, were summarized by the number and percentage of subjects having any AE, and AE in each SOC and PT. All TEAEs were also tabulated by severity. Treatment-emergent AEs suspected of a relationship to study medication were presented in a similar manner. For treatment-emergent, treatment-related AEs, these were also presented by severity when applicable.

Non-fatal serious AEs and AEs causing study treatment discontinuation were listed.

Summary:

Baseline and Demographic Characteristics

Overall subject demographics and baseline characteristics are summarized in Table 14.1.2.1 for the safety population and Table 14.1.2.2 for the ITT population. A total of 40 subjects were included in the safety population; the majority of subjects were female (33, 82.5%), of white – white/Caucasian/European heritage (29, 72.5%), with an overall mean age of 35.7 years (SD = 11.65, range: 18-61 years). Demographic characteristics were similar between safety and ITT populations.

Table 14.1.2.1 presents the baseline Fitzpatrick phototypes for the safety population (Type I: 3 subjects [7.5%]; Type II: 10 subjects [25.0%]; Type III: 16 subjects [40.0%]; Type IV: 11 subjects [27.5%]). Fitzpatrick phototypes were similar in the ITT population (Table 14.1.2.2).

Dermal Response

The frequencies of dermal response score by visit and treatment for the ITT population are presented in Table 1-3. All subjects scored a response of 0, that is there was no evidence of irritation in all subjects in each of the treatment groups (Table 14.2.1.2).

Table 1-3 Frequency of Dermal Response Score by Visit and Treatment - Intent-to-Treat Population

Visit	Score	Serum A (N = 39)	Serum C (N = 39)	Serum G (N = 39)	Serum N (N = 39)	Saline Solution (N = 39)
Visit 3 (15-30 minutes)	No evidence of irritation	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
Visit 4 (24 hours)	No evidence of irritation	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
Visit 5 (48 hours)	No evidence of irritation	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)

Source: Table 14.2.1.1.

Superficial Irritation

The frequencies of superficial irritation (other effects) score by visit and treatment for the ITT population are summarized in Table 1-4. All subjects demonstrated "no effect" for any of the test products and the negative control. The frequencies of combined score by visit and treatment are summarized in Table 14.2.2.2. There were no subjects with combined scores greater than 0.

Table 1-4 Frequency of Superficial Irritation (Other Effects) Score by Visit and Treatment - Intent-to-Treat Population

Visit	Score	Serum A (N = 39)	Serum C (N = 39)	Serum G (N = 39)	Serum N (N = 39)	Saline Solution (N = 39)
Visit 3 (15-30 minutes)	No effect	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
Visit 4 (24 hours)	No effect	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
Visit 5 (48 hours)	No effect	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)

Source: Table 14.2.2.1.

Safety Results:

No AEs were reported within the randomized and non-randomized populations (Listing 16.2.7.1 and Listing 16.2.7.2, respectively). There were no TEAEs reported in the study (Tables 14.3.1.1, 14.3.1.2, 14.3.1.3, and 14.3.1.4). As there were no AEs or serious AEs, no subjects discontinued from the study as the result of serious AEs (Listing 14.3.2.2). No deaths were reported in the study (Listing 14.3.2.1).

Conclusions:

- The primary objective of this study was met as there were no irritation scores observed at any time point for any of the prototype serum formulations.
- All of the prototype serum formulations were generally well-tolerated with no evidence of irritation or other skin effects reported.

Tables, Figures and/or Graphs

Protocol: 207235 Program Run Date: 04JUL2017

Table 14.1.1
Subject Disposition
All Screened Subjects

All Screened Subjects (N=46)

	Overall n	(%)
TOTAL SUBJECTS SCREENED	46	
SUBJECTS NOT RANDOMISED	6	(13.0)
DID NOT MEET STUDY CRITERIA	3	(6.5)
ADVERSE EVENT	0	
LOST TO FOLLOW UP	0	
PROTOCOL VIOLATION	0	
WITHDRAWAL OF CONSENT	3	(6.5)
OTHER	0	
SUBJECTS RANDOMISED	40	
COMPLETED STUDY	39	(97.5)
DID NOT COMPLETE STUDY	1	(2.5)
DID NOT MEET STUDY CRITERIA	0	
ADVERSE EVENT	0	
LOST TO FOLLOW-UP	1	(2.5)
PROTOCOL VIOLATION	0	
WITHDRAWAL OF CONSENT	0	
OTHER	0	
RANDOMISED POPULATION	40	(100.0)
SAFETY POPULATION	40	(100.0)
ITT POPULATION	39	(97.5)

Protocol: 207235 Program Run Date: 07JUL2017

Table 14.1.2.1
Subject Demographics and Baseline Characteristics
Safety Population

Study Population: Safety (N=40)

	Overall (N=40)
SEX n (%)	
MALE	7 (17.5)
FEMALE	33 (82.5)
RACE n (%)	
AFRICAN AMERICAN/AFRICAN HERITAGE	11 (27.5)
AMERICAN INDIAN OR ALASKAN NATIVE	0
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE	0
ASIAN - EAST ASIAN HERITAGE	0
ASIAN - JAPANESE HERITAGE	0
ASIAN - SOUTH EAST ASIAN HERITAGE	0
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0
WHITE - ARABIC/NORTH AFRICAN HERITAGE	0
WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE	29 (72.5)
AGE (YEARS)	
n	40
MEAN	35.7
SD	11.65
MEDIAN	33.5
MINIMUM	18
MAXIMUM	61
FITZPATRICK SCALE FOR SKIN TYPE	
I = ALWAYS BURNS EASILY; NEVER TANS (PALE WHITE SKIN)	3 (7.5)
II = ALWAYS BURNS EASILY; TANS MINIMALLY (WHITE SKIN)	10 (25.0)
III = BURNS MODERATELY; TANS GRADUALLY (LIGHT BROWN SKIN)	16 (40.0)
IV = BURNS MINIMALLY, ALWAYS TANS WELL (MODERATE BROWN SKIN)	11 (27.5)
V = RARELY BURNS, TANS PROFUSELY (DARK BROWN SKIN)	0
VI = NEVER BURNS (DEEPLY PIGMENTED DARK BROWN TO BLACK SKIN)	0

Protocol: 207235 Program Run Date: 04JUL2017

Table 14.1.2.2
Subject Demographics and Baseline Characteristics
Intent to Treat Population

Intent to Treat Population (N=39)

	Overall (N=39)
SEX n (%)	
MALE	6 (15.4)
FEMALE	33 (84.6)
RACE n (%)	
AFRICAN AMERICAN/AFRICAN HERITAGE	11 (28.2)
AMERICAN INDIAN OR ALASKAN NATIVE	0
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE	0
ASIAN - EAST ASIAN HERITAGE	0
ASIAN - JAPANESE HERITAGE	0
ASIAN - SOUTH EAST ASIAN HERITAGE	0
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0
WHITE - ARABIC/NORTH AFRICAN HERITAGE	0
WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE	28 (71.8)
AGE (YEARS)	
n	39
MEAN	36.0
SD	11.62
MEDIAN	35.0
MINIMUM	18
MAXIMUM	61
FITZPATRICK SCALE FOR SKIN TYPE	
I = ALWAYS BURNS EASILY; NEVER TANS (PALE WHITE SKIN)	3 (7.7)
II = ALWAYS BURNS EASILY; TANS MINIMALLY (WHITE SKIN)	10 (25.6)
III = BURNS MODERATELY; TANS GRADUALLY (LIGHT BROWN SKIN)	15 (38.5)
IV = BURNS MINIMALLY, ALWAYS TANS WELL (MODERATE BROWN SKIN)	11 (28.2)
V = RARELY BURNS, TANS PROFUSELY (DARK BROWN SKIN)	0
VI = NEVER BURNS (DEEPLY PIGMENTED DARK BROWN TO BLACK SKIN)	0

Protocol: 207235 Program Run Date: 04JUL2017

Table 14.2.1.1
Frequency of Dermal Response Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population (N=39)

Visit	Score	Serum A (N=39)	Serum C (N=39)	Serum G (N=39)	Serum N (N=39)	Saline Solution (N=39)
VISIT 3 (15-30 min)	MISSING	0	0	0	0	0
	0	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	4	0	0	0	0	0
	5	0	0	0	0	0
	6	0	0	0	0	0
	7	0	0	0	0	0
VISIT 4 (24 hours)	MISSING	0	0	0	0	0
	0	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	4	0	0	0	0	0
	5	0	0	0	0	0
	6	0	0	0	0	0
	7	0	0	0	0	0
VISIT 5 (48 hours)	MISSING	0	0	0	0	0
	0	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
	1	0	0	0	0	0
	2	0	0	0	0	0
	3	0	0	0	0	0
	4	0	0	0	0	0
	5	0	0	0	0	0
	6	0	0	0	0	0
	7	0	0	0	0	0

0 = No evidence of irritation; 1 = Minimal erythema barely perceptible; 2 = Definite erythema, readily visible; minimal edema or minimal popular response; 3 = Erythema and papules;4 = Definite edema; 5 = Erythema, edema and papules; 6 = Vesicular eruption; 7=Strong reaction spreading beyond test site

PPD

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Protocol: 207235 Program Run Date: 07JUL2017

Table 14.2.1.2
Average Dermal Response Score by Visit and Treatment
Intent to Treat Population

Study Population: ITT (N=39)

THERE WERE NO SUBJECTS WITH DERMAL RESPONSE > 0

Protocol: 207235 Program Run Date: 07JUL2017

Table 14.2.2.1
Frequency of Superficial Irritation (other effects) Score by Visit and Treatment
Intent to Treat Population

Study Population: ITT (N=39)

Visit	Score	Serum A (N=39)	Serum C (N=39)	Serum G (N=39)	Serum N (N=39)	Saline Solution (N=39)
VISIT 3 (15-30 min)	NO EFFECT	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
	MISSING	0	0	0	0	0
	GRADE=A/SCORE=0	0	0	0	0	0
	GRADE=B/SCORE=1	0	0	0	0	0
	GRADE=C/SCORE=2	0	0	0	0	0
	GRADE=F/SCORE=3	0	0	0	0	0
	GRADE=G/SCORE=3	0	0	0	0	0
	GRADE=H/SCORE=3	0	0	0	0	0
VISIT 4 (24 hours)	NO EFFECT	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
	MISSING	0	0	0	0	0
	GRADE=A/SCORE=0	0	0	0	0	0
	GRADE=B/SCORE=1	0	0	0	0	0
	GRADE=C/SCORE=2	0	0	0	0	0
	GRADE=F/SCORE=3	0	0	0	0	0
	GRADE=G/SCORE=3	0	0	0	0	0
	GRADE=H/SCORE=3	0	0	0	0	0
VISIT 5 (48 hours)	NO EFFECT	39 (100%)	39 (100%)	39 (100%)	39 (100%)	39 (100%)
	MISSING	0	0	0	0	0
	GRADE=A/SCORE=0	0	0	0	0	0
	GRADE=B/SCORE=1	0	0	0	0	0
	GRADE=C/SCORE=2	0	0	0	0	0
	GRADE=F/SCORE=3	0	0	0	0	0
	GRADE=G/SCORE=3	0	0	0	0	0
	GRADE=H/SCORE=3	0	0	0	0	0

A/0=Slight glazed appearance; B/1=Marked glazed appearance; C/2=Glazing with peeling and cracking; F/3=Glazing with fissures; G/3= Film of dried serous exudate covering all or portion of the patch site; H/3=Small petechial erosions and/or scabs

Protocol: 207235 Program Run Date: 07JUL2017

Table 14.2.2.2
Frequency of Combined Score by Visit and Treatment
Intent to Treat Population

Study Population: ITT (N=39)

THERE WERE NO SUBJECTS WITH COMBINED SCORES > 0

Combined Score: Dermal response Score + "other effect" score(>0)

PPD

Protocol: 207235 Program Run Date: 05JUL2017

Table 14.3.1.1
Treatment Emergent Adverse Events
Safety Population

Study Population: Safety (N=40)

******* No Treatment Emergent AEs Exist *******

n (%) = Number (percent) of subjects; nAE = Number of adverse events.

PPD

Table 14.3.1.2
Treatment Emergent Adverse Events by Severity
Safety Population

Study Population: Safety (N=40)

******* No Treatment Emergent AEs Exist *******

Protocol: 207235 Program Run Date: 07JUL2017

Table 14.3.1.3
Treatment Emergent Treatment Related Adverse Events
Safety Population

Study Population: Safety (N=40)

******* No Treatment Emergent AEs Exist *******

Protocol: 207235 Program Run Date: 07JUL2017

Table 14.3.1.4
Treatment Emergent Treatment Related Adverse Events by Severity
Safety Population

Study Population: Safety (N=40)

******* No Treatment Emergent AEs Exist *******

Study Information

Clinical Protocol 207235

Statistical Analysis Plan for Protocol 207235

Clinical Protocol

207235

CONFIDENTIAL

SUMMARY INFORMATION

Title:	A Human Subject 24 Hour Patch Test to Assess the Irritation Potential of Four Skin Serum Products
Protocol Number:	207235
Sponsor:	GlaxoSmithKline Consumer Healthcare (GSKCH) Rua Hungria, 1240 4º andar, Jardim Europa São Paulo/SP – Brazil, CEP 01455-000 Tel: PPD
Product Name:	Experimental Daily Defense Serum
Development Phase:	N/A

Expert Advice Outside of Normal Working Hours:	Tel: PPD (US)

Key Protocol Authors:	
PRIMARY CONTACT **Clinical Research Scientist:**	PPD MSc GlaxoSmithKline Consumer Healthcare (GSKCH) St. Georges Avenue, Weybridge, Surrey, KT13 0DE. UK Tel. PPD
PRIMARY CONTACT **Clinical Study Manager:**	PPD GlaxoSmithKline Consumer Healthcare (GSKCH) Rua Hungria, 1240 4º andar, Jardim Europa São Paulo/SP – Brazil, CEP 01455-000 Tel: PPD
Biostatistician:	PPD
Other Protocol Authors:	
Clinical Supplies:	PPD
Data Manager:	PPD
Medical Expert:	PPD, MD, Ph.D

Principal Investigator:	Regina M. Doi - Dermatologist
Study Site Name & Address:	AZIDUS BRASIL PESQUISA CIENTÍFICA E DESENVOLVIMENTO LTDA. Rua: General Osório, n° 507 - Bairro: Vila

	Martina - Valinhos – São Paulo – Brazil.
Study Site Telephone Number:	PPD
Study Examiner(s):	Patch assessors will be assigned according to the site schedule (before First Subject First Visit) and documented in the site file.

