ZIIP Acne Protocol
October 5, 2020

Evaluation of the Safety and Efficacy of an Acne Treatment Device

STUDY NUMBER	DCS-46-20
INVESTIGATOR	Zoe Diana Draelos, MD
STUDY SITE	Dermatology Consulting Services, PLLC 2444 North Main Street High Point, NC, 27262 **T** 336-841-2040 **F** 336-841-2044 zdraelos@northstate.net
INSTITUTIONAL REVIEW BOARD	Allendale Institutional Review Board (AIRB) 30 Neck Road Old Lyme, CT 06371 **T** 860-434-5872 **F** 860-434-5892
SPONSOR	ZIIP Inc.
INVESTIGATIONAL DEVICE	ZIIP Device
SPONSOR PRIMARY CONTACT	Jamie Rosen
STUDY DESIGN	Monadic device, historical control
VERSION NUMBER	6

PROTOCOL NUMBER: DCS-46-20

STUDY TITLE: Evaluation of the Safety and Efficacy of an Acne Treatment Device

PROTOCOL SYNOPSIS AND BUDGET DATE: August 1, 2020

PROTOCOL DATE: October 5, 2020

ANTICIPATED STUDY RUN DATES: TBD

ANTICIPATED FINAL REPORT DATE: TBD

This document represents the final approved protocol ready for IRB submission.

_____ _____

Representative Date
ZIIP

_____ _____

Zoe Diana Draelos, M.D. Date
Primary Investigator
Dermatology Consulting Services, PLLC

STUDY NUMBER **1**

1. PROTOCOL SYNOPSIS

Title of Study:	Evaluation of the Safety and Efficacy of an Acne Treatment Device
Study Period:	12 weeks
Test Device and Application Instructions:	ZIIP Device (active) -400 microamps direct current, applied 3 days per week on non-consecutive days, on all areas afflicted by acne The following instructions will be provided: 1. Both silver probes must come in contact with skin throughout treatment. 2. Slowly make continuous circles with the top probe (the one farthest away from the charging port) over acne within each facial zone. **NOTE: Instructional video will be provided for participants to follow** 3. Treat each facial zone for 1 minute. Your device will beep and vibrate at the one minute mark to indicate that treatment of that zone is complete. Only treat the acne zone(s) identified for treatment. 4. After treatment, wipe your device clean with a tissue, being careful to avoid the charging port. Spray the device and a second tissue lightly with rubbing alcohol and wipe again, remaining careful to avoid the charging port. 5. Store safely away from water, moisture or debris.
Ancillary Product and Application Instructions:	Electroconductive Media Apply as a thin layer to all facial areas afflicted with acne
Objective:	The objective of this study is to demonstrate the safety and efficacy of a novel direct current device employed in the treatment of mild to moderate inflammatory acne after 12 weeks of every other day use.
Design:	Male and female subjects will be enrolled in this single-site monadic study to evaluate the effect of a device on acne treatment. Subjects who sign the consent form and meet all inclusion criteria and none of the exclusion criteria will be enrolled at the baseline visit. Subjects will be asked to continue use of their self-selected moisturizer, non-medicated cleanser, and sunscreen they have used without difficulty for the prior 30 days and for the 12-week study. Subjects must also continue all facial products and cosmetics unchanged for the duration of the study. No other oral or topical acne products can be used. Subjects must be washed out of all topical acne products for at least 2 weeks and all oral acne products for at least 4 weeks prior to study participation. Subjects must possess mild to moderate acne with 5-30 inflammatory lesions and no nodules/cysts. At baseline visit, subjects will receive the study acne device to be applied to the areas of the face afflicted by acne following cleansing, every other day. The dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform

