PPD

PPD **Protocol Number:**	PPD
GSKCH Protocol Number:	218005
Title:	Clinical Evaluation of the Sun Protection Factor (SPF) of Sunscreen Products According to the FDA Final Rule: Sunscreen Drug Products (2011).
Objective:	To measure the static SPF of three over-the-counter (OTC) sunscreen lip balms.
Test Products:	ChapStick Active Performance (CAP) UnScented (CCI CAP Herbal Mint Flavour (CCI CAP Mountain Berry Flavour (CCI
Participants:	Eligible male and female volunteers, aged 18-70 with Fitzpatrick skin types I, II or III will be enrolled.
SPF Standard:	7% Padimate-O and 3% Oxybenzone
Sponsor:	GlaxoSmithKline Consumer Healthcare Holdings (US) LLC (GSK CH), PPD Name: PPD Phone: PPD Title: Senior Clinical Study Manager Email:PPD
Contract Site:	PPD
Principal Investigator (PI):	PPD
Institutional Review Board (IRB):	Advarra IRB PPD

Contents

Key Abbreviations:

MED	Minimal Erythema Dose
MEDu	Unprotected MED (i.e., the MED of an untreated site)
MEDuI	Initial Unprotected MED
MEDuR	Repeat Unprotected MED
MEDp	Protected MED (i.e., the MED of a treated site)
ssMEDp	SPF Standard Protected MED (i.e., site treated with SPF standard)
tpMEDp	Test Product Protected MED (i.e., site treated with test product)
ssSPFi	SPF value for the SPF standard for an individual participant
tpSPFi	SPF value for a Test product an individual participant

1.0 Introduction

The 2011 FDA Final Rule [1] describes the procedures for determining the static sun protection factor (SPF) of over-the-counter (OTC) sunscreen products.

The static SPF is defined as the ratio of the minimal erythema dose of ultraviolet (UV) radiation for sunscreen-protected skin to that for unprotected skin. The minimal erythema dose (MED) is the lowest dose of UV radiation that produces the first perceptible erythema with clearly defined borders (covering more than 50% of the exposure site), 16 to 24 hours (hrs) after UV exposure administration. UV radiation doses, expressed in Joules/square meter (J/m^2), are administered using a xenon arc lamp that simulates solar radiation and satisfies the requirements of the FDA Final Rule [1].

2.0 Objective

The objective of this study is to determine the static SPF of three sunscreen lip balms using the methodology described in the FDA Final Rule (2011) [1].

3.0 Test Products

Three sunscreen lip balms will be evaluated; each has a target SPF of 30.

- ChapStick Active Performance (CAP) UnScented (CCI [redacted]
- CAP Herbal Mint Flavour (CCI [redacted]
- CAP Mountain Berry Flavour (CCI [redacted]

An SPF Standard (7% Padimate-O and 3% Oxybenzone) will be evaluated alongside the three test products.

4.0 Study Design/Blinding

Test treatments (SPF standard, test products and unprotected sites) will be randomized to test sites to ensure blinded evaluation of erythemal response. Eligible participants will be assigned to treatment based on the randomization schedule on Day 1 of the study.

To maintain study blinding and avoid bias, the erythema evaluator will not participate in either product application or the administration of UV doses. Treatment application and UV irradiation will be carried out by different individuals on the study team.

Each participant will have up to 8 test sites delineated on the skin of their back. One will be used on Day 1 to determine MEDuI. Assignment of the three test products, SPF standard and an unprotected site (MEDuR) to test site shall follow the randomization schedule generated by PPD according to SOP PPD. If the back of a participant cannot accommodate a minimum of 6 sites (too small, unsuitable areas of anatomical curvature), the participant will be discontinued.

Note: A minimum of 6 test sites is required to evaluate MEDuI, MEDuR, the 3 test products and the SPF standard sunscreen. Up to 8 test sites will be drawn to provide an additional 2 sites should test product reapplication be necessary due to uneven/ inconsistent application to help ensure UV exposures can be completed for all study treatments.

For practical reasons, the only site that may be known to the erythema evaluator is the Initial Unprotected MED (MEDuI) site. If the evaluator has questions about test site locations and/or exposure site locations, the evaluator may receive assistance from the technicians who applied the test materials and administered the UV doses; the technicians should not influence the evaluator in the grading of UV responses.

Study duration is expected to be 3-8 days.

5.0 Participants

Potential study participants will be recruited from PPD Volunteer Database per SOPs PPD .

The FDA Final Rule (2011) [1] requires the test panel to produce a minimum of 10 valid test results for each product tested; invalid data from a maximum of 3 participants per product may be rejected (i.e., 10□13 participants and □ ≤t □□□□□□□□per product). Therefore, a maximum of 23 participants will be enrolled in order to achieve the minimum of 10 valid results per study product required for SPF labeling [1].

Study participants will be healthy male and female volunteers with skin types I, II or III (Table 1: Fitzpatrick Skin Types). Individual Typology Angle (ITA°) will be measured for each participant to determine skin type. No discrimination of any kind (e.g. social class, gender, skin color, ethnicity) should preclude eligible participants from participating in the study.

Table 1. Fitzpatrick Skin Types

ITA Value	Skin Color Categories	Fitzpatrick Skin Type	Fitzpatrick Definitions
>55°	Very Light	I	Always burns easily; never tans
>41° to 55°	Light	II	Always burns easily; tans minimally
>28° to 41°	Intermediate	III	Burns moderately; tans gradually
>10° to 28°	Tan	IV	Burns minimally; always tans well
>-30° to 10°	Brown	V	Rarely burns; tans profusely
□-30°	Black	VI	Never burns; deeply pigmented

Eligible participants must satisfy the following inclusion and exclusion criteria.

5.1 Inclusion Criteria

- Participant must provide a signed and dated, legally effective, informed consent document, which indicates they have been informed of all pertinent aspects of the study, before any study procedures are performed.
- Participant must be 18-70 years old inclusive at the time of consent.
- Participant must provide relevant details of their medical history and current/recent medications and treatments (self-reported).
- Participant must have completed an annual Health Insurance Portability and Accountability Act (HIPAA) Authorization form.
- Participant must have completed a Photo Release Form.
- Participant must be able to read, write, speak and understand English.
- Participant must be in good general health.
- Participant must have uniform skin color over the test area (skin of the back between the shoulder blades and above the waistline) and an ITA value >28°.
- Participant must have Fitzpatrick Skin Type I, II or III
- Participant must have sufficient area of suitable skin on their back for at least six 40cm^2 test sites.
- Willing to have body hair clipped by a technician if participant has excessive hair in the test area.
- Participant must have a valid form of personal identification (photo ID, driver's license, passport, permanent resident card, military ID card; forms cannot be expired).
- Male and female participants of child-bearing potential must agree to use a highly effective method of contraception for the duration of the study and for 14 days after their last treatment application.
  Note: A participant is considered to be of child-bearing potential if, in the opinion of the PI, they are biologically capable of having children and sexually active.

