

# PROTOCOL

## CO-1701-2511-3728-SACT

PROTOCOL TITLE: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

PROTOCOL IDENTIFICATION: CO-1701-2511-3728-SACT

DATE & VERSION: 09 March 2017 Final Version 1.0

SPONSOR: JOHNSON & JOHNSON CONSUMER, INC.

STUDY SITES: Tennessee Clinical Research Center

Nashville, TN 37215

PRINCIPAL INVESTIGATORS (PIs): Michael H Gold, MD

STUDY MANAGER:

STUDY DIRECTOR:

DEPARTMENT HEAD:

DESIGNATED PHYSICIAN REPRESENTATIVE (DPR):

This study will be performed in compliance with International Conference on Harmonization Guidelines for Good Clinical Practice (E6).

CONFIDENTIAL: The information in this document contains trade secrets and commercial information that are privileged or confidential and may not be disclosed unless such disclosure is required by Federal or State law or regulations. Subject to the foregoing, this information may be disclosed only to those persons involved in the study who have a need to know, but all such persons must be instructed not to further disseminate this information to others. These restrictions on disclosure will apply equally to all future information supplied to you, which is indicated as privileged or confidential.

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
 Protocol identification: CO-1701-2511-3728-SACT  
 Date: 9 March 2017 Final Version 1.0

#### VERSION TRACKING

VERSION	DATE	STATE	REASON FOR CHANGE	DESCRIPTION OF CHANGE
1.0	09MAR2017	Final	N/A	N/A

#### SYNOPSIS

<b>PROTOCOL IDENTIFICATION</b>	CO-1701-2511-3728-SACT
<b>PROTOCOL TITLE</b>	A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS
<b>PRINCIPAL INVESTIGATOR</b>	Michael H Gold, MD
<b>STUDY SITE</b>	Tennessee Clinical Research Center [REDACTED]
<b>OBJECTIVE</b>	The objective of this study is to evaluate the tolerance of a light therapy-based acne treatment in subjects with mild to moderate acne and self-reported sensitive skin over a 28-day period.
<b>STUDY DESIGN</b>	This is a single-center, monadic clinical trial to assess the tolerance of the test product on female and male subjects 12-40 years of age with mild to moderate acne vulgaris and sensitive skin. [REDACTED] [REDACTED] Tolerance measures will be signs and symptoms of irritation and adverse events, evaluated by the Investigator and subjects
<b>STUDY POPULATION</b>	Males and females, 12-40 years of age who meet the eligibility criteria of the study. [REDACTED] [REDACTED]
<b>SAMPLE SIZE</b>	A sufficient number of subjects will be screened to enroll up to 45 subjects to complete with 40 total subjects.

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
 Protocol identification: CO-1701-2511-3728-SACT  
 Date: 9 March 2017 Final Version 1.0

<b>INVESTIGATIONAL STUDY MATERIALS</b>	Regimen: Cleanser [REDACTED] [REDACTED] [REDACTED] Acne Mask, [REDACTED] [REDACTED]
<b>DOSE AND MODE OF APPLICATION</b>	ALL: Cleanser: Subjects will use twice a day to wash face, once in the morning and once at evening. Treatment (Acne Mask): Subjects will use the mask once per day, in the evening after washing/drying their face.
<b>STUDY DURATION</b>	This is a 28-day study comprised of 3 visits. Subjects will be assessed at Day 0 Screening/Baseline (Visit 1), Day 14 (Visit 2) and Day 28 (Visit 3).
<b>METHODOLOGY</b>	Evaluation of tolerance: Tolerance will be measured by signs and symptoms of irritation, [REDACTED] and adverse events. [REDACTED]
<b>SUCCESS CRITERIA</b>	[REDACTED]
<b>TOLERANCE MEASURES</b>	Signs and symptoms of irritation as evaluated by the PI based on a four-point scale, 0-3: - Erythema - Dryness/Scaling - Edema

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
 Protocol identification: CO-1701-2511-3728-SACT  
 Date: 9 March 2017 Final Version 1.0

	<p>Signs and symptoms of irritation as self-evaluated by the subject based on a four-point scale, 0-3:</p> <ul style="list-style-type: none"> <li>- Burning/Stinging</li> <li>- Itching</li> <li>- Tightness/Dry Feeling</li> </ul>
<b>SAFETY AND ADVERSE EVENTS</b>	<p>Any Adverse Event (AE), Serious Adverse Event (SAE), or Unanticipated Adverse Device Effect (UADE) related or unrelated to the investigational products must be documented as required (occurrence date, site, outcome, and assessment of causality, severity, and relatedness).</p> <p>SAEs must be reported and relevant supportive documentation must be sent within 24h of learning of the event to the Study Manager or designee.</p>



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

## LIST OF ABBREVIATIONS

Abbreviation	Definition
ADE	Adverse Device Event
AE	Adverse Event
BPO	Benzoyl Peroxide
CRF	Case Report Form
DPR	Designated Physician Representative
EDC	Electronic Data Capture
FDA	US Food and Drug Administration
ICH GCP	International Conference on Harmonization Good Clinical Practice
ICD	Informed Consent Document
IEC	Independent Ethics Committee
IRB	Institutional Review Board
OCMS	Office of Consumer Medical Safety
OTC	Over-the-Counter
PI	Principal Investigator
PIE	Post-Inflammatory Erythema
PIH	Post-Inflammatory Hyperpigmentation
PQC	Product Quality Complaint
Rx	Prescription Medication
SAE	Serious Adverse Event
TEAE	Treatment Emergent Adverse Event
UADE	Unanticipated Adverse Device Effect