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 International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Good Clinical Practice (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.

Investigator Name:	
Investigator Qualifications:	
Investigator Signature:	PPD
Date of Signature/ Agreement:	PPD 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 Institutional Review Board (IRB)/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 IRB/ 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.

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. ~~strikethrough~~

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 ☒	Correction to site telephone number. Update to clarify recording of dermal response scores. Clarify the wording for success criteria.	Informed Consent ☐ Yes ☒ No Safety Statement ☐ Yes ☒ No CRF ☐ Yes ☒ No	Summary Information 6.3 Patch Assessments 7.1.1 Events NOT meeting definition of an AE include: Summary/Statistical methods 9.2.3. Criteria for Evaluation	Signature: PPD Date: PPD
Protocol Version No.: 2.0	Substantial/ Major ☐				

Amendment No.: 2	Non-Substantial/Minor ☒	A new formulation code for one of the test products. Clarification of wording	Informed Consent ☐ Yes ☒ No Safety Statement ☒ Yes ☐ No CRF ☐ Yes ☒ No	Product Information 5.1 Study Product 5.5 Packaging and labelling 4.3 Screening/Baseline Failures 6.1.2 Informed Consent	Signature: PPD
Protocol Version No.: 3.0	Substantial/ Major ☐				Date: PPD
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.:	Non-Substantial/Minor ☐		Informed Consent ☐ Yes ☐ No Safety Statement ☐ Yes ☐ No CRF ☐ Yes ☐ No		Signature: PPD
Protocol Version No.:	Substantial/ Major ☐				Date: PPD
Amendment No.:	Non-Substantial/Minor ☐		Informed Consent ☐ Yes ☐ No Safety Statement ☐ Yes ☐ No CRF ☐ Yes ☐ No		Signature: PPD
Protocol Version No.:	Substantial/ Major ☐				Date: PPD

SCHEDULE OF EVENTS

Procedures	Visit 1 Screen	Visit 2 Day 1	Visit 3 Day 2	Visit 4 Day 3	Visit 5 Day 4
Informed consent	X				
Demographics	X				
Medical History	X				
Current/Concomitant Medications reviewed	X	X	X	X	X
Inclusion and Exclusion criteria	X				
Eligibility to participate determined by Investigator (dermatologist)	X				
Continued eligibility		X	X	X	X
Randomisation		X			
Application of patches to test sites		X			
Removal of patches at study site 24 (± 2hrs) after application			X		
Assessment of test sites 15-30 minutes following patch removal at study centre[a]			X		
Assessment of test sites 24 (± 2hrs) following patch removal at study centre[a]				X	
Final assessment of test sites 48 (± 2hrs) following patch removal at study centre[a]					X
Adverse event assessment[b]		X	X	X	X
Study Conclusion					X

a. A trained (by a dermatologist) blinded evaluator will perform assessments of all test sites for symptoms of irritation using the scoring system detailed in Appendix 2.
b. Subjects are asked to report any adverse events from Visit 2 (or Visit 1 if patch application occurs at Visit 1) and the use of any concomitant medications throughout the study.

NOTE: Visit 1 and visit 2 could occur on the same day, but Visit 2 must be within 7 days of Visit 1.

PROTOCOL SYNOPSIS FOR STUDY 207235

Brief Summary

A cosmetic product that is freely available to the consumer must be safe when applied under normal or reasonably foreseeable conditions of use. For this reason, the raw materials used in a product formulation must be raw materials with proven safety and tolerability. As a general requirement the safety and tolerability of a final formulation must be confirmed before it is marketed. (Guideline for the Safety Evaluation of Cosmetic Products; Agência Nacional de Vigilância Sanitária (ANVISA) 2012).

Cutaneous compatibility studies such as patch tests are designed to confirm the absence of irritation and/or sensitization during single or repeated topical application of a cosmetic product to human subjects.

Among the numerous cutaneous methods, patch tests are a well-recognized diagnostic tool (Lachapelle, 2012).This methodology involves occlusive or semi-occlusive application of test product to the skin, ensuring a higher contact between the components of the product formula and the skin.

The objective of this clinical study is to assess the cutaneous irritation potential of four test products under maximized conditions with dermatologist supervision.

Objective(s) and Endpoint(s)

Objective(s)	Endpoint(s)
Primary	
To assess the irritation potential of four prototype daily defense serum formulations after 24 (± 2) hours under semi-occlusive patch application to the skin of healthy volunteers	Trained evaluator assessment of product tolerability through visual assessment of cutaneous irritation 15-30 minutes, 24 +/- 2 and 48 +/-2 hours after patch removal
Secondary	
To evaluate the general safety of four prototype daily defense serum formulations	Frequency and severity of Adverse Events

Study Design

This is an evaluator (single) blind, test site randomized and intra-subject comparison patch test study to evaluate the cutaneous irritation potential of four experimental daily defense serum formulations, including a saline solution as a negative control.

Subjects will be exposed to 24 hour semi-occlusive patch applications of the test products and negative control.

Type and Planned Number of Subjects

Sufficient subjects will be screened such that approximately 40 subjects will be randomized to ensure approximately 30 evaluable subjects complete the entire study.

Diagnosis and Main Criteria for Inclusion

Healthy male and female volunteers aged 18 to 65 with no active dermatological conditions will be enrolled into this study.

Product Information

	Test Product 1	Test Product 2	Test Product 3	Test Product 4	Reference Product 1
Product Name	Experimental Daily Defense Serum A	Experimental Daily Defense Serum C	Experimental Daily Defense Serum G	Experimental Daily Defense Serum N	Saline Solution Sodium Chloride (NaCl; 0.9% $_{aq}$)
Product Formulation Code (MFC)	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	N/A Site to Supply
Dose	0.02ml/cm^2	0.02ml/cm^2	0.02ml/cm^2	0.02ml/cm^2	0.02ml/cm^2
Route of Administration	Topical application via semi occlusive patch	Topical application via semi occlusive patch	Topical application via semi occlusive patch	Topical application via semi occlusive patch	Topical application via semi occlusive patch

Statistical Methods

The primary evaluation will be the irritation scores after patch removal for each of the four test formulations.

The study will be considered a success if no irritation is observed which is attributable to the test product at any time point, or if any observed irritation for the test product is not clinically differentiable from the saline solution

~~The primary outcome for success is that there will be no evidence of irritation observed in the test products at any time point attributable to the product.~~

No formal statistical inference will be performed. Summary statistics will be presented by product group for skin irritation scores at 15-30 mins, 24 and 48 hours after patch removal. These will include mean irritation scores (if any subjects have reported irritation) and the number and percentage of subjects recording each category of skin irritation scores.

Adverse Events (AE) will be tabulated by the sponsor according to the current version of the Medical Dictionary for Regulatory Activities (MedDRA). Frequencies and percentages will be presented overall, for each system organ class, and for each preferred term. Summaries of treatment-emergent AEs, treatment-related AEs, AEs leading to discontinuation, and serious AEs will be completed. For treatment-related AEs, these will also be presented by product group/test site.

1. INTRODUCTION

In recent years the cosmetic industry has grown considerably, along with its concern for the development of safe and effective products. This heightened industry awareness, combined with consumer and regulatory agency requirements have led cosmetic manufacturers to adopt procedures that provide them with a better understanding of the safety and compatibility of their products. This includes the conduct of clinical tests to assess the safety and efficacy of products under supervision of a dermatologist prior to marketing.

A cosmetic product that is freely available to the consumer must be safe when applied under normal or reasonably foreseeable conditions of use (Guideline for the Safety Evaluation of Cosmetic Products; ANVISA, 2012). The raw materials used in the product formulation must be of proven safety with established use in the cosmetic industry, safety and compatibility of the final formulation must also be confirmed before it is marketed.

Skin contact with topical products such as cosmetics may trigger different types of reactions including eczematous, contact dermatitis, urticaria, acne and spots. Contact dermatitis can arise from two mechanisms: primary irritation, through the action of irritant substances; or sensitization, in the presence of an allergenic ingredient (Birmingham, 1965)

Tests to evaluate the irritation and sensitization potential of a product must take into account a number of variables including the components used in the formulation concentration, absorption, amount applied, skin condition, application directions and frequency, as well as any cumulative effects (Dooms-Goossens, 1993).

Primary irritation results from a direct chemical attack on the skin and is characteristically a rapid response, occurring on first contact with the skin. The effect may be limited to the stratum corneum and may result in symptoms such as dryness, flaking, or cracking. Primary irritation may involve deeper penetration, through the epidermis and into the dermis, where the classic inflammatory response takes place with erythema (reddening) and possibly edema (swelling), vesiculation (blistering) or exudation (weeping).

The human patch test is a well-established industry test for assessing primary skin irritation potential. The products are applied via an occlusive or semi-occlusive patch.

This occlusion provides a higher contact between the components of the product formula and the skin.

This clinical study is being performed to assess the primary irritation potential of the four study products. A standard saline solution will also be included as a negative control.

All test products will be applied via semi-occlusive patches onto the dorsum (scapular region) skin of healthy subjects for a 24 hour period. Subjects will leave the patches in place until they return to the site where the patches will be removed and the skin assessed for any signs of irritation. Visual evaluations of dermal irritancy will be performed by (where ever possible) the same trained assessor 15 to 30 minutes after patch removal, and again at 24 (± 2) and 48 (± 2) hours after the patch removal. The scores will be analyzed to establish the irritation potential of each test product.

2. OBJECTIVE(S) AND ENDPOINT(S)

Objective(s)	Endpoint(s)
Primary	
To assess the irritation potential of four prototype daily defense serum formulations after 24 (± 2) hours under semi-occlusive patch application to the skin of healthy volunteers	Trained evaluator assessment of product tolerability through visual assessment of cutaneous irritation 15-30 minutes, 24 +/- 2 and 48 +/-2 hours after patch removal
Secondary	
To evaluate the general safety of four prototype daily defense serum formulations	Frequency and severity of Adverse Events

3. STUDY PLAN

3.1. Study Design

This is an evaluator (single) blind, single site, randomized and intra-subject comparison patch test study to evaluate the cutaneous irritation potential of four experimental daily defense serum formulations, including a saline solution as a negative control.

Subjects will be exposed to 24 hour semi-occlusive patch applications of the test products and negative control. At all study visits, subjects will be asked by a trained

technician if there have been any feelings of discomfort since the last visit, and also if any medication has been taken during this period.

3.2. Subject Restrictions

Lifestyle/ Dietary
During the entire study (Screening – Last Subject Last Visit (LSLV) the following should be avoided: 1. Applying any other product to the test site. 2. Changing any cosmetic habits, including personal hygiene. 3. Changing dietary habits. 4. Getting the patch test site wet: during showers or bathing, in pools or lakes/ocean, sauna (study site to provide instructions on how to shower/bathe throughout the study). 5. Activities that cause excessive sweating. 6. Removing the patches. 7. Wearing tight or restrictive clothing that can remove the patch through friction or cause redness. 8. Exposure to excessive prolonged sunlight and not to undergo artificial tanning or use tanning beds 9. Introducing new products during the study including soap, laundry detergent, or fabric softener.
Medications and Treatments
During the entire study (Screening – LSLV) the following medications and treatments should be avoided: 1. Subjects will be instructed to avoid cosmetics, moisturizers, and other topical product application on the dorsum (back) area for the duration of their time in the study. 2. Having any body aesthetic or dermatological treatments performed. 3. Changing hormone treatment. 4. Changing contraceptive method. 5. Subjects will be instructed to not use the following medications: a) Systemic or topical corticosteroids b) Systemic or topical immunosuppressive drugs c) Systemic or topical antihistamines d) Vitamin A acid and its derivatives e) Non-steroidal anti-inflammatory drugs 6. Concomitant topical treatment at test sites

3.3. Type and Planned Number of Subjects

Healthy male and female volunteers aged 18 to 65 with no dermatological disorders will be enrolled into this study. Subjects with a Fitzpatrick phototype I to IV (Appendix 3) will be recruited to ensure any reactions are clearly visible on subject's skin. A sufficient number of subjects will be screened such that approximately 40 subjects will be randomized to ensure at least 30 evaluable subjects complete the study.

The sample size has been selected to provide descriptive information on the tolerability and safety of the products.

Subjects will be recruited from the site's database.

3.4. Dose Justification

The prerequisite for a patch test is the requirement that the whole test site is covered with the test product, without spreading or overlapping into other test sites. Previous work (Isaksson, 2007) has shown that the optimal dose to fulfil these requirements is 0.02ml/cm^2.

This is a single-dose study; subjects will have a semi-occlusive patch (adhesive tape) measuring 65cm^2, containing paper discs of 1.2cm^2 onto which 0.02ml/cm^2 (Lee, 2007) each of the four experimental daily defense serum formulations and negative control; saline solution (sodium chloride ($NaCl_{aq}$) 0.9%) will be applied by trained personnel, once, according to the randomisation schedule for 24 (± 2) hours on the dorsum (scapular) region.

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 Safety Statement.

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 18 and 65 years inclusive.

3. GENERAL HEALTH
a.) 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. b.) Subjects must have intact skin on the proposed application site; dorsum (scapular region).

4. Skin Type
Fitzpatrick phototype I to IV

5. COMPLIANCE
Agreement to comply with the procedures and requirements of the study and to attend the scheduled assessment visits.

