STUDY PROTOCOL

ATM-2201

Intralesional Injections of Triamcinolone for Acne Vulgaris

Proof of Concept Study

Version 2.0
28-Oct-2022

Study Sponsor
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PROTOCOL APPROVAL SIGNATURE PAGE

The following individuals approve this version of Protocol ATM-2201. All changes to this version of the protocol must have a prior written approval and require an amendment or administrative letter.

Approved by Sponsor – ACOM Labs Inc.

Paul F Bente IV	CEO
Printed Name	Title
DocuSigned by: Paul F Bente IV Signer Name: Paul F Bente IV Signing Reason: I approve this document Signing Time: 05-Nov-2022 | 09:58:52 EDT 9526E06165164D16B3E30E4B1DC99F01	05-Nov-2022 | 09:59:07 EDT
Signature	Date

Approved by Clinical Research Organization - ethica CRO Inc.

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Signature	Date

INVESTIGATOR SIGNATURE PAGE

I agree to:

- Implement and conduct this study diligently and in strict compliance with the protocol, good clinical practices and all applicable laws and regulations.
- Maintain all information supplied by ACOM Labs, Inc. in confidence and, when this information is submitted to an Institutional Review Board (IRB) or another group, it will be submitted with a designation that the material is confidential.

I have read this protocol in its entirety and I agree to all aspects.

Principal Investigator *(Printed Name)*	Signature	Date

SYNOPSIS

Version	Version 2.0 (28-Oct-2022)	**Study Device**	Intradermal needle adapter
Study Number	ATM-2201		
Phase	Proof of Concept	**Control Product**	Not Applicable
Indication	Inflammatory Acne Lesions	**Study Sites**	1 site (US)
Title	Intralesional Injections of Triamcinolone for Acne Vulgaris		
Sponsor	ACOM Labs, Inc.		
Study Duration	14 days per subject	**Sample Size**	~20 subjects
Study Design	This is an open-label, prospective, single-arm study. Approximately 20 subjects will be enrolled at 1 study site. All subjects will receive standard-of-care intralesional injection with triamcinolone using an intradermal needle adapter at Visit 1 (Day 1). Subjects will then attend in-clinic visits at Visit 2 (24-hours post-injection), Visit 3 (48-hours post-injection), Visit 4 (72-hours post-injection), Visit 5 (Day 7), and Visit 6 (Day 14). Efficacy assessments (target lesion assessments, photography) and safety assessments will be conducted by the Investigator at each study visit. Subjects will conduct lesion pain assessments at each study visit as well as satisfaction assessments at each post-treatment visit.		
Study Objectives	The objective of this proof-of-concept study is to investigate the safety of using an intradermal needle adapter for performing intralesional injections.		
Inclusion Criteria	1. Outpatient, male or female of any race, 18 years of age or older. Female subjects of childbearing potential must have a negative UPT at Baseline. 2. Diagnosed with facial acne vulgaris. 3. At least one (1) identifiable inflammatory lesion that, in the opinion of the investigator, is clinically indicated for standard-of-care intralesional injection(s) of triamcinolone and for which the research participant has already agreed to have standard-of-care intralesional injection(s) of triamcinolone. 4. Able to follow study instructions and likely to complete all required visits. 5. In good general health as determined by medical history at the time of screening (Investigator discretion). 6. Sign the IRB-approved ICF (including HIPAA authorization) prior to any study-related procedures being performed.		
Exclusion Criteria	1. Female subjects who are pregnant or breast-feeding. 2. Known hypersensitivity or previous allergic reaction to any constituent of triamcinolone injection. 3. Active cutaneous viral infection in any treatment area at Baseline. 4. Have concomitant skin disease or infection (other than acne) or presence of skin comorbidities in the areas of skin where study device will be used. 5. History of poor cooperation or unreliability (Investigator discretion). 6. Planning to move out of the area prior to study completion. 7. Subjects who are investigational site staff members or family members of such employees. 8. Exposure to any other investigational /device within 30 days prior to Visit 1.		
Study Treatment	**Intradermal Needle Adapter:** The intradermal needle adapter is an accessory that slips on the end of a standard 32G 0.5" needle and reduces the effective length of the needle to 1mm. The adapter is made of biocompatible 304 Stainless Steel. It is packaged in single use bags and will		