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

## TABLE OF CONTENTS

1	BACKGROUND .....	8
2	OBJECTIVE(S).....	8
3	OVERALL STUDY DESIGN AND PLAN DESCRIPTION.....	8
4	STUDY DURATION .....	9
5	SUBJECT SELECTION AND ENROLLMENT .....	9
5.1	INFORMED CONSENT AND ASSENT .....	10
5.2	STUDY POPULATION .....	10
5.2.1	Inclusion Criteria .....	11
5.2.2	Exclusion Criteria.....	12
5.3	Concomitant and Excluded Medications .....	14
5.4	SUBJECT RESPONSIBILITIES .....	14
5.5	CONCURRENT PRODUCTS .....	14
5.6	SCREENING FAILURE .....	15
6	SAMPLE SIZE DETERMINATION .....	15
7	INVESTIGATIONAL STUDY MATERIALS.....	15
7.1	IDENTITY OF INVESTIGATIONAL STUDY MATERIALS.....	15
7.2	RANDOMIZATION.....	17
7.2.1	Blinding .....	17
7.3	STUDY MATERIAL STORAGE AND ACCOUNTABILITY .....	17
7.4	PRODUCT QUALITY COMPLAINTS .....	17
7.5	USE OF THE INVESTIGATIONAL PRODUCTS AND DEVICE.....	18
8	INVESTIGATIONAL PLAN .....	18
8.1	STUDY PROCEDURES BY VISIT .....	19
8.3	SUBJECT COMPLETION/WITHDRAWAL.....	25
8.3.1	Subject Completion.....	25
8.3.2	Subject Withdrawal.....	25
9	STATISTICAL METHODS.....	26
10	SUCCESS CRITERIA.....	28
11	MANAGEMENT OF INTERCURRENT EVENTS.....	28
11.1	AMENDMENTS TO THE PROTOCOL.....	28
11.2	PROTOCOL DEVIATIONS.....	29
11.3	ADVERSE EVENT REPORTING .....	29

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

11.3.1	Introduction .....	29
11.3.2	Definitions .....	29
11.3.3	Unanticipated Adverse Device Effect (UADE) .....	32
11.3.5	Procedures for Reporting Adverse Events .....	33
11.3.6	Monitoring and Resolution of Adverse Events/Adverse Device Events .....	34
11.4	EXPOSURE IN UTERO .....	35
12	ETHICAL CONSIDERATIONS .....	36
12.1	STUDY SUBMISSION TO INSTITUTIONAL REVIEW BOARD/ INDEPENDENT ETHICS COMMITTEE OR HEALTH AUTHORITIES .....	36
13	DATA HANDLING AND RECORD KEEPING .....	37
14	STUDY MONITORING, QUALITY CONTROL AND QUALITY ASSURANCE .....	38
15	SPONSOR DISCONTINUATION CRITERIA .....	38
16	FINAL REPORT .....	38
17	CONFIDENTIALITY .....	38
18	PUBLICATION .....	39
19	BIBLIOGRAPHIC REFERENCES .....	39
20	PROTOCOL SIGNATURES PAGE .....	40
21	PRINCIPAL INVESTIGATOR RESPONSIBILITY STATEMENT .....	41
22.	APPENDICES .....	42
	Appendix I. Subject Instructions .....	43
	<b>Appendix III. Contact Information .....</b>	<b>47</b>



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

## **1 BACKGROUND**



## **2 OBJECTIVE(S)**

The objective of this study is to evaluate the tolerance of a light therapy-based acne treatment in subjects with mild to moderate acne and self-reported sensitive skin over a 28-day period.

## **3 OVERALL STUDY DESIGN AND PLAN DESCRIPTION**

This is a single-center clinical study to evaluate the tolerance of an acne treatment in sensitive skin subjects with mild to moderate acne. Female and male subjects 12-40 years of age with mild to moderate inflammatory acne vulgaris and self-identified as having sensitive skin will be enrolled. The principal investigator and evaluator may be the same person. The Sponsor will provide the test products.





Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0



#### **4 STUDY DURATION**

This study will take place over a 28-day period, with the subjects presenting to the test center for 3 visits. Visits will be at Screening/Baseline (Day 0/Visit 1), Day 14 (Visit 2) and Day 28 (Visit 3).

#### **5 SUBJECT SELECTION AND ENROLLMENT**

This study can fulfill its objective only if the required number of appropriate subjects is enrolled. The eligibility criteria are designed to select subjects for whom protocol procedures are

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

considered appropriate. All relevant medical and non-medical conditions should be taken into consideration, in addition to the inclusion/exclusion criteria, when deciding if a particular individual is suitable for this protocol. The inclusion and exclusion criteria will be reviewed by the Principal Investigator (PI) or a medically qualified designee (i.e. physician's assistant) in order to determine subject eligibility.

Prior to any review of personal data, Informed Consent and/or Assent documents should be signed.

## **5.1 INFORMED CONSENT AND ASSENT**

The Informed Consent Document (ICD) will be read by the subject (or for a minor, his/her parent or guardian). The PI and/or his qualified 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 (or his/her legally acceptable representative) will express his/her consent to the subject's participation in the study by signing the ICD.

For studies involving children **below the age of consent**, an assent document will be prepared and presented to the subject.

The assent is a document written at an age appropriate level to inform minor subjects (i.e., under the age of consent) about the nature of the research to the extent compatible with their understanding.

Where required by national, regional, or local law, the parent or legal guardian/legally authorized representative may be required to sign an informed consent document.

If the subject qualifies for enrollment in this study they are responsible for the return of the device in the original condition in which it was provided. Failure to comply could result in forfeiture of any compensation due.

No subject will be evaluated without a signed ICD (and/or Assent Document, as applicable), which should be kept by the PI. The ICDs (and/or Assent Documents, as applicable) of subjects who are not enrolled in the study will also be kept.

One copy of the signed ICD or Assent Document must be given to the subject (or the legally acceptable representative); the subject (and/or legally acceptable representative) will remain free to withdraw this consent/assent at any moment without any negative consequence to the subject.

The ICD and Assent Document must be approved by the Sponsor and the IRB/IEC and must be in compliance with ICH GCP, local regulatory requirements, and legal requirements.

## **5.2 STUDY POPULATION**

Individuals must meet all of the following eligibility criteria, and none of the exclusion criteria, in order to qualify and be enrolled in the study.

### **5.2.1 Inclusion Criteria**

1. Subjects must read, sign, and receive a copy of the IRB-approved informed consent /assent as applicable.
2. Females and males.
3. Age: 12 to 40 years old.
4. Subjects with Fitzpatrick Skin Types of I – VI
5. Individuals who are generally in good health as determined by the investigator and study physician, based on medical history reported by the subject.
6. Acne criteria - Subjects must have a mild to moderate acne vulgaris on the face, as defined by an Investigator's Global Assessment Score of 2 or 3 using the Modified Cook's Scale as defined in section 8.2.
7. Sensitive Skin Criteria - Subjects must successfully meet the Sensitive Skin Criteria according to Sensitive Skin Inclusion Criteria questionnaire as defined in section 8.2.
8. Cutaneous Tolerance scores of 0 or 1 (no greater) in all tolerance parameters
9. Subjects must have used current consistent facial products for at least 1 month prior to study start.
10. Individuals who are able to read, speak, write, and understand English.
11. Females determined to be of child-bearing potential must agree to take a pregnancy test to confirm that they are not pregnant, and females must indicate they are not lactating nor do they intend to become pregnant during their participation in the study (subject must document their response in either the source documentation or informed consent form).