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. Any history of significant dermatological diseases or conditions or medical conditions known to alter skin appearance or physiologic response (e.g. diabetes,) which could, in the opinion of the Investigator, preclude topical application of the investigational products and/or interfere with the evaluation of the test site reaction.

b. Presence of open sores, pimples, or cysts at the application site.

c. Active dermatosis (local or disseminated) that might interfere with the results of the study.

d. Considered immune compromised.

e. History of diseases aggravated or triggered by ultraviolet radiation.

f. Participants with dermatographism.

g. Currently using any medication which in the opinion of the investigator, may affect the evaluation of the study product, or place the subject at undue risk.

h. Use of the following topical or systemic medications: immunosuppressants, antihistamines, non-hormonal anti-inflammatory drugs, and corticosteroids up to 2 weeks before screening visit.

i. Oral or topical treatment with vitamin A acid and/or its derivatives up to 1 month before the screening visit.

j. Intention of being vaccinated during the study period or vaccination within 3 weeks of the screening visit.

k. Currently receiving allergy injections, or due to receive an injection within 7 days prior to Visit 1, or expects to begin injections during study participation

4. ALLERGY/ INTOLERANCE

a. Previous history of atopy, allergic reactions, irritation or intense discomfort feelings to topical-use products, cosmetics or medication.

b. Known or suspected intolerance or hypersensitivity to any of the study materials (or closely related compounds) or any of their stated ingredients,

including any component of the patches.

c. History of sensitization in a previous patch study.

5. CLINICAL STUDY/ EXPERMENTAL 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
a. Recent history (within the last 5 years) of alcohol or other substance abuse.

7. DIAGNOSTIC ASSESSMENTS AND OTHER CRITERIA
a. Intense sunlight exposure or sun tanning sessions up to 30 days before the Screening evaluation. b. Intention of bathing, sauna, water sports, or activities that lead to intense sweating. c. Any Subject who, in the judgment of the Investigator, should not participate in the study. d. Any skin marks on the test site that might interfere with the evaluation of possible skin reactions (e.g. pigmentation disorders, vascular malformations, scars, tattoos, excessive hair, numerous freckles). e. Prisoner or involuntary incarcerated subject. f. Subject from an indigenous tribe.

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

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. Re-screening of subjects **CONSIDERED PREVIOUS SCREEN FAILURES** 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, behavioral 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 (CRF). 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:

a) The site must attempt to contact the subject and re-schedule the missed visit as soon as possible.
b) 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.
c) 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.
d) 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.

5. PRODUCT INFORMATION

5.1. Study Product

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

	Test Product 1	Test Product 2	Test Product 3	Test Product 4	Reference Product 1
Product Name	Experimental Daily Defense Serum A	Experimental Daily Defense Serum C	Experimental Daily Defense Serum G	Experimental Daily Defense Serum N	Saline Solution Sodium Chloride ($NaCl_{aq}$; 0.9%)
Product Formulation Code (MFC)	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	N/A Site to supply
Dose	0.02ml/cm^2	0.02ml/cm^2	0.02ml/cm^2	0.02ml/cm^2	0.02ml/cm^2
Route of Administration	Topical application via semi occlusive patch	Topical application via semi occlusive patch	Topical application via semi occlusive patch	Topical application via semi occlusive patch	Topical application via semi occlusive patch

5.2. Dose Schedule

Subjects will be exposed to a 24 ± 2 hour dermal application of the four experimental daily defense serum formulations and negative control. Patches will be applied by trained staff at the study site.

Subjects will be instructed to keep the patches dry and in place for 24 ± 2 hours. The subjects will be asked to return to the clinic where the patches will be removed and discarded. Upon removal of the patches, the subjects will be asked to wait in the clinic for assessments to be made 15-30 minutes post patch removal. Subjects will then return to the clinic for two additional assessments at 24 ± 2 and 48 ± 2 hours after patch removal.

The study products will be applied to discs (or cells) of the patch test adhesive tape. The number of cells available on the patch test tape is 6 (but only 5 cells will be used).

5.3. 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.

5.4. Product Assignment

Each subject will have all 4 test products and the negative control applied to their backs (dorsum region). The location for each study product application for each subject will be assigned in accordance with the randomization schedule generated by the Biostatistics Department, GSKCH, prior to the start of the study, using validated internal software.

5.4.1 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. The randomization number will be associated with the random location assignment of product to test site.

5.4.2 Blinding

The study statistician and other employees of the Sponsor who may influence study outcomes are blinded to the product allocation/test site location. Investigators dispensing the product will be aware of each product's location and must not divulge information to the study staff or assessors. The assessor performing the assessment of irritation will be blinded to the product allocation.

5.4.3 Code Breaks

The blind must only be broken in an emergency where it is essential to know where each product was applied on a subject 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.

5.5. Packaging and Labelling

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.

The Experimental daily defence serums [redacted] will be supplied in pump packs with a study label affixed by the Sponsor. Each study label will contain, but not be limited to, protocol number, product code letter and directions for storage.

The investigator or designee will supply the saline solution (Reference Product 1) with a study label affixed. Each study label will contain the information according to the site specific internal requirements.

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.

5.5.1. Accountability of Product

All products supplied are for use only in this clinical study and should not be used for any other purpose. Products are only to be used and applied by the study site technician.

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:

- The identification of the subject to whom the study product was dispensed.

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 should not be destroyed without prior written authorization by the Sponsor. When destruction of the study products takes place a dated certificate of, or receipt for destruction, will be provided to the Sponsor.

5.5.2. Storage of Product

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

6. STUDY ASSESSMENTS AND PROCEDURES

This section lists the procedures and parameters of each planned study assessment/Visit. The exact timing of each assessment 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 Visit

6.1.1 Telephone Screening

Prior to the screening visit, telephone screening of interested subjects may be conducted using a telephone script. This will be conducted by the site recruitment staff or designee. Subjects who successfully complete the telephone screening will be scheduled for the Screening Visit. At the Screening Visit, the following procedures will be completed:

6.1.2 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~~ **SIGNED AND DATED** 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 after the subject has signed. The subject will be provided with a copy of their signed and dated consent form and any other written information which they are be instructed to retain.

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 CRF.

After signing the Informed Consent Form (ICF), subjects will undergo all the screening assessments to confirm that they meet all the inclusion criteria and none of the exclusion criteria. If the subject is considered eligible by the Investigator (or designee) to participate they are considered enrolled in the study.

6.1.3 Demographics

The following demographic parameters will be captured by the Investigator or designee and recorded on the CRF: Fitzpatrick skin type scale, year of birth, gender and race.

6.1.4 Medical History and Concomitant Medication

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

6.2 Visit 2 (Day 1), Visit 3 (Day 2) and Visit 4 (Day 3)

Visit 2 may be combined with Visit 1 (Screening) but should be no more than 7 days following Visit 1.

At Visit 2 any concomitant therapy taken will be reviewed, and continued eligibility will be checked before product application (and randomisation of product application ordering). This will be reviewed again before each subsequent visit.

6.2.1 Application of patches

Test products and control (0.02ml/cm^{2}of each product) will be applied to a 1.2cm^2 paper disc (or cell) contained within an adhesive patch (measuring 65cm^2). The number of cells available on the patch test tape is 6 (but only 5 cells will be used). The patch is then applied onto the dorsum (scapula region) of each subject for a period of 24 ± 2 hours, the sequence of the product application to the cells will be according to the randomization schedule.

Patch assessments will be performed at Visit 3, 4 and 5 per section 6.3.

6.3 Patch Assessments

Experienced trained assessor (s) will assess all patch sites for the duration of the study according to the scoring scale in Appendix 2. Where ever possible the same experienced trained assessor will perform all skin assessments for a given subject at each time point; 15-30 minutes post patch removal (Visit 3, Day 2) in addition to 24 ± 2 (Visit 4, Day 3) and 48 ± 2 hours (Visit 5, Day 4) post patch removal. Patch sites will be graded using a magnifying glass with a fluorescent daylight lamp. The assessor will be blinded to the treatment allocation.

The results will be presented as individual responses to each test product at each assessment time point.

In any case of a positive reaction a dermatologist will be available to perform secondary assessments and grade the response with any further action as needed. This should occur the same day as the initial assessment performed by the trained assessor.

The intensity of any visual signs of irritation will be recorded by the trained examiner, according to the quantity and grade of the reactions (Appendix 2) according to the skin appearance (Scale 1) and other features indicative of irritation (Scale 2) observed. The trained examiner is responsible for grading the reactions, and the trained examiner's opinion on the interpretation of the results is final.

Any observed response which can be denoted using the irritation criteria summarized in Appendix 2, will not be considered an adverse event. In addition any tape-related irritation will also not be noted as an AE. Only in case of unusual reactions, these reactions and the consequences upon the evaluation of the respective test areas will be documented as AE's.

All responses will be reviewed in context of the grading scale in this protocol (Appendix 2).

6.4 Visit 5 (Day 4) Study Conclusion

Final review of any concomitant therapy taken adverse events experienced since the last visit and continued eligibility will be performed before final patch assessment (48 ± 2 hours) as per Section 6.3.

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 CRF 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

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:
An AE is any untoward medical occurrence in a patient 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. 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:
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.

Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.

New condition(s) detected or diagnosed after study product administration even though it may have been present prior to the start of the study.

Signs, symptoms, or the clinical sequelae of a suspected interaction.

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:

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.

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..

Medical or surgical procedure (e.g., endoscopy, appendectomy): the condition that leads to the procedure is an AE.

Situations where an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).

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.

Any observed response which can be denoted using the irritation criteria summarized in Appendix 2, will not be considered an adverse event. In addition any tape-related irritation will also not be noted as an AE. Only in case of unusual reactions, these reactions and the consequences upon the evaluation of the respective test areas will be documented as AE's.

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-patient 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 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 considered serious. 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:

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

The investigator or site staff will then record all relevant information regarding an AE/SAE in the CRF.

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.

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).

AEs will be collected from the start of the product application and until **5** days following last administration of the study product.

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.

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:

Mild: An event that is easily tolerated by the subject, causing minimal discomfort

and not interfering with everyday activities.

Moderate: An event that is sufficiently discomforting to interfere with normal everyday activities

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:

The investigator is obligated to assess the relationship between study product and the occurrence of each AE/SAE.

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.

The investigator will use clinical judgment to determine the relationship.

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.

The investigator will also consult the Investigator Brochure (IB) and/or Product Information, for marketed products, in the determination of his/her assessment.

For each AE/SAE the investigator **must** document in the medical notes (source document) or CRF that he/she has reviewed the AE/SAE and has provided an assessment of causality.

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.**

The investigator may change his/her opinion of causality in light of follow-up

information, amending the SAE data collection tool accordingly.

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:

AEs will be recorded in the AE section of the CRF.

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 CRF, if not previously well-characterized by the investigator in the subject's medical history.

AEs elicited by the investigator in a standard manner at the study visits should also be recorded in the AE section of the CRF. The investigator or designee must ask the subject the following question during each visit including any 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)?"

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 CRF.

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
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 SAE Coordinator as soon as possible, **but not later than 24 hours** after study site personnel learn of the event. The SAE Coordinator should be notified of the situation by telephone or email.

Brazil SAE Coordinator (PPD):
Tel: PPD
E-mail: PPD

Brazil backup contact (PPD):
Tel: PPD

The 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.

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:

After the initial report, the investigator is required to proactively follow up with each subject and provide further information on the subject's condition.

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.

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.

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.

The investigator will submit any updated AE or SAE data to GSK within the designated reporting time frames.

Regulatory and ethics reporting requirements for SAEs:

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.

GSKCH will comply with country specific regulatory requirements relating to safety reporting to the regulatory authority, IRB/IEC and investigators.

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.

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 GSKCH will file it with the Investigator Brochure (or safety statement) and will notify the IRB or 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:

Pregnancy information will be collected on all pregnancies reported following administration of any investigational product.

Information on pregnancy identified during the screening phase and prior to

investigational product administration does not need to be collected.

7.6.2. Action to be Taken if Pregnancy Occurs

Action to be Taken:
The investigator will collect pregnancy information on any subject who becomes pregnant while participating in the study after administration of the investigational 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. 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. 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. 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. 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 CRF

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 CRF should be specified in the Source Document Designation Form. In some cases the printed CRF 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

A CRF is a printed, optical, or 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, CRF 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 (PII) (including the subject's name or initials or birth date (day and month)) is to be recorded in the CRF or as part of the query text.

Adverse events and concomitant medications terms (if applicable) will be coded by the sponsor using MedDRA and an internal validated medication dictionary, GSKDrug.

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

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

The CRFs (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.

Protocol deviations are any changes or discrepancies from the protocol that have not been approved by IRB. Protocol procedures should be fully followed, taking appropriate action to prevent any deviations from protocol. However, in case of intercurrences, it is up to the Investigator to analyze the occurrence, as well as the measures that should be taken for the incident.

Any deviation from the plan of this protocol should be described and justified in the final report and submitted to the IRB

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 CRF 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) and report appropriately.

The study monitor at the study site will review the CRFs 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 CRFs, to raise manual queries as needed for site clarification or correction.

9. STATISTICAL CONSIDERATIONS AND DATA ANALYSES

9.1. Sample Size Determination

The primary evaluation will be irritation scores after patch removal for each test product at each assessment

No statistical analyses will be performed in this study. The number of subjects to be assessed (N=30 completing the study) was based on clinical considerations.

9.2. General Considerations

9.2.1. Definition of Analysis Populations

The 'Intent to treat' (ITT) population includes all subjects who are randomised into the study and have skin irritation scores from at least one of the test sites available.

Since this is a study to evaluate safety and tolerability, a separate Per Protocol (PP) analysis will not be performed. Protocol deviations will however be listed for review.

The Safety population includes all subjects who received any of the test products. All safety analyses will be performed using the Safety population.

9.2.2. Exclusion of Data from Analysis

No data will be excluded from any analysis.

9.2.3. Criteria for Evaluation

The primary objective will be to assess the skin irritation potential of the test formulations, based on the irritancy score after patch removal. ~~The study will be considered a success if no irritation is observed which is attributable to the test product at any time point.~~ **The study will be considered a success if no irritation is observed which is attributable to the test product at any time point, or if any observed irritation for the test product is not clinically differentiable from the saline solution**

Safety and tolerability will be evaluated by adverse events assessments.

9.2.4. Handling of Dropouts and Missing Data

Missing data will not be replaced or imputed. Dropouts will be included in analyses up to the point of discontinuation.

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).

9.3.1. Demographic and Baseline Characteristics

Age will be summarized descriptively using means, medians and standard deviations. Gender, race, and Fitzpatrick skin type will be summarized using frequency counts and percentages.