5.2 Exclusion Criteria

- Participant with a scheduled or planned Covid-19 vaccination during likely dates of study participation.
- Participant with a history of abnormal response to sunlight/UV radiation.
- Participant with a history of sensitivity to any ingredient of the test material or skin marker pen, or to latex; or any known sensitivities/allergies, including but not limited to cosmetic/toiletry products and topically applied skin treatment products/drugs.
- Participant with any significant dermatological condition, such as atopic dermatitis (eczema), psoriasis, skin cancer, melanoma, active dermal lesions, nevi, blemishes or moles, lupus, diabetes, or connective tissue disease, that would increase the risk associated with participation.
  Note: presence of non-dysplastic nevi, blemishes, or moles would be acceptable if, in the opinion of the PI, they will neither jeopardize participant safety or compromise study outcomes. A participant with dysplastic nevi should be disqualified.

- Participant receiving any treatment with medications that would, in the opinion of the PI, confound study outcomes or increase the risk associated with participation, such as systemic or topical corticosteroids, antibiotics, anti-inflammatory drugs, antihistamines, antihypertension medications, or any other photosensitive medications.
  Note: The prohibited medication list will be available to site staff for reference during screening.
- Participant who has used topical or systemic steroids, antihistamines, antibiotics or anti-inflammatory medications within 7 days of Study Day 1 which, in the opinion of the PI, could interfere with study outcomes.
- Participant who has used/applied any personal care products (e.g. lotions, sunscreens, sunless tanners) and/or topical medications in/on the test area within 24 hrs of Study Day 1.
- Participant who is unwilling to cease use of personal care products (e.g. lotions, sunscreens, sunless tanners) and/or topical medications in/on the test area for the duration of the study.
- Participant with any known communicable disease(s) (e.g. hM dPF6 □dh □□□□□□□2d Hepatitis C, etc.)
- Participant with skeletal protrusions and/or extreme areas of curvature in the test area.
- Participant with a medical treatment/vaccination (other than the Covid-19 vaccination) planned during the study, which would make them ineligible, place them at undue risk, or confound the outcome of the study, per the discretion of the PI.
- Participant who has undergone any surgical procedure in the last 12 months.
- Participant who has undergone chemical or physical treatment procedures in the test area within the last 12 months.
- Planned hospitalization during the study.
- Participant who exceeds a weight limit of 300 pounds due to equipment limitations.
- Participant with any condition that might confound the study results, increase the risk associated with participation, or interfere with study participation.
- Female participant who is pregnant, planning to become pregnant during the study, or breastfeeding (self-reported).
- Participant with any visible sunburn or suntan in test area.
- Participant with visible sun damage, scarring or tattoos in the test area that would interfere with study participation.
- Participant with any sun exposure and/or use of an artificial tanning lamp on the test area within 2 months of Study Day 1.
- Participant who is unwilling to avoid sun exposure and/or cease use of an artificial tanning lamp on the test area for the duration of the study.
- Participant who has participated in any clinical study involving UV exposure within the last 2 months, or any other type of clinical study within the last 1 month.

- Participant who is an employee/contractor or immediate family member of the PI, study site or Sponsor.

5.3 Participant Responsibilities

Lifestyle Considerations:

For the duration of the study, participants should be

- Dependable, willing and able to keep all study appointments, and follow study instructions.
- Willing to not begin another other clinical study while participating in current study.
- Willing to wear loose-fitting clothing to facilitate access to the back during study visits.
- Willing to continue with use of their current personal care products and avoid use of any new personal care products (e.g. makeup, cleanser).
- Willing to cease use of any personal care products (e.g. lotions, sunscreens, sunless tanners) and topical medications on the test area.
- Willing to not use tanning lamps and to not expose the test area to the sun.
- Willing to inform study staff about any side effects, changes in their health/medications, pregnancy and study-related problems.

Contraception:

All male participants able to father children and female participants who are of child-bearing potential, sexually active and at risk of pregnancy must agree to use a highly effective method of contraception, consistently and correctly, for the duration of the study and for 14 days after their last assigned treatment. This requirement does not apply to females of child-bearing potential with same sex partners or to participants who are, and will continue to be, abstinent from penile-vaginal intercourse on a long term and persistent basis, when this is their preferred and usual lifestyle.

The PI, or designee, will discuss the need to use highly effective contraception, consistently and correctly, with the participant; the conversation will be documented. In addition, the PI, or designee, will instruct the participant to call the site immediately if their contraception method is discontinued or if pregnancy is known, or suspected, in either the participant or the [redacted]partner.

The following is an all-inclusive list of female contraceptive methods that meet the GSK definition of highly effective for avoiding pregnancy (i.e., have a failure rate of less than 1 % per year when used consistently and correctly and, when applicable, in accordance with the product label). Periodic abstinence (e.g., calendar, ovulation, sympto-thermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.

- Contraceptive subdermal implant
- Intrauterine device or intrauterine system

- Combined estrogen and progestogen oral contraceptive
- Injectable progestogen
- Contraceptive vaginal ring
- Percutaneous contraceptive patches
- Male partner sterilization with documentation of azoospermia prior to the female participant's entry into the trial, and this male is the sole partner of the female participant. The documentation on male sterility can come from site personnel review of medical records, medical examination and/or semen analysis, or medical history interview provided by her or her partner.

Male participants with female partners of child-bearing potential must comply with the following contraception requirements for the duration of the study and for 14 days after their last assigned test treatment.

- Vasectomy with documentation of azoospermia. The documentation on male sterility can come from site personnel: review of the [redacted]medical records, medical examination and/or semen analysis, or medical history interview.
- Male condom plus partner use of one of the contraceptive options below that meets the effectiveness criteria including a less than 1% rate of failure per year, as stated in the product label:
  - Contraceptive subdermal implant
  - IUD or intrauterine system
  - Combined estrogen and progestogen oral contraceptive
  - Injectable progestogen
  - Contraceptive vaginal ring
  - Percutaneous contraceptive patches

These allowed methods of contraception are only effective when used consistently, correctly and in accordance with the product label. The PI, or designee, will confirm the participant has had instruction in how to properly use their method of contraception from an appropriately trained health care professional and will document this conversation.

5.4 Participant Discontinuation and Withdrawal

A participant may be discontinued or withdraw from study participation at any time if the participant or the PI (or designee) feels it is not in their best interest to continue. The following is a list of possible reasons for study discontinuation.

- Participant develops a condition listed in the exclusion criteria or hypersensitivity, or takes a contra-indicated medication/treatment.
- Non-compliance with the requirements of the protocol.
- Failure to follow site staff instructions.

- Failure to attend scheduled study visits.
- Adverse event (AE) that, in the opinion of the PI, means it would be in the best interest to discontinue study participation.
- Protocol violation requiring documentation of deviation.
- Sponsor request for early termination of study.

Participants are free to withdraw from study participation at any time, for any reason, specified or unspecified, and without prejudice. Reasonable attempts will be made by the PI, or designee, to ascertain the reason for withdrawal. This will be recorded in source documentation and included in the final report.

