PROTOCOL

PROTOCOL TITLE:	A Randomized, Evaluator-Blinded Clinical Study to Evaluate the Efficacy and Tolerability of an Investigational Light Therapy Mask on Subjects with Mild to Moderate Mottled Hyperpigmentation and Moderate to Severe Facial Wrinkles
PROTOCOL IDENTIFICATION:	CO-1705 1113 2943-SACT
VERSION & DATE:	**Amendment 1: Final Version 2.0, 26 September 2017** Original: Final Version 1.0, 28 August 2017
SPONSOR:	Johnson & Johnson Consumer Inc. [redacted]
STUDY SITE:	1001 KGL Skin Study Center, LLC [redacted]
PRINCIPAL INVESTIGATOR (PI):	Stuart Lessin, M.D. KGL Skin Study Center, LLC [redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

See Appendix XI for full contact information.

The principles of the International Council for Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP E6) will be applied to this study.

VERSION TRACKING

VERSION	DATE	STATE	REASON FOR CHANGE	DESCRIPTION OF CHANGE
1.0	28 August 2017	Obsolete	N/A – new protocol	N/A
2.0	26 September 2017	Issued	To correct a typographical error in section 7.2.3.3.1., to correct [redacted]'s first name in Appendix XI, and to remove any reference to expiration dates in the package inserts (Appendix VIII and Appendix X).	See Summary of Changes in Appendix XII.

SYNOPSIS

PROTOCOL TITLE	A Randomized, Evaluator-Blinded Clinical Study to Evaluate the Efficacy and Tolerability of an Investigational Light Therapy Mask on Subjects with Mild to Moderate Mottled Hyperpigmentation and Moderate to Severe Facial Wrinkles
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SPONSOR	Johnson & Johnson Consumer Inc. [redacted]
STUDY SITE	1001 KGL Skin Study Center, LLC [redacted]
PRINCIPAL INVESTIGATOR (PI)	Stuart Lessin, M.D.
OBJECTIVE	The objective of this study is to evaluate the efficacy and tolerability of an investigational light therapy mask in comparison to a sham mask device over a 12-week usage period and after a 12-week regression period for subjects with mild to moderate mottled hyperpigmentation and moderate to severe facial wrinkles.
STUDY DESIGN	Single-center, 2-cell, sham-controlled, randomized, evaluator-blinded clinical usage study
STUDY POPULATION	• Females, 35 to 70 years old • Fitzpatrick skin types I to VI (an approximately equal number of subjects will be enrolled per skin type per cell) • Clinically determined mild to moderate mottled hyperpigmentation on the face (score of 1-6 on 10-point Modified Griffiths Scale[6]) and moderate to severe global facial wrinkling (score of 4-9 on 9-point Fitzpatrick Wrinkle and Elastosis Scale[5]).
SAMPLE SIZE	A sufficient number of subjects will be screened to enroll up to approximately 125 subjects in order to finish with at least 96 subjects (targeting 48 subjects per cell with 8 subjects per Fitzpatrick skin type per cell).

<table>
<tr><td>INVESTIGATIONAL STUDY MATERIALS</td><td>
Investigational Products (IPs) and Auxiliary Products:
<table>
<tr><th rowspan="2">Product</th><th rowspan="2">Identification Number</th><th rowspan="2">Product Type</th><th colspan="2">Included in</th></tr>
<tr><th>Active Cell</th><th>Sham Cell</th></tr>
<tr><td>AM & PM Cleanser</td><td>[redacted]</td><td>Auxiliary Cleanser</td><td>✓</td><td>✓</td></tr>
<tr><td>AM Moisturizer (with SPF 30)</td><td>[redacted]</td><td>Auxiliary Moisturizer</td><td>✓</td><td>✓</td></tr>
<tr><td>PM Mask Treatment</td><td>[redacted]</td><td>IP – Active</td><td>✓</td><td></td></tr>
<tr><td>PM Mask Treatment</td><td>[redacted]</td><td>IP – Sham</td><td></td><td>✓</td></tr>
<tr><td>Mask Activator</td><td>[redacted]</td><td>IP – Active</td><td>✓</td><td></td></tr>
<tr><td>Mask Activator</td><td>[redacted]</td><td>IP – Sham</td><td></td><td>✓</td></tr>
</table>
</td></tr>
<tr><td>DOSE AND MODE OF APPLICATION</td><td>At Screening (Visit 1), each subject will be provided with an auxiliary cleanser and an auxiliary moisturizer to use full-face for the duration of the study. Each subject will be instructed to wash her face twice daily (morning and evening) with the AM & PM Cleanser. In the morning after washing, subjects will apply the AM Moisturizer full-face (the AM Moisturizer may be used again in the evening [after completing the mask treatment, as applicable], if desired).

At Baseline (Visit 2), each subject will be randomly assigned to also use either the active or sham PM Mask Treatment (with respective Mask Activator) for the 12-week treatment period of the study. In the evening after washing, subjects will use the PM Mask Treatment (either active or sham) for 10 minutes.

A 12-week regression period will begin at Week 12 (Visit 5); during the regression period, subjects will continue using the auxiliary products as described previously, but there will be no mask usage.</td></tr>
<tr><td>STUDY DURATION</td><td>The study will consist of 6 visits* over 24 weeks with visits scheduled at Screening (Visit 1, up to 10 days prior to Baseline), Baseline (Week 0; Visit 2), Week 1 (Visit 3), Week 4 (Visit 4), Week 12 (Visit 5), and Week 24 (Visit 6). Baseline to Week 12 (Visit 2 to Visit 5) will comprise a 12-week treatment period, and Week 12 to Week 24 (Visit 5 to Visit 6) will comprise a 12-week regression period.

*If required for scheduling, Visits 2-6 may each be separated into up to three sub-visits (e.g. Visit 2A, 2B, and 2C) such that the imaging and subject questionnaire will occur separately from the clinical and subjective evaluations of efficacy and tolerance (which may themselves be conducted by different Expert Graders at different sub-visits, as needed). See section 7.1 for details.</td></tr>
<tr><td>METHODOLOGY</td><td>• Clinical evaluations of efficacy: fine lines, periorbital wrinkles, global wrinkling, surface roughness, uneven skin tone, mottled</td></tr>
</table>

	hyperpigmentation, sallowness or yellowing, lack of radiance, [redacted] • [redacted]
EVALUATION SCHEDULE [redacted]	The clinical and subjective evaluations of efficacy [redacted] will be conducted at Visits 2-6 (each clinical parameter will be evaluated by the PI plus two additional board-certified dermatologist Expert Graders). [redacted] The evaluations will be conducted after a 15-minute acclimation period. [redacted]
SAFETY AND ADVERSE EVENTS	All Adverse Events (AEs) (including Serious Adverse Events (SAEs)) must be collected (occurrence date; subject identification; location; outcome; end date; and assessment of seriousness; causality; and severity) regardless of causal relationship to the subject's participation in the study. The information should be reported within the required reporting timelines. The AEs will be included in the final study report.
STATISTICAL METHODS	The primary efficacy variable is the change from baseline in global wrinkling at Week 12. The mean global wrinkling change from baseline to Week 12 will be presented for each cell together with a two-sided 95% confidence interval. Superiority to baseline will be concluded if the upper bound of the 95% confidence interval for the mean change is below -5. The active mask will be compared with the sham mask. Treatment means and between-treatment differences will be assessed by means of an Analysis of Covariance (ANCOVA) model with treatment and skin type group as factors and the corresponding averaged baseline score as a covariate. The two-sided 95% confidence interval for the treatment difference will be presented. Analysis of the primary efficacy variable will be based on the average scores from the three Expert Graders as well as separately for the scores from each Expert Grader. Secondary variables (fine lines, periorbital wrinkles, surface roughness, uneven skin tone, mottled hyperpigmentation, sallowness or yellowing, and lack of radiance at Week 1, Week 4, Week 12, and Week 24; plus global wrinkling at Week 1, Week 4, and Week 24) will be analyzed in the same way as the primary variable.

LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
AIDS	Acquired Immunodeficiency Syndrome
ANCOVA	Analysis of Covariance
DPR	Designated Physician Representative
EDC	Electronic Data Capture
EIU	Exposure In Utero
FDA	US Food and Drug Administration
[redacted]	[redacted]
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HRT	Hormone Replacement Therapy
ICD	Informed Consent Document
ICH GCP	International Council for Harmonisation Good Clinical Practice
ID	Identification
IEC	Independent Ethics Committee
IP	Investigational Product(s) (i.e. test products)
IRB	Institutional Review Board
ITT	Intent-to-Treat
LED	Light-Emitting Diode
[redacted]	[redacted]
LOCF	Last Observation Carried Forward
OTC	Over-the-Counter
PI	Principal Investigator
[redacted]	[redacted]
PQC	Product Quality Complaint
PTAE	Pre-Treatment Adverse Event
SAE	Serious Adverse Event
SM	Study Manager
SMF	Site Master File
SPF	Sun Protection Factor
TMF	Trial Master File
[redacted]	[redacted]
UV	Ultraviolet
[redacted]	[redacted]
[redacted]	[redacted]

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1. INTRODUCTION

Exposure to sunlight and artificial light sources containing ultraviolet (UV) radiation is known to accelerate the skin's aging process, resulting in unwanted wrinkles, irregular skin tone, and loss of elasticity. Ablative techniques, such as dermabrasion, deep chemical peels, and ablative laser resurfacing of various wavelengths, are well documented to alleviate the signs of photodamage.[1,2] However, such techniques often require significant post-treatment care and have higher risk profiles than other treatments, with potential side effects including erythema, pigmentation issues, infection, and possible scarring. They may be poorly tolerated by patients who dislike the discomfort, wound care, and prolonged downtime involved.

Non-ablative skin rejuvenation procedures are also effective for improving the appearance of photodamaged skin and are becoming increasingly popular because of their minimal downtime and increased safety. These procedures include intense pulsed light systems, non-ablative lasers, and monochromatic light boxes, which can target facial rhytids, irregular pigmentation, telangiectasia, and skin laxity.[3] Unfortunately, such techniques can be expensive and their use is primarily limited to clinical settings.

However, the light-emitting diode (LED) is a novel light source that is well-suited for non-ablative phototherapy that can be utilized at home for a relatively low price.[4] This study will evaluate the efficacy and tolerance of an LED-based light therapy mask as compared to a sham mask in subjects seeking anti-aging benefits.

2. OBJECTIVE

The objective of this study is to evaluate the efficacy and tolerability of an investigational light therapy mask in comparison to a sham mask device over a 12-week usage period and after a 12-week regression period for subjects with mild to moderate mottled hyperpigmentation and moderate to severe facial wrinkles.

3. STUDY DESIGN

This is a single-center, 2-cell, sham-controlled, randomized, evaluator-blinded clinical usage study utilizing three Expert Graders (i.e. the PI plus two additional board-certified dermatologist Expert Graders; see Appendix XI). Up to approximately 125 subjects will be enrolled to finish with at least 96 subjects (targeting 48 subjects per cell). The target population is 35- to 70-year-old females with mild to moderate mottled hyperpigmentation on the face and moderate to severe facial wrinkles. Enrollment will be evenly distributed across all Fitzpatrick skin types (i.e. an approximately equal number of subjects will be enrolled per skin type per cell).

Subjects will be assessed at Screening, Baseline (Week 0), Week 1, Week 4, Week 12, and Week 24, as described in section 7.

At Screening (Visit 1), each subject will be provided with an auxiliary cleanser (twice daily usage – morning and evening) and an auxiliary moisturizer (once daily usage in the morning after cleansing [plus additional evening usage (after completing the mask treatment, as applicable), as desired]) to use full-face for the duration of the study. At Baseline (Visit 2), each subject will be randomly assigned to also use either the

active or sham light therapy mask (with respective activator; once daily usage for 10 minutes in the evening after cleansing) for the 12-week treatment period of the study. The active and sham masks will be identical in appearance; the Expert Graders will be blind to the IP assignment, and subjects will also be blinded to the extent possible (see section 6.6).

A 12-week regression period will begin at Week 12 (Visit 5); during the regression period, subjects will continue using the auxiliary products as described previously, but there will be no mask usage.

4. SUBJECT SELECTION AND ENROLLMENT

This study can fulfill its objective only if appropriate subjects are enrolled. The eligibility criteria are designed to select subjects for whom protocol procedures are considered appropriate.

All relevant medical and non-medical conditions should be taken into consideration, in addition to the inclusion/exclusion criteria below, when deciding if a particular individual is suitable for this protocol.

No type of discrimination (e.g. social class, gender, skin color, ethnicity, etc.) should preclude an eligible subject from participating in the study. Information that is not relevant to the conduct of the study should not be collected.

Prior to any review of personal data, the Informed Consent Document (ICD) should be signed.

4.1. INFORMED CONSENT

The ICD must be read by the subject and explained to the subject by the PI or designee. The PI or designee must ensure that each study subject is fully informed about the nature and objectives of the study and possible risks associated with participation. After understanding and agreeing, the subject will express her consent to her participation in the study by signing the ICD.

The ICD will be signed and dated by both the PI/designee and by the subject – the signed and dated original will be kept in the Site Master File (SMF) and a signed and dated copy must be given to the subject.

No subject will be evaluated without a signed and dated ICD, which should be kept by the PI as part of the SMF. The ICDs of subjects who are not included in the study will also be part of the SMF.

The ICD must be approved by the Sponsor and the Institutional Review Board/Independent Ethics Committee (IRB/IEC) and must be in compliance with ICH GCP, local regulatory requirements, and legal requirements.

4.2. STUDY POPULATION

An individual must meet all of the inclusion criteria and none of the exclusion criteria to be included in the study. No waivers to inclusion or exclusion criteria will be permitted.

The inclusion and exclusion criteria will be reviewed for each subject and confirmed by the PI in order to determine subject eligibility.

The PI or designee must ensure that the subject is still eligible through the entire conduct of the study.

4.2.1. Inclusion Criteria

a) Has read, understood, signed, dated, and received a copy of the Photograph Release and ICD (including a Health Insurance Portability and Accountability Act [HIPAA] disclosure) after the nature of the study has been fully explained.

b) Female

c) 35 to 70 years old

d) Has clinically determined mild to moderate mottled hyperpigmentation on the face at Visit 1, defined as a score of 1-6 on the 10-point Modified Griffiths Scale (see section 7.2.3.3.1), as determined by the PI.

e) Has clinically determined moderate to severe global facial wrinkling at Visit 1, defined as a score of 4-9 on the 9-point Fitzpatrick Wrinkle and Elastosis Scale (see section 7.2.3.3.1), as determined by the PI.

f) Fitzpatrick Skin Type I, II, III, IV, V, or VI (an approximately equal number of subjects will be enrolled per skin type per cell; Appendix I).

g) Able to read, write, speak, and understand English.

h) Generally in good health based on medical history reported by the subject, as determined by the PI or designee.

i) Intends to complete the study and is willing and able to fulfill the subject responsibilities (see section 4.2.3).

j) Meets one of the following criteria:
   - Is not of child-bearing potential or is in a monogamous relationship with a partner who is not of child-bearing potential, meaning the subject and/or partner:
     - Is post-menopausal (amenorrhea for at least 1 year)
     - Had a surgical sterilization (e.g., vasectomy that has been confirmed effective by sperm count check, tubal occlusion, hysterectomy, bilateral oophorectomy or salpingectomy)
   - Must agree to practice a medically acceptable form of birth control during the study and for 30 days after study completion. Female subjects must have used such birth control for at least 3 months prior to study start. Medically acceptable forms of birth control that may be used by the subject and/or partner include:
     - Established use of hormonal methods of contraception (oral, injected, implanted, hormone patch or vaginal ring)
     - Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps)
     - Intrauterine device or intrauterine system
     - Abstinence from intercourse that could cause pregnancy. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.