9.3.2. Primary Analysis(es)

The primary analysis will be based on the irritation scores assessed using the dermal scale described in Scale 1 of Appendix 2. No formal statistical inference will be performed. Summary statistics will be presented by product group for skin irritation scores at 15-30 mins, 24 and 48 hours after patch removal. This will include mean irritation scores (if any subjects have reported/developed irritation) and the number and percentage of subjects recording each category of skin irritation scores.

9.3.3. Secondary Analysis(es)

Other skin effects, if manifest, will be assessed using the scale described in Scale 2 of Appendix 2. These effects will be summarized descriptively as the number and percent of subjects reporting each category of score. A combined dermal and other effects score will also be derived as the sum of these 2 scores. This combined score will also be summarized descriptively as the number and percent of subjects reporting/developing each category of score.

9.3.4. Safety Analysis(es)

Adverse Events (AE) will be tabulated according to the current version of the MedDRA. Frequencies and percentages will be presented overall, for each system organ class, and for each preferred term. Summaries of treatment-emergent AEs, treatment-related AEs, AEs leading to discontinuation, and serious AEs will be

completed. For treatment-related AEs, these will also be presented by product group/test site.

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 (Resolution nº 466 de 12 December 2012), and with GSK policy.

The study will also be conducted in accordance with ICH GCP and all applicable subject privacy requirements. This includes, but is not limited to, the following:

1. Before initiating a trial, the investigator/institution should have written and dated approval/favorable opinion from the IRB/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.
2. Signed informed consent to be obtained for each subject before participation in the study (and for amendments as applicable)
3. Investigator reporting requirements (e.g. reporting of AEs/SAEs/protocol deviations to IRB/IEC)
4. GSK will provide full details of the above procedures, either verbally, in writing, or both.

The informed consent will also contain the following: As with any other product, this product may cause unexpected reactions, such as “redness”, “swelling”, “itching”, and “burning sensation” in the application site. However, all adverse reactions caused by the test product will be followed by a dermatologist until their resolution and appropriate medication will be provided if necessary. As A benefit for participating in

the study, subjects will be examined before the beginning of the study by an expert physician and, if any problem is identified in the relevant site, they will be notified and advised. Subjects may also learn about their correct skin tone/type (phototype) based on the procedures followed.

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 CRF will serve as the source document.

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

1. Data are authentic, accurate, and complete.
2. Safety and rights of subjects are being protected.
3. 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.

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 IRB/IEC, and should provide the sponsor and the IRB/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 IRB/IEC and provide the IRB/IEC a detailed written explanation of the termination or suspension.
3. If the IRB/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.

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 CRFs 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.

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.

11. REFERENCES

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12. APPENDICES

12.1. Appendix 1 - Abbreviations and Trademarks

Abbreviations

AE	Adverse Event
ANVISA	Agência Nacional de Vigilância Sanitária
aq	Aqueous
CD	Compact Disc
CRF	Case Report Form
EDC	Electronic Data Capture
FSFV	First Subject First Visit
GCP	Good Clinical Practice
GSK	GlaxoSmithKline
GSKCH	GlaxoSmithKline Consumer Healthcare
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
ICF	Informed Consent Form
IRB	Institutional Review Board
ITT	Intention to Treat
LSLV	Last Subject Last Visit
MedDRA	Medical Dictionary for Regulatory Activities
PII	Personally Identifiable Information
PP	Per Protocol
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan

12.2. Appendix 2 – Skin Irritation Scoring System

Scale 1: Dermal Response

Score	Skin Appearance
0	No evidence of irritation
1	Minimal erythema, barely perceptible
2	Definite erythema, readily visible; minimal edema or minimal papular response
3	Erythema and papules
4	Definite edema
5	Erythema, edema and papules
6	Vesicular eruption
7	Strong reaction spreading beyond test site

Effects on superficial layers of the skin should be recorded as follows:

Scale 2: Other Effects

Score (Numeric equivalent)	Observation
A (0)	Slight glazed appearance
B (1)	Marked glazed appearance
C (2)	Glazing with peeling and cracking
F (3)	Glazing with fissures
G (3)	Film of dried serous exudate covering all or portion of the patch site
H (3)	Small petechial erosions and/or scabs

When an "Other Effects" score is observed, each score should be reported as a number and letter combination score and also as a numerical total (i.e. numerical "Dermal Response" score + numeric equivalent for the "Other Effects" lettered score).

A "Strong" reaction to the test patch is defined as a 'dermal response' score of 3-7 or any dermal score combined with 'other effects' rating of 4.

12.3. Appendix 3 - Fitzpatrick Skin Type Grading

The Fitzpatrick scale is a numerical classification that is widely used by dermatologists to classify a person's skin type by their response to sun exposure (Fitzpatrick, 1988).

Skin Type	Sunburn and Tanning History
I	Always burns easily; never tans (pale white skin)
II	Always burns easily; tans minimally (white skin)
III	Burns moderately; tans gradually (light brown skin)
IV	Burns minimally, always tans well (moderate brown skin)
V	Rarely burns, tans profusely (dark brown skin)
VI	Never burns (deeply pigmented dark brown to black skin)

SIGNATURE PAGE

207235 Clinical Protocol

Date	Signed By
06-Mar-2017 10:58:05	PPD
Justification	Approved

Date	Signed By
07-Mar-2017 03:12:13	PPD
Justification	Approved

Date	Signed By
07-Mar-2017 06:38:57	PPD
Justification	Clinical Operations Approval

Date	Signed By
07-Mar-2017 08:35:16	PPD
Justification	Biostatistics Approval

Date	Signed By
Justification	

Date	Signed By
Justification	

CONFIDENTIAL

STATISTICAL ANALYSIS PLAN FOR PROTOCOL 207235

A Human Subject 24 Hour Patch Test to Assess the
Irritation Potential of Four Skin Serum Products

BIOSTATISTICS DEPARTMENT
GLAXOSMITHKLINE CONSUMER HEALTHCARE

Document type:	Statistical Analysis Plan
Authors:	PPD (Principal Statistician)
Document status:	Final 1.0
Release date:	31-May-2017

Table of contents

The purpose of this Statistical Analysis Plan (SAP) is to describe the planned analyses and output to be included in the Clinical Study Report for Clinical Study Protocol (CSP) 207235. This SAP will be finalized prior to database freeze and treatment code un-blinding.

1 Study details

A cosmetic product that is freely available to the consumer must be safe when applied under normal or reasonably foreseeable conditions of use. For this reason, the raw materials used in a product formulation must be raw materials with proven safety and tolerability. As a general requirement the safety and tolerability of a final formulation must be confirmed before it is marketed. (Guideline for the Safety Evaluation of Cosmetic Products; Agência Nacional de Vigilância Sanitária (ANVISA) 2012).

Skin contact with topical products such as cosmetics may trigger different types of reactions including eczematous, contact dermatitis, urticaria, acne and spots. Contact dermatitis can arise from two mechanisms: primary irritation, through the action of irritant substances; or sensitization, in the presence of an allergenic ingredient (Birmingham, 1965).

Tests to evaluate the irritation and sensitization potential of a product must take into account a number of variables including the components used in the formulation concentration, absorption, amount applied, skin condition, application directions and frequency, as well as any cumulative effects (Dooms-Goossens, 1993).

Primary irritation results from a direct chemical attack on the skin and is characteristically a rapid response, occurring on first contact with the skin. The effect may be limited to the stratum corneum and may result in symptoms such as dryness,flaking, or cracking. Primary irritation may involve deeper penetration, through the epidermis and into the dermis, where the classic inflammatory response takes place with erythema (reddening) and possibly edema (swelling), vesiculation (blistering) or exudation (weeping).

The human patch test is a well-established industry test for assessing primary skin irritation potential. The products are applied via an occlusive or semi-occlusive patch.

This occlusion provides a higher contact between the components of the product formula and the skin.

This clinical study is being performed to assess the primary irritation potential of the four study products. A standard saline solution will also be included as a negative control.

The study will be considered a success if no irritation is observed which is attributable to the test product at any time point, or if any observed irritation for the test product is not clinically differentiable from the saline solution.

General safety and tolerability will be assessed based on the frequency and severity of Adverse Events (AEs).

1.1 Study design

This is an evaluator (single) blind, single site, randomized and intra-subject comparison patch test study to evaluate the cutaneous irritation potential of four experimental daily defense serum formulations, including a saline solution as a negative control.

Subjects will be exposed to 24 hour semi-occlusive patch applications of the test products and negative control. At all study visits, subjects will be asked by a trained technician if there have been any feelings of discomfort since the last visit, and also if any medication has been taken during this period.

1.2 Study objectives

Objectives	Endpoints
Primary Objective	**Primary Endpoint**
To assess the irritation potential of four prototype daily defense serum formulations after 24 (± 2) hours under semi-occlusive patch application to the skin of healthy volunteers.	Trained evaluator assessment of product tolerability through visual assessment of cutaneous irritation 15-30 minutes, 24 +/- 2 and 48 +/-2 hours after patch removal.
Secondary Objectives	**Secondary Endpoints**
To evaluate the general safety of four prototype daily defense serum formulations.	Frequency and severity of Adverse Events.

1.3 Treatments

	Test product 1	Test product 2	Test product 3	Test Product 4	Reference product
Product Name	Experimental Daily Defense Serum A	Experimental Daily Defense Serum C	Experimental Daily Defense Serum G	Experimental Daily Defense Serum N	Saline Solution Sodium Chloride ($NaCl_{aq}$; 0.9%)
Product Formulation Code (MFC)	CCI	CCI	CCI	CCI	N/A

	Test product 1	Test product 2	Test product 3	Test Product 4	Reference product
Dose	$0.02ml/cm^2$				
Route of Administration	Topical application via semi occlusive patch				

1.4 Timepoints and visit windows

Deviations from the scheduled assessment times should be avoided or kept to a minimum as possible. The following are the assessment time windows.

Visit	Activity	Time window
Visit 3 (Day2)	Patch Removal	24 (± 2hrs) after application on Day 1
	Test Site Assessment	15~30 mins after patch removal
Visit 4 (Day3)	Test Site Assessment	24 (± 2hrs) after patch removal on Day 2
Visit 5 (Day4)	Test Site Assessment	48 (± 2hrs) after patch removal on Day 2

2 Data analysis

Data analysis will be performed by inVentiv Health Clinical. Prior to database hard lock a Blind Data Review Meeting (BDRM) will be conducted in which various aspects of the trial will be discussed and agreed. The statistical analysis software used will be SAS® version 9.4.

Expect as described below, all listings will be produced for all randomised subjects.

2.1 Populations for analysis

2.1.1 Subject disposition

Screen failures will be defined as subjects who do not satisfy all the inclusion/exclusion criteria. A summary will be provided of the number of subjects screened and the number of screen failures with reasons why subjects were not randomised.

Subject disposition will be summarized as the number and percentage of subjects (out of the number of randomised subjects) who complete the study, with the number who discontinue broken down by reason for discontinuation (Table 14.1.1). The table will also summarize the number and percent of subjects assigned to each analysis population (refer to section 2.1.3).

2.1.2 Protocol violations

Protocol violations will be tracked by the study team throughout the conduct of the study. All violations will be reviewed prior to un-blinding and closure of the database to ensure all important violations are captured and categorised.

Major violations will be defined in the "Review Listing Requirement (RLR)" document.

A list of protocol deviations will be provided (Listing 16.2.2).

2.1.3 Analysis populations

Four populations are defined below.

Population	Definition / Criteria	Analyses Evaluated
All Screened Subjects	• All subjects those who are screened	• Disposition
Randomised	• All subjects who are randomised and may or may not receive the application of the study products.	• Protocol deviations
Safety	• Safety population includes all subjects who are randomised and receive any application of the study products.	• Safety analysis
Intent-to-Treat (ITT)	• The 'Intent to treat' (ITT) population includes all subjects who are randomised and have skin irritation scores from at least one of the test sites available.	• Irritation analysis

2.1.4 Subgroups/Stratifications

Not applicable.

2.1.5 Centers pools

Not applicable.

2.2 Patient demographics/other baseline characteristics

Demographic and Baseline characteristics summaries will be produced for the safety and ITT populations.

2.2.1 Demographic characteristics

Categorical demographic variables include gender, race and Fitzpatrick score. These variables will be summarized by the number and percentage of subjects with each relevant characteristic (Table 14.1.2.1 for safety, Table 14.1.2.2 for ITT). Age will be summarized by the mean, standard deviation, median, minimum and maximum values.

The Fitzpatrick scale is a numerical classification that is widely used by dermatologists to classify a person's skin type by their response to the sun exposure (Fitzpatrick, 1988).

Table 1: Fitzpatrick Scale For The Assessment Of Skin Type

Skin Type	Sunburn and Tanning History

Skin Type	Sunburn and Tanning History
I	Always burns easily; never tans (pale white skin)
II	Always burns easily; tans minimally (white skin)
III	Burns moderately; tans gradually (light brown skin)
IV	Burns minimally, always tans well (moderate brown skin)
V	Rarely burns, tans profusely (dark brown skin)
VI	Never burns (deeply pigmented dark brown to black skin)

2.2.2 General medical history

Medical history data will not be presented in the study report. A data listing will be produced for evaluation of protocol violations only at the blinded data review stage.

2.2.3 Characteristics of Disease

Not applicable.

2.3 Treatments (study drug, rescue medication, other concomitant therapies, compliance)

Not applicable.

2.3.1 Study Product/drug Compliance and Exposure

Any protocol deviation associated with treatment applications or patch adherence will be listed at the blinded data review stage.

2.3.2 Concomitant medication

Concomitant medication/non-drug treatments data will not be presented in the study report. A data listing will be produced for evaluation of protocol violations only at the blinded data review stage.

2.4 Analysis of skin irritation

2.4.1 Primary endpoint

2.4.1.1 Primary skin irritation endpoint definition

The primary analysis will be based on the irritation scores assessed using the dermal scale described below.