	an inflammatory and non-inflammatory lesion count. The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, & 4=severe). The subjects will assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, & 4=severe). Subjects will be given their diaries, study device, and electroconductive media and asked to return to the research center in 2 weeks. A reminder text will be sent to encourage compliance prior to the week 2 visit. Subjects will return to the research center at week 2, week 4, and week 8 for the same study activities as conducted at baseline. However, in addition a subject self-assessment marketing questionnaire provided by the sponsor will be administered. Subject diaries will be checked at each return visit for compliance and completion. Subjects will be re-dispensed electroconductive media as needed at each visit; and the devices will be inspected for continued functionality. Reminder texts will be sent prior to each visit to encourage compliance. Subjects will return to the research center at week 12 for the same study activities as conducted at baseline. Study diaries and devices will be checked and collected. Subjects will terminate their study participation at this time. All investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12. Subjects will be provided with the following device instructions: 1. Begin with clean, dry skin. 2. Inspect your skin and identify which zones of your face have acne. The four facial zones are divided as follows: 1) Upper Left, 2) Upper Right, 3) Lower Left, and 4) Lower Right. The zone(s) identified now will be treated throughout the study. 3. Liberally apply the conductive gel provided to you over each zone which has acne. 4. Turn on your device by pressing the button at the top. You will hear one beep. 5. Place the device on your skin. Lights will illuminate under the device when both silver probes come in contact with your skin. Both probes must keep contact with skin throughout treatment. 6. Slowly make continuous circles with the top probe (the one farthest away from the charging port) over acne within each facial zone. (You may feel a tingling sensation during treatment. That is normal.) 7. Treat each facial zone for 1 minute. Your device will beep and vibrate at the one minute mark to indicate that treatment of that zone is complete. Only treat the acne zone(s) identified for treatment. 8. At the end of treatment, your device will beep twice and turn off.

9. After treatment, wipe your device clean with a tissue, being careful to avoid the charging port. Spray the device and a second tissue lightly with rubbing alcohol and wipe again, remaining careful to avoid the charging port.
10. Store safely away from water, moisture or debris. After treatment, wipe your device clean with a tissue before putting it away.
11. Repeat treatment of the original acne zone(s) through the study. Perform treatments every other day for 12 weeks.
12. If any new areas of acne develop later in the study, you may also treat those additional zones until study completion. For example, if you have acne in the forehead and mouth zones at the start of the study, treat those two zones for every treatment. If additional acne develops on the left cheek later in the study, treat the left cheek zone in addition to the mouth and forehead zones for all remaining treatments

CHARGING:
When you see the orange light flashing while using your device, it's time to charge. To charge, plug in the charging cable provided. The orange light will remain illuminated while charging. You will know that your device is completely charged when the orange light is no longer on.

CONTRAINDICATIONS
ZIIP should not be used in the following areas
- Breast area
- Directly on top of the eyelid
- Midline of neck (bone of neck)
- Groin area
- Do not use this device on patients who have a cardiac pacemaker, implanted defibrillator, or other implanted metallic or electronic device because this may cause electric shock

WARNINGS
Do not submerge the device in water or any other liquid(s). If you store your ZIIP in an area such as a bathroom counter, ensure the product does not come in contact with water or other liquid(s).

ZIIP should not be used by:
• Children
• Pregnant Women
• People subject to seizures
• People with cancer/tumors
• People with a cardiac pacemaker
• People with implanted defibrillators/stimulators
• People with electronic implanted devices

If you have any medical concerns, such as a severe medical illness, epilepsy or seizures, or recent facial surgery, please consult your doctor before using ZIIP.

