CL-AC-21-02
[redacted]

A Proof of Concept Study to evaluate the efficacy and tolerability of Microneedling with SkinPen in female and male Subjects with facial Acne Vulgaris, ages 18 through 45

[redacted]

A Proof of Concept Study to evaluate the efficacy and tolerability of Microneedling with SkinPen in female and male Subjects with facial Acne Vulgaris, ages 18 through 45

SPONSOR STUDY NUMBER:	CL-AC-21-02
SPONSOR:	Crown Laboratories 5005 LBJ Freeway Suite 370 Dallas, TX 75244
SPONSOR'S REPRESENTATIVE:	Mona Alqam, MD Email: [redacted] Brian jones, PhD Email: [redacted]
TESTING FACILITY:	Crown Laboratories [redacted]
INVESTIGATOR:	Joe Blumenau, MD
SUB-INVESTIGATOR:	Mona Alqam, MD

[redacted]

CL-AC-21-02
[redacted]

A Proof of Concept Study to evaluate the efficacy and tolerability of Microneedling with SkinPen in female and male Subjects with facial Acne Vulgaris, ages 18 through 45

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Contents

[redacted]

[redacted]

1. PURPOSE

This single-center, proof of concept trial is being conducted over the course of 42 days followed by 2-month post last treatment visit in order to assess the efficacy and tolerability of the Sponsor's SkinPen device in treating Acne Vulgaris on the face.

There is currently no published medical or scientific literature demonstrating the effect of Microneedling on Acne Vulgaris.

[redacted]

2. STUDY OBJECTIVES

This proof of Concept study serves to evaluate the efficacy and tolerability of Microneedling with SkinPen in female and male Subjects with facial Acne Vulgaris, ages 18 through 45. Overall assessment of clinical outcome and safety will be based on clinic visits. The Investigator will apply an objective and precise assessment, the Lesion Count of inflammatory and non-inflammatory lesions. The Investigator will also perform the IGA assessment. Subjects will be dispensed a Diary to record any new Adverse Events between visits. Subjects will be encouraged to contact the Study Investigator if any adverse events arise.

3. STUDY ENDPOINTS

3.1 Primary Endpoint

- The primary endpoint of the study is reduction of lesion count from Visit 1 (baseline) to Visit 5, in the inflammatory (papules and pustules) and non-inflammatory (open and closed comedones) lesions.

3.2 Secondary Endpoints

- Monitoring of adverse events throughout the course of the study.
- Investigator's Global Assessment (IGA, from jaw line to hairline) performed at Visit 1 (Baseline) and 2-months post treatment (Visit 5) with IGA score improvement

4. TEST MATERIAL INFORMATION

4.1 Study Identification Procedures

Investigator will assign each study device(s) a unique test material identification number (TMIN) in order to provide proper identification in records and reports.

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Hydrogel will be used in conjunction with the SkinPen during treatment to protect against abrasion and friction.

[redacted]

[redacted]

4.6 Treatment Compliance

Any suspected non-compliance will be addressed by the Investigator or designee. The Investigator will make a determination if a subject's non-compliance will have an effect on the outcome of the study and if the subject should be dropped from the study and/or data should be excluded from statistical analyses.

4.7 Method of Treatment Assignment

A total of 15 Subjects with an IGA score between 1 and 3 on the face and meeting eligibility criteria will be enrolled and assigned a number sequentially in the order in which they qualify for entry into the study. This number will remain with the subject throughout the study and should be used in all references to the individual in this study. No number will be reassigned once the study begins.

5. SUBJECT ENROLLMENT AND INSTRUCTIONS

5.1 Informed Consent Form

An IRB-approved informed consent form (ICF), consistent with the requirements in 21 Code of Federal Regulations (CFR) 50.25, will be given to each candidate subject before participation in any study procedures. [redacted]

[redacted].

5.2 Eligibility Criteria

Individuals will be admitted to the study at the discretion of the Investigator or designee, based on medical history and findings of the interview and examination. Individuals will be screened for the eligibility criteria listed below prior to study enrollment.

5.3. Inclusion Criteria

1. Adult males and females, ages 18 through 45, at the time the ICF is signed.
2. Clinical diagnosis of Acne Vulgaris
3. Investigator's Global Assessment (IGA) Score 1,2 or 3
4. Individuals willing to withhold aesthetic therapies to the areas of the face being treated or judged to potentially impact results by the Investigator (e.g. soft tissue fillers and/or any resurfacing procedures, botulinum toxin, injectable fillers, microdermabrasion, IPL (intense pulsed light), peels, facials, laser treatments, and tightening treatments, etc.) for the duration of the study. Waxing and threading is allowed but not facial laser hair removal.
5. Women of childbearing potential agree to take a urine pregnancy test at the Baseline visit. [redacted]
6. Individuals of childbearing potential who use an acceptable method of contraception throughout the study. [redacted]
7. Individuals that are willing to provide written informed consent and are able to read, speak, write and understand the informed consent document.
8. Willingness to cooperate and participate by following study requirements for the duration of the study and to report any changes in health status or medications, adverse event symptoms, or reactions immediately.