Table 2: Skin Irritation Scoring System − Dermal Response

Score	Skin Appearance
0	No evidence of irritation
1	Minimal erythema; barely perceptible
2	Definite erythema; readily visible; or minimal edema; or minimal popular response
3	Erythema and papules
4	Definite edema
5	Erythema, edema, and papules
6	Vesicular eruption
7	Strong reaction spreading beyond test site

Summary statistics will be presented by product group for skin irritation scores at 15-30 mins, 24 and 48 hours after patch removal. Number and percentage of subjects recording each category of skin irritation score will be presented in Table 14.2.1.1. Mean, median, min and max irritation scores will be presented in Table 14.2.1.2.

2.4.1.2 Statistical hypothesis, model, and method of analysis

Not applicable. No formal statistical inference will be performed.

2.4.2 Secondary skin irritation endpoint

2.4.2.1 Secondary skin irritation endpoint definition and analysis

Secondary analysis will include effect on superficial layers of the skin as defined below.

Table 3: Skin Irritation Scoring System – Other Effects

Score (Numeric equivalent)	Observation
A (0)	Slight glazed appearance
B (1)	Marked glazed appearance
C (2)	Glazing with peeling and cracking
F (3)	Glazing with fissures
G (3)	Film of dried serous exudate covering all or portion of the patch site
H (3)	Small petechial erosions and/or scabs

A combined dermal response and other effect score will be derived as the sum of Dermal Response Score plus numerical equivalent for the "Other Effect" lettered score. As an example, if dermal response score=3 and superficial irritation letter ="C" then the combined score will be 3 + 2 = 5. This combined score will also be summarized descriptively as the number and percent of subjects reporting/developing each category of score (Table 14.2.2.1).

"Other effect" score will be summarized descriptively as the number and percent of subjects reporting each category of score (Table 14.2.2.2).

2.4.3 Handling of missing values/censoring/discontinuations

Missing data will not be replaced or imputed. Dropouts will be included in analyses up to the point of discontinuation.

2.5 Analysis of secondary objectives

Not applicable.

2.6 Safety

2.6.1.1 Adverse events and Serious Adverse Events

All adverse events (AEs) will be summarised by primary system organ class and preferred term.

Treatment emergent adverse events (TEAEs), defined as the AEs reported after study product application, will be summarized by the number and percentage of subjects having any adverse event, an adverse event in each System Organ Class, and each individual adverse event (Table 14.3.1.1). All TEAEs will also be tabulated by severity (Table 14.3.1.2). Treatment-emergent AEs suspected of a relationship to study medication and those causing study discontinuation will be presented in a similar manner (Table 14.3.1.3). For treatment emergent-related AEs, these will also be presented by severity, if applicable (Table 14.3.1.4).

Deaths occurring during treatment (if any) will be listed (Listing 14.3.2.1) by treatment, including the date and study day of death, and the principal cause of death. Non-fatal serious adverse events and adverse events causing study treatment discontinuation will be listed (Listing 14.3.2.2).

All AEs will be listed in the Listing 16.2.7.1 and Listing 16.2.7.2.

2.7 Analysis of other variables

Not applicable.

2.8 Interim analysis

No interim analysis is planned.

2.9 Sample size calculation

No statistical analyses will be performed in this study. Approximately 40 subjects will be randomized to ensure at least 30 evaluable subjects complete the study. The number of subjects to be assessed (N=30 completing the study) was based on clinical considerations.

3 Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol version 3.0 [(Dated: 7/Mar/2017)].

4 Appendix 1:

4.1 List of Tables, Listings and Figures

4.2 Tables

Table Number	Table Title (Population)	Template
14.1.1	Subject Disposition (All Screened Subjects)	Appendix 2
14.1.2.1	Subject Demographics and Baseline Characteristics (Safety Population)	Appendix 2
14.1.2.2	Subject Demographics and Baseline Characteristics (ITT Population)	14.1.2.1
14.2.1.1	Frequency of Dermal Response Score by Visit and Treatment (ITT Population)	Appendix 2
14.2.1.2	Average Dermal Response Score by Visit and Treatment (ITT Population)	Appendix 2
14.2.2.1	Frequency of Superficial Irritation (other effects) Score by Visit and Treatment (ITT Population)	Appendix 2
14.2.2.2	Frequency of Combined Score by Visit and Treatment (ITT Population)	Appendix 2
14.3.1.1	Treatment emergent Adverse Event (Safety Population)	Appendix 2
14.3.1.2	Treatment emergent Adverse Event by Severity (Safety Population)	Appendix 2
14.3.1.3	Treatment emergent Treatment Related Adverse Event (Safety Population)	14.3.1.1
14.3.1.4	Treatment emergent Treatment Related Adverse Event by Severity (Safety Population)	14.3.1.2

4.3 Listings

Listing Number	Listing Title (Population)	Template
14.3.2.1	Listing of Deaths (Randomised population)	16.2.7.1
14.3.2.2	Listing of Serious Adverse Events leading to Discontinuation (Randomised population)	16.2.7.1
16.1.7	Randomisation information (Randomised Population)	Appendix 2
16.2.2	Individual Subjects Protocol Violation (Randomised Population)	Appendix 2
16.2.7.1	All Adverse Events (Randomised Population)	Appendix 2
16.2.7.2	All Adverse Events (Non-Randomised Subjects)	16.2.7.1

Note: If there are no data to display generate a null listing.

4.4 Top line Outputs:

Table/Listing Figure Number	Table/Listing/Figure Title (Population)
14.1.1	Subject Disposition (All Screened Subjects)
14.1.2.2	Subject Demographics (ITT Population)
14.2.1.1	Frequency of Dermal Response Score by Visit and Treatment (ITT Population)
14.3.1.1	Treatment emergent Adverse Event (Safety Population)
16.2.7.1	All Adverse Events (Randomised Population)

5 Appendix 2:

5.1 Templates for the Tables, Listings and Figures

This is a guideline which will give the guidance of treatment labels that will be used for the table header and in the figures, listings and in the footnotes.

The treatment labels for the column heading will be as follow:

- Serum A
- Serum C
- Serum G
- Serum N
- Saline Solution

Protocol: 207235 Program Run Date:ddmonyyyy

Table 14.1.1
Subject Disposition
All Screened Subjects

All Screened Subjects (N=XX)

	Overall(N=XX) n (%)
TOTAL NUMBER OF SUBJECTS SCREENED	xx (xx.x)
SUBJECTS NOT RANDOMISED	xx (xx.x)
DID NOT MEET STUDY CRITERIA	xx (xx.x)
ADVERSE EVENTS	xx (xx.x)
ETC.	xx (xx.x)
SUBJECTS RANDOMISED	xx (xx.x)
COMPLETED	xx (xx.x)
DID NOT COMPLETE	xx (xx.x)
ADVERSE EVENT	xx (xx.x)
LOST TO FOLLOW UP	xx (xx.x)
PROTOCOL DEVIATION	xx (xx.x)
WITHDRAWAL OF CONSENT	xx (xx.x)
OTHER	xx (xx.x)
RANDOMISED POPULATION	xx (xx.x)
SAFETY POPULATION	xx (xx.x)
INTENT TO TREAT POPULATION	xx (xx.x)

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Protocol: 207235 Program Run Date:ddmonyyyy

Table 14.1.2.1
Subject Demographics and Baseline Characteristics
Safety Population

Safety Population (N=XX)

	Overall (N=XX)
SEX n (%)	
MALE	xx (xx.x)
FEMALE	xx (xx.x)
RACE n (%)	
ASIAN	xx (xx.x)
BLACK or AFRICAN	xx (xx.x)
AMERICAN INDIAN OR ALASKA NATIVE	xx (xx.x)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	xx (xx.x)
WHITE	xx (xx.x)
MULTIPLE	xx (xx.x)
AGE (YEARS)	
N	XX
MEAN	XX.X
SD	XX.XX
MEDIAN	XX.X
MINIMUM	XX
MAXIMUM	XX
FITZPATRICK SCALE FOR SKIN TYPE	
I = ALWAYS BURNS EASILY NEVER TANS (PALE WHITE SKIN);	xx (xx.x)

	Overall (N=XX)
II = ALWAYS BURNS EASILY; TANS MINIMALLY (WHITE SKIN);	xx (xx.x)
III = BURNS MODERATELY; TANS GRADUALLY (LIGHT BROWN SKIN);	xx (xx.x)
IV = BURNS MINIMALLY, ALWAYS TANS WELL (MODERATE BROWN SKIN);	xx (xx.x)
V = RARELY BURNS, TANS PROFUSELY (DARK BROWN SKIN);	xx (xx.x)
VI = NEVER BURNS (DEEPLY PIGMENTED DARK BROWN TO BLACK SKIN)	xx (xx.x)

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Table 14.2.1.1
Frequency of Dermal Response Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population(N=XX)

Visit	Score	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT 3 (15~30 min)				
	Missing	xx (xx%)	... ...	xx (xx%)
	0	xx (xx%)	... ...	Xx (xx%)
	1	xx (xx%)	... ...	xx (xx%)
	2	xx (xx%)	... ...	xx (xx%)
	3	xx (xx%)	... ...	xx (xx%)
	4	xx (xx%)	... ...	xx (xx%)
	5	xx (xx%)	... ...	xx (xx%)
	6	xx (xx%)	... ...	xx (xx%)
	7	xx (xx%)	... ...	xx (xx%)
VISIT 4 (24 hours)	Same as above			
VISIT 5 (48 hours)	Same as above			

0 = No evidence of irritation; 1 = Minimal erythema barely perceptible; 2 = Definite erythema; readily visible;or minimal edema; minimal popular response; 3 = Erythema and papules;4 = Definite edema; 5 = Erythema, edema and papules; 6 = Vesicular eruption; 7=Strong reaction spreading beyond test site

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Table 14.2.1.2
Average Dermal Response Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population(N=XX)

Visit	variable	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT 3 (15~30 min)				
	N (non-missing)	xx	... ...	xx
	Mean	x.x	... ...	x.x
	SD	x.xx	... ...	x.xx
	Median	x	... ...	x
	Min	X	... ...	x
	Max	X	... ...	X
VISIT 4 (24 hours)	Same as above			
VISIT 5 (48 hours)	Same as above			

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Note: This table will be provided only if there are subjects with dermal responses > 0.

Protocol: 207235 Program Run Date:ddmonyyyy

Table 14.2.2.1
Summary of Combined Score by Visit and Treatment
Intent to Treat Population

Intent to Treat Population (N=XX)

Visit	Combined Scores	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT 3 (15~30 min)	0	xx (xx%)	... ...	xx (xx%)
	1	Xx (xx%)	... ...	Xx (xx%)
	2	xx (xx%)	... ...	xx (xx%)
	3	xx (xx%)	... ...	xx (xx%)
	4	xx (xx%)	... ...	xx (xx%)
	5	xx (xx%)	... ...	xx (xx%)
	6	xx (xx%)	... ...	xx (xx%)
	7	xx (xx%)	... ...	xx (xx%)
	...	...	... ...	...
VISIT 4(24 hours)	same as above			
Visit 5 (48 hours)	Same as above			

Combined Score: Dermal response Score + "other effect" score(>0)

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Note: This table will be provided only if there are subjects with combined scores > 0 .

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Table 14.2.2.2
Frequency of Superficial Irritation (other effects score) by Visit and Treatment
Intent to Treat Population

Intent to Treat Population (N=XX)

Visit	Grade/Score	Serum A (N=XX)	Serum C...Serum N (N=XX)...(N=XX)	Saline Solution (N=XX)
VISIT3 (15~30 min)				
	Missing	xx (xx%)	... ...	xx (xx%)
	GRADE=A/SCORE=0	xx (xx%)	... ...	xx (xx%)
	GRADE=B/SCORE=1	xx (xx%)	... ...	xx (xx%)
	GRADE=C/SCORE=2	xx (xx%)	... ...	xx (xx%)
	GRADE=F/SCORE=3	xx (xx%)	... ...	xx (xx%)
	GRADE=G/SCORE=3	xx (xx%)	... ...	xx (xx%)
	GRADE=H/SCORE=3	Xx (xx%)	... ...	Xx (xx%)
VISIT4 (24 hours)	Same as above			
VISIT5 (48 hours)	Same as above			

A/0=Slight glazed appearance; B/1=marked glazed appearance; C/2=Glazing with peeling and cracking; F/3=Glazing with fissures; G/3= Film of dried serous exudate covering all or portion of the patch site; H/3=Small petechial erosions and/or scabs

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Table 14.3.1.1
Summary of Treatment emergent Adverse Event by SOC and preferref term
Safety Population

Safety Population (N=xx)

SOC and Preferred Term	Serum A (N=XX)		Serum C...Saline (N=XX)...(N=XX)	Overall (N=XX)	
	n (%)	nAE		n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE AE	xx (xx.x)	xx	... ...	xx (xx.x)	xx
NUMBER OF SUBJECTS WITH NO AE	xx (xx.x)	xx	... ...	xx (xx.x)	xx
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	... ...	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	... ...	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	... ...	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	... ...	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	... ...	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	... ...	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx		xx (xx.x)	xx

n (%) = Number (percent) of subjects nAE = Number of adverse events.

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Table 14.3.1.2
Summary of Treatment emergent Adverse Event by Severity
Safety Population

Safety Population (N=xx)

SOC and Preferred Term	Serum A (N=XX)						...	Overall (N=XX)					
	Mild		Moderate		Severe			Mild		Moderate		Severe	
	n (%)	nAE	n (%)	nAE	n (%)	nAE		n (%)	nAE	n (%)	nAE	n (%)	nAE
NUMBER OF SUBJECTS WITH AT LEAST ONE AE	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ERYTHEMA	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DERMATITIS	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
GASTROINTESTINAL SYSTEM	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
ABDOMINAL PAIN	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
DRY MOUTH	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
VOMITTING	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	...	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx

n (%) = Number (percent) of subjects nAE = Number of adverse events.