	Electronic monitoring equipment (such as ECG monitors and ECG alarms) may not operate properly when a ZIIP device is in use. Stimulation should not be applied over, or in proximity to cancerous lesions, or applied over swollen, infected, or inflamed areas or skin eruptions, e.g., phlebitis, thrombophlebitis, broken capillaries, varicose veins, etc. Men should shave before use as hair can interfere with the conductivity of the electrodes. Facial area under a beard or mustache cannot be treated. Do not apply stimulation across your chest as the introduction of electrical current into the chest may cause rhythm disturbances to your heart, which could be lethal. The long-term effects of stimulation are not known. *(There is an allowance for an unscheduled visit at any time, if necessary.)*
Study Population:	Healthy male and female subjects 18-50 years of age of all Fitzpatrick skin types with mild to moderate acne consisting of 5-30 inflammatory lesions and no nodules/cysts.
Number of Patients:	50 subjects
Inclusion Criteria:	1. Subjects with mild to moderate acne (5-30 inflammatory lesions and no nodules/cysts). 2. Male and female subjects age 18-50 years. 3. Subjects with all Fitzpatrick skin types. 4. Subjects of all complexion types (normal, oily, dry, combination). 5. Subjects who have used the same moisturizer without difficulty for 30 days and will continue using same moisturizer during the 12-week study. 6. Subjects agree not to introduce any new colored cosmetics (lipsticks, eye shadows, facial foundations, blush, or powder). 7. Subjects who are using no other acne products for the duration of the study. 8. No known medical conditions that, in the investigator's opinion, may interfere with study participation. 9. Women of childbearing potential must be willing to use a form of birth control during the study. For the purpose of this study, the following are considered acceptable methods of birth control: oral contraceptives, Norplant®, Depo-Provera®, double barrier methods (e.g., condom and spermicide) and abstinence. 10. Subjects have signed an Informed Consent Form in compliance with 21CFR, Part 50: "Protection of Human Subjects." 11. Subjects are dependable and able to follow directions and willing to comply with the schedule of visits. 12. Subjects in generally good physical and mental health.
Exclusion Criteria:	1. Any dermatological disorder, which in the investigator's opinion, may interfere with the accurate evaluation of the subject's skin characteristics, except for the study condition of acne.

	2. Subjects who are not willing to use the assigned study device to their face as instructed. 3. Subjects who have used any topical prescription or OTC acne products for 2 weeks prior to study entry. 4. Subjects who have taken any oral prescription or OTC acne products for 4 weeks prior to study entry. 5. Subjects who have used a non-OTC cleanser without benzoyl peroxide, sulfur or salicylic acid for at least 2 weeks prior to study entry. 6. Subject who have not had any facial treatments in the past 6 months and are willing to withhold all facial treatments during the course of the study including facials, facial peels, photo facials, laser treatments, dermabrasion, botulinum toxin (Botox), injectable filler treatments, intense pulsed light (IPL), acid treatments, tightening treatments, and/or facial plastic surgery. 7. Subjects who are pregnant, breast feeding or planning a pregnancy. 8. Subjects with clinically significant and/or unstable medical disorders. 9. Subjects who are unwilling or unable to comply with the requirements of the protocol. 10. Subjects who have a history of a psychological illness or condition that would interfere with their ability to understand and follow the requirements of the study. 11. Subjects who have undergone recent facial surgery. 12. Subjects currently participating in any other clinical trial. 13. Subjects having started hormone replacement therapies (HRT) or hormones for birth control less than 3 months prior to the study entry; or who plan on starting, stopping or changing doses of HRT or hormones for birth control during the study. 14. Subjects who have a cardiac pacemaker, implanted defibrillator, or other implanted metallic or electronic device. 15. Subjects who are wearing EKG monitoring equipment. 16. Subjects with phlebitis, thrombophlebitis, broken capillaries, or varicose veins. 17. Subjects who have seizures, epilepsy, or cancer/tumors. 18. Subjects who have a history of hypertrophic scarring or keloid formation.
Endpoints:	<u>Tolerability Endpoint:</u> The tolerability endpoint is the investigator-assessed absence of skin irritation from the facial study device at any time during the 12-week study. <u>Safety Endpoint:</u> The safety endpoint is the overall incidence of all adverse events reported during the study. <u>Efficacy Endpoint:</u> The efficacy endpoint is the investigator assessed improvement in investigator global assessment (IGA) after 12 weeks of every other day device use as compared to baseline.
Measures:	<u>Dermatologist Investigator assessed efficacy parameters</u>: Investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost

	clear, 2=mild, 3=moderate, and 4=severe. IGA assessments will be conducted at baseline, week 2, week 4, week 8, and week 12. Dermatologist Investigator lesion counts: inflammatory lesion count (papules, pustules), non-inflammatory lesion count (open comedones, closed comedones). Lesion counts will be conducted at baseline, week 2, week 4, week 8, and week 12. Dermatologist Investigator assessed tolerability parameters: peeling, dryness, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, & 4=severe) at baseline, week 2, week 4, week 8, and week 12. Self-assessment questionnaire: To be provided by sponsor. All assessments will be at week 2, week 4, and week 8, and week 12. Subject assessed tolerability parameters: itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, & 4=severe) at baseline, week 2, week 4, and week 8, and week 12. Photography: all investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.
Statistical Methods:	Along with descriptive statistics (means, standard deviations and percentages), investigator and subject ordinal nonparametric data will be analyzed using the Wilcoxon signed rank test. Acne lesion counts will be assessed using a Student t test. Change will be considered significant at a p value of less than or equal to 0.05.

2. STUDY VISIT SCHEDULE

Procedures	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
	BL	Week 2	Week 4	Week 8	Week 12
Informed Consent Procedure	X				
Inclusion/Exclusion Criteria	X				
Brief Medical History and Concomitant Medications Review	X	X	X	X	X
Investigator Clinical Grading for Tolerability	X	X	X	X	X
Investigator Clinical Facial Grading (IGA)	X	X	X	X	X
Investigator Acne Lesion Counts	X	X	X	X	X
Subject Clinical Grading for Tolerability	X	X	X	X	X
Subject Self Assessment Questionnaire		X	X	X	X
Photography	X	X	X	X	X
Dispense electroconductive media	X	X	X	X	
Device Check/Dispensing	X	X	X	X	
Subject Diary Assessment and Compliance Check		X	X	X	X
Subject Device Accountability and Study Completion					X

3. INTRODUCTION

Acne is a disease that affects individuals of all ages. 85% of Americans 12-24 years of age have acne and epidemiological studies show a similar prevalence in other countries. The etiology of acne is multifaceted, involving abnormal follicular hyperkeratizination, increased sebum production; follicular colonization by *C. acnes*, and inflammation. Hyperkeratinization induced microcomedone formation is the first step in acne lesion formation. As keratinocytes and sebum continue to accumulate, a visible non-inflammatory comedone lesion forms. The continued proliferation of *C. acnes* within the follicle results in follicular wall rupture and eventual formation of an inflammatory papule or pustule. Successful treatment of acne involves interrupting this sequence of events. This research examines the ability of a novel device to treat acne.

4. STUDY OBJECTIVE

The objective of this study is demonstrate the safety and efficacy of a novel direct current device in the treatment of mild to moderate inflammatory acne after 12 weeks of every other day use.

5. STUDY DESIGN OVERVIEW

Male and female subjects will be enrolled in this single-site monadic study to evaluate the effect of a direct-current device on acne treatment. Subjects who sign the consent form and meet all inclusion criteria and none of the exclusion criteria will be enrolled at the baseline visit. Subjects will be asked to continue their self-selected moisturizer, non-medicated cleanser, and sunscreen they have used without difficulty for the prior 30 days and for the 12 week study. Subjects must also continue all facial products and cosmetics unchanged for the duration of the study. No other oral or topical acne products can be used. Subjects must be washed out of all topical acne products for at least 2 weeks and all oral acne products for at least 4 weeks. Subjects must possess mild to moderate acne with 5-30 inflammatory lesions and no nodules/cysts.

At baseline visit, subjects will receive the study acne device to be applied to the areas of the face afflicted by acne following cleansing, every other day. The dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform an inflammatory and non-inflammatory lesion count. The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, & 4=severe).

The subjects will assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, & 4=severe). Subjects will be given their diaries, study device, and electroconductive media and asked to return to the research center in 2 weeks. A reminder text will be sent to encourage compliance prior to the week 2 visit.

Subjects will return to the research center at week 2, week 4, and week 8 for the same study activities as conducted at baseline. However, in addition, a subject self-assessment marketing questionnaire provided by the sponsor will be administered. Subject diaries will be checked at each return visit for compliance and completion. Subjects will be re-dispensed electroconductive media gel at each visit and the devices will be inspected for any problems. Reminder texts will be sent prior to each visit to encourage compliance.