4.2.2. Exclusion Criteria

a) Has known allergies or has had adverse reactions to common topical skincare products or ingredients in the investigational study materials (see Appendix III).

b) Has a known light or photosensitivity disorder, or is currently using medication that may cause sensitivity of the skin to light, as determined by the PI or designee based on subject report.

c) Is currently being treated for skin cancer or has a history of skin cancer.

d) Presents with a facial skin condition that could interfere with evaluations or confound study results (e.g., moderate to severe rosacea, moderate to severe acne, psoriasis, eczema, atopic dermatitis, solar urticaria, solar hypersensitivity, skin cancer, sunburn, observable suntan, scars, tattoo, etc.).

e) Has a self-reported uncontrolled metabolic condition or disease, such as diabetes, hypertension, hyper/hypothyroidism, hypercholesterolemia, asthma, epilepsy, etc. Individuals with a controlled health condition may also be excluded from the study at the discretion of the PI or designee.

f) Has active hepatitis, an immune deficiency disorder (including HIV infection or AIDS), or an autoimmune disease, as reported by the subject.

g) Is taking immunosuppressive drugs within the 3 months prior to Visit 1 or during the study.

h) Is currently using, planning to use during the study (other than the investigational study materials), or has used any of the following in the specified time range:

Any of the following topical products on the face: • Any skin firming, anti-aging, anti-wrinkle, skin lightening products, or any other product or topical known to affect skin aging or dyschromia (products containing alpha/beta/poly-hydroxy acids, vitamin C, soy, Q-10, hydroquinone; topical retinoids, etc.)	1 month prior to Visit 1
Superficial to mid-deep chemical peels or dermabrasion of the face	6 weeks prior to Visit 1
Topical prescription retinoids (e.g. Retin-A®, Retin-A Micro®, Renova®, Avita®, Tazorac®, or Differin®)	4 months prior to Visit 1
Prescription skin lightening products (e.g., hydroquinone, tretinoin, alpha/beta/poly-hydroxyacids, 4-hydroxyanisole alone or in combination with tretinoin, etc.)	4 months prior to Visit 1
Accutane®, Soriatane®, or other oral retinoid	12 months prior to Visit 1
Any of the following on the face: • Thermage treatments or an equivalent type of high energy treatment • Deep facial chemical peel, non-ablative laser, or fractional laser resurfacing	12 months prior to Visit 1
Facial plastic surgery or ablative laser resurfacing on the face	3 years prior to Visit 1

i) Female who (to the best of her knowledge) is pregnant, lactating, or planning to become pregnant during the study or within 30 days of study completion.

j) Intends to begin or change a hormone replacement therapy (HRT) during the study.

k) Is taking medication for a chronic condition (e.g., insulin, antihistamines, steroidal and non-steroidal anti-inflammatory drugs, antibiotics, etc.) or is taking any other medication that could influence the study results and/or affect the individual's safety, within 30 days before inclusion or during the study.

l) Has a history of or a concurrent health condition/situation which, in the opinion of the PI or designee may put the individual at significant risk, confound the study results, or interfere significantly with the individual's participation in the study.

m) Is simultaneously participating in any other clinical study or has participated in any clinical study within 30 days prior to Visit 1.

n) Is a ward of the court or deprived from liberty by a judiciary or administrative decision.

o) Is an employee/contractor or immediate family member of the PI, Study Site staff, or Sponsor.

4.2.3. Subject Responsibilities

During the study, the subject responsibilities are as follows:

- Use the provided AM & PM Cleanser twice daily (morning and evening) to wash your full face for the duration of the study.
- Every morning for the duration of the study: after washing and drying your face, apply the provided AM Moisturizer full-face. (If desired, you may use the AM Moisturizer again in the evening [after completing the mask treatment, as applicable]).
- During the 12-week treatment period: every evening after washing and drying your face, use the provided PM Mask Treatment for 10 minutes.
- During the study, do not use any facial cleansers, moisturizers, sunscreens, or light-based devices other than those provided for this study.
- Do not use any exfoliating, sunless tanning, skin lightening, skin firming, or anti-aging products on your face during the study.
- Do not receive any professional or aesthetic facial spa procedures during the study.
- Continue using your regular brands of color cosmetics (i.e. makeup) and makeup remover during the study. Do not start using any new skincare products or change your currently used brands during the study. Use only facial products reviewed by study staff at Visit 1.
- On the day of study visits: remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit and then do not apply any leave-on facial products until the visit is completed. Note: if you do not follow these directions, you will be asked to remove your makeup/products and wash your face with the provided cleanser on-site prior to the acclimation period.
- Avoid extended periods of sun exposure and all use of tanning beds for the duration of the study. Extra care should be taken to avoid sun exposure from 11 AM to 4 PM.

- Maintain your birth control method for the duration of the study and 30 days after completion.
- If you are using a HRT, do not change it during the study. If you are not using a HRT, do not begin one during the study.
- Attend all scheduled visits.
- Do not begin any other clinical study during the current study.
- Report any side effects, changes in health/medication, pregnancies, issues, or questions to the study staff.
- Bring your study products to all visits. All products must be returned when requested by the Study Site.

See section 6 regarding detailed product usage instructions.

4.3. CONCURRENT PRODUCTS

Subjects may not use any facial cleansers, moisturizers, sunscreens, or light-based devices other than the provided investigational study materials. They may not use any exfoliating, sunless tanning, skin lightening, skin firming, or anti-aging products on their face during the study, nor should they receive any professional or aesthetic facial spa procedures during the study.

Subjects should continue using their regular brands of color cosmetics (i.e. makeup) and makeup remover during the study. They should not start using any new skincare products or change their currently used brands during the study (for both the face and body). At Visit 1, study staff should record each subject's regular facial products that she will continue to use during the study; during the study, subjects should use only facial products that were reviewed by study staff at Visit 1.

4.4. CONCURRENT MEDICATION

If a subject is taking any medication during the course of the study or within 1 month prior to the study, it must be recorded as a concurrent (i.e. concomitant) medication. The minimum information that is required is the name of the medication. If this medication is linked to the treatment of an IP-related or study-related AE, the dose and duration of the treatment should be specified. Medications excluded are indicated in section "Exclusion Criteria"; the use of any excluded medication during the study will result in discontinuation of the subject.

4.5. SCREEN FAILURE

All individuals who signed the ICD and withdraw their consent for participation in the study or fail to meet at least one of the eligibility criteria during the initial evaluation will be considered a "screen failure" and their data will not be considered in the final report (except for screen-failed subjects with an AE, in which case the demography, subject disposition, and AE information will be entered in the electronic data capture [EDC] system).

An individual who is screen-failed but may qualify at a later time may be re-screened at the PI's discretion, but the individual should be treated as a new candidate (i.e. new subject ID, new ICD, etc.). Any individual who screen fails and has an AE will not be re-screened.

5. SAMPLE SIZE

A sufficient number of subjects will be screened to enroll up to approximately 125 subjects in order to finish with at least 96 subjects (targeting 48 subjects per cell). Enrollment will be evenly distributed across all Fitzpatrick skin types (i.e. an approximately equal number of subjects will be enrolled per skin type per cell, targeting 8 subjects per Fitzpatrick skin type per cell to complete the study).

Refer to section 8.4 for the sample size determination rationale.

If the final overall sample size is smaller than expected (i.e. less than 96 subjects complete the study), a protocol deviation should be recorded and communicated to the Sponsor.

6. INVESTIGATIONAL STUDY MATERIALS

The Sponsor has ensured that there is sufficient safety data to support the human use of the investigational study materials (i.e. the IPs and auxiliary products).

6.1. IDENTITY OF INVESTIGATIONAL STUDY MATERIALS

The following investigational study materials will be provided under authorization of the Sponsor:

Table 1. IP and Auxiliary Product List

Product Identity (as Labeled)	Identification Number	Regulatory Classification and US Marketing Status	Product Type	Included in	
				Active Cell	Sham Cell
AM & PM Cleanser[a] (plus commercial name: [redacted])	[redacted]	Cosmetic, Marketed	Auxiliary Cleanser	✓	✓
AM Moisturizer (with SPF 30) (plus commercial name: [redacted])	[redacted]	OTC Monograph Drug, Marketed	Auxiliary Moisturizer	✓	✓
PM Mask Treatment	[redacted]	Device, Non-Marketed	IP – Active	✓	
PM Mask Treatment	[redacted]	Device, Non-Marketed	IP – Sham		✓
Mask Activator[b]	[redacted]	Device, Non-Marketed	IP – Active	✓	
Mask Activator[b]	[redacted]	Device, Non-Marketed	IP – Sham		✓

[a]A few additional units of the cleanser will be provided to the Site for on-site usage by subjects prior to acclimation, as needed.

[b]Each PM Mask Treatment is controlled by a corresponding Mask Activator, which turns the mask on/off (Active cell only) and displays how many treatments are still available for use (with each Mask Activator limited to 5 uses). The active and sham Mask Activators are identical except for battery type (the active Mask Activator has more efficient batteries to facilitate the light therapy treatments). The active and sham PM Mask Treatments are structurally identical except the sham wiring has been disabled. Consequently, subjects in the Active cell will receive a fully functional PM Mask Treatment and Mask Activator which will toggle the mask on/off and track the number of remaining treatments available. Subjects in the Sham cell

will receive a functional Mask Activator that will track the number of remaining "treatments" but will not actually activate the sham PM Mask Treatment. A set of Mask Activators will be supplied to subjects at Baseline (Visit 2) and Week 4 (Visit 4). A countdown timer will also be provided to subjects in each cell to audibly define the 10-minute usage period for parity (since the sham mask will not light up).

The IPs will be manufactured by the Sponsor or its agents according to Good Manufacturing Practices; the auxiliary products will be commercially sourced. A Letter of Non-Significant Risk will be provided to the PI for use of the non-marketed devices in this study. OTC Drug Facts will be provided to the PI as reference safety information for the AM Moisturizer, and the ingredient list for each of the auxiliary products is provided in Appendix III.

6.2. LABELING

A label will be affixed to each IP unit or packaging and any brand markings on the devices will be over-labeled. The IP labels may contain (but are not limited to) fields for the following information:

- Protocol Number
- Product Identity (see table in section 6.1)
- Randomization Number
- "CAUTION: Investigational Device. Limited by United States law to investigational use."
- Directions
- Warnings
- Study Site Identification
- Net Contents
- Site Emergency Contact Information
- Storage Information
- Unit #

One IP starter kit (kit 1) and one IP refill kit (kit 2) will be provided for each randomization number. Each starter kit will contain one PM Mask Treatment and seven Mask Activators (each either active or sham, as applicable for the randomization number). Each refill kit will contain fourteen Mask Activators (either active or sham, as applicable for the randomization number). The subject instructions and cell-specific device package insert (see section 6.5) will be packaged with the products in each kit. Replacement kits will be available, as needed (see section 6.6).

A partial label will be affixed to each auxiliary product unit. The auxiliary product labels may contain (but are not limited to) fields for the following information:

- Protocol Number
- Product Identity (see table in section 6.1)
- "For Participant Use Only"
- Directions
- Study Site Identification
- Site Emergency Contact Information
- Unit #

The auxiliary products will be provided individually (i.e. not in kits) for dispensing as needed. Units of the AM & PM Cleanser will also be available for on-site usage prior to acclimation, as needed.

6.3. STORAGE AND ACCOUNTABILITY

The IP and auxiliary products for this study will be secured in a room or cabinet that is only accessible to Study Site authorized personnel and kept at 5-25°C (41-77°F) with relative humidity up to 60%, with temperature and humidity recorded at least daily on business days.

The PI or designee must maintain adequate records documenting the receipt, use, loss, or other disposition of the IPs and auxiliary products on the Product Dispensing and Accountability Log (or equivalent), which must be filed in the SMF.

The log must identify the IPs and auxiliary products and account for their disposition including specific dates and quantities used/dispensed and returned as applicable.

The log must be signed by the Site designee who used/dispensed and retrieved the IPs and auxiliary products and a copy of the log must be provided to the Sponsor.

At the end of the study, all IP and auxiliary product units (used and/or unused) must be returned to the Sponsor: [redacted]

6.4. PRODUCT QUALITY COMPLAINTS

A Product Quality Complaint (PQC) is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, or safety of a product, including its labeling, delivery system, or packaging integrity. It also includes device malfunctions.

No PQC form should be filed for issues identified during receipt/inventory of a shipment. Instead, these should be reported as indicated on the receipt letter.

Subsequently, any observation/report of a PQC requires immediate notification of the Sponsor. The PI or designee should complete, sign, and securely send a copy of the PQC form to the SM. The PI/site staff is responsible for detecting and reporting PQCs, and for instructing subjects to do the same, whenever applicable. The PI/site staff must also ensure that products presenting PQCs are not used or that they have their use interrupted upon the identification of a PQC.

PQC information must also be included on the Product Dispensing and Accountability Log (or equivalent). The SM can provide assistance and answer questions related to this process. To aid in the initial conversation and understanding of a PQC, the Site staff may be asked to photograph the issue and send the photograph to the SM. The SM will coordinate the replacement or return of the affected products, if necessary.

6.5. APPLICATION/USE OF THE IP/AUXILIARY PRODUCT

At Screening (Visit 1), each subject will be provided with the auxiliary cleanser and the auxiliary moisturizer

to use full-face for the duration of the study. Each subject will be instructed to wash her face twice daily (morning and evening) with the AM & PM Cleanser. In the morning after washing, subjects will apply the AM Moisturizer full-face (the AM Moisturizer may be used again in the evening [after completing the mask treatment, as applicable], if desired). The detailed subject instructions for Visit 1 are in Appendix VI.

At Baseline (Visit 2), each subject will be randomly assigned to also use either the active or sham PM Mask Treatment (with respective Mask Activator) at home for the 12-week treatment period of the study. In the evening after washing, subjects will use the PM Mask Treatment (either active or sham) for 10 minutes. The detailed subject instructions for the treatment period are in Appendix VII, and the device package insert is in Appendix VIII and IX for the Active and Sham cells, respectively.

A 12-week regression period will begin at Week 12 (Visit 5); during the regression period, subjects will continue using the auxiliary products as described previously, but there will be no mask usage. The detailed subject instructions for the regression period are in Appendix X.

See section 7.3 regarding compliance metrics.

6.6. RANDOMIZATION/IP ALLOCATION AND BLINDING

Subjects who sign the ICD will be sequentially assigned a Subject ID. The Subject ID will begin with the four-digit center ID (1001) followed by a unique four-digit subject identifier assigned in ascending order and beginning with "1001," resulting in an eight-digit Subject ID (e.g. "10011001," "10011002," etc.). Once a Subject ID has been assigned to a subject, it cannot be reassigned to another subject.