Male and Female subjects with reproductive potential must agree to practice a medically acceptable form of birth control during the study (through Week 4) or for 30 days following the last dose of investigational product whichever is later. Females must have used such birth control for at least 3 months prior to the Baseline visit.

Medically acceptable forms of birth control that may be used by the subject and/or his/her partner include:

- Established use of hormonal methods of contraception (oral, injected, implanted, patch or vaginal ring) for a minimum of 90 days prior to baseline



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

- Barrier methods of contraception with spermicide: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository.
- Intrauterine device (IUD) or intrauterine system (IUS)
- Surgical sterilization (e.g., vasectomy that has been confirmed effective by sperm count check, tubal occlusion, hysterectomy, bilateral salpingectomy)
- Abstinence from heterosexual intercourse: When this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.

A female subject who is postmenopausal (i.e., amenorrheic for at least 12 months prior to the Baseline visit) is not considered of reproductive potential.

#### 5.2.2 Exclusion Criteria

Subjects with any of the hereafter criteria must be excluded from the study:

1. Has a known light or photo-sensitivity disorder.
2. Subjects with very sensitive skin, atopic dermatitis, and/or known allergies or sensitivities to ingredients contained in the cleanser (i.e. fragrance, preservatives, etc.), and/or other known medical conditions that in the opinion of the Investigator would cause them to be excluded.
3. Subjects with severe acne or acne conglobata.
4. Subjects who have pre-existing, dormant or active facial dermatologic conditions (e.g., psoriasis, rosacea, atopic dermatitis, rashes, many and/or severe excoriations, etc.) that could interfere with the outcome of the study as determined by the Investigator.
5. 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
6. Male whose female partner is (to the best of his/her knowledge) pregnant or planning to become pregnant during the study or within 30 days of study completion.
7. Subjects who report that they have used topical tretinoin (Retin-A®, Retin-A Micro®, Renova®, Adapalene, Tazarotene), Avita®, Tazorac®, Avage®, Differin®, Azelaic acid, benzoyl peroxide, Dapsone, Sodium sulfacetamide, or Epiduo or other similar prescription drug, and/or other prescription medications for acne such as Doxycycline, Minocycline, Clindamycin, Bactrim, Tetracycline, Erythromycin, and Vibramycin within 2-weeks of the study start,



8. Subjects who have taken Accutane or other oral retinoid within the past 6 months.
9. Subjects who report starting a new prescription medication (oral or topical) that can make skin more sensitive, cause photosensitivity, or have an effect on the skin (i.e. antibiotics, hormones (not including those used for contraception), insulin, inhaled steroids (with the exception of inhaled steroids prescribed for allergies) etc.) within 1 month prior to entry. Subjects may continue on a regular course of medication that they have been using for more than 1 month, and for which they will continue using routinely for the full course of the study, if they are stable in the opinion of the Investigator or designee.
10. Subjects using OTC topical medications on the face (excluding sunscreens, which are allowed) and/or soaps/makeups that contain topical medications (including anti-acne or antibacterial agents, topical anti-inflammatories, topical retinoids, salicylic acid etc.) within a 2-week period before the start of the study.
11. Individuals who have observable suntan, scars, nevi, tattoo, excessive hair, etc. or other dermal conditions on the face that might influence the test results in the opinion of the Investigator or designee
12. Subjects concurrently participating in any other clinical study (i.e., dermal patch, use tests, investigational drug or devices, etc.), or having participated in another facial clinical study within 30 days from the start of the study.
13. Subjects viewed by the Investigator as not being able to complete the study.
14. An individual who has any condition which in the PI's judgment makes the candidate inappropriate for study participation.
15. Individuals with a history of immunosuppression/immune deficiency disorders (including HIV infection or AIDS) or currently using immunosuppressive medications (e.g., azathioprine, belimumab, cyclophosphamide, Enbrel, Imuran, Humira, mycophenolate mofetil, methotrexate, prednisone, Remicade, Stelara.), and/or radiation as determined by study documentation.
16. Individuals with an uncontrolled disease such as asthma, diabetes, hypertension, hyperthyroidism, or hypothyroidism. Individuals having multiple health conditions may be excluded from participation even if the conditions are controlled by diet, medication, etc.
17. Individuals with any planned surgeries and/or invasive medical procedures during the course of the study.

18. Subjects who are related to those persons involved directly or indirectly with the conduct of this study (i.e., PI, sub-investigators, study coordinators, other site personnel, employees of Johnson & Johnson subsidiaries, contractors of Johnson & Johnson, and the families of each

### **5.3 Concomitant and Excluded Medications**

- If a subject is taking any medication, the medicine, dose and duration must be recorded on the Concomitant Medication Form.
- Excluded medications are indicated in the Subject Exclusion criteria; the use of any excluded medications during the study may result in discontinuation of the subject, pending review with the study physician, investigator and sponsor to determine the impact of the medicine and duration of use on acne.

### **5.4 SUBJECT RESPONSIBILITIES**

The subject responsibilities are as follows:

- Subjects must not use any other light based devices
- Subjects may not receive professional or aesthetic facial spa procedures during the course of the study.
- Subjects may follow their normal bathing routine
- Subjects must not shave or use other hair removal methods on their faces within 24 hours of visits
- Subjects must be willing and able to follow all study directions, including avoiding excessive sun exposure (including tanning beds), which could lead to a change in the visible appearance of skin such as sunburn or tanning effect, and to commit to all follow up visits for the duration of the study.
- Subjects must be willing to cleanse their face and remove ALL facial and ALL eye makeup at least 30 minutes (and maximum of 2 hours) prior to every study visit. If an individual wears makeup to their visit, they will remove it in the clinic with a Sponsor-provided non-medicated cleanser and undergo a waiting period of at least 15 minutes prior to having grading performed.