Subjects will return to the research center at week 12 for the same study activities as conducted at baseline. Study diaries and devices will be checked and collected. Subjects will terminate their study participation at this time.

20 investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.

6. STUDY POPULATION

6.1 NUMBER OF SUBJECTS

50 subjects enrolled

6.2 SUBJECT CHARACTERISTICS

Healthy male and female subjects 18-50 years of age of all Fitzpatrick skin types with mild to moderate acne consisting of 5-30 inflammatory lesions and no nodules/cysts

6.3 INCLUSION CRITERIA

The following items represent the inclusion criteria:

1. Subjects with mild to moderate acne (5-30 inflammatory lesions and no nodules/cysts).
2. Male and female subjects age 18-50 years.
3. Subjects with all Fitzpatrick skin types.
4. Subjects of all complexion types (normal, oily, dry, combination).
5. Subjects who have used the same moisturizer without difficulty for 30 days and will continue using same moisturizer during the 12 week study.
6. Subjects agree not to introduce any new colored cosmetics (lipsticks, eye shadows, facial foundations, blush, & powder).
7. Subjects who are using no other acne products for the duration of the study.
8. No known medical conditions that, in the investigator's opinion, may interfere with study participation.
9. Women of childbearing potential must be willing to use a form of birth control during the study. For the purpose of this study, the following are considered acceptable methods of birth control: oral contraceptives, Norplant®, Depo-Provera®, double barrier methods (e.g., condom and spermicide) and abstinence.
10. Subjects have signed an Informed Consent Form in compliance with 21CFR, Part 50: "Protection of Human Subjects."
11. Subjects are dependable and able to follow directions and willing to comply with the schedule of visits.

12. Subjects in generally good physical and mental health.

6.4 EXCLUSION CRITERIA

The following items represent the exclusion criteria:

1. Any dermatological disorder, which in the investigator's opinion, may interfere with the accurate evaluation of the subject's skin characteristics, except for the study condition of acne.
2. Subjects who are not willing to use the assigned study device to their face as instructed.
3. Subjects who have used any topical prescription or OTC acne products for 2 weeks prior to study entry.
4. Subjects who have taken any oral prescription or OTC acne products for 4 weeks prior to study entry.
5. Subjects who have used a non-OTC cleanser without benzoyl peroxide, sulfur or salicylic acid for at least 2 weeks prior to study entry.
6. Subject who have not had any facial treatments in the past 6 months and are willing to withhold all facial treatments during the course of the study including facials, facial peels, photo facials, laser treatments, dermabrasion, botulinum toxin (Botox), injectable filler treatments, intense pulsed light (IPL), acid treatments, tightening treatments, and/or facial plastic surgery.
7. Subjects who are pregnant, breast feeding or planning a pregnancy.
8. Subjects with clinically significant and/or unstable medical disorders.
9. Subjects who are unwilling or unable to comply with the requirements of the protocol.
10. Subjects who have a history of a psychological illness or condition that would interfere with their ability to understand and follow the requirements of the study.
11. Subjects who have undergone recent facial surgery.
12. Subjects currently participating in any other clinical trial.
13. Subjects having started hormone replacement therapies (HRT) or hormones for birth control less than 3 months prior to the study entry; or who plan on starting, stopping or changing doses of HRT or hormones for birth control during the study.
14. Subjects who have a cardiac pacemaker, implanted defibrillator, or other implanted metallic or electronic device.
15. Subjects who are wearing EKG monitoring equipment.
16. Subjects with phlebitis, thrombophlebitis, broken capillaries, or varicose veins.
17. Subjects who have seizures, epilepsy, or cancer/tumors.
18. Subjects who have a history of hypertrophic scarring or keloid formation.

6.5 CONCOMITANT MEDICATIONS

All oral and topical prescription medications should remain unchanged during the study. No oral or topical over the counter or prescription acne medications are allowed. No other acne products other than the study products are allowed during the study.