5.5 Disposition of Withdrawn Participants

The date a participant is withdrawn from the study and the reason for discontinuation will be recorded in source documentation. If a participant fails to return for scheduled study visits, the PI, or designee, will make every reasonable effort to contact the participant and determine why they failed to attend. This information will be recorded in source documentation. When a participant is withdrawn (regardless of reason), the PI, or designee, will encourage the participant to return to site to complete all evaluations which may be necessary to assure that the participant is free of untoward effects, and to seek appropriate follow-up for any unresolved AEs.

5.6 Participant Replacement

If participants are discontinued from the study or have their data rejected because results are considered invalid (see Section 9.0), additional participants can be randomized up to a maximum of 20 randomized participants per test product, until the maximum number of invalid data sets (3 per test product) is reached. Any valid data collected up to that point will continue to be used.

6.0 Study Instruments

6.1 Solar Simulators and Radiometer/Detector systems

The solar simulators used in the study will comprise a multiport or single port xenon arc lamp equipped with 1 mm WG320 UVC blocking filters, 1 mm UG-11 visible and infrared blocking filters, and heat-rejecting dichroic mirrors that comply with the 2011 FDA Final Rule [1] (Model 16S/Model 601, Solar Light Co., Philadelphia), as described in Table 2. Solar simulator systems will not be interchanged or replaced during testing (Model 16S to Model 601 or vice versa), except in case of malfunction.

- The Model 16S solar simulator will be used with radiometer PMA2100 and detector Erythema PMA2105 showing output in MED/hr.
- The Model 601 solar simulator will be used with radiometer DCS-2/PMA2100 and detector Erythema PMA2108 showing output in MED/hr.

Table 2. Requirements for Irradiation Source

Each solar simulator will have a minimum warm up time of 20 minutes (mins) prior to capturing the lamp effective irradiance readings.
Continuous, stable emission spectrum from 290 to 400 nanometers (nm).
Emission spectrum measured at least annually, after replacement of lamp bulb or following any change in optical components, using an appropriate spectroradiometer system calibrated to a NIST traceable source.
Daily radiation intensity will be measured (after warm-up period) before and after each photo-test, or at least at the beginning and end of each test day, using an erythemally-weighted radiometer (add model) with a calibration consistent with the spectroradiometer system.
No significant time-related fluctuations in the exposure plane (±10%)
Good beam uniformity (±20% from centerline reading)
UVAII (320-I Vt □□aB□ Ht ≥ □□total UV irradiance
UVAI (340-Vtt □□aB□ St ≥ □□total UV irradiance
F□□□□M□□□□□□□□□□□ H, t □□≤dVtt □□ □≤d, tt Watts/square meter (W/m^2) to avoid inducing excessive heat and/or pain during irradiation
Specification of spectral output is described by the cumulative erythemal effectiveness for successive wavelength bands from 290-400 nm (expressed as a percentage of total erythemal effectiveness from less than 290 nm to 400 nm). Percent erythemal dose contributions are provided in Table 3

Table 3. Percent Erythemal Dose Contributions

Wavelength Range (nm)	Percent Erythemal Dose Contribution
<290	<0.1
290-300	1.0-8.0
290-310	49.0-65.0
290-320	85.0-90.0
290-330	91.5-95.5
290-340	94.0-97.0
290-400	99.9-100.0

6.2 Colorimeter

A hand-held reflectance colorimeter, SmartProbe 400 (IMS, Inc.) or equivalent, will be used to measure the skin color of the test site in the L*a*b* color space. L*, a*, and b* values will be measured from at least 3 different locations on the □□□□□□□□□□□□□□□□ and used to calculate the ITA°. ITA° can be used to estimate the MED of unprotected sites (MED_u).[2]

6.3 Digital Camera

Photographs may be taken of test sites using a Canfield Twin Flash Clinical System 950029 with Nikon D90 Digital SLR (or similar system) to document unexpected results/AEs if requested by the PI, or designee, or the Sponsor. Photographs will not reveal participant identity.

7.0 Study Procedures

Table 4. Study Procedures

Study Procedures	Day 1	Day 2	Day 3
Written Informed Consent	X		
Skin examination; determine ITA°; confirm skin type	X		
Complete medical history/eligibility questionnaire	X		
Identify and document concomitant medications/treatments	X	X	X
Confirm subject qualification against inclusion/exclusion criteria	X		
Delineate 6 test sites on the skin of the back	X		
Administer UV doses* to unprotected site for MED_{uI}	X		
Assess compliance		X	X
Evaluate UV responses (16-24 hours [hrs] later) Determine MED_{uI}		X	
Apply test materials (SPF standard & test products) to their assigned test sites according to the randomization schedule		X	
15 min drying time		X	
Administer UV doses* to unprotected site for MED_{uR}		X	
Administer UV doses* to protected sites		X	
Evaluate UV responses (16-24 hrs later) Determine MED_{uR} and $_{ss}MED_p/_{tp}MED_p$			X
Monitor for Adverse Events†	X	X	X
Study conclusion			X

* For unprotected (untreated) sites, total exposure time is typically 1-2 mins; for protected sites (i.e. treated with either a sunscreen product or SPF standard), total exposure time is typically 11-25 mins. Participants will be informed of this in the ICF.

†Adverse Events (AEs) and therefore all Serious Adverse Events (SAEs will be collected from immediately after participant provides consent to participate in the study by the completion of the Informed Consent Form (ICF).

For consistency of evaluation, study procedures (skin assessments, irradiation, treatment applications) will be performed with the participant in the same position ☐ upright or prone ☐throughout the study. Test material preparation/application, UV exposures and MED assessments will be performed by trained study staff in ambient conditions (as described in SOP PPD).

7.1 Day 1

7.1.1 Enrollment

7.1.1.1 Informed Consent Process

Written informed consent will be obtained from each potential participant prior to entering the study (Informed Consent of Human Subjects, 21 CFR Part 50, Subpart B). The PI will ensure the informed consent process is conducted in accordance with applicable local, state, and federal laws and regulations.

Prospective participants will report to the study site and be provided with a copy of the Informed Consent Form (ICF), with Privacy Rule 45 CFR parts 160 and 164 (details the Federal protection for the privacy of health information), a Photo Release Form and an annual HIPAA authorization form to review. Site staff will answer any questions they may have about the study. If they chose to participate, site staff will obtain the applicable signatures on the enrollment documentation, starting with the ICF. Site staff will then complete a Medical History/Eligibility Questionnaire with the participant and document any concomitant medications/treatments (year of birth, but not full date of birth, may be recorded in source documentation). Enrollment procedures will be completed in a private setting. Each participant will be given a signed copy of the Informed Consent Form. If the participant has questions about their rights, they may contact the IRB at any time during or after trial participation.

If required, site staff may consult the study physician/dermatologist regarding the participant□□medications/treatments and/or responses to the medical history/eligibility questionnaire to confirm qualification.