### **5.5 CONCURRENT PRODUCTS**

- Subjects may continue using their regular brand(s) of non-medicated facial products such as moisturizers, eye makeup removers, color cosmetics, and sunscreens within the following specifications:
  - must have been used for at least one month prior to study start
  - must be non-medicated and do not contain benzoyl peroxide, salicylic acid, alpha hydroxy acids (AHAs), vitamins A (retinol) or C (ascorbic acid) or their analogs or derivatives.



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

- must not have exfoliating properties (cleansers with exfoliating beads, scrubs, masks)
- Subjects must not introduce new product or change products during the course of the study
- **Site staff will record the products that the subject is currently using at baseline [paper capture only].**

## 5.6 SCREENING FAILURE

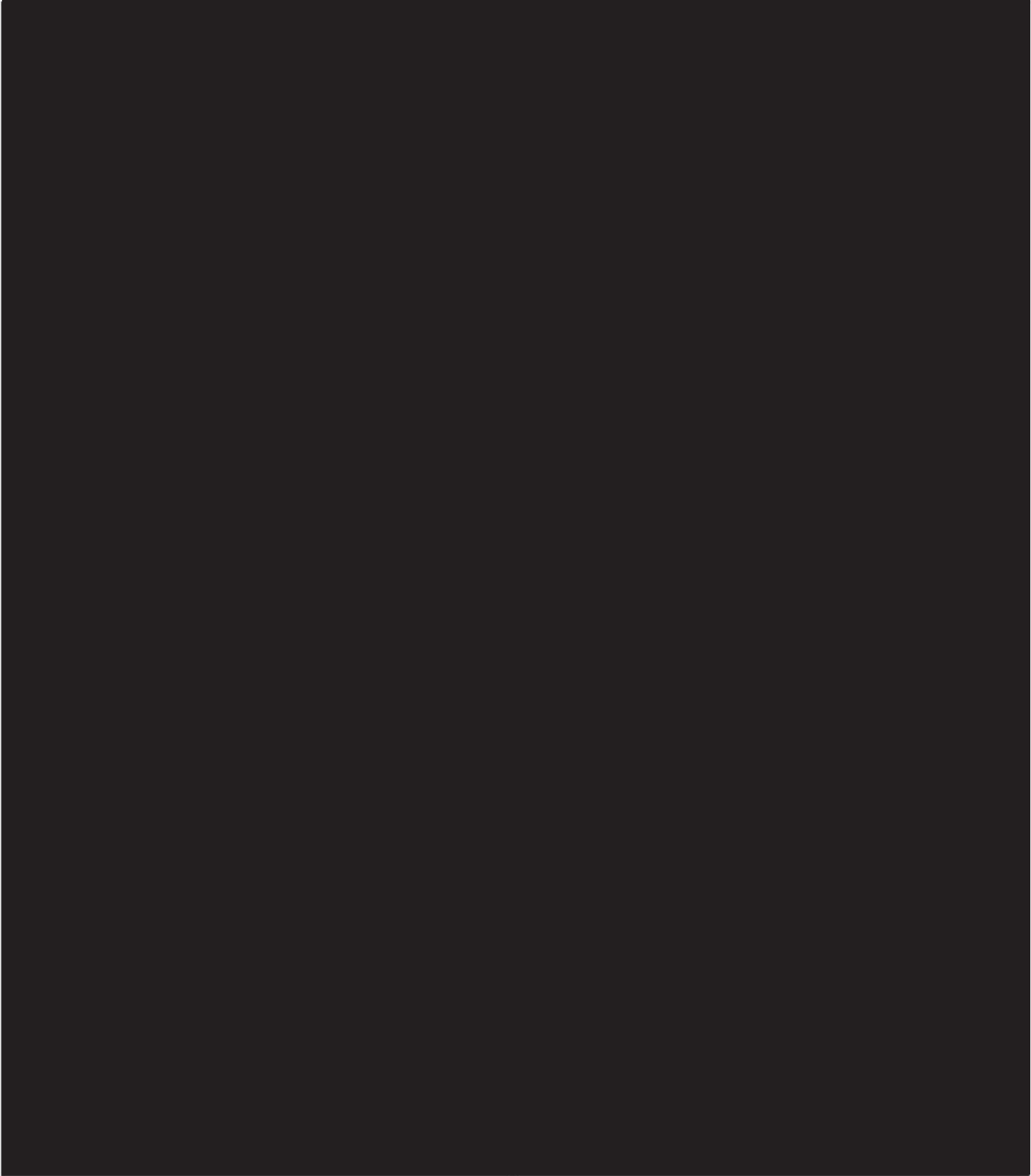
All individuals who sign the ICD/Assent Document and withdraw their participation or fail to meet all of the eligibility/screening criteria during the initial evaluation will be considered a "screening failure."

Data from screen failure subjects will not be considered in the final report.

## 6 SAMPLE SIZE DETERMINATION

A sufficient number of subjects will be screened to enroll up to 45 subjects to complete with 40 total subjects.

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0





## **7.2 RANDOMIZATION**

There will be no randomization.

### **7.2.1 Blinding**

This is an open label, single-arm study. There is no blinding.

## **7.3 STUDY MATERIAL STORAGE AND ACCOUNTABILITY**


The PI must ensure that deliveries of investigational study materials from the Sponsor are correctly received by a responsible person and that the investigational study materials are stored in a secure area under recommended storage conditions: all test products and devices at room temperature (59° - 77°F) in a secured and locked room that is only accessible by authorized site personnel.

The PI must maintain adequate records documenting the receipt, use, loss, damage or other disposition of the investigational products and devices on the Investigational Product Accountability Log or equivalent.

The log must identify the investigational products and devices and account for their disposition on a subject by subject basis, including specific dates and quantities dispensed and returned.

The log must be signed by the individual who dispensed/retrieved the investigational products and devices and a copy must be provided to the Sponsor for the Trial Master File at end of study.

At the end of the study, after final reconciliation of all investigational products and devices is complete, the investigational products and devices must be packaged and returned to the Sponsor at the following address:



## **7.4 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. This does not include effectiveness, preference, or performance measures. Any PQC discovered during the initial inventory should follow the instructions provided on the receipt letter; no PQC form should

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

be filed for issues identified when opening or unpacking a shipment. Subsequently, any observation of a PQC requires immediate notification to the Study Manager via a completed PQC form and telephone call. The PI or designee should complete, sign, and forward a copy of the PQC form to the Study Manager

In addition, PQC information must be included on the Investigational Product accountability and reconciliation Form or equivalent in the comments field. The Study Manager listed can assist you or 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 it to the Study Manager.