	be autoclaved or prepared in the standard manner for typical stainless steel instruments used by the Investigator. **Triamcinolone for Injection:** A commercial supply of triamcinolone for injection will be used for injection. The site will store triamcinolone as per the conditions described in the package insert. A standard 32G 0.5" needle will be fixed to a 1.0 mL luer syringe and the syringe will be loaded with an appropriate volume and concentration of triamcinolone. A total of 0.05 mL to 0.15 mL of triamcinolone 0.5% to 2.5% will be injected into each target lesion. The choice of volume and concentration will be at the discretion of the Investigator as per his clinical judgement. An intradermal needle adapter will then be installed on the needle. At least one (1), and up to three (3) inflammatory target lesions will be selected for intralesional injections of triamcinolone using the intradermal needle adapter.
Blinding	Not applicable
Investigator Assessments	• **Global Severity Score (GSS):** A 5-point scale assessing ranging from 0 (Clear) to 4 (Severe). *Note: only Baseline assessments will be conducted.* • **Target Lesion Erythema:** A 5-point scale ranging from 0 (No Erythema) to 4 (Very Severe Erythema). • **Target Lesion Severity:** A 5-point scale ranging from 0 (None) to 4 (Very Severe). • **Target Lesion Improvement:** A 7-point scale ranging from 1 (Clear; 100%) to 7 (Worse). • **Target Lesion Videography:** A video will be taken of each injected lesion starting from just prior to needle penetration and up to 10 seconds after removed of needle from lesion. • **Target Lesion Photography:** Photographs will be taken at each study visit of each injected inflammatory lesion. At Baseline, photographs will be taken both pre- and post-injection.
Subject Assessments	• **Target Lesion Pain:** Target lesion pain will be self-assessed by the subject using a Visual Analog Scale • **Intralesional Injection Pain:** Target lesion injection pain will be self-assessed by the subject using a Visual Analog Scale. • **Subject Satisfaction:** A 5-point scale ranging from 1 (Very satisfied) to 4 (Very dissatisfied).
Safety Endpoints	Adverse Events
Sample Size	Approximately 20 subjects will be enrolled. This is a POC study and a formal sample size justification is not provided for this study. It is the opinion of the Sponsor that a total of 20 subjects will be sufficient to achieve the objective of the study.
Statistical Methods	For categorical parameters, the number and percentage of subjects/observations in each category will be presented. The denominator will be based on the number of subjects/observations appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will include n (number of subjects or observations), mean, standard deviation, median, and range. Two-sided 95% CIs will be provided for all study outcomes. The modified Intent-to-Treat (mITT) Population (defined as all subjects who were enrolled and received at least one application with the study device) will be used for analyses of safety and effectiveness endpoints. A Per-Protocol (PP) Population will neither be defined nor analyzed.

SCHEDULE OF EVENTS AND PROCEDURES

Visit Number	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**
Day/Week/Month	**Day 1**	**24hr Post-Inj.**	**48hr Post-Inj.**	**72hr Post-Inj.**	**Day 7** *±1 day*	**Day 14** *±2 days*
Assessment and Procedures						
Informed Consent	X					
Inc/Excl Criteria	X					
Demographics, Med Hx	X					
Concomitant Medications	X	X	X	X	X	X
Intralesional Injection(s)	X					
Investigator Assessments						
Global Severity Score	X					
Target Lesion Assessments	X	X	X	X	X	X
Target Lesion Photography	X *pre-/post- inj.*	X	X	X	X	X
Lesion Injection Videography	X					
Subject Assessments						
Target Lesion Pain	X *pre-inj.*	X	X	X	X	X
Intralesional Injection Pain	X *post- inj.*					
Subject Satisfaction		X	X	X	X	X
Safety Assessments						
UPT (as applicable)	X					
Adverse Events	X	X	X	X	X	X

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1 INTRODUCTION

Intralesional injection of corticosteroids is standard of care therapy for stubborn acne lesions. They are typically dosed with triamcinolone acetonide at concentrations of 0.5 mg/mL to 2.5 mg/mL (i.e., 0.5% to 2.5%) in volumes of 0.05 mL to 0.15 mL.

This proof-of-concept study will investigate the safety of using an intradermal needle adapter for delivery of intralesional triamcinolone injections in patients with acne vulgaris. The intradermal needle adapter is an accessory that slips on the end of a standard 32G 0.5" needle and reduces the effective length of the needle to 1mm. The adapter (currently a prototype) is made of biocompatible 304 Stainless Steel and is being developed to allow patients to safely self-inject triamcinolone, rather than depending on injections performed by a physician.

As intralesional triamcinolone injections are standard-of-care, the purpose of this proof-of-concept study is to test the safety of the intradermal needle adapter, not the safety and efficacy of triamcinolone per-se.

2 STUDY OBJECTIVE

The objective of this proof-of-concept study is to investigate the safety of using an intradermal needle adapter for performing intralesional injections.

3 COMPLIANCE STATEMENT

The study will be conducted in accordance with the Clinical Investigation Plan, International Conference on Harmonization (ICH) and Good Clinical Practice (GCP), the Declaration of Helsinki, International Organization for Standardization (ISO) 14155, and the United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312). In addition, the study will be conducted in compliance with all applicable laws and regulatory requirements relevant to the use of new medical devices in the United States.

The sites' Principal Investigator (PI) is responsible for ensuring the privacy, safety and welfare of the subjects during and after the study and must ensure that site personnel are appropriately trained. The PI at each site has the overall responsibility for the conduct and administration of the study at their site, and for contact with study site management, and local authorities.

3.1 Variations to the Protocol

No changes from the final approved (signed) protocol will be initiated without the prior approval by the IRB except 1) when necessary to eliminate immediate hazards to the subjects or when the change involves only logistics or administration, or 2) minor administrative or typographical corrections. The sites' PIs and the Sponsor must sign any protocol amendments.

3.2 Investigational Sites

One (1) U.S. investigational site will participate in this study. The site must obtain written approval from a 21 CFR 56 compliant IRB prior to recruitment and enrollment of any subject into the study. Any changes to the study procedures must be made with the mutual agreement of the PI and the Sponsor, documented in an amendment to the protocol, and approved by the reviewing IRB.