7. CONDUCT OF STUDY: METHODS AND PROCEDURES

7.1 ENROLLMENT

7.1.1 INFORMED CONSENT

A signed informed consent form shall be obtained from each subject prior to study enrollment and performing any study procedures. No study related procedures or activities shall be performed until each subject is fully informed and the consent form is signed and dated.

7.1.2 MEDICAL HISTORY

An abbreviated medical history including current medications shall be recorded.

7.1.3 DERMATOLOGICAL EXAMINATION

A dermatological examination shall be performed to insure subjects possess acne and meet all inclusion criteria and none of the exclusion criteria.

7.1.4 STUDY PROCEDURES

The subjects will be screened for the inclusion and exclusion criteria prior to study enrollment. Only subjects who meet all the requirements, have signed an informed consent, and have given a medical history shall be entered into the study. All other subjects shall be considered screening failures.

7.1.5 STUDY MATERIAL ADMINISTRATION

All subjects will use the active ZIIP device as currently marketed. The ZIIP Device will be customized for the delivery of acne treatment with -400 microamps direct current, applied 3 days per week on non-consecutive days, on each facial zone afflicted by acne. A electroconductive media will be applied to each facial zone afflicted by acne prior to initiation of the device treatment.

7.1.6 SCREENING PROCEDURES

Potential volunteers will be enrolled based on the presence of mild to moderate acne and their ability to meet the inclusion/exclusion criteria required for study enrollment.

7.2 STUDY CONDUCT PROCEDURES

7.2.1 BASELINE

Male and female subjects will be enrolled in this single-site monadic study to evaluate the effect of a direct current device on acne treatment. Subjects who sign the informed consent form and meet all inclusion criteria and none of the exclusion criteria will be enrolled at the baseline visit. Subjects will be asked to continue their self-selected moisturizer, nonmedicated cleanser, and sunscreen they have used without difficulty for the prior 30 days and for the 12 week study. Subjects must also continue all facial products and cosmetics unchanged for the duration of the study. No other oral or topical acne products can be used. Subjects must be washed out of all topical acne products for at least 2 weeks and all oral acne products for at least 4 weeks. Subjects must possess mild to moderate acne with 5-30 inflammatory lesions and no nodules/cysts.

At baseline visit, the dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform an inflammatory and noninflammatory lesion count within each facial quadrant (zone). The subjects will then be provided the study device and electroconductive media for every other day use after cleansing to the acne afflicted facial zones. The first use of the device will occur at the research center to ensure all subjects are using the device properly.

The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will then assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). Subjects will be given their diaries and asked to return to the research center in 2 weeks. A reminder text will be sent to encourage compliance prior to the week 2 visit.

All investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.

7.2.2 WEEK 2

At the week 2 visit, the dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform an inflammatory and noninflammatory lesion count within each facial quadrant. The study device

will be inspected for proper operation and the study diary will be inspected for compliance.

The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will then assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will also complete a sponsor provided marketing questionnaire. Subjects will be asked to return to the research center at week 4. A reminder text will be sent to encourage compliance prior to the week 4 visit.

All investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.

7.2.3 WEEK 4

At the week 4 visit, the dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform an inflammatory and noninflammatory lesion count within each facial quadrant. The study device will be inspected for proper operation and the study diary will be inspected for compliance.

The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will then assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will also complete a sponsor provided marketing questionnaire. Subjects will be asked to return to the research center at week 8. A reminder text will be sent to encourage compliance prior to the week 8 visit.

All investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.

7.2.4 WEEK 8

At the week 8 visit, the dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform an inflammatory and

noninflammatory lesion count within each facial quadrant. The study device will be inspected for proper operation and the study diary will be inspected for compliance.

The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will then assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will also complete a sponsor provided marketing questionnaire. Subjects will be asked to return to the research center at week 12. A reminder text will be sent to encourage compliance prior to the week 12 visit.

All investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.