When enrolling subjects into this study, it is the site's responsibility to instruct subjects not to use the investigational product if they have a concern related to the labeling, investigational product) or package integrity and to immediately report it using the instruction on the ICD or investigational product label.

## **7.5 USE OF THE INVESTIGATIONAL PRODUCTS AND DEVICE**

Prior to use, the subject will receive education and documentation on proper use of the product and device. Subjects will acknowledge understanding of the instructions and a copy of signed acknowledgement will be sent home with them for reference. The first use of the investigational products or device will be under clinic supervision on Visit 1/Day 0.

When the products are distributed, the subjects will be given detailed instructions for use as directed in Appendix I, as well as in the inserts provided with the test products.

Subjects will also receive an IRB approved diary to track compliance.

### **7.5.1 INSTRUCTIONS:**

Detailed subject instructions are in Appendix I.

## **8 INVESTIGATIONAL PLAN**

Subjects will report to the test site on Visit 1/Day 0 and go through the informed consent process. Eligibility criteria, medical history, concomitant medications, and concurrent products will be reviewed and recorded. Subject will complete the Sensitive Skin Inclusion Questionnaire parts A and B as part of the inclusion/exclusion eligibility criteria. Should they qualify, the subjects will acclimate to ambient room temperature conditions for at least 15 minutes. After acclimation, the PI will perform Investigator Global Acne assessment, and Cutaneous Tolerance scores. Females of child-bearing potential will have a urine pregnancy test to prove that they are currently not pregnant. If the subject qualifies, he/she will be entered into the study.

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS


Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

The subjects will receive written and verbal instructions on how to use the device and products as per section 7.5.1 and Appendices I. The subjects will use the products and the device for the first time, on site, under the supervision of a site staff member.

Subsequent visits will be carried out according to section 8.1.

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0





Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

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

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

## 2. Investigator Global Acne Assessment – Modified Cook's Scale (Visit 1)

The following scale will be used for the global acne assessment (no half-points may be used):

0	Clear
1	Almost Clear
2	Mild
3	Moderate
4	Severe



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
 Protocol identification: CO-1701-2511-3728-SACT  
 Date: 9 March 2017 Final Version 1.0

5	Very Severe	
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### 3. Cutaneous Tolerance Scores (Visit 1, Visit 2 and Visit 3)

**Note: For enrollment (see Inclusion Criterion #8), an individual must have a score of 0 or 1.0, not higher, for all tolerance parameters at baseline.**

To be evaluated by the Investigator

<b>Erythema</b>	
0 = None	
1 = Mild	
2 = Moderate	
3 = Severe	
<b>Dryness/Scaling</b>	
0 = None	
1 = Mild	
2 = Moderate	
3 = Severe	
<b>Edema</b>	
0 = None	
1 = Mild	
2 = Moderate	
3 = Severe	

**To be evaluated by the subject:** (No half points to be used)

<b>Burning/Stinging</b>	
0 = None	
1 = Mild	
2 = Moderate	
3 = Severe	
<b>Itching</b>	
0 = None	

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

1 = Mild	
2 = Moderate	
3 = Severe	

Tightness/Dry Feeling	
0 = None	
1 = Mild	
2 = Moderate	
3 = Severe	



5.1) Sensitive Skin Inclusion Criteria Questionnaire Parts A and B (Visit 1 only)  
(see separate document)

PART A: Sensitive Skin Inclusion Criteria Questionnaire

Subjects must answer either "All of the time" or "Most of the time" to the following question:

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

Do you consider your facial skin to be sensitive?

- ☐ None of the time
- ☐ Some of the time
- ☐ Most of the time
- ☐ All of the time

PART B: Sensitive Skin Inclusion Criteria Questionnaire

Subjects must answer "yes" to at least 1 of the following 4 questions.

<u>Question #</u>	<u>Question</u>	<u>Response</u>
1	In the past, have you ever experienced skin irritation (itching, burning, redness, dryness, stinging) when using topical acne treatments?	Yes or No
2	In the past, have you ever stopped using a topical acne treatment due to skin irritation (itching, burning, redness, dryness, stinging)?	Yes or No
3	Have you ever been told by a dermatologist, physician, esthetician or other professional that you have sensitive skin on your face?	Yes or No
4	When purchasing skincare products (facial cleansers, facial moisturizers, makeup, etc.), do you look for products labelled "for sensitive skin" or similar?	Yes or No



#### 6) Subject Diaries (Visit 1 through Visit 3)

Subject diaries will be completed at home morning and night to record their product use every day.

### **8.3 SUBJECT COMPLETION/WITHDRAWAL**

#### **8.3.1 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.

#### **8.3.2 Subject Withdrawal**

When an individual who has signed the ICD is not enrolled in the study or withdraws/is withdrawn prior to completing the study, the reason is to be documented on the Screening and Enrollment log and will be noted in the final study report.

Reasons for subject withdrawal may include:

- Adverse Event / SAE (must be reported in accordance with the reporting requirements defined in the AE/SAE section).
- Not enrolled (e.g. fails to meet inclusion/exclusion criteria, chooses not to enroll, etc)
- Participant is determined to be ineligible after enrollment
- Subject's choice to withdraw
- Investigator terminated (e.g. noncompliance, etc.)
- Study terminated by sponsor
- Lost to follow-up
- Screen Failure

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

- Death
- Pregnancy
- 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, three (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 adverse events.

Should a subject withdraw from the trial and also withdraw 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 withdrawal or dropouts, subjects may be replaced based on overall enrollment numbers and with the approval of the sponsor.

If a subject misses a scheduled visit, but notifies the study site, they will be allowed to re-schedule their missed visit if it is within the (visit window) as specified in Table 1: Schedule of Events. If, it is outside the visit window, they should return for the next study visit. Study staff will need to assess compliance to test product and/or device to ensure missed visit did not result in lack of compliance. This will be documented as a deviation and the sponsor should be notified.