5.4 Exclusion Criteria

A subject will not be eligible to participate if they meet any of the following exclusion criteria.

1. Individuals diagnosed with known allergies to facial or general skin care products.
2. Individuals who have presence of an active systemic or local skin disease, other than Acne Vulgaris, that may affect wound healing.
3. Individuals who have severe solar elastosis.
4. Individuals with sensitivity to topical lidocaine.
5. Individuals who have physical or psychological conditions unacceptable to the Investigator.
6. Individuals who have a recent history of significant trauma to the face (< 6 months).
7. Individuals who have significant scarring, other than atrophic acne scars, in the area(s) to be treated.
8. IGA Score 0 or 4.
9. Individuals who have a recent or current history of inflammatory skin disease other than Acne Vulgaris, [redacted]
10. Individuals who currently have or have a history of hypertrophic scars, or keloid scars.
11. Individuals who currently have cancerous or pre-cancerous lesions in the areas to be treated and/or with a history of skin cancer.
12. Individuals who have the inability to understand instructions or to give informed consent.
13. [redacted]
14. Individuals who have a history of chronic drug or alcohol abuse.
15. [redacted]
16. Individuals who, in the Investigator's opinion, have a history of poor cooperation, noncompliance with medical treatment, or unreliability.
17. Individuals who are current smokers or have smoked in the last 5 years.
18. [redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

19. Individuals with a history of using the following prescription and over-the-counter medications:

- [redacted]

20. Individuals who are nursing, pregnant, or planning to become pregnant during the study according to subject self-report.

21. Individuals having a health condition and/or pre-existing or dormant dermatologic disease, [redacted]

22. Individuals with a history of immunosuppression/immune deficiency disorders (including HIV infection or AIDS) [redacted]

23. Individuals with an uncontrolled disease [redacted]

24. Individuals with any planned surgeries, overnight hospitalization, and/or invasive medical procedures during the course of the study.

25. Individuals who are currently participating in any other study [redacted]

[redacted]

26. Individuals who have observable suntan, nevi, excessive hair, etc. or other dermal conditions on the face that might influence the test results in the opinion of the Investigator or designee.

27. Individuals who have any condition, which in the opinion of the Investigator makes the patient unable to complete the study per protocol [redacted]

28. Individuals who started hormone replacement therapies (HRT[redacted]

29. Subjects who have received radiation therapy and/or anti-neoplastic agents within 90 days prior to baseline

5.4 Subject Instructions

[redacted]

[redacted]

5.4.3 Subject Instructions for Study Visits

Wash off all make up and skincare products on the face, at least 30 minutes prior to each scheduled clinic visit. [redacted]

5.4.4 General Study Instructions

- Avoid extended periods of sun exposure and all use of tanning beds for the duration of the study.
- [redacted]

6. STUDY DESIGN

This single-center, proof of concept clinical trial is being conducted in order to assess the efficacy and tolerability of the Sponsor's SkinPen II when used to treat facial acne in male and female Subjects, ages 18 through 45.

[redacted]

[redacted]

6.1 Outline of Procedures

[redacted]

([redacted]

[redacted]

[redacted]

6.2. Conduct of Study

6.2.1 Baseline: Visit 1

1. Candidate subjects will be given an IRB-approved informed consent form (ICF) [as described in section 5.1] to read and sign. They will have all their study related questions answered by the

Investigator or designated staff, and if they agree, they will sign the ICF and will receive a copy of the signed ICF.

2. Candidate subjects will complete a Medical History Form which will be reviewed by the investigator or designee.
3. Potential Subjects that sign the initial paper-work will be assigned a Subject Number
4. [redacted]

6.2.2 Subsequent Treatment Visits- Visits 2, 3, and 4 (Days 14, 28, and 42)

1. A clinician will record concomitant medications and will ask subjects if they have experienced any changes in their health since the previous visit. If an adverse event (AE) is reported then the Investigator will be informed and an AE form will be completed.
2. Lesion count and IGA will be completed prior to treatment.
3. [redacted]

6.2.3 Post treatment Follow up visit- Visit 5 (Day 102)

1. A clinician will record concomitant medications and will ask subjects if they have experienced any changes in their health since the previous visit. If an adverse event (AE) is reported then the Investigator will be informed and an AE form will be completed. Refer to section 8 for AE reporting procedures.
2. Collect and review Subject diary.
3. [redacted]

[redacted].

7. ASSESSMENTS

7.1 Lesion Count

[redacted].