Participants deemed eligible based on inclusion/exclusion criteria will continue to the screening skin evaluation. Ineligible participants will be discontinued.

7.1.1.2 ITA/Skin type determination

The □□□□□□□□□□□□□□□□□□□□back, between the beltline and shoulder blades, will be examined for uneven skin tones and blemishes using a Woods Lamp. All participants will acclimate at room temperature (as described in SOP PPD) for 10 mins prior to the skin being examined. ITA° will then be determined by a study technician; mean L *, a*, b* values will be calculated from at least 3 measurements on the back of each participant. An ITA° calculation range greater than a 10-point difference will result in disqualification (example: 34.6°-45.4°).

Qualified participants will be enrolled and scheduled for study procedures. Ineligible participants will be disqualified. Each qualifying participant will be assigned a unique identifying study number in order of study enrollment.

7.1.2 Initial Unprotected MED (MEDuI) Dose Administration

Using an indelible marker and template, and with the participant in an upright or prone position, a study technician will draw up to 8 rectangles (minimum 6), i.e., up to 8 test sites (minimum 6) on the skin of the back (between the belt-line and shoulder blades, lateral to the midline, avoiding any areas with extreme curvature). Each rectangle will be 40 square centimeters (cm^2) in area, with at least 1 cm between the borders of adjacent test sites. Each test site will be further sub-divided into 5 subsites (exposure sites). The area of each subsite will be ☐ 0.5 cm^2; the distance between the borders of each subsite will be at least 0.8 cm; the distance between any subsite and the edge of its test site will be ☐ 1 cm.

With the participant in an upright or prone position, a series of 5 timed UV doses, increasing in 25 percent increments (J/m^2), will be administered to the designated ☑ 56 ☐ test site.

Table 6. UV Dose Series for MEDuI

Expected MEDu				
0.64	0.80	1.00	1.25	1.56

After irradiation is complete, an immediate response code will be recorded for each subsite in source documentation.

Table 7. Immediate Response Codes

N	No immediate response
D	Immediate darkening or reddening
H	Immediate generalized heat response spreading beyond the subsite

The technician will document the identities of the solar simulator, radiometer and detector; UV doses; the lamp effective irradiance reading before UV doses (*optional:* after UV doses lamp effective irradiance reading per request of the Study Sponsor); Immediate Response Codes; and the UV dose series completion time stamp in source documentation.

Participants will be instructed to avoid UV exposure; they will be reminded of the study requirements/lifestyle considerations and asked to return to the study site 16 to 24 hrs after completion of Day 1 UV doses.

7.2 Day 2

7.2.1 MEDuI Determination

Participants will return to the study site 16 to 24 hrs later for erythemal response evaluation. Each will be questioned non-directively to assess compliance with the requirements of the protocol and to identify changes in health/concomitant medications. Any changes/AEs will be recorded in source documentation. All

participants will acclimate at room temperature for 10 minutes prior to response evaluation (as described in SOP PPD).

A trained evaluator will grade the responses of the UV exposed sites, under warm white fluorescent or tungsten illumination of at least 450 lux, using the grading scale shown in Table 8. Grades will be recorded, along with any comments, in source documentation and the evaluator will time stamp the evaluation completion.

Table 8. Grading Scale for Erythema Responses

0	No erythema response
1	Minimally perceptible erythema with no clearly defined borders
2	Perceptible erythema with clearly defined borders (covering more than 50% of the exposure site)
3	Moderate erythema with sharp borders*
4	Dark red erythema with sharp borders*
5	Dark red erythema with sharp borders and possible edema*
6	Intense erythema with sharp borders and edema*

* If moderate, dark red or intense erythema does not reach borders of exposed site, an explanation will be provided in the source documentation.

The MEDuI is defined as the first exposure site in the series with erythema □□□□□ H.

Participants whose MEDuI can be determined will continue with study procedures. Participants whose MEDuI cannot be determined will be discontinued.

The progression of erythema grades must be consistent with the UV doses administered.

Participants with pronounced tanning responses are not considered good candidates for SPF studies with an erythema endpoint. They should be discontinued from the study and another participant should be added.

To facilitate study scheduling, participants may leave the study site after MEDuI determination and return up to 1 week later to resume study procedures. Re-scheduled participants whose testing has been paused will be questioned non-directively on their return to assess compliance with the requirements of the protocol and to identify changes in health/concomitant medications. to confirm ongoing qualification. Any changes/AEs will be recorded in source documentation.

7.2.2 Application of Study Treatments

7.2.2.1 SPF Standard Application

The study technician will apply 80 ± 2 mg (2.0mg/cm^2 ± 0.05 mg/cm^2) of the SPF standard to its assigned test site using a fingercot. A double-weighing procedure (weighing the syringe/pipette + product + fingercot, prior to and after application) to ensure the required quantity of SPF standard is delivered. Using the fingercot and light pressure, the SPF standard will be evenly spread over the test site; spreading time will be 35 ± 15 secs, depending on the ease of application.

7.2.2.2 Test Product Application

The study technician will apply 80 ± 2 mg (2.0mg/cm^2 ± 0.05 mg/cm^2) of the test [redacted] using a fingercot. A double-weighing procedure (weighing boat + product + fingercot, prior to and after application) to ensure the required quantity of product is delivered. Using the fingercot and light pressure, the test product will be evenly spread over the test site; spreading time will be 35 ± 15 secs, depending on the ease of application.

7.2.2.3 Additional Application Instructions for All Test Materials

- The study technician will ensure test materials are homogenous (thoroughly mixed and/or shaken well) prior to application
- Test sites may be cleaned using a dry cotton pad or equivalent prior to test material application.
- Evenness of application will be verified by observation with a Woods Lamp. If non-uniformity or streaking of the test material is noted, the test site shall be rejected and may not be used for testing. If another test site is available, re-application of the test material should be attempted.
- Test material dispensing (test site allocation, weight (mg), spreading time, drying time) will be recorded in source documentation.
- Wait at least 15 mins after applying the test materials before commencing UV irradiation of unprotected and protected sites.

7.2.4 UV Doses for Unprotected and Protected Sites

7.2.4.1 Repeat Unprotected Minimal Erythema Dose (MEDuR) Determination

A series of 5 (timed) UV doses, increasing by 25 percent increments (J/m^2) across the 5 subsites, will be administered to the assigned unprotected test site of the back The UV exposure selected for each subsite will be based on the previous MEDuI evaluation, which appears as the [redacted] point, as shown above in Section 7.1.2, Table 6.

Immediate Response Codes and procedural information will be recorded in source documentation as described in Section 7.1.2, Table 7.

7.2.4.2 Protected Minimal Erythema Dose (tpMEDp/ssMEDp) Determination

A series of 5 (timed) UV doses, increasing by 25 percent increments (J/m²) across the 5 subsites, will be administered to each protected test site (i.e., the sites treated with SPF standard [ssMEDp] and test products [tpMEDp). The UV exposure selected for each subsite will be determined by the previously determined MEDuI and the expected SPF of the test materials, as shown in Table 9.