4 OVERVIEW OF STUDY DESIGN

This is an open-label, prospective, single-arm study. Approximately 20 subjects will be enrolled at 1 study site. A full description of the inclusion and exclusion criteria can be found in Section 5.

All subjects will receive standard-of-care intralesional injection with triamcinolone using an intradermal needle adapter at Visit 1 (Day 1). Subjects will then attend in-clinic visits at Visit 2 (24-hours post-injection), Visit 3 (48-hours post-injection), Visit 4 (72-hours post-injection), Visit 5 (Day 7), and Visit 6 (Day 14).

5 STUDY POPULATION

Potential study participants may be identified and recruited into the study through various methods, such as:

- Database of individuals who have agreed to be contacted for future studies;
- In-person recruitment;
- Physician to physician referrals;
- Internet advertisement;
- Print advertisement.

Note that scripts and advertisement fliers will be submitted to the IRB as necessary.

5.1 Inclusion Criteria

1. Outpatient, male or female of any race, 18 years of age or older. Female subjects of childbearing potential must have a negative UPT at Baseline.

   A female is considered of childbearing potential unless she is:
   - *postmenopausal for at least 12 months prior to study device administration;*
   - *without a uterus and/or both ovaries; or*
   - *has been surgically sterile for at least 6 months prior to study device administration.*

2. Diagnosed with facial acne vulgaris.
3. At least one (1) identifiable inflammatory lesion that, in the opinion of the investigator, is clinically indicated for indicated for standard-of-care intralesional injection(s) of triamcinolone and for which the research participant has already agreed to have standard-of-care intralesional injection(s) of triamcinolone.
4. Able to follow study instructions and likely to complete all required visits.
5. In good general health as determined by medical history at the time of screening (Investigator discretion).
6. Sign the IRB-approved ICF (including HIPAA authorization) prior to any study-related procedures being performed.

5.2 Exclusion Criteria

1. Female subjects who are pregnant or breast-feeding.
2. Known hypersensitivity or previous allergic reaction to any constituent of triamcinolone injection.
3. Active cutaneous viral infection in any treatment area at Baseline.

4. Have concomitant skin disease or infection (other than acne) or presence of skin comorbidities in the areas of skin where study device will be used.
5. History of poor cooperation or unreliability (Investigator discretion).
6. Planning to move out of the area prior to study completion.
7. Subjects who are investigational site staff members or family members of such employees.
8. Exposure to any other investigational /device within 30 days prior to Visit 1.

5.3 Subject Withdrawal

Subjects are free to withdraw from participating in this study at any time and for whatever reason, specified or unspecified, and without prejudice. All premature discontinuations and their reasons must be carefully documented by the PI in the source documents, CRF, and (if applicable), on the AE form.

6 SUBJECT NUMBERING, RANDOMIZATION AND BLINDING

This is an open-label, non-randomized, single-group study. All subjects who are enrolled will receive treatment with the study device. Randomization and blinding are not applicable.

All enrolled subjects will receive a 3-digit subject number, starting at 001. Subject numbers will be assigned in ascending order. The subject number will be used to identify the subject throughout the study. Subjects withdrawn from the study will retain their subject number; new subjects will be allocated a new subject number. Screen Failures will not be entered in the eCRF.

7 CONCOMITANT AND PROHIBITED MEDICATION/PROCEDURES

7.1 Concomitant Medications and Procedures

All treatment/procedures received by the subject throughout the treatment period, including the name of the treatment/procedure, must be recorded in the CRF with end dates, if applicable. Every attempt should be made to keep concomitant therapy dosing constant during the study. Any change to concomitant therapy should be noted in source documents and the CRF.

There are no prohibited medications defined for the study. Any necessary therapies that are deemed appropriate by the Investigator are permitted. Subjects currently taking medications to treat acne should be instructed to maintain their current dosing throughout the study.

8 INVESTIGATIONAL PRODUCT MANAGEMENT

8.1 Intradermal Needle Adapter

The intradermal needle adapter is an accessory that slips on the end of a standard 32G 0.5” needle and reduces the effective length of the needle to 1mm (Figure 1). The adapter is made of biocompatible 304 Stainless Steel. It is packaged in single use bags and will be autoclaved or prepared in the standard manner for typical stainless steel instruments used by the Investigator.

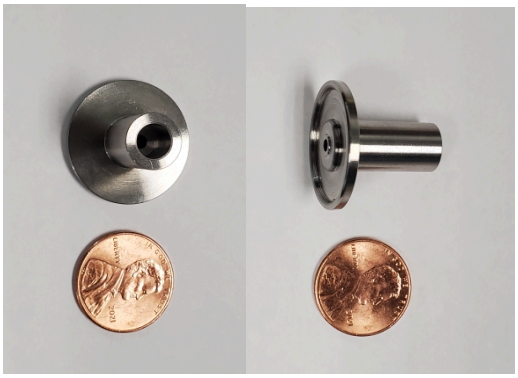

Figure 1. Intradermal Needle Adapter

8.2 Triamcinolone for Injection

A commercial supply of triamcinolone 10% for injection will be provided to the site and diluted with Saline to the appropriate concentration. The site will store triamcinolone as per the conditions described in the package insert.