Definitions for each lesion type can be seen in the table below:

ACNE LESIONS: NAMES AND DEFINITIONS	
Lesion Name	**Lesion Definition**
Closed Comedone	Non-inflammatory lesion; whitehead, skin-colored or slightly inflamed “bump” in the skin
Open Comedone	Non-inflammatory lesion; blackhead, surface of the plugged sebaceous follicle has a blackish appearance
Papule	Inflammatory lesion; small (≤ 5 mm in diameter), solid palpable lesion, usually with inflamed elevation of the skin that does not contain pus
Pustule	Inflammatory lesion; small (≤ 5 mm in diameter), inflamed skin swelling that is filled with pus
Nodules and Cysts	Cyst or nodule; palpable solid or soft lesion > 5 mm in diameter

7.2 Investigator’s Global Assessment

[redacted]

[redacted]

INVESTIGATOR’S GLOBAL ASSESSMENT	
Score	**Description**
0	Clear skin with no inflammatory or non-inflammatory lesions
1	Almost clear; rare non-inflammatory lesions with no more than one small inflammatory lesion

[redacted]

2	Mild severity; greater than Grade 1; some non-inflammatory lesions with no more than a few inflammatory lesions (papules/pustules only, no nodular lesions)
3	Moderate severity; greater than Grade 2; up to many non-inflammatory lesions and may have some inflammatory lesions, but no more than one small nodular lesion
4	Severe; greater than Grade 3; up to many non-inflammatory and inflammatory lesions, but no more than a few nodular lesions

7.3 Photography

Prior to photography procedures, clinic personnel will ensure that subjects have a make-up free face with no skincare products as described in the study procedures. [redacted]

7.4 Noninvasive Procedures

Bioinstrumentation: DermaLab Combo, Cortex Technology (Denmark) will be used to obtain skin erythema. [redacted]

7.5 Other Procedures

Urine Pregnancy Test: The female Subject will be asked to provide a urine sample if applicable and determined by the Investigator, for a Urine Pregnancy test. [redacted]

Patient Satisfaction Questionnaires [redacted]

8. ADVERSE EVENTS

8.1 Definition of an Adverse Event

[redacted]

8.2 Assessment of Severity and Relationship

[redacted]

[redacted]

8.3 Definition of a Serious Adverse Event

A serious adverse event (SAE) is any experience or reaction occurring at any dose that results in any of the following outcomes:

- death,
- is life threatening,
- inpatient hospitalization or prolongation of hospitalization,
- a persistent or significant disability/incapacity, or
- a congenital anomaly/birth defect.

[redacted]

8.4 Procedures for Reporting Adverse Events

[redacted]

[redacted]

[redacted]

[redacted]

8.5 Procedures for Reporting Serious Adverse Events

[redacted]

8.6 Procedures for Reporting Pregnancies

[redacted]

8.7 Medical Treatment for Adverse Events and Serious Adverse Events

[redacted]

8.9 Unanticipated Adverse Reactions

[redacted]

[redacted]

8.10 Anticipated Reactions

Expected side effects: After the procedure, the skin will be red and flushed in appearance, similar to a moderate sunburn. The patient many also experience skin tightness and mild sensitivity to touch on certain areas. This will diminish significantly within a few hours following the procedure. Within the next 24 hours, the skin will have returned to normal. After three days, there is rarely any evidence that the procedure has taken place.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

9. PROTOCOL MODIFICATIONS

[redacted]

[redacted]

[redacted]

10. ETHICAL AND REGULATORY PROCEDURES

10.1 Research Standards and Good Clinical Practice

The conduct of this study will follow all applicable guidelines for the protection of human subjects for research as outlined in 21 CFR 50, in accordance with the accepted standards for Good Clinical Practice (GCP), International Conference on Harmonization (ICH), and the standard practices of the Clinical Research Site.

10.2 Quality Control and Quality Assurance

[redacted]

10.3 Institutional Review Board

This study (protocol, ICF and all addenda) will be reviewed and approved by an Institutional Review Board (IRB). [redacted]

11. BIOSTATISTICS AND DATA MANAGEMENT

11.1 Statistical Analysis Population and Plan

[redacted]

11.2 Data management and Review

[redacted]

APPENDIX I: SkinPen Precision System Instructions

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SkinPen® Precision Instructions for Use with SkinPen® Precision

OVERVIEW
SkinPen® Precision is an automated, non-surgical microneedling device designed for use by licensed healthcare practitioners or individuals directed by practitioners. The device incorporates a sterile microneedle cartridge and BioSheath for single use only.

SkinPen® Precision Handpiece Model#100

SkinPen® Precision Charger Base Model #101

CAUTION: Federal law restricts this device to sale by or on the order of a physician.

INTENDED USE
The SkinPen® Precision system is a microneedling device and accessories intended to be used as a treatment to improve the appearance of facial acne scars in adults aged 22 years or older.

CONTRAINDICATIONS
Are there any reasons why a patient should not receive SkinPen® Precision treatments? The use of the SkinPen® Precision System should not be used on patients who:

- Have active skin cancer in the treatment area(s)
- Have open wounds, sores, or irritated skin in the treatment area(s)
- Have an allergy to stainless steel or anesthetics
- Have a hemorrhagic (bleeding) disorder or hemostatic (bleeding) dysfunction
- Are pregnant or nursing
- Are currently taking drugs with the ingredient isotretinoin (such as Accutane)

NOTE: This product is not intended for transdermal (under the skin) delivery of topical products such as cosmetics, drugs, or biologics.

WARNINGS
Do not use any equipment not designed specifically for SkinPen® Precision as to avoid interference with the device's intended performance.