Table 9. FDA Final Rule Dose Series

Expected SPF	Multiple of expected SPF and Participant MEDuI				
< 8	0.64	0.80	1.00	1.25	1.56
≥ 8 to 15	0.69	0.83	1.00	1.20	1.44
> 15	0.76	0.87	1.00	1.15	1.32

Immediate Response Codes and procedural information will be recorded in source documentation as described in Section 7.1.2.

While administering treatment evaluation UV doses for any Model 16S (single port) testing, as required, the technician may adopt the following procedure to accommodate participant scheduling needs.

- Reduce the test material UV exposure times by the correct UV dose series multiplier and immediately continue UV exposures.

Management approval to adopt this approach and the outcome will be recorded in source documentation.

Participants will be instructed to avoid UV exposure; they will be reminded of the study requirements/lifestyle considerations and asked to return to the study site 16 to 24 hrs after completion of Day H UV doses.

7.3 Day 3

7.3.1 MEDuR, ssMEDp and tpMEDp Determination

Participants will return to the study site 16 to 24 hrs later for erythemal response evaluation. Each will be questioned non-directively to assess compliance with the requirements of the protocol and to identify changes in health/concomitant medications. Any changes/AEs will be recorded in source documentation. All participants will acclimate at room temperature for 10 minutes prior to response evaluation (as described in SOP PPD).

A trained blinded evaluator will grade the responses of the UV exposed sites, under warm white fluorescent or tungsten illumination of at least 450 lux, using the grading scale shown in Table 8. Grades will be recorded, along with any comments, in source documentation and the blinded evaluator will time stamp the evaluation completion.

Note: the same blinded evaluator should evaluate erythemal response throughout the study.

MED (MEDuR, ssMEDp and tpMEDp) is defined as the first exposure site in the series □□□□□□□□□□□□□□□□□□□□ Hs Erythema grades, comments and the evaluation completion time stamp will be recorded in source documentation.

Photographs of the test sites, which do not reveal participant identity, may be taken to document unexpected results and/or AEs.

8.0 Statistical Analysis

Statistical analyses will be performed by PPD using Microsoft Excel 365 (2021). Since all methodologies for the summary and statistical analyses of the data collected in this study are specified in the protocol, a separate Reporting Analysis Plan (RAP) will not be created. Any major modification of the analysis plan will be documented as a protocol amendment.

8.1 Analysis Population

The analysis population will include all eligible participants (qualified based on the inclusion/exclusion criteria) who are randomized, received study treatment and provide valid results.

8.2 Participant Disposition and Demography

Participant disposition and demographic characteristics will be tabulated and presented with summary descriptive statistics (sample size, mean, standard deviation, median, minimum and maximum) for continuous variables (e.g., age) and frequency distributions for categorical variables (e.g., sex).

8.3 SPF Computation

The SPF values of each test product (tpSPFi) and the SPF standard (ssSPFi) will first be computed for each individual participant (to one decimal place) as follows:

$$\mathbf{SPFi = MEDp/MEDuR}$$

The arithmetic mean SPF and standard deviation (SD) will then be calculated separately for each test product and the SPF standard from valid SPFi data; the standard error (SE) of the mean will also be calculated (n= no. participants who provide valid test results).

$$\mathbf{SPF = (\Sigma SPFi)/n}$$

SD = □□v□P[b□) □(v□P[b□a²/n) / (n-1))]

P5 3 P6u□□

The t value from □□□□H-□□□□□□Student-t distribution table corresponding to the upper 5% point with n-1 degrees of freedom will be obtained.

The labeled SPF value will be determined as the largest whole number less than the following calculation:

Labeled SPF = Mean SPF – (t * SE)

For the SPF determination of the test products to be considered valid, in compliance with the FDA Final Rule 2011, the SPF value of the SPF standard should fall within the SD range of the expected SPF (i.e. 16.3 ± 3.43 or 12.87 to 19.73). [1]

8.4 Summary Analyses

Calculations and statistical analyses will be performed in compliance with the FDA Final Rule (2011) [1] and reviewed by PPD Quality Assurance. Individual participant results will be tabulated along with summary statistics, including mean SPF, valid test data used in the SPF calculations, SD, SE and t-value (as described in Section 8.3). Passed or failed grades will also be listed, along with excluded participants and reasons for exclusion.

9.0 Rejected Test Data:

9.1 Invalid Data

Test data are deemed invalid and shall be excluded under the following circumstances:

- Erythema is not present on either the unprotected or protected test site(s).
- Erythema is present at all subsites on either the unprotected or protected test site(s).
- The responses are inconsistent with the series of UV doses administered.

Data from a maximum of three participants per test material may be invalidated for the above reasons.[1]

9.2 Other Reasons for Data Rejection

Test data may be excluded for other reasons, examples include:

- Participant was non-compliant with study protocol
- Participant lost to follow up
- Participant unable to complete the study
- Participant discontinued due to an AE
- Participant disqualified due to an administrative/technical failure
- Participant dismissed due to product wash off
- Participant discontinued/withdrawn (See Section 5.4)

10.0 Adverse Events

The safety population is defined as all randomized participants who received at least one dose of a study treatment.

The PI, or designated designee(s), is responsible for detecting, documenting and reporting events that meet the definition of an AE or SAE.

The PI, or designated designee(s), is responsible for following up serious AEs (SAEs); AEs considered to be test product (or study procedure) related; and AEs that caused the participant to discontinue or be withdrawn from the study.

10.1 Definition of an Adverse Event (AE)

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a test product, whether or not considered related to the test product. 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 a test product.

Events Meeting the AE Definition:

- Unexpected or unusual reactions which occur within a test site that cannot be completely described by the scale in Table 8 (e.g., hives) will be recorded as AEs.
- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (e.g., ECG, radiological scans, vital sign measurements), including those that worsen after test product administration, considered clinically significant in the medical and scientific judgment of the PI or medically qualified designee (i.e., not related to progression of underlying disease).
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition after test product administration.
- New conditions detected or diagnosed after test product administration, even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either test product or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.
- □lack of efficacy□per se will not be reported as an AE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE if they fulfill the definition of an AE.

Events NOT meeting the AE definition:

- Any clinically significant abnormal laboratory findings (if applicable) or other abnormal safety assessments which are associated with an underlying disease, unless judged by the PI, or medically qualified designee, to be more severe than expected for the participant's condition.
- A medical or surgical procedure (e.g., endoscopy, appendectomy) is not an AE. The condition that leads to the procedure is the AE (e.g., gastritis, appendicitis).
- Situations where an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations in a pre-existing disease/condition present or detected at the start of the study that did not worsen.
- Localized erythema caused by exposure of the skin to UV radiation is expected and will not be reported as an adverse event.

10.2. Definition of a Serious Adverse Event (SAE)

An SAE is a particular category of AE where the adverse outcome is serious. If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met.