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Protocol: 207235 Program Run Date:ddmonyyyy

Listing 16.1.7
Randomisation information
Randomised Population

Subject Number	Age/Sex/Race[1]	Randomization Number	Test Site/Treatment Randomised	Date of randomization (dd/mmm/yyyy)
PPD				PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

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Listing 16.2.2
Individual Subjects Protocol Deviation
Randomised Population

Subject Number	Age/Sex/Race[1]	Visit	DeviationSequence	Protocol Deviation
PPD				xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

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Protocol: 207235 Program Run Date:ddmonyyyy

Listing 16.2.7.1
All Adverse Events
Randomised Population
Treatment Group: Serum X

Subject Number	Age/Sex/ Race[1]	Adverse Event (Preferred Term) (System Organ Class)	Start Date /Study Day[2]	Start Time	End Date	End Time	Frequency /Intensity[3]	Related to Study Product?	Action Taken re Study Product	Outcome	Serious?	Withdrew? [4]
PPD												

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H =Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.
[2] Study day is the day relative to start of treatment, day 1 being the day of first treatment.
[3] INT = Intermittent and SGLE = Single.
[4] Did subject withdraw from study as a result of this adverse event?

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Programming Note for Listing 16.2.7.2:

- Repeat the same layout for listing 16.2.7.2
- Population should be used ‘Non randomised Subjects’
- The fourth column should be only ‘Start Date’
- Add footnote ‘Only SAEs are collected for non randomised subjects’
- Delete the footnote related to study day and adjust the numbers accordingly.

Subject Data Listings

Protocol: 207235 Program Run Date: 13JUL2017

Listing 14.3.2.1
Listing of Deaths
Randomised Population

Study Population: Randomised Subjects (N=40)

******* NO Deaths Reported During the Study *******

Listing 14.3.2.2
Listing of Serious Adverse Events leading to Discontinuation
Randomised Population

Study Population: Randomised Subjects (N=40)

******* NO Serious AEs Reported During the Study *******

Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation

PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

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Protocol: 207235 Program Run Date: 13JUL2017

Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation

PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

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Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation

PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

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Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation

PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

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Protocol: 207235 Program Run Date: 13JUL2017

Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation

PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

PPD

Protocol: 207235 Program Run Date: 13JUL2017

Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation
PPD				

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

PPD

Protocol: 207235 Program Run Date: 13JUL2017

Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation

PPD

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

PPD

Listing 16.1.7
Randomisation Information
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race [1]	Randomisation Number	Treatment Sequence	Date of Randomisation
PPD				

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

PPD

Protocol: 207235 Program Run Date: 13JUL2017

Listing 16.2.2
Individual Subjects Protocol Violation
Randomised Population

Study Population: Randomised Subjects (N=40)

Subject Number	Age/Sex/Race[1]	Visit	Deviation Sequence	Protocol Deviation
PPD				

(Page 1 of 1)

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.

PPD

Page 110 of 112

Protocol: 207235 Program Run Date: 05JUL2017

Lisitng 16.2.7.1
All Adverse Events
Randomised Population

Study Population: Randomised Subjects (N=40)

******* NO AEs Reported During the Study *******

[1] Age in years; Sex: F = Female, M = Male ; Race: A = Asian, B = Black or African American, I = American Indian or Alaska Native, H = Native Hawaiian or Other Pacific Islander, W = White, O = Multiple.
[2] Study day is the day relative to start of treatment, day 1 being the day of first treatment.
[3] INT = Intermittent and SGLE = Single.
[4] Did subject withdraw from study as a result of this adverse event?

PPD

Listing 16.2.7.2
All Adverse Events
Non-Randomised Population

Study Population: Non-Randomised Subjects (N=6)

******* NO AEs Reported During the Study *******

SIGNATURE PAGE

207235 Synopsis Report

Date	Signed By
24-Oct-2017 06:57:39	PPD
Justification	Biostatistics Approval

Date	Signed By
24-Oct-2017 07:02:01	PPD
Justification	Approved

Date	Signed By
24-Oct-2017 10:02:35	PPD
Justification	Approved

Date	Signed By
Justification	

Date	Signed By
Justification	

Date	Signed By
Justification	

GlaxoSmithKline	Document Name	gsk-207235-clinical-study-report.pdf		
	Type	Version	Document Identifier	Effective Date
	eldo_controlled	NT; Most-Recent; In Review	090032d581254d35	
	Reason For Issue			

Annotated Study Book for Study Design: 207235

Study Design Version: 1.0

Sponsor: GlaxoSmithKline Consumer Healthcare

Protocol: 207235

GSKCH 207235 Study

Generated by Central Designer TM

May 10, 2017 1:04PM

Time and Events Sch r Study Design: 207235

	Element		System		CORE_LIB_ELEMENTS						
	Assessment	CRF	SCREEN (SCR) [S]	ENROLL (ENR) [S]	SCREENING (VISIT 1) [S]	DAY 1 (VISIT 2) [S/D]	DAY 2 (VISIT 3) [S/D]	DAY 3 (VISIT 4) [S/D]	DAY 4 (VISIT 5) [S/D]	AE/CONMED/NONDRUG (AE/CONMED/NONDRUG) [S]	STUDYCONC (STUDYCONC) [S]
	Visit Start Hours		0	0	0	24	48	72	96	120	144
1	INFORM SCREENING	SCREEN	1								
2	SUBJECT ENROLLMENT	ENROL		1							
3	DATE OF VISIT/ASSESSMENT	DOV			1	1	1	1	1		
4	SUBJECT IDENTIFICATION	SUBID			2						
5	CONSENT	CONSENT			3						
6	DEMOGRAPHY	DEMO			4						
7	ANY MEDICAL HISTORY	ANY MEDHIST			5						
8	MEDICAL HISTORY	MEDHIST			6-DF						
9	FITZPATRICK ASSESSMENT	FITZPAT			7						
10	INCLUSION CRITERIA	INCLUS			8						
11	EXCLUSION CRITERIA	EXCLUS			9						
12	SUBJECT ELIGIBILITY (Screening)	ELIG			10						
13	COMBINE(V1/V2)	COMBINE (V1/V2)			11						
14	SUBJECT CONTINUED ELIGIBILITY	ELIG				2-DF	2	2	2		
15	SUBJECT RANDOMISATION	RAND				3					
16	TREATMENT PATCH APPLICATION	PATAPP				4					
17	TREATMENT PATCH REMOVAL	PATREM					3				
18	PATCH TEST SITE ASSESSMENT	PATTEST					4	3	3		
19	ANY ADVERSE EVENTS AND PAST/CONCOMITANT MEDICATIONS	AE-CONMED-NONDRUG								1	
20	CONCOMITANT MEDICATIONS	CONMED								2-DF-C-RF	
21	CONCOMITANT NON-DRUG TREATMENT/PROCEDURES	NONDRUG								3-DF-C-RF	
22	ADVERSE EVENTS	AE								4-DF-C-RF	
23	ANY PROTOCOL DEVIATIONS	ANY DEVIATION									1
24	PROTOCOL DEVIATIONS	DEVIATION									2-DF
25	STUDY CONCLUSION	STUDYCONC									3

Key: [S] = Scheduled Visit [D] = Dynamic Visit [U] = Unscheduled Visit [R] = Repeating Visit
C = Common Form DF = Dynamic Form RF = Repeating Form

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Reason For Issue			

207235: INFORM SC (SCREEN)

INFORM SCREENING

1.	Year of Birth [Year of Birth]	**[DOBDT]**

Note: Hidden items are not displayed.

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eldo_controlled Record For Issue	NT; Most-Recent; In Review	090032d581254d35	

207235: SUBJECT ENROLMENT (ENROL)

SUBJECT SCREENING NUMBER

1.	Subject Screening Number [Subject Screening Number]	**[txtSubjectNumber]**

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eldo_controlled	NT; Most-Recent; In Review	090032d581254d35	

207235: DATE OF VISIT ASSESSMENT (DOV)

DATE OF VISIT/ASSESSMENT

1.	Date of Visit [Date of Visit]	**[DOV]** / /

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eldo_controlled Document Type	NT; Most-Recent; In Review	090032d581254d35	

207235: SUBJECT IDENTIFICATION (SUBID)

SUBJECT IDENTIFICATION

1.	Subject Screening Number [Subject Screening Number]	**[txtSubjectNumber]**

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Reason For Issue			

207235: CONSENT (GlaxoSmithKline)

CONSENT

1.	Date of Consent [Date of Consent]	**[CONSDT]** / /

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Reason For Issue			

207235: DEMOGRAP O)

DEMOGRAPHY

1.	Year of Birth [Year of Birth]	**[DOBDT]**
2.	Age [Age]	**[AGE]**
3.	Sex [Sex]	**[SEX]** Male Female
4.	Race [Race]	**[cmpRACECD]** **(Check all that apply)** **[RACECD11]** African American/African Heritage **[RACECD12]** American Indian or Alaskan Native **[RACECD13]** Asian - Central/South Asian Heritage **[RACECD14]** Asian - East Asian Heritage **[RACECD15]** Asian - Japanese Heritage **[RACECD16]** Asian - South East Asian Heritage **[RACECD17]** Native Hawaiian or Other Pacific Islander **[RACECD18]** White - Arabic/North African Heritage **[RACECD19]** White - White/Caucasian/European Heritage

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Reason For Issue:

207235: ANY MEDIC ORY (ANY MEDHIST)

ANY MEDICAL HISTORY

List relevant previous and current medical conditions (including allergies or drug sensitivity) and surgery that the subject has experienced.
NOTE: If treatment is currently taken for any medical conditions, complete the Concomitant Medications page.

1.	Are there any medical conditions to report? [Any Medical History]	**[MHANY]** ◯ Yes ◯ No **If Yes, complete Medical History page**

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207235: MEDICAL H MEDHIST)

	Medical Condition	Start Date	Ongoing Medical Condition
1.			

MEDICAL HISTORY Entry

List any relevant previous and current medical conditions (including allergies or drug sensitivity) and surgery that the subject has experienced.
NOTE: If treatment is currently taken for any medical conditions, complete the Concomitant Medications page.

1.1	Medical Condition [Medical Condition]	**[MHTERM]**
1.2	Start Date [Start Date]	**[MHSTDT]** / /
1.3	Ongoing Medical Condition? [Ongoing Medical Condition]	**[MHONGO]** Yes **[MHENDT]** No, provide End Date: / /

Note: Hidden items are not displayed.

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207235: FITZPATRICK SKIN TYPE ASSESSMENT (FITZPAT)

FITZPATRICK ASSESSMENT

1.	Fitzpatrick Skin Type Grading [Fitzpatrick Grading]	**[FITZPATCD]** I - Always burns easily; never tans (pale white skin) II - Always burns easily; tans minimally (white skin) III - Burns moderately; tans gradually (light brown skin) IV - Burns minimally, always tans well (moderate brown skin) V - Rarely burns, tans profusely (dark brown skin) VI - Never burns (deeply pigmented dark brown to black skin)

207235: INCLUSION CRITERIA (INCLUS)

INCLUSION CRITERIA

Mark the correct answers to the following Inclusion Criteria questions.

1.	Inclusion #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. [Inclusion #1) Consent]	**[IECRTNUMI01]** ◯ Yes ◯ No
2.	Inclusion #2) Age - Aged between 18 and 65 years inclusive. [Inclusion #2) Age]	**[IECRTNUMI02]** ◯ Yes ◯ No
3.	Inclusion #3a) 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. [Inclusion #3a) Compliance]	**[IECRTNUMI03A]** ◯ Yes ◯ No
4.	Inclusion #3b) General Health - Subjects must have intact skin on the proposed application site; dorsum(scapular region). [Inclusion #3b) General Health]	**[IECRTNUMI03B]** ◯ Yes ◯ No
5.	Inclusion #4) Skin Type - Fitzpatrick phototype I to IV. [Inclusion #4) Skin Type]	**[IECRTNUMI04]** ◯ Yes ◯ No
6.	Inclusion #5) Compliance - Agreement to comply with the procedures and requirements of the study and to attend the scheduled assessment visits. [Inclusion #5) Compliance]	**[IECRTNUMI05]** ◯ Yes ◯ No

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207235: EXCLUSION CRITERIA (EXCLUS)

EXCLUSION CRITERIA

Mark the correct answers to the following Exclusion Criteria questions.

1.	Exclusion #1) Pregnancy - Women who are known to be pregnant or who are intending to become pregnant over the duration of the study. [Exclusion #1) Pregnancy]	**[IECRTNUME01]** Yes No NA
2.	Exclusion #2) Breast-feeding - Women who are breast-feeding. [Exclusion #2) Breast-feeding]	**[IECRTNUME02]** Yes No NA
3.	Exclusion #3a) Concurrent Medication/Medical History - Any history of significant dermatological diseases or conditions or medical conditions known to alter skin appearance or physiologic response (e.g. diabetes) which could, in the opinion of the Investigator, preclude topical application of the investigational products and/or interfere with the evaluation of the test site reaction. [Exclusion #3a) Concurrent Medication/Medical History]	**[IECRTNUME03A]** Yes No
4.	Exclusion #3b) Concurrent Medication/Medical History - Presence of open sores, pimples, or cysts at the application site. [Exclusion #3b) Concurrent Medication/Medical History]	**[IECRTNUME03B]** Yes No
5.	Exclusion #3c) Concurrent Medication/Medical History - Active dermatosis (local or disseminated) that might interfere with the results of the study. [Exclusion #3c) Concurrent Medication/Medical History]	**[IECRTNUME03C]** Yes No
6.	Exclusion #3d) Concurrent Medication/Medical History - Considered immune compromised. [Exclusion #3d) Concurrent Medication/Medical History]	**[IECRTNUME03D]** Yes No
7.	Exclusion #3e) Concurrent Medication/Medical History - History of diseases aggravated or triggered by ultraviolet radiation. [Exclusion #3e) Concurrent Medication/Medical History]	**[IECRTNUME03E]** Yes No
8.	Exclusion #3f) Concurrent Medication/Medical History - Participants with dermatographism. [Exclusion #3f) Concurrent Medication/Medical History]	**[IECRTNUME03F]** Yes No
9.	Exclusion #3g) Concurrent Medication/Medical History - Currently using any medication which in the opinion of the investigator, may affect the evaluation of the study product, or place the subject at undue risk. [Exclusion #3g) Concurrent Medication/Medical History]	**[IECRTNUME03G]** Yes No
10.	Exclusion #3h) Concurrent Medication/Medical History - Use of the following topical or systemic medications: immunosuppressants, antihistamines, non-hormonal anti-inflammatory drugs, and corticosteroids up to 2 weeks before screening visit. [Exclusion #3h) Concurrent Medication/Medical History]	**[IECRTNUME03H]** Yes No
11.	Exclusion #3i) Concurrent Medication/Medical History - Oral or topical treatment with vitamin A acid and/or its derivatives up to 1 month before the screening visit. [Exclusion #3i) Concurrent Medication/Medical History]	**[IECRTNUME03I]** Yes No
12.	Exclusion #3j) Concurrent Medication/Medical History - Intention of being vaccinated during the study period or vaccination within 3 weeks of the screening visit. [Exclusion #3j) Concurrent Medication/Medical History]	**[IECRTNUME03J]** Yes No
13.	Exclusion #3k) Concurrent Medication/Medical History - Currently receiving allergy injections, or due to receive an injection within 7 days prior to Visit 1, or expects to begin injections during study participation. [Exclusion #3k) Concurrent Medication/Medical History]	**[IECRTNUME03K]** Yes No
14.	Exclusion #4a) Allergy/Intolerance - Previous history of atopy, allergic reactions, irritation or intense discomfort feelings to topical-use products, cosmetics or medication. [Exclusion #4a) Allergy/Intolerance]	**[IECRTNUME04A]** Yes No
15.	Exclusion #4b) Allergy/Intolerance - Known or suspected intolerance or hypersensitivity to any of the study materials (or closely related compounds) or any of their stated ingredients, including	**[IECRTNUME04B]** Yes No