Use of this equipment adjacent to or stacked with other equipment should be avoided because it could result in improper operation. Use of accessories other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

PRECAUTIONS
What precautions should patients be advised about?

Safety and Effectiveness for settings greater than 1.5 mm has not been evaluated.

Universal precautions are necessary during microneedling. Microneedling should not be used within the orbital rim of the eye, such as the eyelids.

The SkinPen Precision System has not be evaluated in the following patient populations (i.e. patients with the following conditions or taking the following medications): Actinic (solar) keratosis; active acne; collagen vascular diseases or cardiac abnormalities; diabetes; eczema, psoriasis and other chronic conditions in the treatment area or on other areas of the body; immunosuppressive therapy; history of contact dermatitis; raised moles in the treatment area; rosacea; active bacterial, fungal, or viral infections (i.e. herpes, warts); keloid scars (a scar that grows outside of the boundaries of an original scar); patients on anticoagulants; scars and stretch marks less than one year old; scleroderma; and wound-healing deficiencies.

SKINPEN® PRECISION CHARGING:
Ensure the charger base is plugged into an outlet and the SkinPen® Precision handpiece is placed onto the base with the power button facing up.

IMPORTANT: Keep dry.

PRE-PROCEDURE PRECAUTIONS
- Avoid excessive sun exposure/burns 24 hours prior to procedure.
- Discontinue use of topical retinoids 24 hours prior to procedure.
- Avoid treatment on patients with active breakouts or open lesions.
- Allow at least 24 hours after autoimmune therapies before a SkinPen® Precision treatment.
- Wait six months following oral isotretinoin use.
- Although not seen in the clinical study, in Fitzpatrick IV–VI, pigment may darken prior to lightening.

PROCEDURE INSTRUCTIONS
1. Have patient complete consent form.
2. Explain the SkinPen® procedure to the patient and set expectations.
3. Apply single use, non-latex gloves.
4. Cleanse patient's face with a gentle cleansing complex to effectively remove makeup, sunscreen and surface oils.
5. Take "before" pictures of the procedure area.
6. Open the SkinPen® Treatment Kit and remove all contents.
7. Apply the disposable BioSheath to the SkinPen®.
8. Install the cartridge onto SkinPen®.

***NOTE: The cartridge contains a lock-out feature and cannot be re-installed on the SkinPen® Precision device once removed. This safety feature ensures only a sterile single-use application.**

9. If a numbing agent was applied to provide patient comfort, the numbing agent must be removed from the skin with an antiseptic solution prior to the microneedling procedure.
10. Apply a thin layer of Skinfuse® Lift HG to protect the skin against abrasion and friction during the SkinPen® Precision treatment. If the layer is too thick the microneedle cartridge may become clogged.

Please refer to Skinfuse Lift HG instructions for additional details.

Note: if the patient is allergic to any of the following ingredients, which are in the Skinfuse Lift HG hydrogel: purified water, glycerin, carbomer, potassium hydroxide, disodium EDTA, phenoxythanol, caprylyl glycol, sorbic acid, SkinPen® Precision treatment may not be safe.

11. Ensure the needle is set to "0" before starting a new procedure.
12. Power on by pressing and holding the on/off button on the front of SkinPen® Precision for two seconds.
13. Adjust needle depth settings on the SkinPen® Precision cartridge. New settings will be indicated by a "click" into place.

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SKINPEN® IFU 10330009 Rev.A

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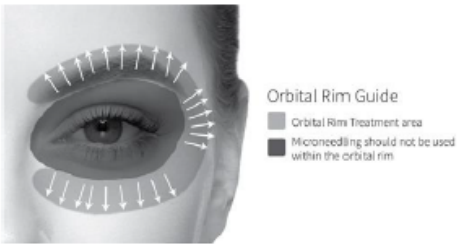
SkinPen® Precision Instructions for Use with SkinPen® Precision

14. Select SkinPen® Precision microneedle position based on patient needs. Start at a depth setting of 0.25mm. Increase in increments of 0.25 mm or 0.5mm until desired erythema is reached, with a maximum depth of 1.5 mm on the face. Lower to 0.25-0.5 mm to perform procedure around orbital rim.

Acne Scar Procedure Depth (Suggested Guidelines)	
Forehead (0.25-1.0 mm)	Nose (0.25-0.75 mm)
Around the Orbital Rim* (0.25-0.5 mm)	Facial Acne Scars (up to 1.5 mm)

*Note: treatment can be performed around but not within the orbital rim



15. Divide the face into four quadrants. Start with the right cheek, move to the chin/perioral/nose, then to left cheek, and finish with forehead.
16. Hold the skin taut and glide the pen in controlled horizontal motions.
    Repeat with vertical motions in the same area. Repeat the pattern if the erythema endpoint is not reached. Depth may be increased within guidelines if necessary. Gentle, one-directional circular motions in small targeted areas is acceptable if needed to assist in reaching the erythema endpoint.
17. For treatment of acne scar tissue, a needle depth of 1.5mm may be used on the face.