A serious adverse event is any untoward medical occurrence at any dose that:

- **Results in death**
- **Is life-threatening**
  - The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant 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.
- **Requires inpatient hospitalization or prolongation of existing hospitalization**
  - In general, hospitalization signifies that the participant 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 outpatient 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.
- **Results in persistent or significant disability /incapacity**
  - 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 an uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

- **Results in congenital anomaly/birth defect**
- **Other situations:**
  - Medical or scientific judgment should be exercised in deciding whether SAE 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 participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.
  - Examples of such events include 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.

Note: Classification of an AE as 'serious' is based on the outcome of the event and is a factor in determining reporting requirements.

10.3 Expected Events

UV Expected Events:

Possible/expected side effects on and/or around the test sites associated with UV exposure include the following:

- Erythema (sunburn)
- Mild discomfort
- Itching
- Edema (swelling)
- Dryness/Tightness
- Peeling
- Papules
- Stinging/Burning
- Ulceration or irritation
- Heat
- Hyperpigmentation/hypopigmentation are possible

Any expected side effects experienced by the participant after UV exposure of the test sites are not to be considered AEs. Test products may not perform up to the expected protection level. Under protection outcomes are potential anticipated events and are also not to be considered AEs. However, if any of these parameters/outcomes appear

to be highly exacerbated, more than normally associated with the test procedures as determined by the PI, or designee, and lead to discontinuation, the event will be documented as an AE.

Skincare Product Expected Events:

There is always the possibility of irritation or a skin reaction to any product applied to the skin. Examples of possible skincare product reactions are:

- Redness
- Dryness/tightness
- Peeling
- Itching
- Burning/stinging
- Allergic reaction

Any skin reaction associated with the application of a test product to the test site will be considered an AE and documented as such.

10.4. Time Period and Frequency for Collecting AE and SAE Information

All AEs, and therefore all SAEs, will be collected immediately after a participant provides consent to participate in the trial by the completion (signing) of the ICF and until 14 days following last administration of test product (or last study procedure). Medical occurrences that began before obtaining informed consent will be recorded in the source documentation as Medical History/Current Medical Conditions, not as AEs.

All SAEs will be recorded and reported to the Sponsor, or designee, immediately and under no circumstance should this exceed 24 hours. The PI, or designee, will submit any updated SAE data to the Sponsor within 24 hours of it being available.

The PI is not obligated to actively seek AEs or SAEs after the conclusion of study participation. However, if the PI learns of any SAE, including a death, at any time after a participant has been discharged from the study, and they consider the event to be reasonably related to the test product or study participation, the PI must promptly notify the Sponsor.

10.5. Reporting Procedures

The PI, or medically qualified designee, is responsible for detecting, documenting and reporting all events that meet the definition of an AE and remains responsible for following up on AEs that are serious or considered to be related to a test product, participation in the study or a study procedure, or that caused the participant to discontinue a test product or the study.

Each participant will be questioned about AEs. Spontaneously reported AEs and those elicited by asking non-directive questions (such as "How do you feel?") will be assessed, recorded in AE-specific source documentation and reported appropriately.

The PI, or medically qualified designee, is to report all directly observed AEs and all AEs spontaneously reported by a participant.

Each AE should be assessed to determine if it meets the criteria for a SAE. If an SAE occurs, expedited reporting will follow local and international regulations, as appropriate.

When an AE occurs, it is the responsibility of the PI, or medically qualified designee, to review all documentation (e.g., hospital progress notes, laboratory and diagnostics reports) related to the event. The PI, or designee, will record all relevant information regarding an AE in AE-specific source documentation and all details relating to an SAE on the paper SAE form provided.

It is not acceptable for the PI, or medically qualified designee, to send photocopies of a participan□□□medical records to GSK CH in lieu of completion of AE-specific source documentation or the SAE form. There may be instances when copies of medical records are requested by GSK CH. In this instance, all participant identifiers, except for the participant number, will be redacted prior to sharing with GSK CH.

The PI, or medically qualified designee, will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. The diagnosis should be the documented as the AE/SAE, where known, and not the individual signs/symptoms (e.g., upper respiratory tract infection, seasonal allergy; not cough, runny nose).

AEs elicited by the PI, or medically qualified designee, during study visits should be recorded in AE-specific source documentation and/or using the SAE form, as appropriate. Care will be taken not to introduce bias when questioning a participant about changes in their health. Open-ended and non-directive verbal questioning should be used.

Reporting an Adverse Event:

AEs will be reported using AE-specific source documentation by the PI or site staff and the Sponsor-supplied SAE form, when appropriate, using concise medical terminology. Where the same data are collected, AE-specific source documentation and the SAE form must be completed in a consistent manner; the same AE terms should be used on both.

Reporting a Serious Adverse Event:

In addition to recording the details in AE-specific source documentation, an SAE form should be completed, as fully as possible. Hard copies of the paper SAE form will be provided for the Investigator Site Master File. Original SAE forms should be retained in the Investigator Trial Master File.

It is essential to enter the following information:

- Protocol and participant identifiers

- Participant demography
- Description of event(s), with diagnosis if available
- PI opinion of relationship to test product (or study procedure, if appropriate)
- Criterion for seriousness

The following are desirable and are of particular relevance for PI and GSK CH assessment of the SAE report:

- Date of onset of event
- Date event stopped, if relevant
- Test product start date
- Test product end date, if relevant
- Action taken in relation to the test product
- Outcome if known

The SAE form, completed as fully as possible, must be scanned and e-mailed to the GSK CH Clinical Operations Safety Reporting email box with the GSK CH study number and participant number in the title field of the email **immediately and under no circumstance should this exceed 24 hours** after study site personnel learn of the event. The PI will submit any updated SAE data to the sponsor **immediately and under no circumstance should this exceed 24 hours** of it being available. The GSK CH Study Manager should also be notified of the situation by telephone or email.

Email Serious Adverse Events to:

PPD

The GSK CH Study Manager, or designee, will be responsible for forwarding the SAE form to the Case Management Group, Global Clinical Safety and Pharmacovigilance mailbox PPD . The initial report will be followed up with more information as relevant, or as requested by the Sponsor.

10.6. Evaluating Adverse Events

Assessment of Intensity:

The PI, or medically qualified designee, will assess intensity for each AE reported during the study and will assign one of the following categories.

- **Mild:** An event that is easily tolerated by the participant, 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.

NOTE: An AE classified as ☒severe☐should not be confused with an SAE.

"Severe" is a category utilized to classify the intensity of an event; both non-serious AEs and SAEs can be classified as "severe". For example, a headache may be "severe" (interferes significantly with the participant's usual function) but would not be classified as "serious" unless it met one of the criteria for an SAE, as described above (Section 1.2.2.). An event is defined as 'serious' when it meets at least 1 of the pre-defined outcomes as described in Section 1.2.2., not when it is classified as "severe".

Assessment of Causality

Causality is one of the criteria used to determine regulatory reporting requirements. For each AE (serious and non-serious), the PI, or medically qualified designee, must provide an assessment of causality in the AE-specific source documentation and, for SAEs, on the SAE form.