## **9 STATISTICAL METHODS**

### **Statistical Analysis Population**

The cutaneous tolerability evaluations and self-assessment questionnaire data analysis will be performed for subjects in full analysis set (FAS) which is defined as all subjects who use study products and have baseline and at least one post-baseline assessment.

The safety analysis will be based on all subjects who use study products. AE will be listed for safety analysis population.

### **Demographic Data**

Demographic and baseline characteristics [including data from the investigator global acne assessment and the sensitive skin questionnaire at baseline (part A & B)] will be summarized for all subjects who are enrolled in the study. For continuous variables, descriptive summary will include number of subjects, mean, standard deviation, median, minimum and maximum values. For Categorical variables, descript summary will include number and percentage of subjects in each response category.

### **Cutaneous Tolerance Scores**

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

A descriptive statistical summary will be provided for cutaneous tolerance evaluation scores by the investigator and by the subject. The descriptive statistical summary will include the number of observations (N), mean, median, standard deviation (SD), minimum (MIN) and maximum (MAX) at all available visits.

Mean of the change from baseline (defined as post-baseline value minus baseline value) will be estimated at post-baseline time points for applicable parameters. The null hypothesis, that the mean change from baseline is zero, will be tested for applicable parameters using methods described in the Statistical Analysis Plan table.

The following will also be calculated and reported at the applicable post-baseline time point(s):

$$\text{Percent mean change from baseline} = \frac{(\text{visit mean score} - \text{baseline mean score}) \times 100}{\text{baseline mean score}}$$

$$\text{Percent of subjects whose score improved/worsened} = \frac{(\text{number of subjects whose score improved/worsened from baseline}) \times 100}{\text{total number of subjects}}$$


Cutaneous tolerance scores will also be tabulated with count and percent.

#### Adverse Events


A listing of AEs will be provided, differentiating treatment-emergent AEs.

#### Statistical Analysis Plan Table





All statistical tests will be 2-sided at significance level  $\alpha=0.05$ . P-values will be reported to 3 decimal places (0.000). No multiple testing corrections will be considered in the study. Statistical analyses are performed using SAS software version 9.4 or later series (SAS Statistical Institute). The statistical results will be sent to the Sponsor along with the raw data in a Microsoft Excel document at the completion of the study.



## **11 MANAGEMENT OF INTERCURRENT EVENTS**

### **11.1 AMENDMENTS TO THE PROTOCOL**

Neither the PI nor Sponsor will modify this protocol without obtaining the concurrence of the other. The party initiating a modification will confirm it in writing.

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

## **11.2 PROTOCOL DEVIATIONS**

Protocol deviations should be avoided whenever possible. When a protocol deviation occurs, it must be captured in the source documents.

The PI or designee will also contact the Study Manager (see Appendix III) should a Protocol Deviation occur. Contact with the Study Manager 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, if any, will also be notified. The final report will describe the deviation from the protocol and the circumstances requiring it.

## **11.3 ADVERSE EVENT REPORTING**

### **11.3.1 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.

### **11.3.2 Definitions**

#### **11.3.2.1 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) would be considered an AE and recorded appropriately.

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

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

- Investigational product overdose,
- Investigational product withdrawal,
- Investigational product abuse,
- Investigational product misuse,
- Investigational product interactions,
- Medication errors,
- Investigational product dependency,
- Exposure *in utero*, and
- Study related procedure.

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 adverse event 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.

#### **11.3.2.2 Treatment Emergent AE (TEAE)**

TEAE is defined as any event not present prior to the initiation of the treatment/Investigational device.

Note that AEs will be summarized for all subjects who signed the ICD, differentiating TEAEs.

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

#### **11.3.2.3 Serious Adverse Event (SAE)**

An SAE is an AE (untoward medical occurrence) that fulfills at least one of the following criteria:

For Products:

- 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 suspected transmission of any infectious agent via a medicinal product (medically significant) and should be reported as an SAE in the category "*Other medically important conditions*";
- results in a congenital anomaly/birth defect;
- is another medically significant event (i.e. a medically significant condition that may jeopardize the subject or require medical or surgical intervention to prevent any of the previously listed outcomes). Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in situations other than those 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).

#### 11.3.2.4 Severity

The severity of all AEs must be evaluated by the PI or, if the PI does not have a medical background, by a medically qualified individual (MD/DO). 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.

#### 11.3.2.5 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, if the PI does not have a medical background, a medically qualified individual (MD/DO) 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).

### 11.3.3 Unanticipated Adverse Device Effect (UADE)

An unanticipated adverse device effect (UADE) is any serious adverse effect on health or safety, or any life-threatening problem or death caused by, or associated with, a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of the subject.

If an unanticipated adverse device effect occurs, the Investigator must promptly notify the Sponsor of such an event within 24 hours of first learning of the event.

A medical device adverse event is **serious** when both the following criteria are fulfilled:

- The event involves patient/subject/consumer contact
- The event results in:
  - Death
  - Serious deterioration in state of health. This includes:
    - Life-threatening illness or injury
    - Permanent impairment of a body function
    - Permanent damage to a body structure
  - A condition that requires medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

### 11.3.4 Anticipated Adverse Device Effects

The anticipated reactions may be found in the product inserts located in Appendices IV and V.



### 11.3.5 Procedures for Reporting Adverse Events

All AEs/ADEs 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).

Self-reported AEs/ADEs that occur between the end of study and 30 calendar days after completion of the study will only be reported to the Sponsor if they are serious using paper source documents. SAE/UADEs 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 beyond the time frame specified in the protocol.

Subjects are encouraged to report AEs/ADEs 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/ADE reported by the subject or observed by the study team, the study team member should notify the PI, Study Physician, or designee, who will review collected information about the event.

All AEs and ADEs, regardless of seriousness, severity, or presumed relationship to study procedures, must be recorded using medical terminology on the source document and then entered into the electronic data capture system (EDC). AE/ADEs must be entered into this electronic database within 5 business days of the subject's visit.

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, if the PI does not have a medical background, a medically qualified individual (MD/DO) designee, must record or confirm on the source and in the EDC system, their opinion concerning the seriousness, severity, and relationship of the AE to the study. All measures required for AE management must be recorded in the source document and reported according to Sponsor instructions.