PLEASE NOTE: The SkinPen® Precision device allows for incremental increase in settings of up to 2.5 mm to allow for the variability in thickness of healthy skin and acne scar tissue. However, the device has not been clinically evaluated at cartridge settings of greater than 1.5 mm. As there are fine structures (i.e., nerve branches and accompanying blood vessels) that run under the skin and are essential to proper tissue function, it is not recommended to treat at needle depths greater than 1.5mm. It is essential that the thickness of the patient's skin in each anatomical area to be treated is assessed by a qualified clinician to address any potential risk of injuring these structures. Such structures include (but are not limited to) the supraorbital nerve (the terminal branch of the frontal nerve that provides the sensory innervations for the skin of the forehead, mucosa of frontal sinus, and the skin of the upper eyelid) and the temporal, buccal and marginal mandibular branches of the facial nerve (motor nerve that controls facial muscle movement). No adverse events were observed relating to such structures in the SkinPen® Precision clinical study when treating at needle depth of up to 1.5mm. Please refer to Bellus provided training module on superficial nerve and vessel facial anatomy for additional information.

NOTE: Microneedling should not be used within the orbital rim, such as the eyelids.

IMPORTANT: Microchannels created during the procedure may remain open up to 24 hours. NOTE: This product is not intended for transdermal (under the skin) delivery of cosmetics, drugs, or biologics.

Unexpected complications may occur when products not proven safe for use with microneedling are applied post-procedure.

POST PROCEDURE INSTRUCTIONS

1. Gently use sterile gauze to pat down the affected area.
2. Apply a generous layer of Skinfuse® Lift HG after the procedure.
3. Skinfuse® Lift HG may be applied additionally the day of the procedure to prevent the skin from drying out post procedure. The patient can re- apply, as needed, up to 24 hours post procedure.
4. Advise patient to avoid sweaty exercise and sun exposure for 72 hours post-procedure.
5. It is recommended to avoid other facial aesthetic treatments the month following the SkinPen Precision treatment.
6. Schedule next appointment after at least 4 weeks.
7. Take "after" pictures before next appointment.

How to remove the BioSheath and clean the SkinPen Precision Device:

- Hold the SkinPen Precision perpendicular to the floor, or with the cartridge attachment tip pointing downwards. Use one hand to remove the cartridge and dispose of the cartridge in a sharps container.

- Continue to hold the SkinPen Precision device perpendicular to the floor, with the cartridge tip pointed downwards, and pull apart the adhesive strip of the BioSheath.

- Remove the BioSheath by carefully rolling it down the SkinPen Precision to prevent soiling the handpiece.

- Dispose of the BioSheath in a biohazard container. BioSheaths are not intended to be reused.
- Disinfection of the SkinPen Precision should be completed with the use of Sani-Cloth HB® wipes, See section 9- Cleaning of SkinPen Precision and Charger Base.
- After removal of the BioSheath and disinfection with Sani-Cloth HB® wipes is performed, users' gloves should be removed, hands cleaned, and a new pair of clean gloves worn before proceeding to the next patient.

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SkinPen® Precision Instructions for Use with SkinPen® Precision

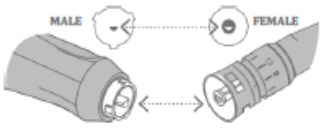
NOTE: Soiled gloves should always be disposed of in a biohazard container. Do not reuse disposable gloves.

NOTE: The purpose of a sheath is to provide a covering that helps prevent the transmission of pathogens from one patient to another. SkinPen Precision is intended to be used only with provided BioSheath.

How to install/uninstall disposable SkinPen® Precision cartridge:

- Ensure SkinPen® Precision is powered off.

- Open the cartridge package by holding it right- side up and pulling back the protective covering at the sealed chevron.
- Align the lock and key mechanism on the SkinPen® Precision microneedling cartridge and the SkinPen® Precision device.



- Start with the ▲ symbol to the right of the power indicator and rotate the cartridge left to align with the power indicator. The SkinPen® Precision cartridge is now secure.
- To remove the cartridge, rotate until the cartridge is removed.
- The SkinPen® Precision cartridge is designed for single use, with a lock-out feature prohibiting re- installation of the cartridge after use.

- Dispose of used SkinPen® Precision cartridge via a Sharps container.

*If a SkinPen® Precision Cartridge becomes inadvertently contaminated before or during installation (ie. Dropped on floor, open/broken package, needles subjected to possible contamination), discard, and obtain new SkinPen® Precision cartridge.

CLEANING OF SKINPEN® PRECISION HANDPIECE AND CHARGER BASE

#Ensure SkinPen® Precision device is powered off before cleaning, and that the SkinPen® Precision charger base is unplugged.