Enrollment in the study will be evenly distributed across all Fitzpatrick skin types. Six strata will be created, with one stratum for each of the six Fitzpatrick skin types. A randomization scheme will be performed separately for each stratum. Upon enrollment in the study, subjects will be allocated to one of the six strata based on their Fitzpatrick skin type. Within each stratum, subjects will then be randomly assigned to one of two treatment cells (Active or Sham). An extra stratum will be created to provide replacement kits as needed (e.g. if a subject misplaces or breaks the PM Mask Treatment in the starter kit) so that there will be a total of seven strata in the study. In the event of a replacement, the site should contact the Sponsor's Clinical Supplies department; subjects will be given a new randomization number from this stratum based on their original treatment assignment. Once a randomization number has been assigned to a subject, it cannot be reassigned to another subject. The randomization scheme will be devised by the Sponsor's Quantitative Sciences Department.

The randomization numbers will be incorporated into the IP labeling, as described in section 6.2.

This study will be evaluator-blinded, so the PI/evaluators will not know which treatment cell (Active or Sham) each subject is in. Personnel dispensing the IPs or supervising IP use will not participate in the evaluation of subjects in order to minimize potential bias. IPs will be kept separate from the site personnel involved in assessing or evaluating the subjects, and subjects will be instructed not to discuss their assigned IPs with the evaluators or other subjects. Subjects will also be blinded to the extent possible given the nature of the IPs (as described in section 6.1); to this end, the ICD will indicate, "Not all energy is visible to the human eye. You may not see the LEDs light up." Meanwhile, the package insert for the Active cell (Appendix VIII) indicates "Not all energy emitted by the Mask is visible. You will not see all of the LEDs light up;" the package insert for the Sham cell (Appendix IX) indicates "The Mask is not intended

to emit visible light, so you will not see the LEDs light up." Subjects should not be exposed to the other cell's IPs or device package inserts.

The randomization schedule will be used by the Sponsor to generate randomization number-specific single disclosure envelopes. In the event that the PI or medically qualified designee believes an un-blinding is necessary and circumstances allow, the PI or designee will contact the SM who will consult with the DPR to determine whether a code break is needed. If there is a medical emergency and the PI or medically qualified designee deems it necessary to urgently know which IP the subject is using for the subject's proper medical care, then the PI or designee may break the treatment code immediately by opening the provided randomization number-specific disclosure envelope for that subject. The time, date, and reason for the un-blinding should be noted in the subject's source document and documentation should be provided to the Sponsor. Upon completion of the study, all disclosure envelopes will be returned to the Sponsor.

Blinding should only be broken for serious, unexpected, and related AEs, and only for the subject in question, or when required by local regulatory authorities.

7. INVESTIGATIONAL PLAN

7.1. STUDY DURATION

The study will consist of 6 visits* over 24 weeks with visits scheduled at Screening (Visit 1**), Baseline (Week 0; Visit 2), Week 1 (Visit 3), Week 4 (Visit 4), Week 12 (Visit 5), and Week 24 (Visit 6). Baseline to Week 12 (Visit 2 to Visit 5) will comprise a 12-week treatment period, and Week 12 to Week 24 (Visit 5 to Visit 6) will comprise a 12-week regression period.

As necessary, Visit 3 may be adjusted ± 2 days and Visits 4-6 may be adjusted ± 3 days. All scheduling windows are versus the Baseline visit (Visit 2 or [if applicable] the final Visit 2 sub-visit, as described below).

*If required based on Expert Grader availability, Visits 2-6 may each be separated into up to three sub-visits. In such cases, each sub-visit will be identified by the suffix -A, -B, or -C (e.g. Visit 2A, 2B, and 2C); the date and procedures for that sub-visit will be clearly recorded in the source documentation, and all sub-visits for a particular time point should still occur within the prescribed scheduling window. Imaging and the subject questionnaire may be conducted at one sub-visit, while the clinical and subjective evaluations of efficacy and tolerance may occur at (a) separate sub-visit or sub-visits (before or after the imaging visit, as needed). The subject acclimation and interviews for AEs, compliance, and changes in health/medications will be conducted at each sub-visit. If Baseline (Week 0, Visit 2) is split, the sub-visits will occur within 3 days of one another (e.g. if Visit 2A is on a Monday, the final sub-visit will be completed by Thursday), and subjects will be instructed not to begin IP usage until the final sub-visit is complete. If Visit 5 is split, subjects will be instructed to continue the treatment period instructions until the final sub-visit is complete (i.e. IP will be collected and the regression period will begin at the final Visit 5 sub-visit). If Visit 6 is split, subjects will be instructed to continue the regression period instructions until the final sub-visit is complete (i.e. auxiliary products will be collected at the final Visit 6 sub-visit). The Site will use the fewest sub-visits possible.

**Screening will occur up to 10 days prior to Baseline (or the first Visit 2 sub-visit, as applicable). If Baseline (or Visit 2A) immediately follows Screening (on the same day), the Visit 1 AE collection and Visit 2 (or Visit 2A) interview for compliance may be waived. All Visit 1 procedures must be completed prior to Visit 2 commencing.

If a subject misses a scheduled visit but notifies the study site, he/she will be allowed to re-schedule the missed visit if it is within the scheduling window as specified above. If it is outside the scheduling window, the SM should be notified to determine if the visit should be rescheduled outside the scheduling window. Study staff will need to assess subject compliance with product usage to ensure the missed/altered visit did not result in a lack of compliance. A lack of compliance will be documented as a deviation and the Sponsor should be notified.

7.2. STUDY PROCEDURES AND EVALUATION SCHEDULE

Table 2 summarizes the study procedures and evaluation schedule.

Table 2. Schedule of Events

Time Points[a]/Procedures	Prior to Treatment Period	Treatment Period				Regression Period
	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
	Screening[b]	Baseline (Week 0)	Week 1 (± 2 days)	Week 4 (± 3 days)	Week 12 (± 3 days)	Week 24 (± 3 days)
ICD with HIPAA disclosure & photograph release	X					
Collect demographics (including Fitzpatrick skin type and oiliness level), general medical history, & concomitant medications	X					
Interview for compliance		X*	X	X	X	X
15-minute acclimation	X	X	X	X	X	X
Clinical and subjective evaluations of efficacy [redacted]	X[d]	X	X	X	X	X
Review of eligibility	X					
Subject qualification by PI	X					
Enrollment & randomization	X					
[redacted]						
[redacted]						
IP and auxiliary product dispensed (as applicable) with subject instructions and daily diary[e]	X *Auxiliary products; Appendix VI instructions; daily diary*	X *IP starter kit & auxiliary products; Appendix VII instructions*		X *IP refill kit & auxiliary products; Appendix VII instructions*	X *Auxiliary products; Appendix X instructions*	
Daily diary reviewed		X	X	X	X	X
IP/auxiliary product checked for use compliance (as applicable)		X	X	X	X	X
IP/auxiliary product and daily diary collected					X *All IPs*	X *Auxiliary products and daily diary*
Collect/record AEs and changes in health/medications	X* *AEs only*	X	X	X	X	X
Subject disposition						X[f]

[a]See section 7.1 regarding possible separation of Visits 2-6 into sub-visits.

[b]Screening will occur up to 10 days prior to Baseline (or Visit 2A, as applicable). If Visit 2 (or Visit 2A) immediately follows Screening (on the same day), the denoted (*) AE collection and interview for compliance (for Visit 2 or Visit 2A, as applicable) may be waived. All Visit 1 procedures must be completed prior to Visit 2 commencing.

[c]The efficacy [redacted] evaluations will be conducted independently by each of three Expert Graders (except at Screening[d]), but only the PI will question the subject for the subjective parameters.

[d]Only the "mottled hyperpigmentation" and "global wrinkling" parameters will be conducted at Screening as part of the eligibility review. The evaluations will be conducted only by the PI.

[e]Additional IP, auxiliary product, and daily diary units may be dispensed as needed/previous units collected at the Site's discretion.

[f]Subject disposition will be recorded at final study visit or at the time of subject discontinuation from the study.

7.2.1. Recruiting

Candidate subjects will be recruited using IRB-approved materials. Interested candidates will be scheduled for Visit 1.

7.2.2. Visit 1 (Screening)

Selected candidates will report to the test facility. On the day of the study visit, candidate subjects should remove all leave-on facial products (including eye makeup) and arrive at the visit with a clean face. Note: if a candidate subject arrives with facial products on, she may remove the facial products and wash her face with a non-medicated cleanser on-site prior to the acclimation period. This will not be recorded as a deviation. Candidate subjects will take part in the following procedures:

7.2.2.1. Informed Consent

Informed consent will be obtained as described in section 4.1. The ICD will include a HIPAA disclosure. Subjects will also review and sign a Photograph Release. Subjects who sign the ICD and Photograph Release will be sequentially assigned a Subject ID (see section 6.6).

7.2.2.2. Acclimation

Subjects will acclimate to conditions in the facility for at least 15 minutes before the clinical evaluations of eligibility (see section 7.2.2.3) are conducted.

7.2.2.3. Medical History, Concomitant Medications, and Review of Eligibility

The demographics (including Fitzpatrick skin type [Appendix I] and oiliness level [Appendix II]), medical history, and concomitant medications of each candidate subject will be collected and reviewed (this interview may occur during the acclimation period).

All of the eligibility requirements of the study will also be reviewed to assess each candidate subject's eligibility. As part of this review, the "mottled hyperpigmentation" and "global wrinkling" clinical evaluations will be conducted by the PI as described in section 7.2.3.3.1 after the acclimation period is completed in order to determine if the individual meets the eligibility requirements (see inclusion criteria [d] and [e] in section 4.2.1). In addition, the PI or designee will review each subject's facial products to ensure the subject meets the eligibility criteria (see exclusion criterion [h] in 4.2.2) and approve/record each subject's regular facial products that she will continue to use during the study (see section 4.3).

The PI will review the above information (medical history, concomitant medications, and eligibility review) to confirm the eligibility of each subject prior to their enrollment in the study.

7.2.2.4. Enrollment and Randomization

Upon enrollment, each subject will be assigned a randomization number (see section 6.6).

7.2.2.5. Auxiliary Product Dispensing and Instructions

Each enrolled subject will receive a unit of the auxiliary cleanser and the auxiliary moisturizer, along with a daily diary for the subject to record her product usage throughout the study (note: the Site may dispense/collect diary units at its discretion throughout the study). The site designee will review the subject instructions in Appendix VI with each subject. The subject instructions in Appendix VI contain the instructions relevant between Visit 1 and initiation of IP usage. Subjects will begin using the auxiliary products on the night of Visit 1.

7.2.2.6. AE Collection

Individuals that have signed the ICD will be questioned and assessed for AEs before leaving the facility. (Note: if Visit 2 or Visit 2A will occur on the same day as Visit 1, the Visit 1 AE collection may be waived).

7.2.3. Visit 2 (Week 0, Baseline)

On the day of the study visit, subjects should remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit. No other topical products should be applied to the face until the study visit has been completed. Note: if a subject does not follow these directions, she will be asked to remove her facial products and wash her face with the auxiliary cleanser on-site prior to the acclimation period (Note: this will not be considered a deviation). Subjects will take part in the following procedures:

7.2.3.1. AE Collection & Interview for Compliance

The PI or designee will interview the subjects to collect and record any AEs or changes to health/concomitant medications that may have occurred since the previous visit. Subjects will also be interviewed for compliance with study directions. (Note: this interview may be skipped at Visit 2 [or Visit 2A, as applicable] if Visit 1 occurred on the same day). This interview may occur during the acclimation period.

7.2.3.2. Acclimation

Subjects will acclimate to conditions in the facility for at least 15 minutes before the clinical and subjective evaluations of efficacy [redacted] are conducted.

7.2.3.3. Clinical and Subjective Evaluations of Efficacy [redacted]

The following evaluations will be conducted after the acclimation period:

7.2.3.3.1. Efficacy

The PI and two other Expert Graders* (see Appendix XI) will each separately assess each subject's facial skin for the appearance of the following aging parameters using the applicable grading scales shown in Appendix IV:

- Fine lines
- Periorbital wrinkles
- Global wrinkling*
- Surface roughness
- Uneven skin tone
- Mottled hyperpigmentation*
- Sallowness or yellowing
- Lack of radiance
- [redacted]

**Note: At Visit 1, these evaluations will be conducted only by the PI. For enrollment at Visit 1 (see Inclusion Criteria [d] and [e] in section 5.2.1), an individual must have a score of 1-6 for the "mottled hyperpigmentation" parameter and a score of 4-9 for the "global wrinkling" parameter, as determined by the PI.*

[redacted]

[redacted]

7.2.3.5. IP Dispensing and Instructions

Each subject will receive a starter kit for the randomly assigned product cell (see section 6). Additional auxiliary product will also be dispensed, as needed. The site designee will review the treatment period instructions (Appendix VII) with the subjects. If Visit 2 is split into sub-visits, subjects will be instructed to begin following the treatment period instructions only after completion of the final Visit 2 sub-visit.

7.2.3.6. AE Collection

Subjects will be questioned and assessed for AEs before leaving the facility.

7.2.4. Visit 3 (Week 1), Visit 4 (Week 4), & Visit 5 (Week 12)

On the day of each study visit, subjects should remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit. No other topical products should be applied to the face until the study visit has been completed. Note: if a subject does not follow these directions, she will be asked to remove her facial products and wash her face with the auxiliary cleanser on-site prior to the acclimation period (Note: this will not be considered a deviation).

At each visit:

- Subjects will be interviewed for compliance with study instructions. This may occur during the acclimation period.
- Subjects will acclimate to conditions in the test facility for at least 15 minutes before the clinical and subjective evaluations of efficacy [redacted] are conducted.
- The clinical evaluations of efficacy [redacted] will be repeated as described in section 7.2.3.3.
- [redacted]
- A trained site designee will review each subject's daily diary and inspect the IPs/auxiliary products to assess subject compliance (see section 7.3).
- Additional auxiliary products will be dispensed, as needed. Used Mask Activators and used auxiliary products will be collected and retained by study staff at the Site's discretion.
- *Visit 4 only*: An IP refill kit will be dispensed.
- *Visit 5 only*: all IPs will be collected and retained by study staff. Additional auxiliary product will be dispensed to subjects with instructions for the regression phase of the study (Appendix X). If Visit 5 is split into sub-visits, this will be completed at the final Visit 5 sub-visit.
- Subjects will be questioned and assessed for AEs and any changes in their health or concomitant medications.

7.2.5. Visit 6 (Week 24)

On the day of the study visit, subjects should remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit. No other topical products should be applied to the face until the study visit has been completed. Note: if a subject does not follow these directions,

she will be asked to remove her facial products and wash her face with the auxiliary cleanser on-site prior to the acclimation period (Note: this will not be considered a deviation).

At the visit:

- Subjects will be interviewed for compliance with study instructions. This may occur during the acclimation period.
- Subjects will acclimate to conditions in the test facility for at least 15 minutes before the clinical and subjective evaluations of efficacy [redacted] are conducted.
- The clinical evaluations of efficacy [redacted] will be repeated as described in section 7.2.3.3.
- [redacted]
- [redacted]
- A trained site designee will review each subject's daily diary and inspect the auxiliary products to assess subject compliance (see section 7.3).
- The daily diary and all auxiliary products will be collected and retained by study staff. If Visit 6 is split into sub-visits, this will be completed at the final Visit 6 sub-visit.
- Subjects will be questioned and assessed for AEs and any changes in their health or concomitant medications.