A standard 32G 0.5" needle will be fixed to a 1.0 mL luer syringe and the syringe will be loaded with an appropriate volume and concentration of triamcinolone. A total of 0.05 mL to 0.15 mL of triamcinolone 0.5% to 2.5% will be injected into each target lesion. The choice of volume and concentration for each individual lesion will be at the discretion of the Investigator as per his clinical judgement. The intradermal needle adapter will then be installed on the needle.

At least one (1), and up to three (3) inflammatory target lesions will be selected for intralesional injections of triamcinolone using the intradermal needle adapter.

9 STUDY EVALUATIONS

9.1 Visit Procedures

9.1.1 Visit 1 (Baseline; Day 1)

- Written informed consent (incl. HIPAA and California Bill of Rights)
- Inclusion / exclusion criteria
- UPT (if female subject of childbearing potential)
- Medical history and demographics
- Concomitant medications/treatments
- Investigator Assessments
  - *Global Severity Score (GSS)*
  - *Target Lesion Assessments: lesion erythema, lesion severity*
  - *Target Lesion Photography (pre- and post-injection)*
  - *Target Lesion Injection Videography*
- Subject Assessments
  - *Target lesion pain (pre-injection)*
  - *Intralesional injection pain (post-injection)*
- Intralesional injection(s)
- AE Assessment

9.1.2 Visits 2 to 6 (24hr, 48hr, 72hr, 7 days±1 day, 14 days±2 days)

- Investigator Assessments
  - *Target Lesion Assessments: lesion erythema, lesion severity, improvement*
  - *Target Lesion Photography*
- Subject Assessments
  - *Target lesion pain*
  - *Subject Satisfaction*
- Concomitant medications/treatments
- AE Assessment

9.2 Investigator Assessments

9.2.1 Global Severity Score (GSS)

The Investigator will use the following GSS scale to determine subjects' Baseline acne severity (Table 1).

Table 1: Global Severity Score

Score	Grade	Description
0	**Clear**	Normal, clear skin with no evidence of acne vulgaris
1	**Almost Clear**	Rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red
2	**Mild**	Some non-inflammatory lesions are present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)
3	**Moderate**	Non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and there may or may not be one nodulocystic lesion
4	**Severe**	Inflammatory lesions are more apparent, many comedones and papules/pustules, there may or may not be up to 2 nodulocystic lesions

9.2.2 Target Lesion Assessments

Up to 3 inflammatory lesions on the face will be chosen for intralesional injections of triamcinolone using the study device as per Section 8 (i.e., target lesions).

Each injected lesion will be individually assessed as per the following methods.

9.2.2.1 Target Lesion Erythema

The Investigator will use the following scale to determine the severity of erythema for each target lesion (Table 2).

Table 2: Target Lesion Erythema

Grade	Description
0	No Erythema
1	Mild Erythema
2	Moderate Erythema
3	Severe Erythema
4	Very Severe Erythema

9.2.2.2 Target Lesion Severity

The Investigator will determine the severity of each target lesion as per the scale in Table 3.

Table 3: Target Lesion Severity

Grade	Description
0	None
1	Mild
2	Moderate
3	Severe
4	Very Severe

9.2.2.3 Target Lesion Improvement

The Investigator will determine the improvement seen with each target lesion as per the scale in Table 4. Lesion improvement will not be assessed at Baseline.

Table 4: Target Lesion Improvement

Grade	Description
1	Clear (100%)
2	Almost clear (90% to <100%)
3	Marked improvement (75% to <90%)
4	Moderate improvement (50% to <75%)
5	Fair improvement (25% to <50%)
6	No change
7	Worse

9.2.2.4 Target Lesion Videography

A video will be taken of each injected lesion starting from just prior to needle penetration and up to 10 seconds after removed of needle from lesion.

9.2.2.5 Target Lesion Photography

Photographs will be taken at each study visit of each injected inflammatory lesion. At Baseline, photographs will be taken both pre- and post-injection.

9.3 Subject Assessments

9.3.1 Target Lesion Pain

For each inflammatory lesion to be injected, lesion pain will be self-assessed by the subject using a 10 cm Visual Analog Scale (VAS) Pain Scale. Lesion pain at Baseline will be recorded prior to injection(s). The occurrence of inflammatory lesion pain is expected and will not be considered an AE.

9.3.2 Intralesional Injection Pain

Injection pain will be self-assessed at each study visit by the subject using the Visual Analog Scale (VAS). Lesion pain at Baseline will be recorded prior to injection(s). Injection Site Pain during injection will be assessed for all injected lesions immediately after the final lesion has been injected. Ten (10) minutes after these assessments, injection pain will be assessed again for all injected lesions. The occurrence of injection site pain is expected and will not be considered an AE.

9.3.3 Subject Satisfaction

Subject Satisfaction will be assessed by the subject using the following subjective 5-grade scale as detailed in Table 5. Subject will be instructed: "Rate your level of satisfaction with the effect of study treatment on inflammatory acne lesions by using the following scale":

Table 5. Subject Satisfaction Scale

Grade	Description
1	Very satisfied
2	Satisfied
3	Neither satisfied nor dissatisfied
4	Dissatisfied
5	Very dissatisfied

9.4 Safety

9.4.1 Adverse Events

All observed or volunteered AEs regardless of suspected causal relationship to the study device will be recorded in the CRF. Subjects will be questioned for the occurrence of any new or worsening signs or symptoms at each visit.