- The device should be cleaned while holding the SkinPen® facing straight down while wiping the rotary area. Do not clean near the seal.
- Sani-Cloth HB® wipes should be used to clean the SkinPen® after each procedure. Sani-Cloth HB® wipes may also be used to clean the SkinPen® Charger Base. Sani-Cloth HB wipes should be used to carefully wipe the SKINPEN® PRECISION for more than 1 minute, according to their directions for use, found on the Sani-Cloth HB® labeling. Attention should be paid to clean areas such as crevices, seams, and areas around where the SkinPen® Precision Cartridge attaches to the device.
- Sani-Cloth HB® wipes Directions for use: Special Instructions for Cleaning & Decontamination against HIV-1 and HBV of surfaces/objects soiled with blood/body fluids: Personal Protection: Specific barrier protection items to be used when handling items soiled with blood or body fluids are disposable latex gloves, gowns, masks, or eye coverings.
- CLEANING PROCEDURE: Blood and other body fluids must be thoroughly cleaned from surfaces and objects before application of the disinfectant.
- DISPOSAL OF INFECTIOUS MATERIALS: Blood and other body fluids should be autoclaved and disposed of according to federal, state and local regulations for infectious waste disposal.
- CONTACT TIME: Leave surfaces wet for 30 seconds and 10 minutes for HIV- 1 and HBV, respectively. Use the 10 minute contact time to mitigate other viruses, bacteria and fungi listed on the label.
- Do not immerse in liquids.
- Do not use solvents to clean device.

CLINICAL STUDY SUMMARY

A clinical study was conducted to support the safety and effectiveness of the SkinPen Precision System for the treatment of acne scars on the face.

The study was conducted at a single center and included treatments on day 1, day 30, and day 60, with follow-up visits at 1 month and 6 months after the final (day 60) treatment. Treatments were conducted by a trained aesthetician (skin care specialist). The face was cleaned and numbed prior to treatment. A thin layer of Skinfuse Lift HG was applied prior to treatment to protect against abrasion and friction during the procedure.
The aestheticians were instructed to start at the lowest depth setting and gradually increase the depth until erythema was observed, with a maximum depth of 1.5mm. The instructions included a precaution that microneedling was used around but not within the orbital rim. The face was divided into quadrants for treatment to ensure that all acne scars were treated. Following treatment, Skinfuse Lift HG was applied to prevent the skin from drying out post procedure.

A total of 41 subjects completed the study. Only 20 of these subjects were treated with the SkinPen Precision System. The other 21 subjects were treated with a prototype device. There are technological differences between the SkinPen Precision System and the prototype device, including a greater number of needles in the SkinPen Precision cartridge and faster motor speed in the SkinPen Precision device, which may affect the device

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effectiveness results. Therefore, the safety assessments collected for both treatment groups are included in the summary below. However, for the effectiveness results, only the data for the SkinPen Precision group was considered.

Subjects enrolled in the study included both men (31.7%) and women (68.3%) over the age of 21. The study included 11/41 subjects with Fitzpatrick Skin Type (FST) V and VI.

Table 3: Summary of Demographic Information

	SkinPen Precision System		All Subjects	
N	20		41	
Age (years)				
Mean (standard deviation)	43.8 (12.7)		44 (11.9)	
Minimum, Median, Maximum	23, 48, 60		21, 46, 60	
	N	(%)	N	(%)
Sex				
Male	7	35	13	31.7
Female	13	65	28	68.3
Ethnicity				
Hispanic or Latino	6	30	13	31.7
Not Hispanic or Latino	14	70	28	68.3
Race				
American Indian or Alaska Native	1	5	2	4.9
Asian	3	15	9	22.0
Black or African American	6	30	10	24.4
White	10	50	20	48.8
Fitzpatrick Skin Type				
II	2	10	3	7.3
III	4	20	10	24.4
IV	7	35	17	41.5
V	4	20	7	17.1
VI	3	15	4	9.8

At each clinical visit, digital images were taken of each subject's facial acne scars. On day 1, day 30, and day 60, imaging was performed prior to treatment. A total of 3 full-face images were collected. Images were also collected at the 1 month and 6 month follow-up visit. These images were graded by two separate Board Certified Dermatologists after completion of the study using the following assessment tools and timepoints [Table 4]. Details of each of these assessment tools are provided below in Tables 5-7. The results of the study are provided in Tables 8-12.

Table 4: Study Endpoints

Primary effectiveness endpoints	Acne Scar Assessment Scale graded by two blinded dermatologists using photographs taken at baseline, day 30, day 60, 1-month post-treatment, and 6-months post-treatment
	Clinician's Global Aesthetic Improvement Assessment graded by two blinded dermatologists using photographs taken at 1-month post-treatment, and 6-months post-treatment
Secondary effectiveness endpoints	Self-assessed Scar Improvement Scale completed by subjects at baseline, 1-month post-treatment, and 6-months post-treatment
	Subject Global Aesthetic Improvement Scale completed by subjects at baseline, 1-month post- treatment, and 6-months post-treatment
	Patient Satisfaction Questionnaire completed by subjects at 1-month post-treatment and 6-months post-treatment
Safety Endpoint	Subject safety diaries provided to the subject at each treatment visit (day 1, 30, and 60) and completed for 30 days to record treatment responses
	Adverse event monitoring at each visit; baseline, day 30, day 60, 1-month post-treatment, and 6-months post-treatment

The photo grading included the following effectiveness assessments:

- Acne Scar Assessment Scale[1]

Table 5: Acne Scar Assessment Scale

Grade	Term	Description
0	Clear	No depressions are seen in the treatment area. Macular discoloration may be seen.
1	Very mild	A single depression is easily noticeable with direct lighting (deep). Most or all of the depressions seen are only readily apparent with tangential lighting (shallow).
2	Mild	A few to several, but less than half of all the depressions are easily noticeable with direct lighting (deep). Most of the depressions seen are only readily apparent with tangential lighting (shallow).
3	Moderate	More than half of the depressions are apparent with direct lighting (deep).
4	Severe	All or almost all the lesions can be seen with direct lighting (deep).