The PI or designee must also report AEs to the appropriate IRB unless otherwise required and documented by the IRB. *Check with the IRB for reporting requirements.*

If an **SAE/UADE** occurs, in addition to the above reporting procedures, the Site will **immediately** notify the Study Manager by telephone or encrypted e-mail to:





Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

Subsequent to a telephone or encrypted e-mail report of an SAE/UADE, a Clinical Trial SAE/UADE Report Form (provided to the study site at the initiation of the study) must be completed by the investigational staff with as much information as possible (however at a minimum, the subject identification number, name of investigational product [if applicable], SAE/UADE description, investigator's assessment of causality, and name of site personnel reporting event are required), signed by the PI (or the medically qualified designee), and securely transmitted to the Study Manager **within 24 hours** of becoming aware of the event.

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

In the rare event that the Investigator's site does not become aware of the occurrence of a SAE/UADE immediately (e.g., if an outpatient study subject initially seeks treatment elsewhere), the Investigator's site is to report the event immediately after learning of it as described and document the time of the study site's first awareness of the SAE/UADE.

The Study Manager or designee will notify the Study Director and the DPR or designee within 1 calendar day of SAE/UADE information receipt. The DPR will request more information as necessary. The Study Manager or designee will send appropriate documents to Sponsor's OCMS group per local procedures within the following timelines:

- fatal/life-threatening reports: within 2 calendar days from regulatory clock start date
- other SAEs and pregnancy exposure reports: within 3 calendar days from regulatory clock start date

For all SAEs/UADEs, the PI is obligated to pursue and provide information to the Sponsor in accordance with the timeframes for reporting specified above. In addition, the PI may be requested by the Sponsor to obtain specific additional follow-up information in an expedited fashion. This information may be more detailed than that captured on the source document. In general, this will include a description of the SAE/UADE 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 available 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 Sponsor or its designated representative.

### **11.3.6 Monitoring and Resolution of Adverse Events/Adverse Device Events**

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

#### **11.3.6.1 Non-Serious AEs/ADEs**

All study and treatment related AEs/ADEs 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 in the source document and entered into the EDC system.

#### **11.3.6.2 Serious AEs (SAEs)**

The PI or, if the PI does not have a medical background, the medically qualified designee (MD/DO) will monitor SAEs until resolution or until one of the conditions in 11.3.6.3 is met. The information will be captured in the source document and entered into EDC system. The PI/designee will also document follow-up information on an updated Clinical Trial SAE form, which will be reviewed by the PI or medically qualified individual designee and sent securely to the Study Manager or designee. The Study Manager or designee will forward the document(s) to the DPR, the Study Director or designee, and to OCMS per local procedures.

#### **11.3.6.3 Resolution**

The PI will be required to assess the outcome of each AE as one of the following:

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

Serious AEs 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).

### **11.4 EXPOSURE IN UTERO**

For IPs within clinical studies, an exposure *in utero* (EIU) occurs if:

1. A woman is exposed to the IP at any time between her last menses prior to conception through the delivery of the baby.



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

2. There is a possibility of intrauterine exposure to investigational study material via semen from the male partner who is taking the investigational product from time of conception throughout pregnancy thereby possibly exposing the fetus to the investigational product.

If any study subject or study subject's partner becomes or is found to be pregnant during the study subject's participation, the PI must report the pregnancy to the Sponsor on a Pregnancy Notification Form (to be provided by the Sponsor when applicable). Initial notification via telephone to the Sponsor's study team contact must occur immediately upon the Investigator site's awareness of the pregnancy. The Pregnancy Notification Form must then be sent to the Sponsor within 24 hours of the site's awareness. The information submitted should include the anticipated date of delivery (see below for information to document termination of pregnancy).

Follow-up is conducted to obtain pregnancy outcome information on all EIU reports. The PI will follow the pregnancy until completion or until pregnancy termination (i.e., induced abortion) and then notify the Sponsor of the outcome. The PI will provide this information as a follow-up to the initial Drug Exposure During Pregnancy Collection Form A and/or End of Pregnancy Collection Form B (provided by the Sponsor when applicable). The reason(s) for an induced abortion should be specified. An EIU report is not created when an ectopic pregnancy report is received since this pregnancy is not usually viable. Rather, a SAE case is created with the event of ectopic pregnancy.

The PI should follow the procedures for reporting SAEs if the outcome of the pregnancy meets the criteria for immediate classification as a SAE (i.e., spontaneous abortion, stillbirth, neonatal death, or congenital anomaly [including that in an aborted fetus, stillbirth, or neonatal death]). In the case of a live birth, the "normality" of the newborn can be assessed at the time of birth (i.e., no minimum follow-up period of a presumably normal infant is required before an End of Pregnancy Collection Form B can be completed). The "normality" of an aborted fetus can be assessed by gross visual inspection, unless pre-abortion test findings are suggestive of a congenital anomaly.

Additional pregnancy outcomes that are classified as SAEs and should be reported as such include:

- "Spontaneous abortion" includes miscarriage and missed abortion;
- All neonatal deaths that occur within 1 month of birth, without regard to causality;
- Any infant death after 1 month that the PI assesses as possibly related to in utero exposure to the investigational product.

## **12 ETHICAL CONSIDERATIONS**

Privacy information, such as the ICD of the subjects, will be kept confidential during the study.

### **12.1 STUDY SUBMISSION TO INSTITUTIONAL REVIEW BOARD/ INDEPENDENT ETHICS COMMITTEE OR HEALTH AUTHORITIES**

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:

IntegReview



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

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Email: [integreview@integreview.com](mailto:integreview@integreview.com) / Web: <http://www.integreview.com>

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

The study will not be activated, subjects will not be recruited, consented, or receive test 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 IRB/IEC should be retained in the SMF. Copies of IRB/IEC approvals should be forwarded by the monitor or via the IRB portal to the Sponsor and will be filed in the Sponsor TMF.

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.

#### **14 STUDY MONITORING, QUALITY CONTROL AND QUALITY ASSURANCE**

The study will be monitored (in accordance with a study specific Monitoring Plan) by the Sponsor, or its designee. In addition to on-site monitoring, 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 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 ICH GCP is/was being followed. The monitors may review source documents to confirm that the data recorded is complete and accurate. The PI and institution will allow the Sponsor's monitors or its designee and appropriate regulatory authorities direct access to study documentation. If there are any issues noted, the PI will be notified.

Any contact concerning this study should be made with the Study Manager or the Study Director, see Appendix III.