The PI, or medically qualified designee, will use clinical judgment to determine causality, having also consulted the Safety Statement provided by the Sponsor for this study. Alternative causes, such as underlying disease(s), concomitant therapy, other risk factors and the temporal relationship of the event to the test product will also be taken into consideration and investigated.

There may be situations where an SAE has occurred, and the PI has minimal information to include in the initial report to GSK CH. The PI is required to make an assessment of causality prior to the initial transmission of the SAE form to GSK CH; they may change their opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.

Relationship to Test Material

The relationship or association of the AE to test product will be characterized as "unlikely", "possible" or "probable" (Table 10).

A "reasonable possibility" of relationship conveys there are facts, evidence and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out. The facts, evidence and/or arguments which suggest a causal relationship should be provided in the AE report.

For safety analyses, AEs classified as a "possible" or "probable" association to test product shall be considered test product-related AEs.

Follow-up of an AE, after discontinuation of exposure to test product is required if the AE or its sequelae persist. Follow-up is required until the event or its sequelae resolve or stabilize at a level acceptable to the PI and to the Medical Monitor.

Table 10: Causality Assessment

Causality Term	Assessment Criteria
Probable	Event or laboratory test abnormality, with plausible time relationship to test product exposure
	Unlikely to be attributed to condition (or disease) or other products in use by participant
	Response to withdrawal clinically reasonable
	Re-challenqe satisfactory or not required
Possible	Event or laboratory test abnormality, with reasonable time relationship to test product use
	Could also be explained by condition (or disease) or other products in use by participant
	Response to withdrawal unclear or lacking
Unlikely	Event or laboratory test abnormality, with a time to test product use that makes a relationship improbable (but not impossible)
	Condition (or disease) or other products provide plausible explanations

10.7. Follow-up of AEs and SAEs

After the initial AE/SAE report, the PI, or medically qualified designee, is required to proactively follow up with each participant and provide further information on the participant's condition. All AEs (serious and non-serious) will be followed until resolution, until the condition stabilizes, until the event is otherwise explained or until the participant is lost to follow-up.

The PI, or medically qualified designee, is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as may be indicated or as requested by GSK CH to elucidate as fully as possible the nature and/or causality of an AE. This may include additional laboratory tests or investigations, histopathological examinations or consultation with other health care professionals. New or updated information will be recorded on the AE CRF page and, for SAEs, on the SAE form. The PI, or designee, will submit updated SAE data to GSK CH within 24 hours of receipt of the information.

The PI is not obliged to actively seek AEs in former study participants. However, if the PI learns of a SAE, including death, at any time after a participant has been discharged from the trial, and considers the event reasonably related to the test product or study participation, they will promptly notify GSK CH by emailing the information to the GSK CH Clinical Operations Safety Reporting email box PPD).

The GSK CH Study Manager, or designee, will be responsible for forwarding the information to the Case Management Group, Global Clinical Safety and Pharmacovigilance group mailbox at GSK PPD).

The PI, or medically qualified designee, will submit any updated SAE data to GSK CH within the designated reporting time frames.

10.8. Withdrawal Due to an Adverse Event

Withdrawal due to an AE should be distinguished from withdrawal due to other causes, according to the definition of an AE noted earlier, and recorded in the appropriate AE-specific source document. When a participant withdraws because of an SAE, the SAE must be reported as already described.

10.9. Regulatory Reporting Requirements for SAEs

GSK CH 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 PI to GSK CH is essential so that legal obligations and ethical responsibilities towards the safety of study participants are met.

GSK CH will comply with country specific regulatory requirements relating to safety reporting to the regulatory authority and IRB, and other investigators if applicable.

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions (SUSAR) according to local regulatory requirements and sponsor policy and forwarded to investigators, as required.

An investigator who receives an investigator safety report describing a SAE or other specific safety information (e.g., summary or listing of SAE from the sponsor) will review it, file it with the Safety Statement in the Investigator Trial Master File and then notify the IRB, if appropriate, according to local requirements.

10.10. Pregnancy

Time Period for Collecting Pregnancy Information

Pregnancy information will be collected on all pregnancies reported while a female participant is taking part in the study, from the signing of informed consent until 14 days after last administration of test product.

Action to be Taken if Pregnancy Occurs

The PI, or designee, will record pregnancy information on the pregnancy form supplied by the Sponsor. The completed form should be scanned and e-mailed to the GSK CH Clinical Operations Safety Reporting email box PPD within 24 hours of learning of the pregnancy. The GSK CH Study Manager, or designee, will be responsible for forwarding the pregnancy form to the Case Management Group, Global Clinical Safety and Pharmacovigilance mailbox PPD). Original pregnancy information forms should be retained in the Investigator Trial Master File.

The female participant 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 by the PI, or designee, to the GSK CH Clinical Operations Safety Reporting email box and the GSK CH Study Manager, or designee, will forward this information to the Case Management Group, Global Clinical Safety and Pharmacovigilance group mailbox at GSK PPD. Generally, follow-up will be no longer than 6 to 8 weeks after the estimated delivery date. Any termination of the pregnancy will be reported.

While pregnancy itself is not considered to be an AE, abnormal pregnancy outcomes (e.g., spontaneous abortion, fetal death, stillbirth, congenital anomalies, ectopic pregnancy) are, and should be recorded as an SAE. Any female participant who becomes pregnant during the study will be withdrawn. If a female participant later discovers they were pregnant during the study, i.e., after their participation completed, their data will be considered valid for statistical analysis purposes.

11.0 Data Recording and Study Record Maintenance

Safety/efficacy data and additional clinical observations will be recorded in source documentation (e.g., case report forms [CRFs]) in accordance with the ALCOA+ principles of data integrity; data should be attributable, legible, contemporaneous, original, accurate, complete, consistent, enduring and available. Correction of data recorded in source documentation will be carried out accordance with PPD SOPs.

Source documents will include completed ICFs, original records of clinical/instrumental observations, test product disposition/product accountability, AE reports, results and activities necessary to reconstruct and evaluate the study. Source documents will be peer-reviewed by the site staff as per PPD standard practice and/or in accordance with PPD SOPs.

Source documents and other study records (e.g., protocol, protocol amendments/ deviations, IRB approval(s), correspondence with the Sponsor/IRB, monitor log/reports) will be maintained in the Investigator Trial Master File in accordance with the intent and purpose of GCP guidelines, PPD SOPs and all applicable laws and regulations.

12.0 Ethical Review

The Sponsor, Monitor(s) and PI will assure all aspects of the study are conducted in accordance with applicable regulations and laws guiding the protection of human subjects, including regulations requiring informed consent (Informed Consent of Human Subjects, 21 CFR Part 50, Subpart B) and the approval and ongoing review of the research by an IRB (Institutional Review Boards, 21 CFR Part 56). The study will be conducted in accordance with the principles of the Declaration of Helsinki (as amended), the Belmont Report and Good Clinical Practice (GCP).