[1]Jwala Karnik, Leslie Baumann, Suzanne Bruce, Valerie Callender, Steven Cohen, Pearl Grimes, John Joseph, Ava Shamban, James Spencer, Ruth Tedaldi, William Philip Werschler, Stacy R. Smith, "A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars" Journal of the American Academy of Dermatology 71(1):77-83 (2014).

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In addition to the clinician graded effectiveness measures, the following patient-reported measures were recorded throughout the study:

- Self-assessed Scar Improvement Scale

Table 6: Self-assessed Scar Improvement Scale

Rating	Description
-1	Exacerbation of Acne Scars
0	No change in appearance of acne scars
1	1% - 25% improvement in appearance of acne scars
2	25% - 50% improvement in appearance of acne scars
3	50% - 75% improvement in appearance of acne scars
4	75% - 99% improvement in appearance of acne scars

- Subject Global Aesthetic Improvement Scale

Table 7: Subject Global Aesthetic Improvement Scale

Rating	Description
1	**Very Much Improved:** Optimal cosmetic result.
2	**Much Improved:** Marked improvement in appearance from the initial condition, but not completely optimal.
3	**Improved:** Obvious improvement in appearance from initial condition.
4	**No Change:** The appearance is essentially the same as the original condition.
5	**Worse:** The appearance is worse than the original condition.

- Patient Satisfaction Questionnaire

Three questions were asked to the subjects in the study regarding their level of satisfaction with the treatment. It was included as a secondary endpoint in the study. See individual questions and results in the section below. Safety information was collected throughout the study using subject safety diaries. Safety diaries were provided to the subject at each treatment visit (day 1, 30, and 60). The subject was instructed to record any observations related to treatment including common treatment responses.

Common treatment responses are side effects that result from treatment which resolve on the order of days. Common treatment responses that persist may be categorized as adverse events when assessed by the investigator at the next visit. Subjects were informed of the following potential common treatment responses in the informed consent process: skin will be red and flushed similar to a moderate sunburn, skin tightness and mild sensitivity to the touch, redness, burning, tingling, stinging, itching, and/or scaling/ dryness, edema (swelling), tenderness/discomfort, a possibility of developing an infection (an increase in redness, warmth, itching, or pus formation). The diaries included space for daily recording of observations for the 30 days in between treatment visits. Adverse events were assessed by the investigator at each subsequent visit.

Results:

Safety:

At the 6-month post-treatment visit, no adverse events persisted.

The following common treatment responses were reported in the subject safety diaries which were sent home with the subject:

- Dryness in 5/41 (12%) subjects lasting from 1-6 days
  - o These responses were reported by 3 subjects with FST III, 1 subject with FST VI, and 1 subject with FST V
- Rough Skin in 3/41 (7%) of subjects lasting from 1-2 days
  - o These responses were reported by 1 subject with FST III, and 2 subjects with FST V
- Tightness in 2/41 (4%) of subjects lasting from 1-2 days
  - o These responses were reported by 2 subjects with FST VI
- Redness, Itching, Peeling Discomfort and Tenderness in 13/41 (31%) of subjects lasting 1-3 days
  - o These responses were reported by 6 subjects with FST III, 2 subjects with FST VI, 3 subjects with FST V, and 2 subjects with FST V
- Burning in 4/41 (9%) of subjects lasting 1-3 days
  - o These responses were reported by 1 subject with FST III, 1 subject with FST VI, and 2 subjects with FST V

Over the course of the study, 1 subject reported an arthropod bite on the inner right thigh that was determined to be moderate and unlikely related to SkinPen prototype device. 1 subject (1/41, 2.4%) experienced an AE (skin striae [linear marks, ridges, or grooves] on the forehead and both sides of the face) that was determined to be mild and possibly related to use of the SkinPen Precision System. This AE was thought to be due to subject exposure to excess sunlight soon after treatment which was against study instructions, yet resolved without any additional complications.

Effectiveness:

Acne Scar Assessment Scale:

Results of photo grading using the Acne Scar Assessment Scale demonstrated that at baseline the mean population score was mild at 2.80. Following the three treatments and 6 months of follow-up, the mean population score was reported as mild at 2.35.

The evaluation by the blinded assessors indicated that seven subjects (7/20, 35%) had a 1-grade reduction in the Acne Scar Assessment Scale at 6-months post-treatment compared to baseline. The seven subjects reporting a 1-grade reduction included 1 subject with FST II, 2 subjects with FST III, 1 subject with FST IV, 2 subjects with FST V, and 1 subject with FST VI.