	any component of the pat [Exclusion #4b) Allergy/I	◯ ◯
16.	Exclusion #4c) Allergy/Intolerance - History of sensitization in a previous patch study. [Exclusion #4c) Allergy/Intolerance]	**[IECRTNUME04C]** ◯Yes ◯No
17.	Exclusion #5a) Clinical Study/Experimental Product - Participation in another clinical study (including cosmetic studies) or receipt of an investigational drug within 30 days of the screening visit. [Exclusion #5a) Clinical Study/Experimental Product]	**[IECRTNUME05A]** ◯Yes ◯No
18.	Exclusion #5b) Clinical Study/Experimental Product - Previous participation in this study. [Exclusion #5b) Clinical Study/Experimental Product]	**[IECRTNUME05B]** ◯Yes ◯No
19.	Exclusion #6a) Substance Abuse - Recent history (within the last 5 years) of alcohol or other substance abuse. [Exclusion #6a) Substance Abuse]	**[IECRTNUME06A]** ◯Yes ◯No
20.	Exclusion #7a) Diagnostic Assessments And Other Criteria - Intense sunlight exposure or sun tanning sessions up to 30 days before the Screening evaluation. [Exclusion #7a) Diagnostic Assessments And Other Criteria]	**[IECRTNUME07A]** ◯Yes ◯No
21.	Exclusion #7b) Diagnostic Assessments And Other Criteria - Intention of bathing, sauna, water sports, or activities that lead to intense sweating. [Exclusion #7b) Diagnostic Assessments And Other Criteria]	**[IECRTNUME07B]** ◯Yes ◯No
22.	Exclusion #7c) Diagnostic Assessments And Other Criteria - Any subject who, in the judgment of the Investigator, should not participate in the study. [Exclusion #7c) Diagnostic Assessments And Other Criteria]	**[IECRTNUME07C]** ◯Yes ◯No
23.	Exclusion #7d) Diagnostic Assessments And Other Criteria - Any skin marks on the test site that might interfere with the evaluation of possible skin reactions (e.g. pigmentation disorders, vascular malformations, scars, tattoos, excessive hair, numerous freckles). [Exclusion #7d) Diagnostic Assessments And Other Criteria]	**[IECRTNUME07D]** ◯Yes ◯No
24.	Exclusion #7e) Diagnostic Assessments And Other Criteria - Prisoner or involuntary incarcerated subject. [Exclusion #7e) Diagnostic Assessments And Other Criteria]	**[IECRTNUME07E]** ◯Yes ◯No
25.	Exclusion #7f) Diagnostic Assessments And Other Criteria - Subject from an indigenous tribe. [Exclusion #7f) Diagnostic Assessments And Other Criteria]	**[IECRTNUME07F]** ◯Yes ◯No
26.	Exclusion #8) Personnel - An employee of the sponsor or the study site or members of their immediate family. [Exclusion #8) Personnel]	**[IECRTNUME08]** ◯Yes ◯No

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207235: SUBJECT EL[illegible]'Y (ELIG)

SUBJECT ELIGIBILITY

NOTE: If the subject is not eligible to continue in the study, complete the Study Conclusion visit.

1.	On the basis of Visit assessment(s), is the subject eligible and fit to participate in the next part of the study? [Subject eligible to continue in the study]	**[ELIG]** ◯ Yes ◯ No

207235: COMBINE V [illegible]OMBINE(V1/V2))

COMBINE V1/V2

1.	Is visit 1 combined with visit 2? [Visit 1 combined with Visit 2]	**[COMVST]** ◯ Yes ◯ No

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207235: SUBJECT CONTINUED ELIGIBILITY (ELIG)

SUBJECT CONTINUED ELIGIBILITY

NOTE: If the subject experienced any new Adverse Events, please complete the Adverse Event form.
NOTE: If there are any changes to the subject's medications, please complete the Concomitant Medications form.

1.	Have there been any deviations from the protocol since the last visit? [Any Deviations]	**[ELIGDEV]** ○ Yes ○ No **If Yes, please provide details on the Protocol Deviations form.**
2.	Has the subject adhered to lifestyle restrictions since the last visit? [Adhered to lifestyle restrictions]	**[ELIGADH]** ○ Yes ○ No **If No, please provide details on the Protocol Deviations form.**
3.	Is the subject eligible to continue in the study? [Eligible to continue]	**[ELIGCON]** ○ Yes ○ No **If No, the subject should be discontinued from the study. Please complete the Study Conclusion form.**

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207235: SUBJECT RANDOMISATION (RAND)

SUBJECT RANDOMISATION

1.	Was subject randomised? [Subject randomised]	**[RANDYN]** ○ **[cmpRAND_Yes]** **[RANDNUM]** Yes, provide: Randomisation Number [ ] **[RANDDTTM]** Randomisation Date [ ] / [ ] / [ ] ○ No

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207235: TREATMENT PATCH APPLICATION (PATAPP)

TREATMENT PATCH APPLICATION

1.	Date and Time of Patch Application [Date and Time of Patch Application]	**[PAADTTM]** / / : *24-hour clock*

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207235: TREATMENT PATCH REMOVAL (PATREM)

TREATMENT PATCH REMOVAL

1.	Date and Time of Patch Removal [Date and Time of Patch Removal]	**[PARDTTM]** / / : *24-hour clock*

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GlaxoSmithKline Restricted

207235: PATCH TEST ASSESSMENT (PATTEST)

DATE AND TIME OF ASSESSMENT

1.	Date and Time of Assessment [Date and Time of Assessment]	**[PADTTM]** / / : *24-hour clock*

PATCH ASSESSMENT-TEST SITE 1

2.	Dermal Response [Dermal Response]	**[PADERS1CD]** 0 - No evidene of irritation 1 - Minimal erythema, barely perceptible 2 - Definite erythema, readily visible; minimal edema or minimal papular response 3 - Erythema and papules 4 - Definite edema 5 - Erythema, edema and papules 6 - Vesicular eruption 7 - Strong reaction spreading beyond test site
3.	Other Effects [Other Effects]	**[PAEFFCTS1]** **[PAOBSCD]** Yes, Select the score: A(0) - Slight glazed appearance B(1) - Marked glazed appearance C(2) - Glazing with peeling and cracking F(3) - Glazing with fissures G(3) - Film of dried serous exudate covering all or portion of the patch site H(3) - Small petechial erosions and/or scabs No
4.	Score [Score]	**[PASCORS1]**

PATCH ASSESSMENT-TEST SITE 2

5.	Dermal Response [Dermal Response]	**[PADERS2CD]** 0 - No evidene of irritation 1 - Minimal erythema, barely perceptible 2 - Definite erythema, readily visible; minimal edema or minimal papular response 3 - Erythema and papules 4 - Definite edema 5 - Erythema, edema and papules 6 - Vesicular eruption 7 - Strong reaction spreading beyond test site
6.	Other Effects [Other Effects]	**[PAEFFCTS2]** **[PAOBSS2CD]** Yes, Select the score: A(0) - Slight glazed appearance B(1) - Marked glazed appearance C(2) - Glazing with peeling and cracking F(3) - Glazing with fissures

		G(3) - Film of dried serous exudate covering all or portion of the patch site H(3) - Small petechial erosions and/or scabs No
7.	Score [Score]	**[PASCORS2]**
PATCH ASSESSMENT-TEST SITE 3		
8.	Dermal Response [Dermal Response]	**[PADERS3CD]** 0 - No evidene of irritation 1 - Minimal erythema, barely perceptible 2 - Definite erythema, readily visible; minimal edema or minimal papular response 3 - Erythema and papules 4 - Definite edema 5 - Erythema, edema and papules 6 - Vesicular eruption 7 - Strong reaction spreading beyond test site
9.	Other Effects [Other Effects]	**[PAEFFCTS3]** **[PAOBSS3CD]** Yes, Select the score: A(0) - Slight glazed appearance B(1) - Marked glazed appearance C(2) - Glazing with peeling and cracking F(3) - Glazing with fissures G(3) - Film of dried serous exudate covering all or portion of the patch site H(3) - Small petechial erosions and/or scabs No
10.	Score [Score]	**[PASCORS3]**
PATCH ASSESSMENT-TEST SITE 4		
11.	Dermal Response [Dermal Response]	**[PADERS4CD]** 0 - No evidene of irritation 1 - Minimal erythema, barely perceptible 2 - Definite erythema, readily visible; minimal edema or minimal papular response 3 - Erythema and papules 4 - Definite edema 5 - Erythema, edema and papules 6 - Vesicular eruption 7 - Strong reaction spreading beyond test site
12.	Other Effects [Other Effects]	**[PAEFFCTS4]** **[PAOBSS4CD]** Yes, Select the score: A(0) - Slight glazed appearance B(1) - Marked glazed appearance C(2) - Glazing with peeling and cracking F(3) - Glazing with fissures

		G(3) - Film of dried serous exudate covering all or portion of the patch site H(3) - Small petechial erosions and/or scabs No
13.	Score [Score]	**[PASCORS4]**
PATCH ASSESSMENT-TEST SITE 5		
14.	Dermal Response [Dermal Response]	**[PADERS5CD]** 0 - No evidene of irritation 1 - Minimal erythema, barely perceptible 2 - Definite erythema, readily visible; minimal edema or minimal papular response 3 - Erythema and papules 4 - Definite edema 5 - Erythema, edema and papules 6 - Vesicular eruption 7 - Strong reaction spreading beyond test site
15.	Other Effects [Other Effects]	**[PAEFFCTS5]** **[PAOBSS5CD]** Yes, Select the score: A(0) - Slight glazed appearance B(1) - Marked glazed appearance C(2) - Glazing with peeling and cracking F(3) - Glazing with fissures G(3) - Film of dried serous exudate covering all or portion of the patch site H(3) - Small petechial erosions and/or scabs No
16.	Score [Score]	**[PASCORS5]**

207235: ANY ADVERSE EVENTS, PAST/CONCOMITANT MEDICATIONS AND NON-DRUG TREATMENTS (AE-CONMED-NONDRUG)

ANY ADVERSE EVENTS, PAST/CONCOMITANT MEDICATIONS AND NON-DRUG TREATMENTS

1.	Is the subject taking past / concomitant medications? [Any Medications]	**[CMANY]** ◯ Yes ◯ No **If Yes, complete Concomitant Medications page**
2.	Did the subject have any Non-Drug Treatment / Procedures during the study? [Any Non-Drug Treatment / Procedures]	**[NDANY]** ◯ Yes ◯ No **If Yes, complete Concomitant Non-Drug Treatment / Procedures page**
3.	Did the subject experience any adverse events? [Any AE]	**[AEANY]** ◯ Yes ◯ No **If Yes, complete Adverse Events page**

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207235: PAST/CONCOMITANT MEDICATIONS (CONMED) - Repeating Form

#	Drug Name	Reason for Medication	Route of Administration	Dose per Administration	Dose Frequency	Start Date	Ongoing Medication
1							

PAST/CONCOMITANT MEDICATIONS

1.	Drug Name ***(trade name preferred)*** ***[Drug Name]***	**[CMTERM]**
2.	Reason for Medication [Reason for Medication]	**[CMREAS]**
3.	Route of Administration [Route of Administration]	**[CMROUTCD]** **[clROUTE]**
4.	Dose per Administration [Dose per Administration]	**[cmpCMDOSE]** **[CMUDOS]** **[CMDOSU]** Dose Unit **[clDOSUNIT]**
5.	Frequency [Dose Frequency]	**[CMFREQ]** **[clDOSEFREQ]**
6.	Start Date [Start Date]	**[CMSTDT]** / /
7.	Ongoing Medication? [Ongoing Medication]	**[CMONGO]** Yes **[CMENDT]** No, provide End Date: / /

Note: Hidden items are not displayed.

Document Name	gsk-207235-clinical-study-report.pdf		
Type	Version	Document Identifier	Effective Date
eldo_controlled	NT; Most-Recent; In Review	090032d581254d35	

207235: CONCOMITANT DRUG TREATMENT/PROCEDURES (NONDRUG) - Repeating Form

#	Non-Drug Treatment / Procedure Name	Reason for Non-Drug Treatment / Procedure	Frequency	Start Date	Ongoing Non-Drug Treatment / Procedure
1					

CONCOMITANT NON-DRUG TREATMENT/PROCEDURES

1.	Name of Non-Drug Treatment / Procedure [Non-Drug Treatment / Procedure Name]	**[NDTERM]**
2.	Reason for Non-Drug Treatment / Procedure [Reason for Non-Drug Treatment / Procedure]	**[NDREAS]**
3.	Frequency [Frequency]	**[NDFREQ]**
4.	Start Date [Start Date]	**[NDSTDT]** / /
5.	Ongoing Non-Drug Treatment / Procedure? [Ongoing Non-Drug Treatment / Procedure]	**[NDONGO]** Yes **[NDENDT]** No, provide End Date: / /

Note: Hidden items are not displayed.