7.3. SUBJECT COMPLIANCE METRICS

IP/auxiliary product review, daily diary, and subject interview will be used to assess subject compliance. The AM & PM Cleanser and AM Moisturizer will not be weighed but should be visually assessed for usage compliance. Each Mask Activator supplied to the subjects should be reviewed by study staff for usage compliance and the remaining number of treatments will be recorded; the counter on each Mask Activator allows for 5 treatment-sessions and will reduce by 1 with each use.

The diary and Mask Activator must indicate at least 90% compliance (i.e. 3 usage misses in 30 days is allowed); anything less than that will be documented as a compliance deviation and the subject will be re-instructed on proper product usage or be dropped from the study at the PI's or designee's discretion after consultation with the Sponsor.

[redacted]

[redacted]

7.5. SUBJECT COMPLETION/WITHDRAWAL

7.5.1. Subject Completion

Subjects are considered to have completed the study when all study procedures have been completed as designated by the protocol. Completion should be noted on the Screening and Enrollment Log (or equivalent) as well as in the EDC system on the Subject Disposition page.

7.5.2. Subject Discontinuation

When an individual who has signed the ICD is not included in the study or discontinues/is discontinued prior to completing the study, the reason is to be documented on the Screening and Enrollment Log (or equivalent) and (only for randomized subjects plus screen failed subjects with a reported AE) in the EDC system on the Subject Disposition page. The subject disposition should also be summarized in the final study report. Reasons for subject discontinuation may include:

- Screen Failure (i.e. fails to meet inclusion/exclusion criteria or chooses not to participate)
- Participant is determined to be ineligible after enrollment
- Withdrawal by subject
- Non-compliance with study treatment (including non-compliance with product use/study directions)
- Lack of efficacy
- Protocol deviation/violation (other than non-compliance)
- Death (must be reported in accordance with the reporting requirements defined in the SAE section)
- Other AE/Serious AE (must be reported in accordance with the reporting requirements defined in section 10.3.3)
- Pregnancy (must be reported in accordance with the reporting requirements defined in section 10.3.5)
- Study terminated by Sponsor
- Lost to follow-up
- Other

Subjects may withdraw from the trial at any time at their request, or they may be withdrawn at any time at the discretion of the Sponsor, PI, or designee for safety, behavioral, or administrative reasons. If a subject does not return for a scheduled visit, at least 3 documented attempts will be made to contact the subject in order to establish the reason for withdrawal, and the outcome will be documented. The PI or designee should inquire about the reason for withdrawal, request that the subject return for a final visit, if applicable, and follow-up with the subject regarding any unresolved AEs.

When a subject withdraws from the trial and also withdraws consent for disclosure of future information, no further evaluations should be performed and no additional data should be collected. The PI and staff may retain and continue to use any data collected before such withdrawal of consent.

In case of early subject withdrawal, subjects may be replaced based upon overall enrollment numbers and with the approval of the Sponsor.

8. STATISTICAL ANALYSIS METHODS

The Sponsor's Quantitative Sciences Department will be responsible for the data management and statistical analyses of this trial.

Demographic and baseline characteristics will be summarized by treatment. For continuous variables, descriptive summary will include number of subjects, mean, standard deviation, median, minimum and maximum values. For categorical variables, descriptive summary will include the number and percentage of subjects in each response category.

8.1. STATISTICAL ANALYSIS POPULATIONS

[redacted] efficacy data will be evaluated for all intent-to-treat (ITT) subjects who used the IP and had baseline and at least one post-baseline data point. AEs will be summarized for all subjects who signed the ICD, differentiating Pre-Treatment Adverse Events (see section 10.3.2.1).

8.2. EFFICACY ANALYSIS

For each efficacy variable, summary statistics will be provided by treatment group at each time point. For continuous variables, descriptive summaries will include number of subjects, mean, standard deviation, median, minimum and maximum values. Distributions of categorical variables will be summarized by presenting the number and percent of subjects in each response category.

8.2.1. Analysis of Primary Variable

The primary efficacy variable is the change from baseline in global wrinkling at Week 12. Scores from the 3 Expert Graders will be averaged for the baseline readings as well as the Week 12 readings before computing the change. For each subject, the change from baseline is then computed by subtracting post-baseline mean global wrinkling from baseline mean global wrinkling. The mean change from baseline for each cell will be presented together with a two-sided 95% confidence interval. Superiority to baseline will be concluded if the upper bound of the 95% confidence interval for the mean difference is below -0.5. The active mask will be compared with the sham mask. Treatment means and between-treatment differences will be assessed by means of an ANCOVA model with treatment and skin type group as factors and the corresponding averaged baseline score as a covariate. The two-sided 95% confidence interval for the treatment difference will be presented. Analysis of the primary efficacy variable will be based on the average scores as well separately for the scores from each Expert Grader.

If global wrinkling is missing at Week 12 for more than 5% of the subjects, the missing value will be imputed by using the last observation carried forward (LOCF) method.

8.2.2. Analysis of Secondary Variables

The secondary efficacy variables are the change from baseline in the following endpoints at Week 1, Week 4, Week 12, and Week 24. Scores from the 3 Expert Graders will be averaged for the baseline as well as each post-baseline visit before computing the change.

- Global wrinkling (excluding Week 12, the primary time point)
- Fine lines
- Periorbital wrinkles
- Surface roughness
- Uneven skin tone
- Mottled hyperpigmentation
- Sallowness or yellowing
- Lack of radiance

The active mask will be compared with the sham mask. Treatment means and between-treatment differences will be assessed by means of an ANCOVA model with treatment and skin type group as factors and the corresponding averaged baseline score as a covariate. The two-sided 95% confidence interval for the treatment difference will be presented.

8.2.3. Analysis of Tertiary Variables

[redacted]

8.3. [redacted] Safety Analysis

[redacted]

The safety analysis will be based on all randomized subjects who use IP. The number and percentage of subjects experiencing AEs during the clinical study will be presented by MedDRA System Organ Class, preferred term, and treatment. A listing of AEs will be provided for all subjects who signed the ICD, differentiating Pre-Treatment Adverse Events.

8.4. SAMPLE SIZE DETERMINATION

The total sample size of 96 (48 per treatment cell) completed subjects provides 92% power to detect a treatment effect of 0.7 using a two-sided test at the 0.05 significance level. The 0.7 effect size is estimated based on a previous study of similar design using the 9-point Fitzpatrick Wrinkle and Elastosis Scale.

[redacted]

10. MANAGEMENT OF INTERCURRENT EVENTS

10.1. AMENDMENTS TO THE PROTOCOL

Neither the PI/Site nor the Sponsor will modify this protocol without obtaining the agreement of the other.

Amendments must be approved by the Sponsor and the IRB/IEC prior to implementation.

Note that submission of administrative change/non-substantial amendments to regulatory authorities and/or IRB/IECs for approval prior to study implementation is determined after consultation with the local regulatory representative and/or IRB/IEC policy and may vary by country/region.

The only circumstance in which an amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the PI must notify the IRB/IEC and the Sponsor in writing within 3 working days after the implementation.

10.2. PROTOCOL DEVIATIONS

Protocol deviations should be avoided whenever possible. When a protocol deviation occurs, it must be captured on the Protocol Deviation Log.

If a significant deviation occurs, the PI or designee will also contact the SM (see contact information in Appendix XI). Contact with the SM will be made as soon as possible in order to discuss the situation and agree on an appropriate action. If it is determined that the subject safety/well-being was affected, the IRB/IEC will also be notified. The final study report will describe any deviation from the protocol and the circumstances requiring it.

10.3. ADVERSE EVENT REPORTING

10.3.1. Introduction

Timely, accurate, and complete reporting and analysis of safety information from clinical studies are crucial for the protection of subjects, investigators, and the Sponsor, and are mandated by regulatory agencies worldwide. The Sponsor has established procedures in conformity with regulatory requirements to ensure appropriate reporting of safety information.

If a screen-failed subject reports an AE, only the safety data (demography, subject disposition, and AE information) will be entered in the EDC system.

10.3.2. Definitions

10.3.2.1. Adverse Event (AE)

An AE is any untoward medical occurrence in a clinical study subject temporally associated with the clinical investigation, whether or not the event has a causal relationship to the subject's participation in the trial. It is therefore any unfavorable and unintended sign (including an abnormal finding), symptom, or disease that occurs during the trial. This can include any occurrence that is new in onset, an aggravation of severity/frequency of a baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

Examples of AEs include but are not limited to:

- Abnormal test findings,
- Clinically important symptoms and signs,
- Changes in physical examination findings,

- Hypersensitivity, and
- Progression/worsening of underlying disease.

Any change in existing medical condition (medical history) may be considered an AE and recorded appropriately.

Additionally, they may include the signs or symptoms resulting from:

- Product overdose,
- Product withdrawal,
- Product abuse,
- Product misuse,
- Product interactions,
- Medication errors,
- Product dependency,
- Exposure in utero (EIU), and
- Study related procedures.

The criteria for determining whether an abnormal objective test finding should be reported as an AE are as follows:

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention, and/or
- Test result leads to a discontinuation from the study, significant additional concomitant treatment, or other therapy, and/or
- Test result is considered to be an AE by the PI or the Sponsor.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an AE. Any abnormal test result that is determined to be an error does not require reporting as an AE.

Expected Events

Any signs or symptoms of irritation are considered a clinical endpoint and may or may not be coded as AEs based on the PI's or trained designee's assessment. Irrespective of whether the sign(s) or symptom(s) is (are) coded as an AE, the signs or symptoms must be documented on the clinical evaluation source documentation. If any of these irritation parameters appear to be exacerbated, more than normally associated with use of these types of products, the event will be recorded as an AE. This can only be determined by the PI or trained designee. If a subject is discontinued due to worsening of a sign or symptom (including worsening of the signs and or symptoms recorded as part of the evaluations), then it should be recorded as an AE.

Pre-Treatment AE (PTAE)

A PTAE is defined as any AE present prior to the initiation of the IP usage.

10.3.2.2. Serious Adverse Event (SAE)

AEs are considered serious and require immediate reporting if they meet the definition of a **Serious Adverse Event** (SAE).

An AE (untoward medical occurrence) will be considered an SAE if it meets either of the following definitions:

Definition 1:

The event fulfills at least one of the following criteria:

- Results in death
- Is life-threatening (immediate risk of death)
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- Is a congenital anomaly/birth defect
- Is considered a medically significant event (medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not result in death, be life-threatening, or require hospitalization but may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the other outcomes listed above. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasia, or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse, or malignancy)
- Is a suspected transmission of any infectious agent via a product (medically significant)

Definition 2:

- the event involves subject contact with a device AND
- the event results in:
    - death
    - serious injury, which means an injury or illness that:
        - is life-threatening (immediate risk of death)
        - results in permanent impairment of a body function or permanent damage to a body structure, or
        - necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure (*permanent means irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage*).
    - Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
    - Congenital anomaly/birth defect
    - Any suspected transmission of any infectious agent via a product (medically significant).

10.3.2.3. Severity

The severity of all AEs must be assessed by the PI (or a medically qualified designee). The severity classifications are:

- **Severe** – Extreme distress, causing significant impairment of functioning or incapacitation; interferes significantly with subject's usual function; prevents normal everyday activities.
- **Moderate** – Sufficient discomfort is present to cause interference to some extent with subject's usual function or normal everyday activity.
- **Mild** – Awareness of symptoms that are easily tolerated, causing minimal discomfort and not interfering with subject's usual function or normal everyday activities.

Note the distinction between the severity and the seriousness of an AE. A severe event is not necessarily a serious event. For example, a headache may be severe (interferes significantly with subject's usual function) but would not be classified as serious unless it met one of the criteria for SAEs, listed above.

10.3.2.4. Causality Assessment

An AE (serious or non-serious) is considered "study-related" if the causality assessment is possible, probable, or very likely. The PI (or a medically qualified designee) determines the causality by using the following definitions:

- **Not related** – an AE that is not related to the participation in the study.
- **Doubtful** – an AE for which an alternate explanation is more likely (e.g. concomitant drug), or the relationship in time suggests that a causal relationship is unlikely.
- **Possible** – an AE that might be a result of participation in the study. An alternative explanation is inconclusive and the relationship in time is reasonable so a causal relationship cannot be excluded.
- **Probable** – an AE that might be a result of participation in the study. The relationship in time is suggestive (e.g. confirmed by the challenge). An alternative explanation is less likely.
- **Very Likely** – an AE that is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation. The relationship in time is very suggestive (e.g. confirmed by dechallenge and rechallenge).

10.3.3. Procedures for Reporting AEs

All AEs will be reported from the time a signed and dated ICD is obtained until completion of the subject's last study procedure or visit (or termination if the subject terminates early from the study for any reason).

AEs that occur within 30 calendar days after completion of the study will only be reported to the Sponsor if they are serious (i.e. SAEs). SAEs are reportable beyond this period if the event is considered study-related. The Sponsor will evaluate any safety information that is spontaneously reported by the PI/Site beyond this time frame.

Subjects are encouraged to report AEs spontaneously and in response to questioning during the visit (e.g. if they have had any side effects/issues or changes in their health since their last appointment). For each AE reported by the subject or observed by the Site team, the Site team member should notify the PI or designee, who will collect information about the event.

All AEs, regardless of seriousness, severity, or presumed relationship to study procedures, must be recorded using medical terminology. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (e.g., cough, runny nose, sneezing, sore throat, and head congestion should be reported as "upper respiratory infection"). The PI (or medically qualified designee) must record or confirm their opinion concerning the seriousness, severity, and relationship of the AE to the study. All measures required for AE management must be recorded and reported according to Sponsor instructions.

These events must then be entered into the EDC system within 3 business days of the site's awareness.

Tabulation of AEs

AEs will be reported in a table detailing the different AE types highlighted in this protocol:

- Pre-Treatment AEs (PTAEs)
- Expected AEs
- AEs related to the product/study
- AEs non-related to the product/study
- SAEs related to the product/study
- SAEs non-related to the product/study

Additional Reporting Procedures

The PI or designee must also report AEs to the appropriate IRB/IEC unless otherwise required and documented by the IRB/IEC.

If a **SAE** occurs, in addition to the above reporting procedures, the Site will **immediately** upon SAE awareness notify the SM by telephone or encrypted e-mail (see Appendix XI for Contact Information).

Subsequent to a telephone or encrypted e-mail report of an SAE **and within 24 hours of awareness of the SAE**, the Site will complete and securely send (MBOX, Cisco, Secure mail) the Clinical Investigation SAE Report Form signed by the PI (or medically qualified designee) to the SM with as much information as possible, including:

- The PI/designee's assessment of causality
- The subject identification number, the identity of SAE reporter, the IP/auxiliary product information (if applicable), the SAE description/outcome
- Any relevant supporting documentation (e.g., medical history, concomitant medications). Note that if relevant supporting documentation requires translation, these translations must be sent securely **within 3 business days after initial notification.**

This above process also applies to additional new information (follow-up) on previously forwarded SAE reports.

The PI may be requested by the Sponsor to obtain specific additional follow-up information or more detailed information in an expedited fashion. In general, this will include a description of the SAE in sufficient detail to allow for a complete medical assessment of the case and independent determination

of possible causality. Information on other possible causes of the event, such as concomitant medications and illnesses, must be provided.

In the case of a subject death, a summary of autopsy findings (if available) and death certificate should be collected if permission is obtained from the subject's family.

For a hospitalization, a copy of the hospital discharge summary should be requested. If obtained, these documents (with subject's personal identifiers redacted) should be securely submitted as soon as possible to the SM.

All the documentation pertaining to the SAE will be filed in the SMF.