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

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

#### **15 SPONSOR DISCONTINUATION CRITERIA**

Premature termination of this clinical trial may occur because of a change in opinion of the IRB/IEC, investigational device 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. 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 Sponsor, all trial materials must be collected, all CRFs completed to the greatest extent possible, and termination reported to the IRB/IEC.

#### **17 CONFIDENTIALITY**

All the information, data and results of the study will be confidential. Every person having access to these data will be informed of this confidentiality.

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

Medical information concerning the subjects obtained by the investigator during the recruitment and admission will be handled confidentially

## **18 PUBLICATION**

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

## **19 BIBLIOGRAPHIC REFERENCES**

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2. Willis, C. M., et al. "Sensitive skin: an epidemiological study." *British Journal of Dermatology* 145.2 (2001): 258-263.
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Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS

Protocol identification: CO-1701-2511-3728-SACT

Date: 9 March 2017 Final Version 1.0

**20 PROTOCOL SIGNATURES PAGE**



Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

## 21 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 the protocol agreed to by the Sponsor and in accordance with U.S. FDA regulations, applicable local regulations, and International Conference on Harmonisation Guidelines for Good Clinical Practice (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.*

[REDACTED]

[REDACTED]

[REDACTED]

Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

## 22. APPENDICES

Appendix I. Subject Instructions .....	43
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Appendix III. Contact Information .....	47
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Protocol Title: A SINGLE-CENTER CLINICAL STUDY TO EVALUATE THE TOLERANCE OF AN ACNE  
TREATMENT IN SENSITIVE SKIN SUBJECTS WITH MILD TO MODERATE ACNE VULGARIS  
Protocol identification: CO-1701-2511-3728-SACT  
Date: 9 March 2017 Final Version 1.0

#### **Appendix I. Subject Instructions**

##### **Subject Treatment Regimen Instruction Sheet – Baseline through End of Study**

**Study # is CO-1701-2511-3728-SACT**

**See separate document**

#### **Directions:**

##### **In the morning (AM):**

Step 1 – Wet face, pump cleanser into hands, and work into a lather. Massage face gently, rinse and pat dry.

Record regimen completion in dairy.

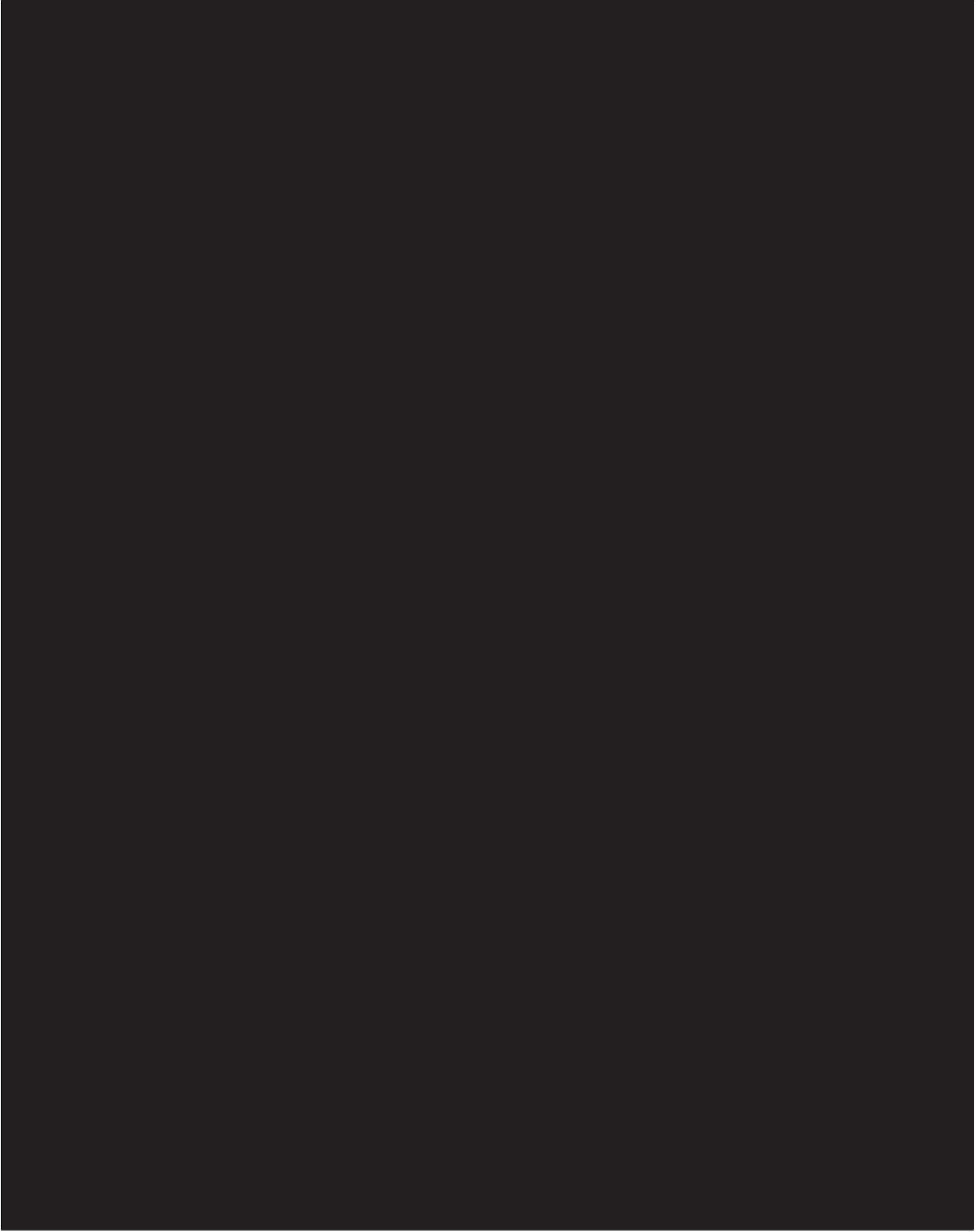
##### **In the evening (PM):**

Step 1 – Wet face, pump cleanser into hands, and work into a lather. Massage face gently, rinse and pat dry. Ensure face is dry.


Step 2 – Put on acne light mask



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Date: 9 March 2017 Final Version 1.0

**Appendix III. Contact Information**

**SPONSOR:**



**STUDY SITE:**