9.4.1.1 Definition of Adverse Event

An AE is any untoward medical occurrence in a patient or clinical investigation subject administered a study device and which does not necessarily have a causal relationship with the study device. AEs include any unfavorable and unintended illness, sign, symptom, clinically significant laboratory test abnormality, or disease temporally associated with the use of a study device that has appeared or worsened during the course of the clinical trial, regardless of causal relationship to the study device under study.

The collection of non-serious AEs and serious adverse events (SAEs) will begin following the subject's signature of the informed consent form.

9.4.1.2 Documenting Adverse Experiences

The PI is responsible to document all AEs that occur during the study. AEs should be documented as a single medical diagnosis. When this is not possible, AEs should be documented in terms of signs/symptoms observed by the PI or reported by the subject at each study visit. Each AE that appears to be independent of any prior event will be reported separately.

All AEs occurring after the subject signs the informed consent form through the last study visit must be reported, regardless of AE causality. All AEs, whether in response to a query, observed by the study site personnel, or reported spontaneously by the subject, will be recorded.

At each visit during the study, the subject will be assessed for the occurrence of new and ongoing AEs. The following data will be collected on all AEs and recorded on the appropriate CRF:

- Event name (diagnosis preferred, if unknown, record the signs/symptoms)
- Onset date and end date
- Maximum intensity (severity)
- Seriousness
- Action taken regarding study device
- Corrective treatment, if given

- Outcome
- Investigator assessment of causality

9.4.1.3 Serious Adverse Events

All AEs will be assessed as either serious or non-serious.

An SAE is defined as any untoward medical occurrence that at any dose:

- Results in death
- Is immediately life threatening, (the term "life threatening" in the definition of "serious" refers to an event in which the subject is at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization for elective surgery for a baseline condition is not considered an AE)
- Results in persistent or significant disability/incapacity (permanent or substantial disruption of a person's ability to conduct normal life functions)
- Is a congenital anomaly/birth defect
- Is a medically important event that may not be immediately life threatening or result in death or hospitalization but may jeopardize the subject and may require medical or surgical intervention to prevent one of the above listed outcomes. Examples of such events include, but are not limited to, allergic bronchospasm requiring intensive treatment in an emergency room or at home; blood dyscrasias or convulsions that do not result in inpatient hospitalization.

Note: A spontaneous abortion will be considered an SAE and must be reported per Reporting of SAEs under Section 9.4.1.6.

9.4.1.4 Assessment of Severity

The severity assigned to an AE should be determined by the maximum severity of the AE. The categories described below should be used to estimate the severity of AEs:

- **Mild:** Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required
- **Moderate:** Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required
- **Severe:** Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalization or prolongation of current hospitalization possible; may be incapacitating or life threatening

9.4.1.5 Assessment of Causality

The PI should assess the relationship of the AE to the study device as either "Related" or "Not Related". The following should be considered when assessing AE causality:

- **Related:** There is at least a reasonable possibility that the AE/SAE is related to the study device. Reasonable possibility means that there is evidence to suggest a causal relationship between the study device and the AE.

- **Not Related:** There is little or no reasonable possibility that the AE/SAE is related to the study device. This assessment implies that the AE/SAE has little or no temporal relationship to the study device and/or a more likely or certain alternative etiology exists.

9.4.1.6 Reporting of Serious Adverse Events

Adverse events classified as "serious" require expeditious handling and reporting to ethica CRO within 24 hours of investigational center notification.

All SAEs, whether related or unrelated to study device, must be immediately reported to the ethica CRO Clinical Project Manager (or designate) within 24 hours of the PI's awareness of the event. All SAEs must be reported via confirmed facsimile or email transmission and must be submitted on a written SAE report form signed by the PI within 24 hours of the PI's awareness of the event.

PIs should not wait to receive additional information to fully document the event before notifying ethica CRO of an SAE. If only limited information is initially available, follow-up reports are required. Additional relevant information such as hospital records and autopsy reports should be provided to the Sponsor as soon as they are available.

The PI should take all appropriate measures to ensure the safety of the subjects, notably he/she should follow a subject with an SAE until the event has resolved or the condition has stabilized. This may imply that follow-up will continue after the subject has left the study, and that additional investigations may be requested by the Sponsor. When an SAE persists at the end of the study, the PI will conduct follow-up contacts with the subject until the PI/Sponsor agree the event is satisfactorily resolved and/or stabilized.

9.4.1.7 Pregnancy

During the study, all female subjects of childbearing potential should be instructed to contact the PI immediately if they suspect they might be pregnant (e.g., missed or late menstrual period).

If a subject or PI suspects that the subject may be pregnant prior to study enrolment, the study device must be withheld until the results of laboratory pregnancy testing are available. If pregnancy is confirmed, the subject must not receive study device and must not be enrolled in the study.

If pregnancy is suspected while the subject is receiving study device, the study device must immediately be withheld until the result of pregnancy testing is known. If pregnancy is confirmed, the study device will be permanently discontinued, and the subject will be followed until the pregnancy comes to term.

All confirmed pregnancies must be reported via confirmed facsimile or email transmission and must be submitted on an Unanticipated Problems Reporting Form within 24 hours of the PI's awareness of the pregnancy using the same reporting as procedure for an SAE under Section 9.4.1.6.