10.3.4. Monitoring and Resolution of AEs

10.3.4.1. Non-Serious AEs

All study-related AEs will be followed until resolution, until a stable clinical endpoint is reached, or at least 30 days post-study withdrawal/completion. This information will be captured and entered into the EDC system.

10.3.4.2. Serious AEs (SAEs)

All SAEs will be followed by the PI, if medically qualified, or the designated study physician until resolution or until one of the conditions in the next section ("Resolution") is met. This information will be captured and entered into the EDC system. The PI/designee will also document follow-up information on an updated Clinical Investigation SAE Report Form, which will be reviewed by the PI (or medically qualified designee) and securely sent to the SM as described above.

10.3.4.3. Resolution

The PI (or medically qualified designee) will be required to assess the outcome of each AE as one of the following:

- Resolved
- Not Resolved
- Fatal
- Resolved with sequelae
- Resolving
- Unknown

SAEs that have not been resolved by the end of the study, or that have not been resolved upon discontinuation of the subject's participation in the study, must be followed until any of the following occurs:

- the event resolves
- the event stabilizes
- the event returns to baseline, if a baseline value is available

- the event can be attributed to factors unrelated to study conduct
- when it becomes unlikely that any additional information can be obtained (subject or healthcare practitioner refusal to provide additional information; lost to follow-up after demonstration of due diligence with follow-up efforts).

10.3.5. Pregnancy Reporting and Exposure In Utero (EIU)

Pregnancy in a female study subject is reportable to the Sponsor. Pregnancies will be reported from the time a signed and dated ICD is obtained until completion of the subject's last study procedure (or termination if the subject terminates early from the study for any reason). Pregnancies that occur between the subject's last visit and 30 calendar days after their last visit will only be reported to the Sponsor if there could have been EIU (according to date of last menses).

Pregnancies occurring in subjects classified as screen failures do not require follow-up unless the screening procedures could have had an effect on the pregnancy outcome or the screen failure was detected after study procedures and IP application was already started.

Follow-up on pregnancy data (e.g., outcome of pregnancy) must occur regardless of whether or not the subject remains in the study. The PI or designee will follow-up the pregnancy until its successful completion or early termination (i.e. abortion) and then notify the Sponsor of the outcome.

If a reportable pregnancy/EIU occurs, the PI or designee must:

- For initial notification, complete and securely send the "*Pregnancy Notification Form*" to the SM or designee within 24 hours of awareness.
- Complete and securely send the "*Product Exposure During Pregnancy – Form A*" within 24 hours from when the information becomes available, which must be no later than 30 calendar days from the initial "*Pregnancy Notification Form*" completion.
- Follow-up with the subject to determine the pregnancy outcome. At the end of the pregnancy, complete and securely send the "*End of Pregnancy Collection – Form B*" within 24 hours from when the information becomes available.

The PI or designee should follow the procedures for reporting SAEs if the outcome of the pregnancy meets the criteria for immediate classification as a SAE, such as spontaneous abortion, stillbirth, neonatal death, congenital anomaly (including that in an aborted fetus, stillbirth, or neonatal death), or any infant death that the PI assesses as possibly related to EIU.

In the case of a live birth, the viability of the newborn will be assessed at the time of birth; no minimum follow-up period of a presumably normal infant is required before an "End of Pregnancy Collection – Form B" can be completed.

All the documentation pertaining to the pregnancy will be filed in the SMF.

11. ETHICAL CONSIDERATIONS

11.1. STUDY SUBMISSION TO INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE

This study (protocol, ICD, recruiting material [advertisements, phone script, etc.], and all addenda) will be reviewed and approved by an Institutional Review Board/Independent Ethics Committee (IRB/IEC) contacted by the Study Site.

Details of the IRB/IEC for this study are included in Appendix XI.

It is the responsibility of the PI to have IRB/IEC approval of the study protocol, protocol amendments, ICD(s), and other relevant documents, e.g., advertisements, as applicable.

The study will not be activated and subjects will not be recruited, consented, or receive study materials until such time as the IRB/IEC has approved the required documentation. In addition, the IRB/IEC will review the study before any significant change in the protocol is initiated. After each review, the IRB/IEC's approval letter will be forwarded to the Sponsor. All correspondence with the IRB/IEC should be retained in the SMF.

The only circumstance in which an amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the PI must notify the IRB/IEC and the Sponsor in writing within 3 working days after the implementation.

12. DATA HANDLING AND RECORD KEEPING

All subject source documents are the Site's subject records and are to be maintained at the Study Site. The study source documents must be attributable, legible, contemporaneous, original, accurate, and complete, and must collect only relevant data required by this protocol. All documentation should be completed using good documentation and data integrity practices.

All data will be captured on source documentation first and then the relevant data needed for analysis will be entered in the Sponsor's EDC system.

EDC pages should be completed for each randomized subject. The completed pages of the EDC system are the sole property of the Sponsor and should not be made available in any form to third parties, except for authorized representatives of the Sponsor or appropriate regulatory authorities, without written permission from the Sponsor.

It is the PI's responsibility to ensure completion and to review and approve all information captured in the EDC system. The subject's data in the EDC system must be electronically signed by the PI. These signatures serve to attest that the information contained in the EDC system is true. At all times, the PI has final personal responsibility for the accuracy and authenticity of all clinical data entered in the EDC system.

The Sponsor or its designee will have responsibility for verifying for accuracy of the data entered into the EDC system against the source documents.

All data entered in the EDC system will be sent to the Sponsor's Quantitative Sciences Department for statistical analysis. All final data recorded in the EDC system will be retained in the Trial Master File (TMF) and the SMF.

The Study Site shall maintain and archive the SMF for 2 years from the time the final report is issued. The Sponsor must be notified before the disposal of any study record, even if retention requirements are met.

If it becomes necessary for the Sponsor or a Regulatory Authority to review any documentation relating to the study, the PI/Site must permit access to such records.

If the PI relocates, retires, or for any reason withdraws from the study, the Sponsor must be prospectively notified.

13. STUDY MONITORING, QUALITY CONTROL AND QUALITY ASSURANCE

The study will be monitored by the Sponsor in accordance with a monitoring plan. Frequent communications (via telephone or e-mail) will be utilized to provide Sponsor oversight and to assist in resolving any difficulties encountered while the study is in progress. The monitoring visits may occur during the trial or shortly after study completion to ensure that the investigation is/was conducted according to the protocol and that the principles of ICH GCP are/were being followed. The monitors may review study documents to confirm that the data recorded is complete and accurate.

The PI/Site will allow the Sponsor's monitors or its representatives and appropriate regulatory authorities direct access to study documents to perform monitoring. If there are any issues noted, the PI will be notified.

Any contact concerning this study should be made with the SM or Study Director (see contact information in Appendix XI).

The Study Site may be subject to review by the IRB/IEC, to quality assurance audits performed by the Sponsor, and/or to inspection by appropriate regulatory authorities.

It is important that the PI and relevant Site personnel are available during monitoring and possible audits or inspections and that sufficient time is devoted to the process.

All study documents must be approved by the Sponsor before use in the study.

14. SPONSOR DISCONTINUATION CRITERIA

Premature termination of this clinical trial may occur because of a change in opinion of the IRB/IEC, IP or study safety problems, or at the discretion of the Sponsor. If a trial is prematurely terminated or discontinued, the Sponsor will promptly notify the PI/Site. After notification, the PI or designated staff must contact all participating subjects within 10 business days (phone, voicemail, or certified letter), as applicable. As directed by the Sponsor, all trial materials must be collected, all documents completed to the greatest extent possible, and termination reported to the IRB/IEC.

15. FINAL REPORT

The draft report will be prepared by the Study Site within 4 weeks after statistical analysis results are received from the Sponsor.

The draft report will be submitted to the Sponsor for review and changes may be made to the draft report at the Sponsor's request. Upon Sponsor's/study team's approval, the report will be finalized and forwarded to the Sponsor. The final report will include (but is not limited to) the following information: study design and protocol, subject population demographics, statistical methods used, results, description of AEs (if any), protocol deviations, discussions, and conclusions.

16. CONFIDENTIALITY

All of the subjects' private information, the data, and the study results are confidential. This information will only be made available to the study team, authorized Sponsor personnel or designees, and authorized external personnel, according to the local requirements and regulations.

17. PUBLICATION

The publication agreement, if any, between the Sponsor and the site is detailed in the clinical trial agreement.

18. BIBLIOGRAPHIC REFERENCES

1) Fitzpatrick RE. Laser resurfacing of rhytids. *Dermatol Clinics.* 1997; 15:431-447.

2) McCullough JL, Kelly KM. Prevention and treatment of skin aging. *Ann NY Acad Sci.* 2006; 1067:323-331.

3) Weiss RA, McDaniel DH, Geronemus RG. Review of non-ablative photorejuvenation: reversal of the aging effects of the sun and environmental damage using laser and light sources. *Semin Cutan Surg.* 2003; 22:93-106.

4) Kim JW. Clinical trial of nonthermal 633 nm Omnilux LED array for renewal of photoaging: clinical surface profile metric results. *Korea Soc Las Med Surg.* 2005; 9:69-76.

5) Fitzpatrick RE, Goldman MP, Satur NM, Tope WD. Pulsed carbon dioxide resurfacing of photoaged facial skin. *Arch Dermatol*. 1996; 132:395-402.

6) Griffiths CEM, Wang TS, Hamilton TA, Vorhees JJ, Ellis CH. A photonumeric scale for the assessment of cutaneous photodamage. *Arch Dermatol.* 1992; 128:347-351.

19. PROTOCOL SIGNATURES PAGE

20. PRINCIPAL INVESTIGATOR RESPONSIBILITY STATEMENT

I have read and understood this study protocol, attached appendices, and any amendments and/or supplements thereto.

I agree to conduct the study in compliance with this protocol and in accordance with U.S. Food and Drug Administration (FDA) regulations, applicable local regulations, and the principles of ICH GCP as outlined herein.

Furthermore, I agree to make no additions and/or changes without the consent of the Sponsor, except when necessary to protect the safety of the subjects.

I will provide copies of the final approved protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure that they are fully informed regarding the protocol and conduct of this study.

I undertake the responsibility of promptly communicating to the IRB/IEC and to the Sponsor any complications that may occur during the course of the study.

I further undertake the responsibility of following up on all the measures required to ensure the safety and the rights of the subjects.

Signature and Date:

[redacted]

Stuart Lessin, M.D.
Principal Investigator

21. APPENDICES

Appendix I. Fitzpatrick Skin Type Classification

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

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

Appendix II. Skin Type – Oiliness Level

At Screening (Visit 1), subjects will rate their self-perceived skin type in terms of oiliness as per the scale below:

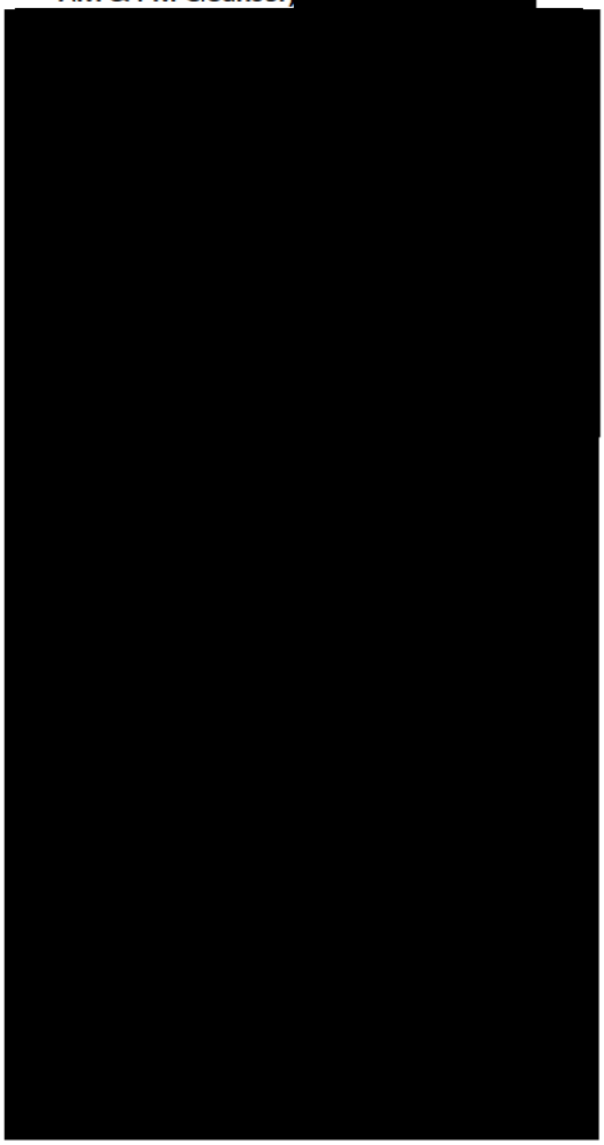
How would you classify your facial skin?

- Oily
- Dry
- Normal
- Combination

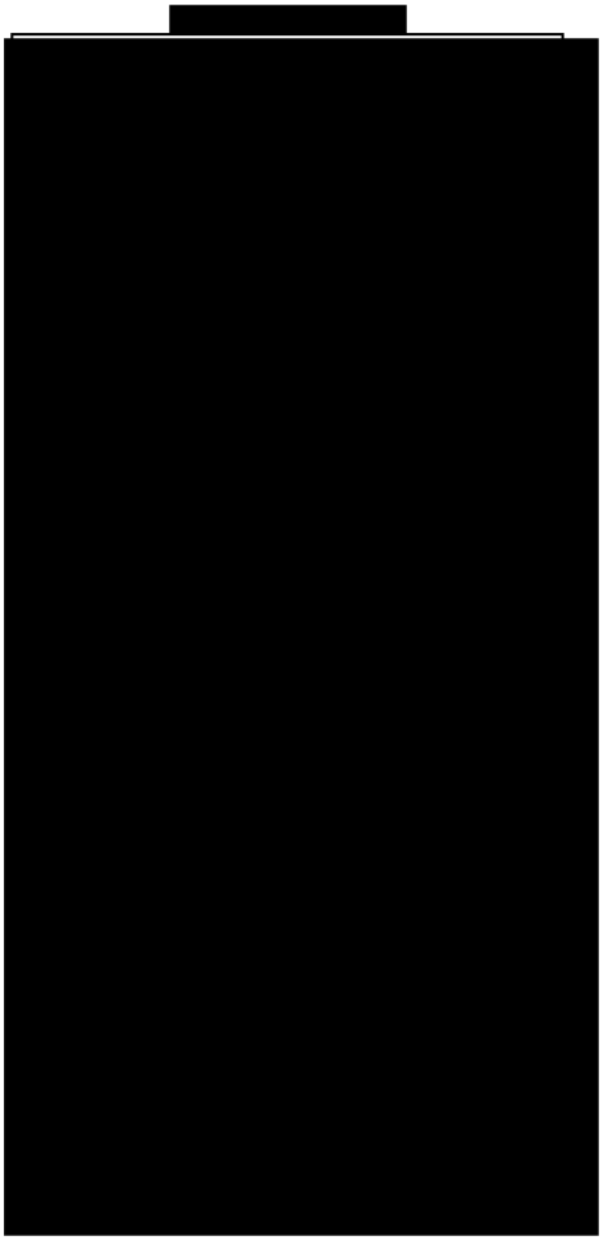
This is for demographic information collection purposes only and is not considered an evaluation endpoint.