The PI will submit the protocol for the proposed clinical investigation, the ICF , an ingredients listing for each test product and the SPF standard, the Sponsor-supplied Safety Statement, advertising materials and any other relevant documents, as appropriate, to the following duly constituted Institutional Review Board (IRB) for review. Written IRB approval of each item is required prior to study initiation.

Advarra IRB

PPD

The PI will assure that all aspects of the institutional review are conducted in accordance with current federal regulations. The letter documenting IRB approval (with the names and titles of the IRB members) will be provided to the Sponsor. Amendments to the protocol or the ICF will be subject to the same IRB review requirements as the original documents.

Should study duration be extended, the PI will submit a progress report, at least annually, to the IRB. This report will include: the total number of test products evaluated; a description of any changes in study procedures or amendments to the protocol; deviations from the protocol; the number and type of participants evaluated; the number of participants who discontinued (and the reasons for discontinuation); the number of participants who completed the trial; a description of any AEs/SAEs.

13.0 Protocol/ICF Amendment

Any change to the approved protocol and/or ICF must be made by formal amendment of the original document. The amended document must be approved in writing by the PI and the Sponsor prior to implementation. Depending on the nature of the change, IRB approval may also be required prior to implementation; administrative changes will be notified to the IRB.

14.0 Protocol Deviation

The PI and site staff will not deviate intentionally from this protocol for any reason without prior approval of the Sponsor and the IRB, except when the change is necessary to eliminate an apparent immediate hazard to study participants. In that event, the PI must notify the Sponsor and the IRB in writing within 5 working days of the change being implemented.

15.0 Clinical Study Report (CSR)

On completion of the study, the PI will provide the Sponsor with three CSRs (one per test product). Each CSR will include (but not be limited to): study start and end dates; test product identification and expected SPF; SPF standard identification and expected SPF; characterization of the UV source; tabulation of participant demographics; erythema grades; MEDs; descriptive and inferential statistics including SPFi values with valid and rejected data for test products and SPF control, and mean SPF values with

SD; summary of safety data (AEs/SAEs), or confirmation there were no AEs; protocol amendments; protocol deviations; conclusions; identification of the technician who conducted the irradiation procedures, by participant, and lamp calibration data; any other reporting requirements for static SPF studies specified in the FDA Final Rule [1].

16.0 Quality Control and Quality Assurance

This study will be conducted under pertinent Good Clinical Practice Guidelines, other applicable regulatory requirements, and testing facility Standard Operating Procedures.

16.1 Study Monitoring by the Sponsor

In accordance with current FDA regulations and GCP guidelines, study monitors and other Sponsor representatives may periodically inspect study-related data at the study site at pre-agreed, mutually convenient times, during or after completion of the study (Guidance for Industry: Oversight of clinical investigations - A risk-based approach to monitoring, DHHS, FDA, August 2013.). Monitoring provides the Sponsor with the opportunity to evaluate the progress of the study, verify the accuracy and completeness of source documentation, assure all protocol requirements, applicable FDA laws and regulations and the PI's obligations are being fulfilled, and to resolve any issues.

16.2 Study Review by PPD Quality Assurance

Study related documents, including source documents, raw data, statistical outputs and CSRs will be examined for completeness, accuracy and proper documentation practices by PPD Quality Assurance personnel.

17.0 Medical Oversight

The Sponsor will ensure access to an appropriately experienced GSK CH physician/ clinical research scientist to be contacted by study staff for advice on medical questions or problems in the event that the established communication pathways between the study site and P[redacted]are not available. The contact details of this individual (Medical Monitor) will be documented in the Study Contact List located in the Investigator Trial Master File held at the study site.

Contact details for the Medical Monitor are not intended for direct use by study participants. To facilitate access to appropriately qualified medical personnel for study-related medical questions and/or problems, participants will be provided with a contact card. The contact card will provide, as a minimum, protocol identifiers, the [redacted] study identification number, contact information for the study site/PI. The site should contact the Medical Monitor in the event that the PI cannot be reached to provide advice on a medical question or problem identified by a healthcare professional other than the PI.

18.0 Clinical Study Products

Prior to use in the clinical study, the test products will be securely stored at room temperature and humidity and protected from direct sunlight. Unused test products will be returned to the Sponsor.

The Sponsor assumes responsibility for the purity, stability, characterization and adequate preservation of the test products. The Sponsor assumes responsibility for determining the test products are safe for use in humans as described in this protocol.

19.0 Record Retention

All original documentation and records pertaining to the conduct of this study will be retained by PPD for 15 years from the time the final CSRs are issued.

At any time prior to the completion of the 15th archival year, the Sponsor may submit a written request to obtain custody of these documents and records once the PPD archive period has been completed. This transfer shall be performed at the expense of the Sponsor. In the absence of such written requests, related records and documents shall be destroyed at the end of the CPT archive period, with no further notice, in a manner that renders them useless.

20.0 Participant Confidentiality

PPD will ensure the names/identities of all study participants are kept confidentialc [redacted]names/identities will not appear in any source documents or study-related records provided to the Monitor/Sponsor. Should study records be required for inspection, participant[redacted]names/identities should be redacted and replaced by their study ID number.

21.0 Indemnification

The Sponsor agrees to indemnify, defend, and hold harmless PPD from any demands, costs, or judgements arising out of or connected with the non-negligent use of the test products or performance of activities to be carried out pursuant to this Protocol. PPD shall notify the Sponsor within 10 working days after receipt of notice of injury, claim or lawsuit. In cases where a service agreement exists, the terms of the service agreement prevail.

22.0 Communication and Publication of Results

The Sponsor shall retain ownership of all study data, data analysis and reports which result from this study. All information generated by the study should be regarded as confidential. CSRs are for the exclusive use of the person, partnership, or corporation to whom they are addressed, and neither the reports, nor the name of PPD nor any member of its staff, may be used in connection with the advertising or sale of any product or process without prior written authorization by a legally binding officer of PPD

23.0 Protocol Approvals

For PPD .: Electronic Signature

PPD

PI (Signature)

For Sponsor: Electronic Signatures

Name	GSK CH Position
PPD	Head of Clinical Development
PPD	Regional Clinical Operations Director
PPD	Head of Biostatistics and Data Management

24.0 References

1. U. S. Food and Drug Administration. Labeling and Effectiveness Testing; Sunscreen Drug Products for Over-the-Counter Human Use; Final Rule; 21 CFR Parts 201 and 310. Federal Register, Vol. 76, No. 117, June 17, 2011. pp. 35660-35665.
2. Guideline for the colorimetric determination of skin color typing and prediction of the minimal erythema dose (MED) without UV exposure. Colipa, 2007.

Signature Page for 218005 TMF-215846 v2.0

Reason for signing: Approved	Name: PPD Role: A Date of signature: PPD
Reason for signing: Approved	Name: PPD Role: A Date of signature: PPD
Reason for signing: Approved	Name: PPD Role: A Date of signature: PPD

Signature Page for TMF-215846 v2.0