10 STATISTICS

There is no inferential statistical testing conducted for this study. Descriptive data summaries will be prepared for all outcome variables.

For categorical parameters, the number and percentage of subjects/observations in each category will be presented. The denominator will be based on the number of subjects/observations appropriate for the purpose of analysis. For continuous parameters, descriptive statistics will

include n (number of subjects or observations), mean, standard deviation, median, and range. Two-sided 95% CIs will be provided for all study outcomes.

10.1 Sample Size Determination

Approximately 20 subjects will be enrolled. This is a POC study and a formal sample size justification is not provided for this study. It is the opinion of the Sponsor that a total of 20 subjects will be sufficient to achieve the objective of the study.

10.2 Assessment of Safety

10.2.1 Adverse Events

All AEs occurring during the study will be recorded and classified on the basis of MedDRA terminology. Descriptions of AEs will include the date of onset, the date the AE ended, the severity of the AE, the relationship to study medication, the action taken regarding study medication usage, the action taken to treat the AE, and the outcome. All reported treatment-emergent AEs (TEAEs) and treatment-related events (TRAEs) will be summarized by the number of Subjects reporting AEs, system organ class, severity, seriousness, and relationship to study medication.

AEs will be summarized by treatment group and severity, and by treatment group and relationship to study device. Each subject will be counted only once within a system organ class or a preferred term by using the AEs with the greatest relationship within each category.

10.3 Analysis Populations

10.3.1 Intent-to-Treat (ITT) Population

The modified Intent-to-Treat (mITT) Population is defined as all subjects who were enrolled and received at least one application with the study device. The mITT Population will be used for analyses of safety and effectiveness endpoints.

10.3.2 Per-Protocol (PP) Population

A Per-Protocol (PP) Population will neither be defined nor analyzed.

10.3.3 Subject Disposition

A tabulation of subject disposition will be provided which will include the numbers of subjects who enter, complete, and discontinue the study. The reasons for discontinuation will be included.

10.3.4 Protocol Deviations and Violations

All protocol deviations and violations will be reported to the Sponsor and recorded throughout the study. A tabulation of protocol deviations will be included in the final study report.

10.3.5 Multicenter Issues

Not applicable

10.3.6 Missing Data Imputations

Data will be analyzed as observed; no imputations will be made for missing data.

10.3.7 Statistical Hypothesis Testing and Control of Multiplicity

Not Applicable.

10.4 Interim Analyses

No interim analyses are planned.

11 QUALITY CONTROL AND QUALITY ASSURANCE

11.1 Study Monitoring

An initiation webinar will be conducted with the PI and study coordinator(s) by Sponsor and/or its designee. During this meeting, an extensive review and discussion of the protocol, all study procedures, source documents, and CRFs will be conducted. Evaluation scales will be reviewed extensively.

The Clinical Project Manager(s) and Clinical Trial Associate(s) will be trained prior to study initiation.

The conduct of the study will be closely monitored by the Sponsor (or designate) following GCP guidelines. The reports of these verifications will also be archived with the study report. In addition, inspections or on-site audits may be carried out by local and/or federal authorities. The PIs will allow the Sponsor's representatives and any regulatory agency to examine all study records, corresponding subject medical records, clinical dispensing records and storage area, and any other documents considered source documentation. The PIs agree to assist the representative, if required.

11.2 Audits and Inspections

The study will be conducted under the Sponsorship of the Sponsor in conformation with all appropriate local and federal regulations, as well as ICH guidelines.

11.3 Protocol Deviations

The PIs must read the protocol thoroughly and must follow the instructions exactly.

A deviation from the protocol is an unintended and/or unanticipated departure from the procedures and/or processes approved by the Sponsor and the IRB and agreed to by the PI. Deviations usually have an impact on individual subjects or a small group of subjects and do not involve inclusion/exclusion or tolerability and cosmetic endpoint criteria.

A protocol violation occurs when there is non-adherence to the protocol that results in a significant, additional risk to the subject, when the subject or PI has failed to adhere to significant protocol requirements (inclusion/exclusion criteria) and the subject was enrolled without prior Sponsor approval, or when there is non-adherence to ICH GCP guidelines.

The issue of noncompliance may be either on the part of the subject, the PI, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

All protocol deviations and violations must be addressed in study subject source documents. A completed copy of the ethica CRO Inc. Protocol Deviation Form must be maintained in the regulatory file, as well as in the subject’s source document. Protocol deviations must be sent to the IRB per its guidelines.

12 ETHICS AND ADMINISTRATIVE ISSUES

12.1 Ethical Conduct of the Study

This study will be conducted in accordance with the ethical principles originating from the Declaration of Helsinki, ICH guidelines, GCP, and in compliance with local regulatory requirements. The PI agrees, when signing the protocol, to adhere to the instructions and procedures described in it and thereby to adhere to the principles of GCP.

12.2 Ethics Review

The study protocol, informed consent form and other information to subjects, and all appropriate amendments will be reviewed and approved by an Institutional Review Board (IRB). A signed and dated notification of the IRB approval will be provided to the Sponsor and PI prior to study initiation. The name and occupation of the chairman and members of the IRB will be supplied to the Sponsor to the extent allowable by the IRB. The PI will provide required progress reports and report all SAEs to the IRB as required by the IRB.