Appendix III. Ingredient Lists

AM & PM Cleanser, [redacted]



AM Moisturizer (with SPF 30), [redacted]



Appendix IV. Clinical and Subjective Evaluations of Efficacy [redacted] – Grading Scales

A) Efficacy: To be independently evaluated by the PI and 2 other Expert Graders (note: only the PI will evaluate the subject at Screening [Visit 1]).

1) Each subject's face will be evaluated for the following efficacy parameters using the **Fitzpatrick Wrinkle and Elastosis Scale**[5] shown below. One score will be assigned by each grader for each parameter. Half points are allowed.

- Fine lines
- Periorbital wrinkles
- Global wrinkling

Fitzpatrick Wrinkle and Elastosis Scale:

Class	Score	Wrinkling	Degree of Elastosis
I	1-3	Fine wrinkles	Mild (fine textural changes with subtle skin lines)
II	4-6	Fine to moderate depth, moderate number of lines	Moderate (distinct popular elastosis, individual papules with yellow translucency, dyschromia)
III	7-9	Fine to deep wrinkles, numerous lines, with or without redundant skin	Severe (multipapular and confluent elastosis, thickened yellow and pallid cutis rhomboidalis)

2) Each subject's face will be evaluated for the following efficacy parameters using the **Modified Griffiths Scale**[6] shown below. One score will be assigned by each grader for each parameter. Half points are allowed.

- Surface roughness – this factor represents a combined assessment of the appearance and feel of the skin's roughness.
- Uneven skin tone
- Mottled hyperpigmentation – this factor represents a visual assessment of light, patchy, mottled hyperpigmentation and solar freckling (including melasma) based on quantitative and qualitative criteria such as the area/density of pigment, color intensity (dark vs. light), and uniformity of distribution (i.e., the more uneven or blotchy, the greater the score). Lentigines, nevi, and other pigmented lesions are not to be included in this assessment.
- Sallowness or yellowing – this factor represents a visual assessment of color tone from no yellow undertones to very sallow or pronounced yellow undertones.
- Lack of radiance

[redacted]

Modified Griffiths Scale:

Rating (Score)	Category	Description
0	None	**See below for parameter-specific descriptions.**
1-3	Mild	
4-6	Moderate	
7-9	Severe	

Surface Roughness (using Modified Griffiths Scale):

Rating (Score)	Category	Description
0	None	Skin perfectly smooth.
1-3	Mild	Slight laxity of skin. Some surface roughness visible.
4-6	Moderate	Tactile and/or visible roughness demonstrable.
7-9	Severe	Topography of skin (visible and tactile) is undulating and rough.

Uneven Skin Tone (using Modified Griffiths Scale):

Rating (Score)	Category	Description
0	None	Uniform natural skin color; perfect evenness.
1-3	Mild	"Barely" to "slightly" to "slightly to mildly"…perceivable areas of redness, yellowness, or darkness.
4-6	Moderate	"Mildly to moderately" to "moderately" to "pronounced"…perceivable areas of redness, yellowness, or darkness
7-9	Severe	"Pronounced" to "pronounced to significantly" to pronounced (severe)"… perceivable areas of redness, yellowness, or darkness

Mottled Hyperpigmentation (using Modified Griffiths Scale):

Rating (Score)	Category	Description
0	None	Perfectly even in tone (no redness or hyperpigmentation).
1-3	Mild	Early color variation; no lentigines (freckles may be present).
4-6	Moderate	Early to moderate dyspigmentation/telangiectasia may be present; one or more lentigines.
7-9	Severe	Dyschromia (mottled and/or discrete) is likely, or it may be replaced by quite definite yellowing.

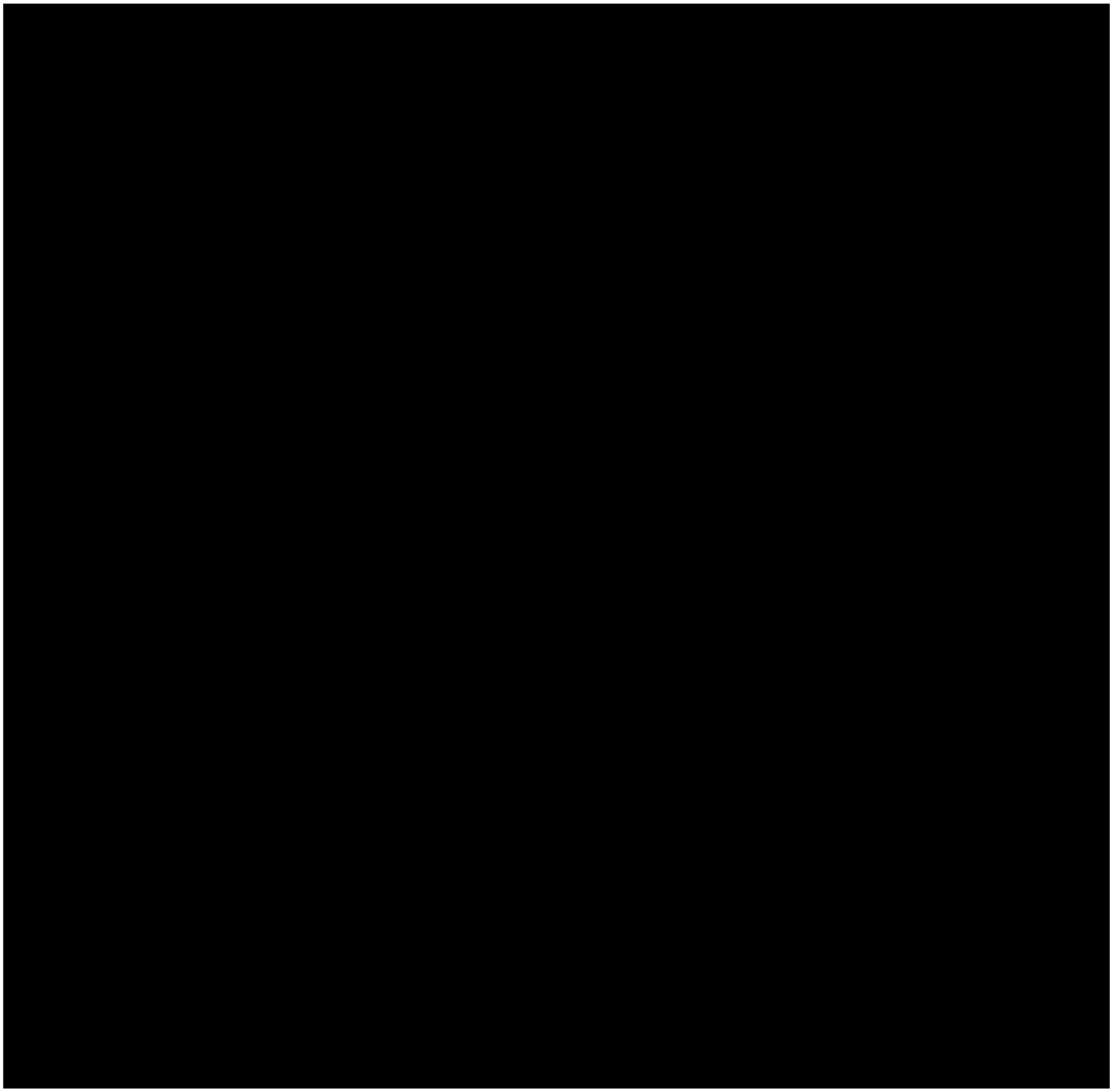
Sallowness or Yellowing (using Modified Griffiths Scale):

Rating (Score)	Category	Description
0	None	No evidence of yellowing; depending on Fitzpatrick skin type, the skin may be very pink and rosy.
1-3	Mild	No yellowing; depending on Fitzpatrick skin type, the skin may be pink and rosy to slightly pink and rosy.
4-6	Moderate	Early evidence of yellowing; one or more lentigines; depending on Fitzpatrick skin type, the skin may be slightly pink and rosy to sallow and pale.
7-9	Severe	Quite definite yellowing. Depending on Fitzpatrick skin type, the skin may be sallow and pale to very sallow and pale.

Lack of Radiance (using Modified Griffiths Scale):

Rating (Score)	Category	Description
0	None	Extremely bright, clear, radiant
1-3	Mild	"Very" to "mildly" to "mildly to moderately"...bright, clear, radiant
4-6	Moderate	Moderately bright, clear, radiant skin, but with some matte appearance to mildly dull/matte appearance to moderately dull/matte appearance.
7-9	Severe	"Moderately to pronounced" to "pronounced" to "significantly (severe)" dull/matte appearance

[redacted]



Appendix VI. Subject Instructions – Prior to Treatment Period

Subject Instructions – Prior to Treatment Period
Protocol # CO-1705 1113 2943-SACT; Site Study # 8376

You have been provided with an **AM & PM Cleanser** and an **AM Moisturizer (with SPF 30).** Please use them as follows:

- Wash your face twice daily (morning and evening) with the **AM & PM Cleanser**. In the morning after washing, apply the **AM Moisturizer** full-face. In the evening after washing, you may apply the AM Moisturizer again, if desired. See the detailed instructions below.

In the morning:

1. Wash your face with the **AM & PM Cleanser**:
   Wet your face. Pump cleanser into your hands, add water, and work into a lather. Massage your face gently and rinse thoroughly. Pat dry.

2. Apply the **AM Moisturizer** full-face:
   Apply liberally over your entire face in gentle massaging strokes until fully absorbed. After product dries, you may apply your makeup as usual.

In the evening:

1. Wash your face with the **AM & PM Cleanser**:
   Wet your face. Pump cleanser into your hands, add water, and work into a lather. Massage your face gently and rinse thoroughly. Pat dry.

2. If desired, you may apply the AM Moisturizer again after washing and drying your face.

Other Instructions:

- During the study, do not use any facial cleansers, moisturizers, sunscreens, or light-based devices other than those provided for this study.
- Do not use any exfoliating, sunless tanning, skin lightening, skin firming, or anti-aging products on your face during the study.
- Do not receive any professional or aesthetic facial spa procedures during the study.
- Continue using your regular brands of color cosmetics (i.e. makeup) and makeup remover during the study. Do not start using any new skincare products or change your currently used brands during the study. Use only facial products reviewed by study staff at Visit 1.

-- Continued on Back --

- On the day of study visits: remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit and then do not apply any leave-on facial products until the visit is completed. Note: if you do not follow these directions, you will be asked to remove your makeup/products and wash your face with the provided cleanser on-site prior to the acclimation period.
- Avoid extended periods of sun exposure and all use of tanning beds for the duration of the study. Extra care should be taken to avoid sun exposure from 11 AM to 4 PM.
- Maintain your birth control method for the duration of the study and 30 days after completion.
- If you are using a hormone replacement therapy (HRT), do not change it during the study. If you are not using a HRT, do not begin one during the study.
- Attend all scheduled visits.
- Do not begin any other clinical study during the current study.
- Report any side effects, changes in health/medication, pregnancies, issues, or questions to the study staff.
- Bring your study products to all visits. All products must be returned when requested by the Study Site.

Appendix VII. Subject Instructions – Treatment Period

Subject Instructions – Treatment Period
Protocol # CO-1705 1113 2943-SACT; Site Study # 8376

You have been provided with an **AM & PM Cleanser**, an **AM Moisturizer (with SPF 30)**, and a **PM Mask Treatment**. Use the products as follows for 12 weeks:

- **Start using them after your visit on <Site to insert date of final Visit 2 sub-visit>** (until then, continue following the "Prior to Treatment Period" instructions).
- Wash your face twice daily (morning and evening) with the **AM & PM Cleanser**. In the morning after washing, apply the **AM Moisturizer** full-face. In the evening after washing, use the **PM Mask Treatment** for 10 minutes. After completing the mask treatment, you may apply the AM Moisturizer again, if desired. See the detailed directions below.

In the morning:

1. Wash your face with the **AM & PM Cleanser**:
   Wet your face. Pump cleanser into your hands, add water, and work into a lather. Massage your face gently and rinse thoroughly. Pat dry.

2. Apply the **AM Moisturizer** full-face:
   Apply liberally over your entire face in gentle massaging strokes until fully absorbed. After product dries, you may apply your makeup as usual.

In the evening:

1. Wash your face with the **AM & PM Cleanser**:
   Wet your face. Pump cleanser into your hands, add water, and work into a lather. Massage your face gently and rinse thoroughly. Pat dry.

2. Use the **PM Mask Treatment** for 10 minutes.
   *Refer to **package insert** for detailed instructions, warnings, etc.*

3. If desired, you may apply the AM Moisturizer again after completing the mask treatment.

Other Instructions:

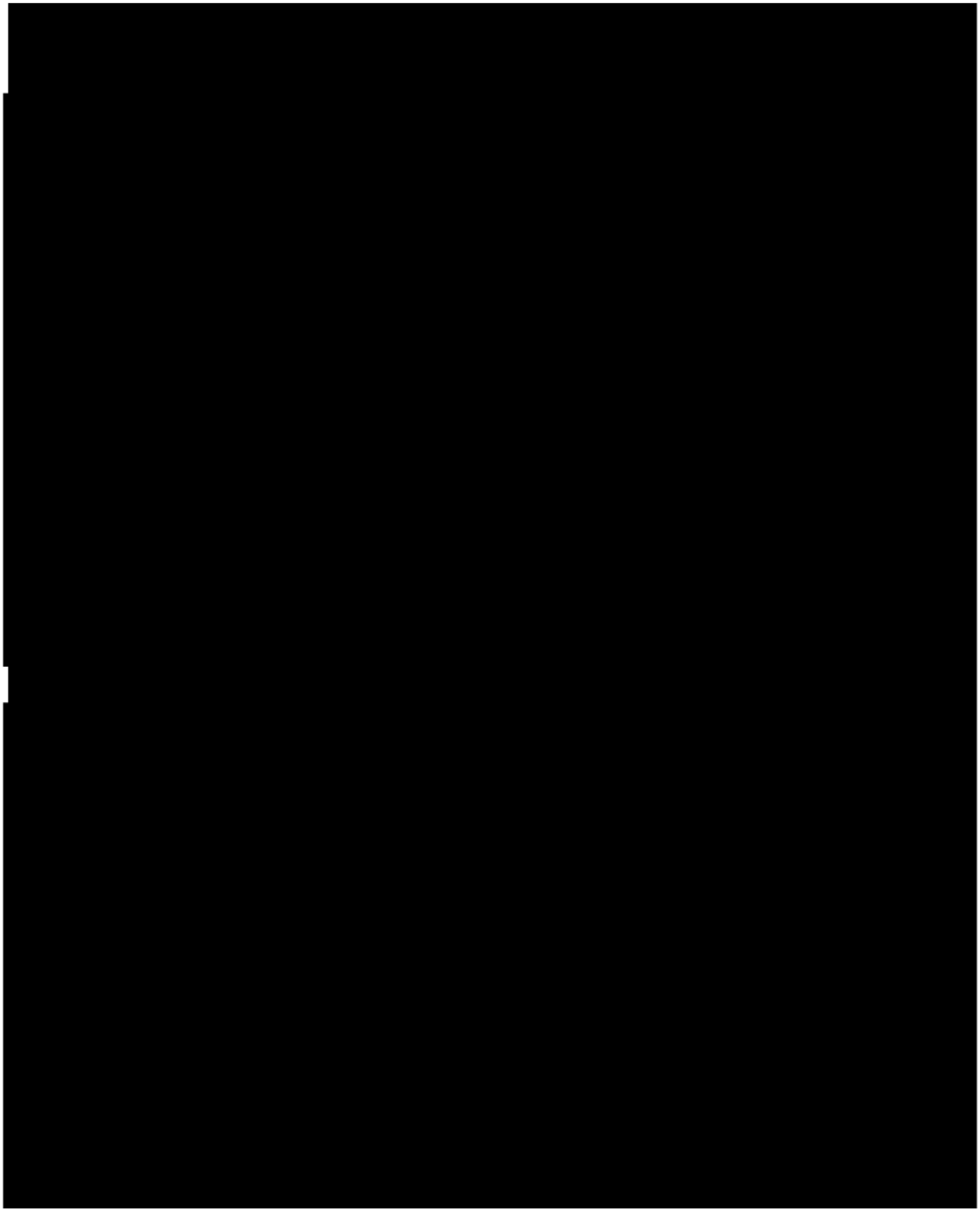
- During the study, do not use any facial cleansers, moisturizers, sunscreens, or light-based devices other than those provided for this study.
- Do not use any exfoliating, sunless tanning, skin lightening, skin firming, or anti-aging products on your face during the study.
- Do not receive any professional or aesthetic facial spa procedures during the study.