In addition, 4 subjects (20%) showed an improvement greater than 0 but less than 1 on the Acne Scar Assessment Scale, giving a total of 55% (11/20) of subjects showing improvement at 6-months post-treatment when compared with baseline. At 6-months post-treatment, the remaining 9 subjects (45%) reported no change in score when compared to baseline. The visual improvements seen in the photo grading results were considered to be clinically meaningful.

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Table 8: Results of Photo Grading of Acne Scar Assessment Scale for SkinPen Precision System

Time Point	N	Mean	Standard Deviation	Minimum	Median	Maximum
Baseline	20	2.80	0.52	2.00	3.00	4.00
Day 30	20	2.78	0.57	2.00	2.75	4.00
Day 60	20	2.70	0.55	2.00	2.50	3.50
1-Month Post-Treatment	20	2.68	0.49	2.00	2.50	3.50
6-Months Post-Treatment	20	2.35	0.69	1.50	2.50	3.50

Table 9: Change from Baseline for Photo Grading of Acne Scar Assessment Scale for SkinPen Precision System

Time Point	N	Subject Improved (%)	Subject Worsened (%)	Mean Change	Standard Deviation for Change	Mean Change (%)
Day 30	20	30.0	20.0	-0.03	0.50	-0.9
Day 60	20	35.0	20.0	-0.10	0.50	-3.6
1-Month Post-Treatment	20	40.0	20.0	-0.13	0.58	-4.5
6-Months Post-Treatment	20	55.0	0.0	-0.45	0.46	-16.1

Self-assessed Scar Improvement Scale:

Treatment with SkinPen Precision produced an improvement in SASIS scores at 1-month post-treatment and 6-months post-treatment. At 1-month post-treatment, 17 (85%) subjects reported some percentage of improvement in the appearance of their acne scars, with 3 (15%) subjects reporting no change. At 6-months post-treatment, 18 (90%) subjects reported some percentage of improvement in the appearance of their acne scars, with 2 (10%) subjects reporting no change. The mean value for the population was = 1.65 and 1.70, at 1-month post-treatment and 6-months post- treatment respectively (1%-25% improvement in appearance of acne scars) when compared with a score of 0 (no change in appearance of acne scars). No subjects reported a negative score (i.e., exacerbation of acne scars) at either post-treatment timepoint.

Subject Global Aesthetic Improvement Scale:

Treatment with SkinPen Precision produced an improvement in SGAIS scores at 1-month post-treatment and 6 months post-treatment. At 1-month post-treatment, 7 (35%) subjects reported much improved, 9 (45%) subjects reported improved, and 4 (20%) subjects reported no change. At 6-months post-treatment, 2 (10%) subjects reported very much improved, 8 (40%) subjects reported much improved, 8 (40%) subjects reported improved, and 2 (10%) subjects reported no change. The mean value for the population was = 2.85 and 2.50, at 1-month post-treatment and 6-months post-treatment respectively (improved) when compared with a score of 4 (no change). No subjects reported a score of 5 (worse) at either post treatment timepoint.

Patient Satisfaction Questionnaire:

The results of the patient satisfaction questionnaire for all subjects indicated that a greater proportion of subjects selected favorable responses regarding treatments at 1 month and 6 months post-treatment for the following inquiries:

- Question 1: Do you notice any improvement in how your acne scars look in the treated area?

Table 10: Results of Patient Satisfaction Questionnaire - Question 1

Time Point	Yes [N (%)]	No [N, (%)]
1-Month Post-Treatment	16 (80.0)	4 (20.0)
6-Months Post-Treatment	18 (90.0)	2 (10.0)

- Question 2: How would you characterize your satisfaction with the treatment?

Table 11: Results of Patient Satisfaction Questionnaire – Question 2

Time Point	Extremely Satisfied [N (%)]	Satisfied [N (%)]	Slightly Satisfied [N (%)]	Neither Satisfied nor Dissatisfied [N (%)]
1-Month Post-Treatment	3 (15.0)	9 (45.0)	5 (25.0)	3 (15.0)
6-Months Post-Treatment	3 (15.0)	9 (45.0)	5 (25.0)	1 (5.0)

Time Point	Slightly Dissatisfied [N (%)]	Dissatisfied [N (%)]	Very Dissatisfied [N (%)]
1-Month Post-Treatment	0 (0.0)	0 (0.0)	0 (0.0)
6-Months Post-Treatment	1 (5.0)	1 (5.0)	0 (0.0)

- Question 3: Would you recommend this treatment to your friends and family members?

Table 12: Results of Patient Satisfaction Questionnaire – Question 3

Time Point	Yes [N (%)]	No [N, (%)]
1-Month Post-Treatment	18 (90.0)	2 (10.0)
6-Months Post-Treatment	18 (90.0)	2 (10.0)

For additional information refer to the SkinPen® Precision User Manual Rev.V2.0

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APPENDIX III: Subject Treatment Satisfaction Questionnaire:

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