12.3 Written Informed Consent

This study will be conducted in compliance with 21 CFR Part 50 for informed consent.

The study coordinator will obtain written informed consent from each subject before any procedures or assessments are done and after the aims, methods, anticipated benefits, potential hazards, compensation and/or honoraria, and insurance arrangements in force are explained. It will also be explained to the subject that they are free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment. The Investigator will be available to respond as needed to questions raised by the participant.

Written and/or oral information about the study in a language understandable by the subject will be given to all subjects. The subjects will be given the opportunity to discuss the procedure, risks, benefits, alternative therapies and the study requirements with the Investigator (or qualified designee) and have any and all questions answered to the subject's satisfaction.

The subject's willingness to participate in the study will be documented in writing on a consent form, which will be signed by the subject with the date and time of that signature indicated.

The site will keep the original consent forms and copies will be given to the subjects.

12.4 Subject Data Protections

Subject data will be protected by ensuring that no captured data contain subject names, addresses, telephone numbers, email addresses, or other personally identifying information. It is acknowledged that subject initials, demographics (including birthdates), medical histories, and prior concomitant medication uses, along with the name and address of the enrolling PI may allow for personal identification of study participants. Other than where necessary to meet regulatory requirements, all data collected in this study will be presented in tabulated (i.e., aggregate) form and listings containing information that could be used to identify an individual subject will not be included in any public disclosures of the study data or the study results.

As part of the study database, study data will be stored at Equinix and Amazon Web Services facilities in Germany and Ireland that are SOC 1, SOC 2, ISO 27001, and FISMA examined and certified. Security monitoring includes biometric scanning protocols, continuous surveillance, and

24x7 production environment management. Data privacy complies with Canadian and US standards, as well as the European Union's General Data Protection Regulation (GDPR).

The study database utilizes encryption to safeguard data and all data is durably stored with National Institute of Standards and Technology (NIST) approved ciphers, transport layer security (TLS) technology, and AES 256-bit at-rest encryption.

12.5 Data Monitoring Committee

Not applicable.

12.6 Investigator Obligation

The PI agrees, when signing the protocol, to adhere to the instructions and procedures described in it and thereby to adhere to the principles of Good Clinical Practice (GCP).

12.7 Changes to the Protocol

The PIs must read the protocol thoroughly and must follow the instructions exactly. Whenever possible, any planned deviations should be agreed to by prior discussion between the Sponsor and the PI, with appropriate documentation of Sponsor approval prior to effecting the changes agreed upon. Any amendment to the protocol containing major modifications (particularly if it may involve an increased risk to the subjects) will be approved by the IRB before it may be implemented. No change in the conduct of the study can be instituted without written approval from the Sponsor.

12.8 Confidentiality Regarding Study Subjects

All the data furnished to the PI and his/her staff and all data obtained through this protocol will be regarded as confidential and proprietary in nature and will not be disclosed to any third party without written consent from the Sponsor.

12.9 Reporting and Publication of Results

ACOM Labs, Inc., as the Sponsor, has a proprietary interest in this study. Authorship and manuscript composition will reflect joint between the PI and ACOM Labs, Inc. personnel.

All information, including but not limited to information regarding the study device or the Sponsor's operations supplied by the Sponsor to the PI and not previously published, along with any data generated as a result of this study are considered confidential and remain the sole property of the Sponsor. The PI agrees to maintain this information in confidence and will use the information only to perform the study.

The Sponsor or its designee is responsible for publicly registering this study on http://www.clinicaltrials.gov/ prior to initiating enrolment.

12.10 Financing and Insurance

A separate financial agreement (Clinical Study Agreement) will be made between the Sponsor and the PI at each site.

ACOM Labs, Inc. will procure and maintain for the duration of the study a policy of insurance covering its liabilities in the conduct thereof. The certificate of insurance will be provided upon request.

13 APPENDICES

Appendix A: Protocol Version History
Appendix B: Adjustment of Visits and Assessments due to COVID-19

APPENDIX A: PROTOCOL VERSION HISTORY

Version and Date	Description
v.1.0; 17-Oct-2022	*Final Protocol*
v.2.0; 28-Oct-2022	*Revisions made in response to 28-Oct-2022 conditional IRB approval.*

APPENDIX B: ADJUSTMENT OF VISITS AND ASSESSMENTS DUE TO COVID-19

1. General Guidance

Subject safety and preserving the integrity of the data are of the highest priority. Any federal, state, and local rules, guidances, or laws shall be followed.

Study visits and procedures should be followed per-protocol whenever possible. Any specific changes in study conduct that deviate from the protocol should be communicated to the Sponsor via reporting to the Clinical Project Manager (CPM) and IRB, as applicable. All protocol deviations which occur as a result of COVID-19 disruptions (including remote visits), will be differentiated from other deviations, and must be documented on the appropriate reporting forms/source document, and clearly annotated "protocol deviations due to COVID-19 illness/restrictions/etc.". If the subject is unable or unwilling to come to the site due to COVID-19, the PI needs to ask for the reasons and document them in the source documents.

The PI is responsible for ensuring subjects' safety and for monitoring all active subjects per protocol. PI must ensure that study subjects are kept informed of changes to the study and monitoring plans that could impact them.