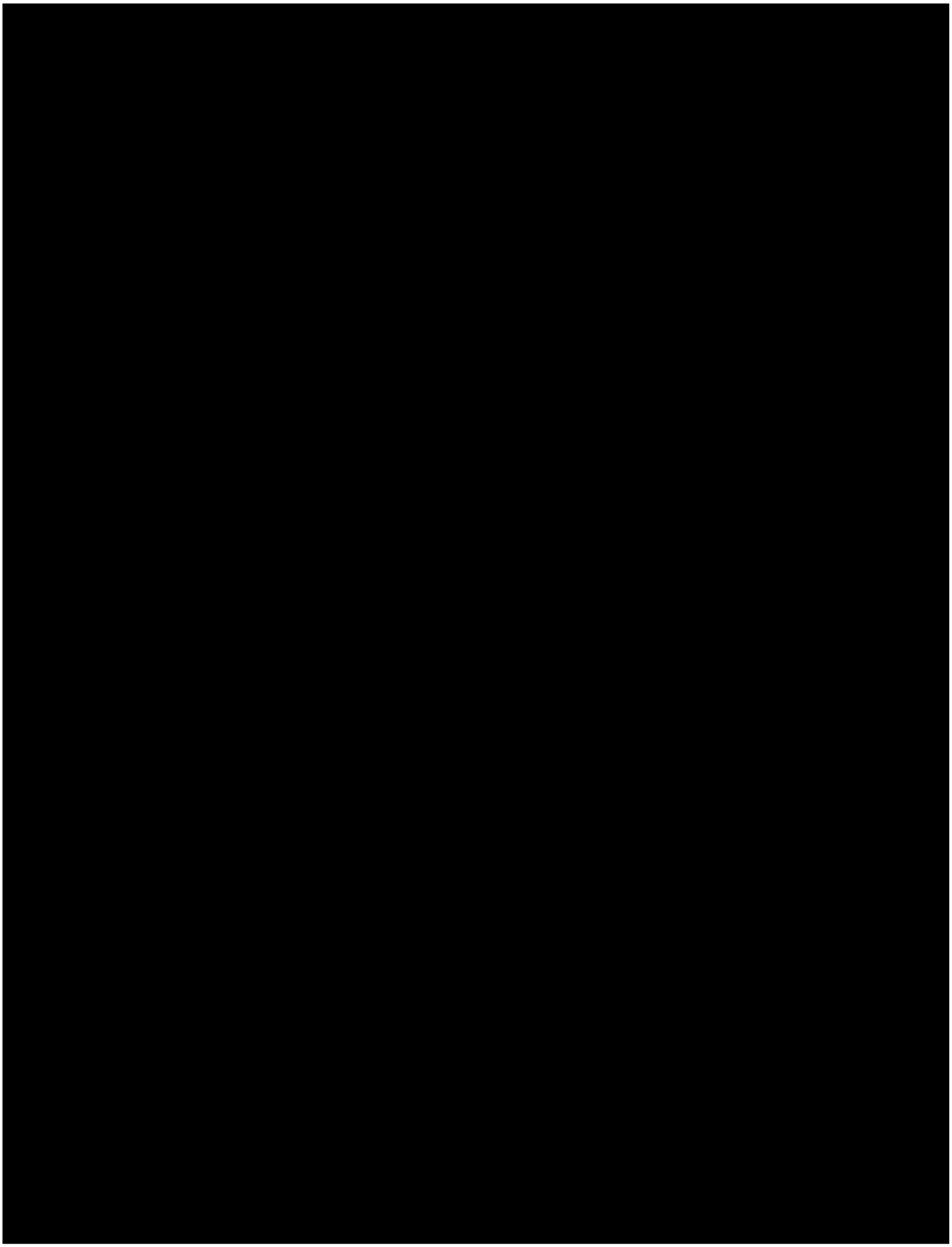
-- Continued on Back --

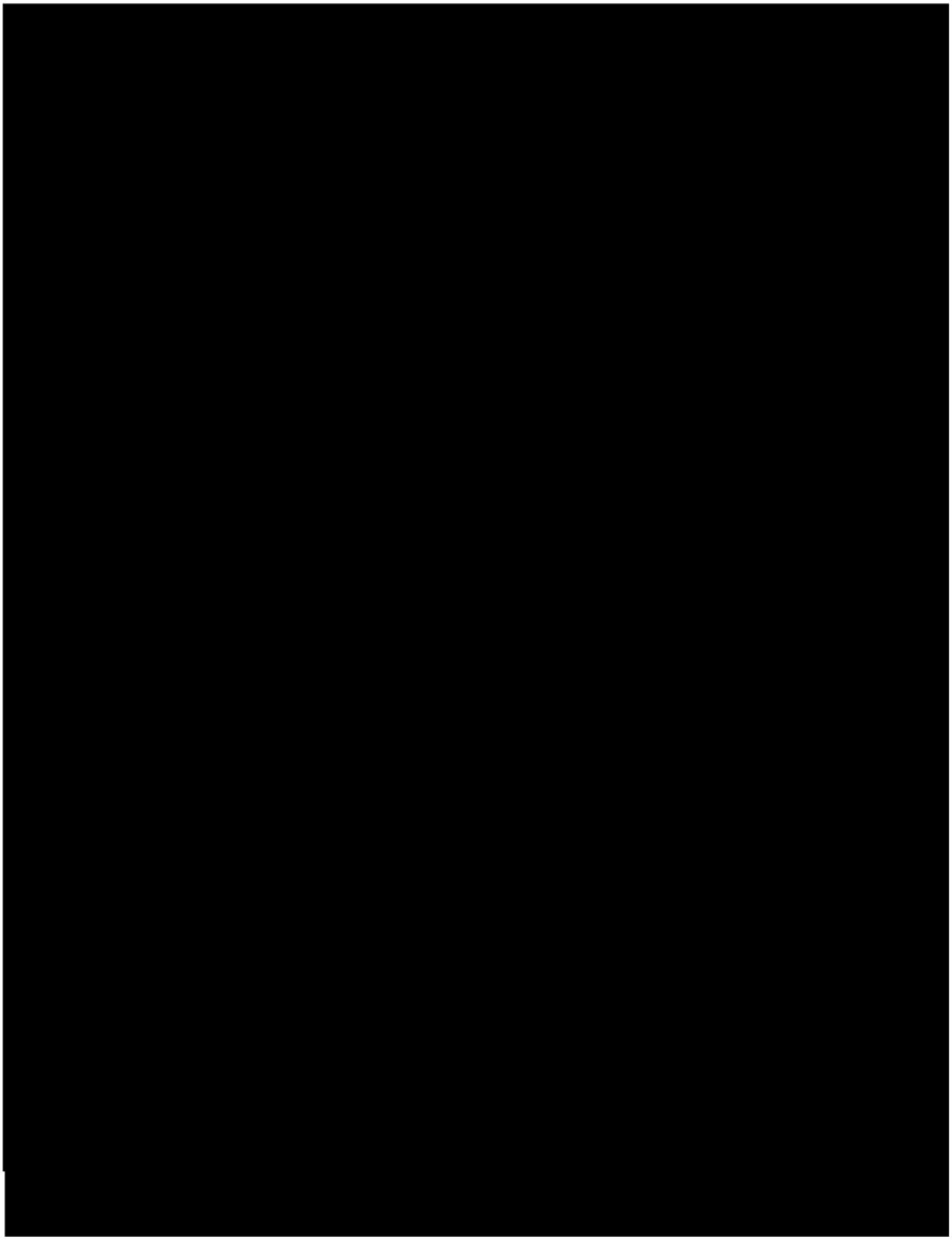
- Continue using your regular brands of color cosmetics (i.e. makeup) and makeup remover during the study. Do not start using any new skincare products or change your currently used brands during the study. Use only facial products reviewed by study staff at Visit 1.
- On the day of study visits: remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit and then do not apply any leave-on facial products until the visit is completed. Note: if you do not follow these directions, you will be asked to remove your makeup/products and wash your face with the provided cleanser on-site prior to the acclimation period.
- Avoid extended periods of sun exposure and all use of tanning beds for the duration of the study. Extra care should be taken to avoid sun exposure from 11 AM to 4 PM.
- Maintain your birth control method for the duration of the study and 30 days after completion.
- If you are using a hormone replacement therapy (HRT), do not change it during the study. If you are not using a HRT, do not begin one during the study.
- Attend all scheduled visits.
- Do not begin any other clinical study during the current study.
- Report any side effects, changes in health/medication, pregnancies, issues, or questions to the study staff.
- Bring your study products to all visits. All products must be returned when requested by the Study Site.