7.2.5 WEEK 12

At the week 12 visit, the dermatologist investigator will assess the face for the investigator global acne assessment (IGA) based on the following 5 point ordinal scale: 0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe. In addition, the dermatologist investigator will perform an inflammatory and noninflammatory lesion count within each facial quadrant. The study device will be inspected for proper operation and the study diary will be inspected for compliance. The diary and the study materials will be collected.

The dermatologist investigator will assess the tolerability of the device in terms of peeling, dryness, redness, and swelling on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will then assess device tolerability in terms of itching, burning, redness, and swelling. All assessments will be made on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, and 4=severe). The subjects will also complete a sponsor provided marketing questionnaire. Subjects will complete their study participation at this time.

All investigator selected subjects will be photographed with the Canfield VISIA CR using Standard 1 lighting at baseline, week 2, week 4, and week 8, and week 12.

8. EFFICACY MEASURES

8.1 SUBJECT COMPLIANCE

Compliance will be determined from the diary sheets. Subjects will record device and electroconductive media application and any comments on the

provided weekly diary. Diary sheets will remain at the study center as part of the source documentation records.

9. FINAL SUBJECT STATUS

A study termination form will be completed for each study subject who receives study product. This includes subjects who completed the study or who withdrew or were withdrawn from study.

9.1 COMPLETED, DISCONTINUED OR INCOMPLETE SUBJECTS

A completed subject is a subject who has satisfied all study entry criteria and completed the 12-week study. For any subject who has started study and terminated from the study prematurely, every effort will be made to obtain final evaluations of clinical status. Reasonable effort will be made to contact any subject lost to follow-up during the course of the study in order to complete assessments and retrieve any outstanding data and clinical supplies. The investigator will choose the description that best describes the status of the subject at termination.

1. Subject completed the 12 week study period

OR INCOMPLETE/DISCONTINUED DUE TO:

2. Contact dermatitis
3. Adverse experience
4. Serious adverse experience
5. Pregnancy
6. Protocol violation
7. Subject withdrew consent
8. Subject lost due to follow-up issues (e.g., attendance issues)
9. Other (provide reason)

10. STUDY PRODUCTS & ADMINISTRATION

10.1 FORMULATIONS

The study will consist of the ZIIP device programmed for the treatment of acne and the electroconductive media

10.2 PRECAUTIONS

Study products should be used as instructed and not orally consumed or placed in the eyes or around the orbital area of the eye. The device should be used as described below:

1. Begin with clean, dry skin.
2. Apply the conductive medium provided to you liberally over any areas where you have acne.
3. Turn on your device by pressing the button at the top. You will hear one beep.
4. Place the device on top of your skin. Lights will illuminate under the device when both silver probes come in contact with your skin. Both probes must keep contact with skin throughout treatment.
5. Follow along with the video, slowly making circles with the top probe (the one farthest away from the charging port) over acne within each zone. (You may feel a tingling sensation during treatment. That is normal.)
6. Do not treat a single spot more than one minute at a time. Only treat the facial zones identified for treatment.
7. At the end of treatment, your device will beep twice and turn off.
8. After treatment, wipe your device clean with a tissue, being careful to avoid the charging port. Spray the device and a second tissue lightly with rubbing alcohol and wipe again, remaining careful to avoid the charging port.
9. Store safely away from water, moisture or debris.

CHARGING:
When you see the orange light flashing while using your device, it's time to charge.
To charge, plug in the charging cable provided. The orange light will remain illuminated while charging. You will know that your device is completely charged when the orange light is no longer on.

CONTRAINDICATIONS
ZIIP should not be used in the following areas
- Breast area
- Directly on top of the eyelid
- Midline of neck (bone of neck)
- Groin area
- Do not use this device on patients who have a cardiac pacemaker, implanted defibrillator, or other implanted metallic or electronic device because this may cause electric shock

WARNINGS
Do not submerge the device in water or any other liquid(s). If you store your ZIIP in an area such as a bathroom counter, ensure the product does not come in contact with water or other liquid(s).