Should a subject develop any symptoms that could be related to COVID-19 or any other acute infection disease, the subject will be instructed to:

- Contact the PI as soon as possible
- Contact their general physician to be examined and determine the course of action according to the standard of care.

The PI or designee will follow-up with the subject as needed but at least within 72 hours of awareness to obtain an update on the subject's health and to obtain information on whether COVID-19 has been diagnosed or not. If the subject has been diagnosed with COVID-19, the event will be reported as an AE.

2. Adjustment of Study Visits

Telemedicine is understood as a possible solution due to COVID-19 disruption and it is not mandatory; if the situation allows it, study visits should be done in person.

On-site Study Visit: If the local situation allows for conduct of on-site study visits, the PI and study personnel must take all necessary steps/precautionary measures at the site to minimize or eliminate immediate hazards of viral transmission within and/or outside the clinical site premises.

Before any research activities occur on-site, both subjects and research staff should be screened for symptoms or risk of COVID-19 infection. Subjects should be pre-screened by phone before their on-site study visit.

If the local situation only allows for completion of some study procedures, the PI will prioritize the research activities that absolutely require an in-person visit in order to maintain the viability and integrity of the research. The PI may consider conducting the other assessments (e.g., medical history review, subject questionnaires) using telemedicine to minimize subject time on site and risk of exposure at the site. However, all efforts should be made to conduct all assessments at the scheduled visits, if possible.

Remote Study Visit: If the local situation does not allow for an on-site study visit to be conducted or if a subject does not wish to come to the study site due to COVID-19 disruption, a remote study visit may be conducted via video conferencing in lieu of an on-site visit. Phone call may also be used to perform some assessments if a subject has no video conferencing capabilities.

The PI or study personnel who will conduct remote visits must be trained on how to conduct real-time video conferencing visits. Also, procedures should be put in place to maintain the subject's privacy, as would be done for a clinical visit:

- **Before the scheduled date of the visit:**
  - The site personnel should determine if the subject can accommodate for video conferencing (e.g., internet access, PC, smartphone, video conference apps, etc.).
  - The PI or site personnel conducting the remote visit should obtain the subject's verbal consent before proceeding with the visit and document it in the source document. The PI or personnel should also explain to the subject how the visit will be conducted.
  - The site personnel should send all required study material to conduct the visit to the subject (e.g., UPTs, etc.).
  - A test call may also be completed with the subject prior to the appointment.
- **On the day of the scheduled visit:**
  - Both the PI/site delegate and the subject should confirm their respective identities with one another before engaging in a real-time video conference visit. For example, the site personnel will state their name and role and the subject may be identified by using two subject identifiers (e.g., name and date of birth) and a photo ID.
  - The date and time of the real-time video interaction, the location of the subject, and the location of the PI or site personnel conducting the remote visit should be documented in the source document.
  - Remote collection of data by PI or delegate will be conducted as described in Section 3 below.

3. Adjustment of Study Assessments

Informed consent: The following process will be followed for consenting a prospective subject remotely:

- Each subject will be provided with an IRB-approved electronic consent form to aid in the consent discussion before the consent process begins.
- The PI and/or site delegate will participate in the consent process via video conference. All parties must introduce themselves and their role in the consenting process.
- The consent form will be reviewed in detail and the subject will be invited to ask any questions and to have them addressed by the study team.
- If the subject is interested in joining the research study, the subject will be asked to electronically sign the consent document.
- The PI and appropriate witness(es) will also provide electronic signatures as required.

- The site should ensure to obtain all electronic signature pages from the subject and to document the consent process in the source document. The site should also provide a softcopy of the consent form to the subject and a hardcopy (in person or by mail).

Inclusion/Exclusion Criteria: The list of inclusion/exclusion criteria will be reviewed via video conference or phone call with the subject to confirm that they are eligible for the study. Data will be documented in the source documents and CRF.

For potential subjects in a high-risk population for COVID-19 (e.g., 60 years old and older, with comorbidities such as diabetes, cardiovascular disease, respiratory system issues, etc.), deferring participation should be considered to minimize risks of exposure.

Investigator Assessments of Efficacy and Safety: Investigator assessments of efficacy and safety can be conducted remotely via FaceTime and photos taken by the subject using his/her phone.

Subject Assessments: Subject assessments of lesion pain cannot be conducted remotely. Subject Satisfaction Assessment can be conducted remotely and reviewed via video conference at each remote visit and reported in the source documents and CRF.

Urine Pregnancy Tests: UPTs can be conducted remotely and reviewed via video conference at each remote visit and reported in the source documents and CRF.

Demographics: Demographic information will be collected via video conference or phone call from the subject at the remote screening visit and will be documented in the source documents and CRF.

Medical History / Concomitant Medications: Medical history and concomitant medications will be reviewed via video conference or phone call at each remote visit and reported in the source documents and CRF.

Adverse Events: AEs will be reviewed remotely via video conference or phone call with the subject at each remote study visit. Any AE/SAE (including suspected / confirmed COVID-19 cases) elicited by a subject during a remote visit / phone call must be immediately captured, and all attempts should be done to capture the necessary clinical and medical information. Reporting of AEs and SAEs to the Sponsor and IRB should follow the protocol procedure and IRB requirements.