Appendix VIII. PM Mask Treatment & Mask Activator Package Insert – Active Cell

PM Mask Treatment & Mask Activator Package Insert

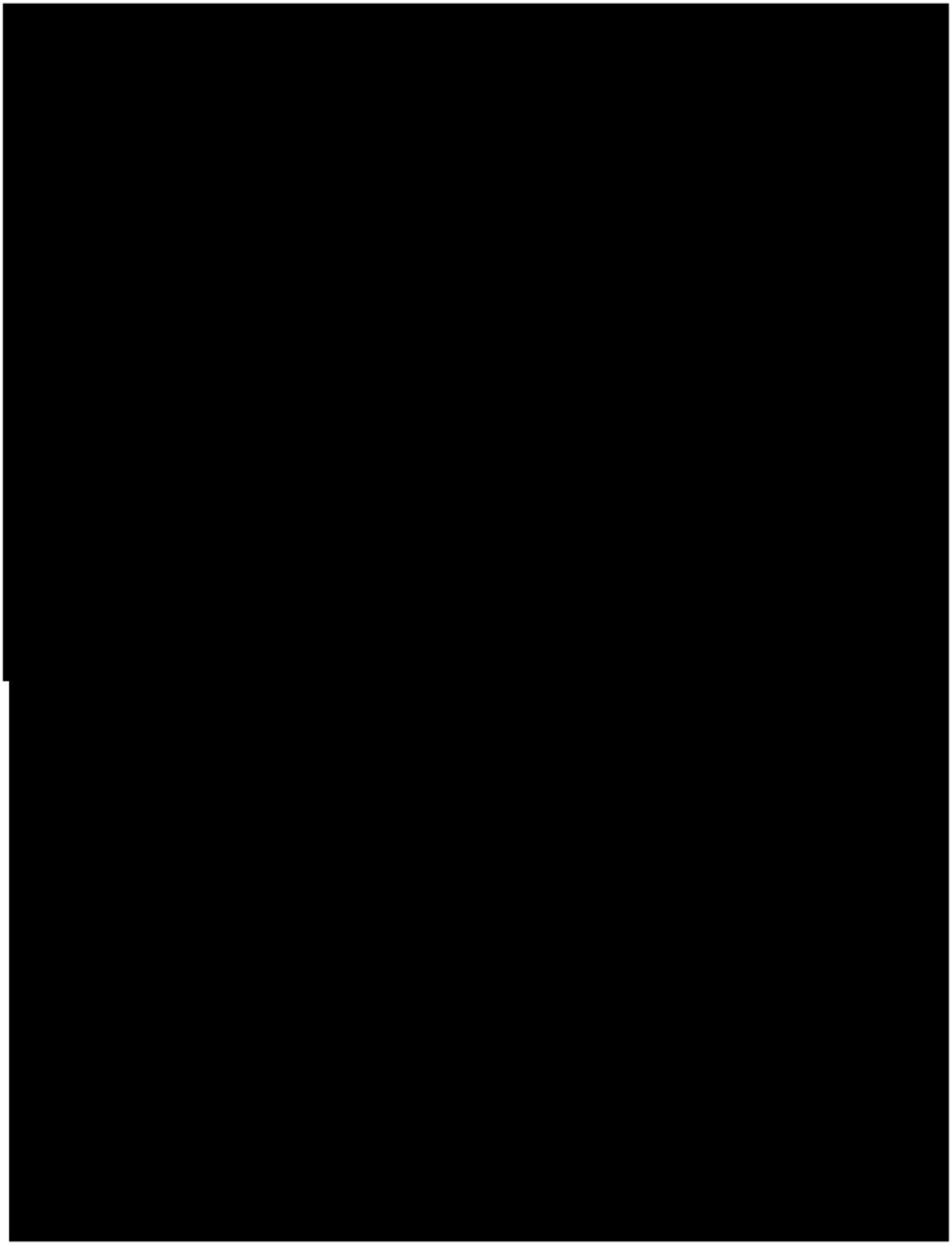


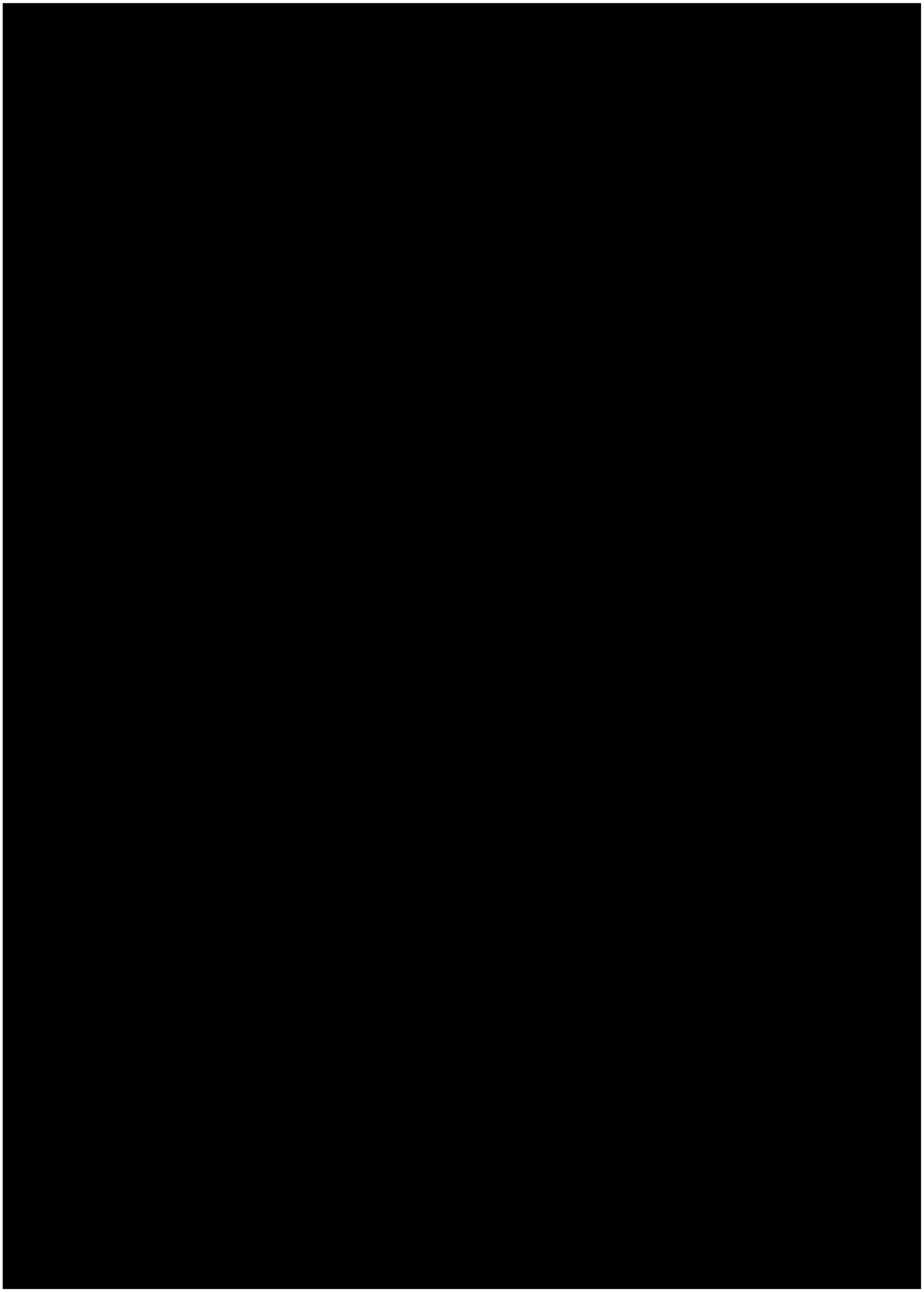


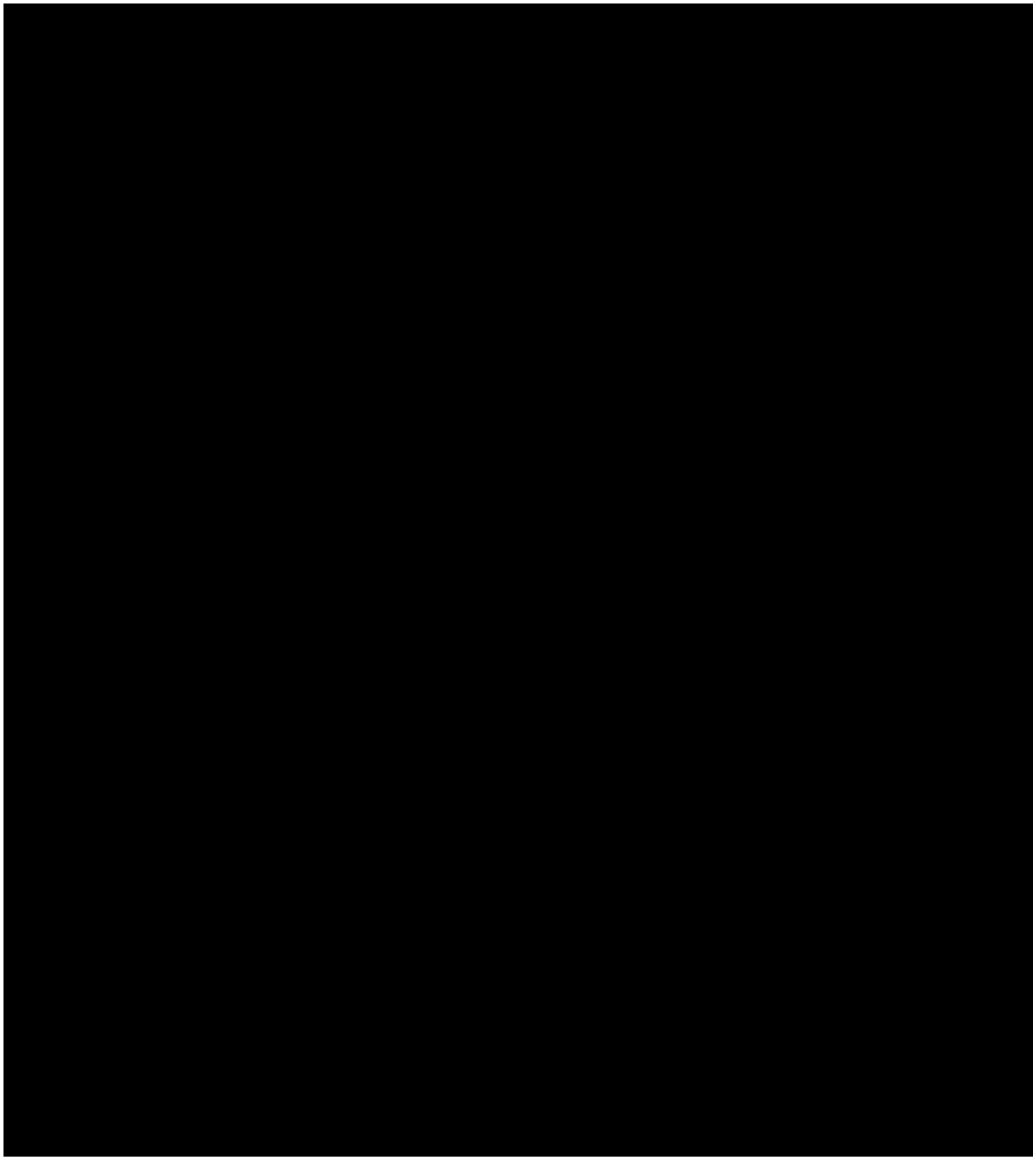


Appendix IX. PM Mask Treatment & Mask Activator Package Insert – Sham Cell

PM Mask Treatment & Mask Activator Package Insert







Appendix X. Subject Instructions – Regression Period

Subject Instructions – Regression Period
Protocol # CO-1705 1113 2943-SACT; Site Study # 8376

You have been provided with an **AM & PM Cleanser** and an **AM Moisturizer (with SPF 30)** for the 12-week regression period. You will no longer be using the PM Mask Treatment. Please use the provided products as follows for the next 12 weeks:

- Wash your face twice daily (morning and evening) with the **AM & PM Cleanser**. In the morning after washing, apply the **AM Moisturizer** full-face. In the evening after washing, you may apply the AM Moisturizer again, if desired. See the detailed directions below.

In the morning:

1. Wash your face with the **AM & PM Cleanser**:
   Wet your face. Pump cleanser into your hands, add water, and work into a lather. Massage your face gently and rinse thoroughly. Pat dry.

2. Apply the **AM Moisturizer** full-face:
   Apply liberally over your entire face in gentle massaging strokes until fully absorbed. After product dries, you may apply your makeup as usual.

In the evening:

1. Wash your face with the **AM & PM Cleanser**:
   Wet your face. Pump cleanser into your hands, add water, and work into a lather. Massage your face gently and rinse thoroughly. Pat dry.

2. If desired, you may apply the AM Moisturizer again after washing and drying your face.

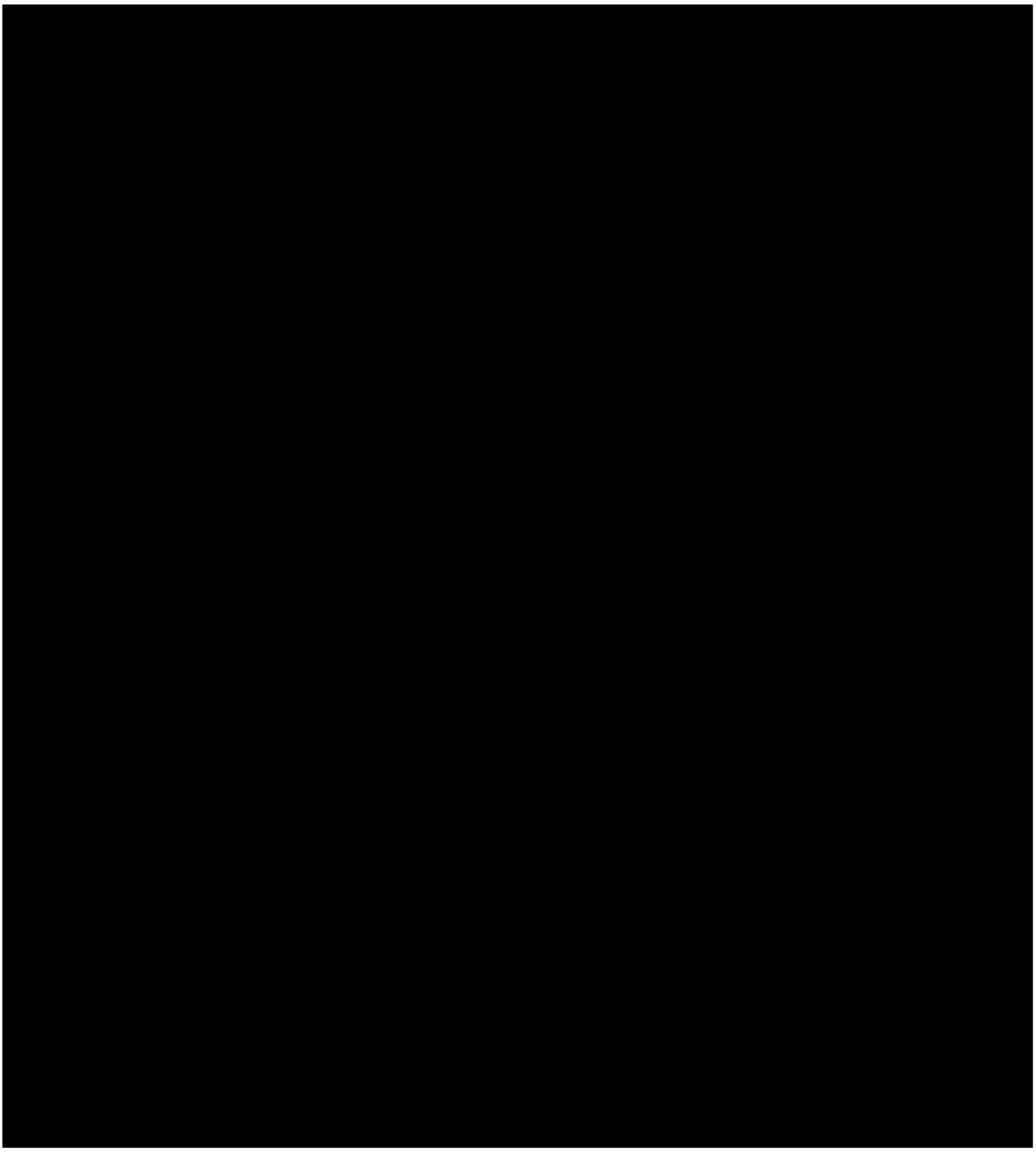
Other Instructions:

- During the study, do not use any facial cleansers, moisturizers, sunscreens, or light-based devices other than those provided for this study.
- Do not use any exfoliating, sunless tanning, skin lightening, skin firming, or anti-aging products on your face during the study.
- Do not receive any professional or aesthetic facial spa procedures during the study.
- Continue using your regular brands of color cosmetics (i.e. makeup) and makeup remover during the study. Do not start using any new skincare products or change your currently used brands during the study. Use only facial products reviewed by study staff at Visit 1.

-- Continued on Back --

- On the day of study visits: remove all leave-on facial products (including eye makeup) and wash with the provided facial cleanser prior to the visit and then do not apply any leave-on facial products until the visit is completed. Note: if you do not follow these directions, you will be asked to remove your makeup/products and wash your face with the provided cleanser on-site prior to the acclimation period.
- Avoid extended periods of sun exposure and all use of tanning beds for the duration of the study. Extra care should be taken to avoid sun exposure from 11 AM to 4 PM.
- Maintain your birth control method for the duration of the study and 30 days after completion.
- If you are using a hormone replacement therapy (HRT), do not change it during the study. If you are not using a HRT, do not begin one during the study.
- Attend all scheduled visits.
- Do not begin any other clinical study during the current study.
- Report any side effects, changes in health/medication, pregnancies, issues, or questions to the study staff.
- Bring your study products to all visits. All products must be returned when requested by the Study Site.

Appendix XI. Contact Information



Appendix XII. Summary of Changes – Amendment 1

CLINICAL PROTOCOL: CO-1705 1113 2943-SACT AMENDMENT 1

A Randomized, Evaluator-Blinded Clinical Study to Evaluate the Efficacy and Tolerability of an Investigational Light Therapy Mask on Subjects with Mild to Moderate Mottled Hyperpigmentation and Moderate to Severe Facial Wrinkles

SUMMARY OF CHANGES

Protocol Number:	CO-1705 1113 2943-SACT
IND / IDE / EudraCT number:	N/A
Phase:	N/A
Sponsor:	Johnson & Johnson Consumer Inc.
Version & Date:	Amendment 1: Final Version 2.0, 26 September 2017 Original: Final Version 1.0, 28 August 2017

1. REASONS FOR THE AMENDMENT TO THE FINAL PROTOCOL

Sections of protocol # CO-1705 1113 2943-SACT, "A Randomized, Evaluator-Blinded Clinical Study to Evaluate the Efficacy and Tolerability of an Investigational Light Therapy Mask on Subjects with Mild to Moderate Mottled Hyperpigmentation and Moderate to Severe Facial Wrinkles," dated August 28, 2017 (Final Version 1.0), have been revised to correct a typographical error in section 7.2.3.3.1 and to correct [redacted]'s first name in Appendix XI. In addition, any reference to expiration dates will be removed from the package inserts in Appendix VIII and Appendix IX; the expiration dates will be over-labeled on the devices due to their positioning next to the etched lot number (which could un-blind the products and therefore will be over-labeled). The study will be completed prior to the expiration date of the devices.

2. PROTOCOL SECTIONS REVISED

The protocol sections that were revised are detailed below. The format is as follows:

- The "Change From" section represents the original text in Protocol # CO-1705 1113 2943-SACT, Final Version 1.0, dated August 28, 2017.
- The "Change To" section represents the revised text in Protocol # CO-1705 1113 2943-SACT, Final Version 2.0, dated September 26, 2017.
- The "Removed" section represents the original text in Protocol # CO-1705 1113 2943-SACT, Final Version 1.0, dated August 28, 2017, that was removed for Final Version 2.0, dated September 26, 2017.

2.1. Efficacy (Section 7.2.3.3.1)

Change From:

- Mottled hyperpigmentation

Change To:

- Mottled hyperpigmentation*

2.2. PM Mask Treatment & Mask Activator Package Insert – Active Cell (Appendix VIII)

Removed:

Shelf Life
For the Activator: refer to the expiration date on the back panel of the Activator.
For the Mask: refer to the expiration date on the eyeglass arm.

2.3. PM Mask Treatment & Mask Activator Package Insert – Sham Cell (Appendix IX)

Removed:

Shelf Life
For the Activator: refer to the expiration date on the back panel of the Activator.
For the Mask: refer to the expiration date on the eyeglass arm.

2.4. Contact Information (Appendix XI)

[redacted]

[redacted]

[redacted]