Document Name	gsk-207235-clinical-study-report.pdf		
Type	Version	Document Identifier	Effective Date
eldo_controlled Ready For Issue	NT; Most-Recent; In Review	090032d581254d35	

207235: ADVERSE E[illegible]E) - Repeating Form

#	Adverse Event	Start Date and Time	Outcome	Frequency	Intensity	Relationship to Investigational Product	Action Taken with the Investigational Product	Serious	Subject Withdrawn
1									

ADVERSE EVENTS

1.	Adverse Event [Adverse Event]	**[AETERM]**
2.	Start Date and Time [Start Date and Time]	**[AESTDTTM1]** / / : *24-hour clock*
3.	Outcome / End Date and Time [Outcome]	**[AEOUTCD]** **[AEENDTTM1]** Recovered/Resolved, provide End Date and Time: / / : *24-hour clock* Recovering/Resolving Not recovered/Not resolved **[AEENDTTM2]** Recovered/Resolved with sequelae, provide End Date and Time: / / : *24-hour clock* **[AEENDTTM3]** Fatal, provide Death Date and Time: / / : *24-hour clock*
4.	Frequency [Frequency]	**[AEFREQCD]** Single Episode Intermittent
5.	Intensity [Intensity]	**[AESEVCD]** Mild Moderate Severe
6.	Is there a reasonable possibility that the AE may have been caused by the investigational product? [Relationship to Investigational Product]	**[AEREL]** Yes No
7.	Action taken with the investigational product as a result of the AE [Action Taken with the Investigational Product]	**[AEACTRCD]** Investigational product(s) withdrawn Dose reduced Dose increased Dose not changed Dose interrupted Not applicable
8.	Serious [Serious]	**[AESER]** Yes No

		NOTE: All serious adverse events must be reported to the study manager within 24 hours and require additional reporting on an SAE form
9.	Did the subject withdraw from study as a result of this AE? [Subject Withdrawn]	**[AEWD]** ◯ Yes ◯ No **If Yes, complete the Study Conclusion page with primary reason for withdrawal as Adverse Event**

Note: Hidden items are not displayed.

Document Name	gsk-207235-clinical-study-report.pdf		
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207235: ANY PROTOCOL DEVIATIONS (ANY DEVIATION)

ANY PROTOCOL DEVIATIONS

1.	Have there been any protocol deviations? [Any Deviations]	**[DVANY]** ◯ Yes ◯ No **If Yes, complete Deviations page**

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207235: PROTOCOL DEVIATIONS (DEVIATION)

	Protocol Deviation	Start Date/Time of Deviation	End Date/Time of Deviation
1.			

PROTOCOL DEVIATIONS Entry

1.1	Protocol Deviation [Protocol Deviation]	**[DVTERM]**
1.2	Start Date/Time of Deviation [Start Date/Time of Deviation]	**[DVSTDTTM]** / / : *24-hour clock*
1.3	End Date/Time of Deviation [End Date/Time of Deviation]	**[DVENDTTM]** / / : *24-hour clock*

Note: Hidden items are not displayed.

Document Name	gsk-207235-clinical-study-report.pdf		
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207235: STUDY CON [illegible] (STUDYCONC)

STUDY CONCLUSION

1.	Date of subject completion or withdrawal [Date of subject completion or withdrawal]	**[DSSTDT]** / /
2.	Was the subject withdrawn from study? [Subject withdrawn from study]	**[DSFAIL]** ○ **[DSRSCD]** Yes, provide primary reason for withdrawal: ○ **[DSRSSP1]** Subject did not meet study criteria; specify the criterion or assessment not met **NOTE: If the subject failed Inclusion/Exclusion criteria, specify the criteria numbers failed with a prefix of I(Inclusion criteria) or E(Exclusion criteria)** ○ Adverse Event, complete Adverse Events page ○ Lost to Follow-up ○ **[DSRSSP4]** Protocol Violation, specify details ○ **[DSRSSP5]** Withdrawal of consent, specify details ○ **[DSRSSP99]** Other, specify details ○ No

"Pages removed- Out of Scope of phase 1 of Policy 0070 – Investigator's Curriculum Vitae"

Participant Information and Informed Consent Form (ICF) - Study 207235

CCI [redacted]

A Human Subject 24 hour Patch Test to Assess the Irritation Potential of Four Skin Serum Products

Introduction

You are being invited to take part in a research study. The sponsoring company for this study is GlaxoSmithKline Consumer Healthcare, and it will be performed at one of AZIDUS BRASIL PESQUISA CIENTÍFICA E DESENVOLVIMENTO LTDA company units (main unit located at Rua General Osório, n° 507 - Bairro: Vila Martina – Valinhos – SP). Before you decide whether or not you wish to take part in this study, it is important that you read this document carefully and fully understand why the research is being done and what it will involve. The study procedures will be fully explained to you. This document may include a few technical terms that you may not be familiar with. Please feel free to ask the Principal Investigator or Study Staff any questions you may have about this research.

The information and any materials or items that you are given during the study should be considered confidential information of the sponsoring company. You are, of course, free to discuss the study with your friends and family while considering whether or not to participate, or at any time when discussing your present or future healthcare.

What is the purpose of the study?

The purpose of this study is to evaluate the skin irritation potential after a single 24 hour application of 4 different experimental skin serums (moisturizers) compared to a control, a neutral salt water solution. The products will be applied on the skin of your upper back by the shoulder blade area under a semi-occlusive patch system (moisture and vapor permeable) and anchored with hypoallergenic tape and left in place for 24 hrs. A total of 5 test sites each 1.2cm^2 will be individually evaluated during this study.

What are the products being tested?

There are 4 test cosmetic skin serums being tested which contain standard cosmetic ingredients found in many products sold in the market place and are safe for you to use in this study. There is also a control product which is a standard saline (salt water) solution.

Is my participation voluntary?

You are free to decide whether or not you wish to take part in the study. If you decide to take part, you will be asked to sign the consent form at the end of this information after all your questions have been answered and be provided a copy. You are still free to withdraw from the study at any time and you do not have to give a reason. You should inform the study staff if you wish to withdraw. The Investigator or Sponsoring Company may discontinue your participation in the study at any time without your consent for safety, ethical, administrative and non-compliance on your part with study schedule and restrictions. The withdrawal before completing all visits does not affect the benefits you are entitled to.

PARTICIPANT INITIALS: _____ PERSON TAKING CONSENT INITIALS: _____

Are there any reasons why I can't take part?

To take part, you should be aged 18 to 65 years old, in good general health with healthy skin in your upper back and have a suitable skin type.

IF YOU ARE FEMALE YOU CANNOT TAKE PART IF YOU ARE PREGNANT, OR PLANNING TO BECOME PREGNANT, OR BREASTFEEDING.

Are there any restrictions I will have to comply with if I take part?

- You should not have any body aesthetic or dermatological treatments performed.
- You should not change hormone treatment.
- You should not change contraceptive method.
- You should not participate in another research study
- You should not use the following medications:
  - Systemic or topical corticosteroids
  - Systemic or topical immunosuppressive drugs
  - Systemic or topical antihistamines
  - Vitamin A acid and its derivatives
  - Non-steroidal anti-inflammatory drugs
- You should not remove the test patch.
- You will be asked to avoid applying any other products to the test sites.
- You should not get the patch test site wet: during showers or bathing, swimming or sauna.
- You should avoid excessive sweating, or wearing restrictive clothing that could remove the patch.
- You should avoid exposure to prolonged sunlight, and not undergo artificial tanning (including tanning beds).
- Avoid changing dietary habits, cosmetic or personal hygiene habits or introducing new products, including soap, laundry detergent or fabric softener.

What will happen to me if I decide to take part?

Your involvement in the study will last approximately 4-10 days (from screening to final assessment). Over this time you will be asked to make up to 5 visits to the study centre.

STUDY PROCEDURES:

Visit 1 – Screening Visit (Approximately 4 hours)

- You will be asked to read this consent form. Study staff will then tell you about the study and what your involvement will be. You will have the opportunity to ask questions.
- If you wish to take part, you will be asked to sign two copies of this consent form. One copy will be kept by us and the other copy will be given to you to keep. Please keep this consent form handy during the study as it contains instructions and important telephone numbers. If you would rather not take part, please hand

PARTICIPANT INITIALS: _____ PERSON TAKING CONSENT INITIALS: _____

the forms back to the staff member and tell them you no longer wish to take part in the study.

- Once you have consented to take part, study staff will ask you about your general health and any medications you are taking, and ask you a series of questions that will help us to decide if you are suitable to take part.

If you have any questions or issues, you can contact the Principal Investigator: Regina M. Doi (Dermatologist) or the medical staff PPD (business hours) or PPD (24 hours).

- When the paperwork is complete, a medical dermatologist (skin specialist) will examine your back to assess your skin health and the suitability for the study
- If you are suitable to continue, you may then have the products test and control applied to your back the same day or be asked to return within 7 days for the test and control products application.

Visit 2: DAY 1 – Patch Application (Approximately 4 hours)

- This Visit may occur on the same day as your screening visit or within 7 days. Staff will ask you if there have been any feelings of discomfort in your back area or changes in your health or medications since your last visit, to check if you are still suitable to continue in the study and randomly assign the order of application of each of the 4 test products and saline solution.
- The test area on your back will be 65 cm2. A total of 0.024 ml of each of the test products and the saline control will be applied in random order to 5 separate filter discs (each measuring 1.2 cm2) within the test area. The discs will be anchored to your skin with a semi-occlusive tape. The patch system willl remain in place for 24 (± 2) hours. You will be asked to return at the same time the next day.

Visit 3: DAY 2 – Patch removal and assessment (Approximately 4 hours)

- Staff will ask you if there have been any feelings of discomfort in the test area or changes in your health or medications since your last visit
- The patch system (adhesive tape and discs) will be removed and you will be asked to wait for 15-30 minutes before each patch test site is assessed by a trained technician, and dermatologist if necessary.
- After the assessment you will be asked to return the following day.

Visit 4: DAY 3 – Patch assessment (Approximately 4 hours)

- Staff will ask you if there have been any changes in your health, medications or feeling of discomfort in the test area since your last visit.
- The evaluator will again check each patch test site on your back where the patch was applied and record any observed findings.
- After the assessment you will be asked to return the following day.

Visit 5: DAY 4 – Patch assessment (Approximately 4 hours)

- Staff will ask you if there have been any changes in your health, medications or feeling of discomfort in the test area since your last visit.
- The evaluator will again check each patch test site on your back where the patch was applied and record any observed findings.

PARTICIPANT INITIALS: _____ PERSON TAKING CONSENT INITIALS: _____

- A dermatologist will perform a final check.
- At this point, you have completed the study.

Are there any possible side effects of the products or risks from the study procedures?

All of the ingredients identified within the study products are considered to be of low toxicity, however since there is always the possibility that a rare or previously unknown side effect may occur in somebody using this or any other product, trained medical staff will be available at the site. You may experience effects such as itching, redness, and swelling and burning at the product application site, but in the event of any type of reaction, you will be assessed and monitored by a medical dermatologist. You are encouraged to report to the study staff any discomfort you may experience on the test area at each visit.

If you experience any problems after leaving the site and for up to 5 days after your last visit, please contact a member of the study staff at the telephone numbers listed above.

How many people will be taking part in the study?

Around 40 participants will be taking part in this study.

What are the possible benefits in taking part?

Your participation in this research will contribute to the launch of products for topical use which don't cause skin irritation in the research group; you will be also examined by a medical specialist before the research start and, in case any problem is observed at the assessed area, you will be informed accordingly.

What if new information becomes available?

If new information about the study test skin serums becomes available during the course of the study, staff will tell you about it promptly and you will have an opportunity to decide whether or not you want to continue with the study.

Will my taking part in this study be confidential?

If you consent to take part in this study, Azidus and the sponsoring company, in accordance with international regulatory guidelines and local resolution 466/12, will store the information collected during the study. The information may also be made available within and outside Brazil to auditors, members of the Ethics Committee and staff from regulatory authorities, for the purposes of data verification. Only the study site staff and the monitors will know that the information is related to you and this information is kept separate and confidential.

The results of the study may be published in the medical literature, but your identity will not be revealed. Data will be transferred outside of Brazil for data processing and analysis. The research summary will be posted on a publicly available protocol register and a summary of the study results will be posted on a publicly available results register but your personal information will always be kept confidential.

Will I be paid for taking part in this study?

PARTICIPANT INITIALS: _____ PERSON TAKING CONSENT INITIALS: _____

You will not be paid for participating in the research, however you will receive a reimbursement for the expenses related to the visits to the institute, such as transportation and food. Participation in this study will not cost you any money.

Is there a contact for further information?

Claims or complaints can be made directly to the Research Ethics Committee by phone PPD .

For any further information on this study, including questions about your rights as a participant, trial related injury and about any study procedures, please contact the research site:

PPD **(business hours) or** PPD **(24 hours)**

Other considerations:

Your consent does not exempt the research centre organizers of their responsibilities;

You are aware that, at one or more study visits, a representative of the sponsor company may be present in order to observe the research;

We assure that any adverse reaction (skin reactions, irritations or discomfort feelings) will be monitored by a dermatologist and/or responsible specialist for the project until its resolution, and if necessary, the adequate medication or medical treatment will be provided. Obligations to you by the study site and Sponsoring Company are assured (eventual indemnities).

PARTICIPANT INITIALS: _____ PERSON TAKING CONSENT INITIALS: _____

- I confirm that I have read and understand this consent form for this study and have had the opportunity to ask questions.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- I give permission for the anonymised data to be transferred to countries outside Brazil.
- I agree to take part in the above study and understand/agree to provide accurate information.

_____

Name of Subject (Print Name)

_____ _____

Date Signature

Impartial Witness (fill only if required): I attest that the information in the consent and any other written information was accurately explained to, and apparently understood by the subject. The subject named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____

Name of Impartial Witness (Print Name)

_____ _____

Date *Signature*

_____

Name of Person Taking Consent (Print Name)

_____ _____

Date Signature

One signed copy of this consent form to be retained by Azidus, another to be given to the subject.

PARTICIPANT INITIALS: _____ PERSON TAKING CONSENT INITIALS: _____