ZIIP should not be used by:
• Children
• Pregnant Women
• People subject to seizures
• People with cancer/tumors

- People with a cardiac pacemaker
- People with implanted defibrillators/stimulators
- People with electronic implanted devices

If you have any medical concerns, such as a severe medical illness, epilepsy or seizures, or recent facial surgery, please consult your doctor before using ZIIP.

Electronic monitoring equipment (such as ECG monitors and ECG alarms) may not operate properly when a ZIIP device is in use.

Stimulation should not be applied over, or in proximity to cancerous lesions, or applied over swollen, infected, or inflamed areas or skin eruptions, e.g., phlebitis, thrombophlebitis, broken capillaries, varicose veins, etc. Men should shave before use as hair can interfere with the conductivity of the electrodes. Facial area under a beard or mustache cannot be treated.

Do not apply stimulation across your chest as the introduction of electrical current into the chest may cause rhythm disturbances to your heart, which could be lethal.

The long-term effects of stimulation are not known.

10.3 STUDY PRODUCT ADMINISTRATION

Subjects will use the acne device for applied 3 days per week on non-consecutive days, on all facial zones afflicted by acne. The electroconductive media will be applied to the face prior to the use of the device. The following instructions will be provided:

1. Both silver probes must come in contact with skin throughout treatment.
2. Slowly make continuous circles with the top probe (the one farthest away from the charging port) over acne within each facial zone.

NOTE: Instructional video will be provided for participants to follow

3. Treat each facial zone for 1 minute. Your device will beep and vibrate at the one minute mark to indicate that treatment of that zone is complete. Only treat the acne zone(s) identified for treatment.
4. After treatment, wipe your device clean with a tissue, being careful to avoid the charging port. Spray the device and a second tissue lightly with rubbing alcohol and wipe again, remaining careful to avoid the charging port.
5. Store safely away from water, moisture or debris.

10.4 PACKAGING, LABELING, DISTRIBUTION

Study products will be dispensed in the packaging provided by the sponsor.

10.5 STORAGE AND ACCOUNTABILITY OF STUDY PRODUCT

The study product will be stored at room temperature, away from sunlight, in a locked, limited access area at the study site. Access to the study product will be limited to the investigator and staff members designated to dispense study medication. A study product log will be used to record the dispensation and return of all study products. The subject number/initials, and the initials and date of the person dispensing and receiving the returned study product will be documented on this form.

10.6 CODE DISCLOSURE

The study coordinator will not develop a code as all subjects will use the active device and electroconductive media in this monadic study.

11. ADVERSE EVENTS

11.1 ADVERSE REACTIONS PREVIOUSLY REPORTED

The study product has been reported to rarely produce skin irritation.

11.2 ADVERSE EXPERIENCES

An adverse experience is defined as any untoward medical occurrence (sign, symptom or laboratory finding), regardless of severity and whether or not attributed to the study product.

The investigator/coordinator will report all adverse experiences (AEs) that occur throughout the study. All AEs will be recorded in the appropriate AE log. The report will include: date of onset, a description of the AE, severity, seriousness, action taken, relationship to the study drug, outcome of the event, and date of resolution.

11.2.1 ASSESSMENT OF SEVERITY

The intensity or severity of an AE is characterized as:
Mild: AE which is easily tolerated.
Moderate: AE sufficiently discomforting to interfere with daily activity.
Severe: AE which prevents normal daily activities.

Subjects who are withdrawn from the study due to any AE will be followed by the investigator until the outcome is determined. The investigator will summarize and document all information relating to the AE and follow up.

11.2.2 RELATIONSHIP TO STUDY PRODUCT

The relationship is characterized as:

Not Related - applies to any adverse experience that is clearly not related to use of the study product.
Possible - means the association of the adverse experience with the study product is unknown; however, a relationship between study product and experience cannot be ruled out.
Probable - there is a reasonable temporal relationship between the use of the study product and the adverse experience. Based upon the investigator's clinical experience, the association of the event with the study product seems likely.
Definite - The AE occurs following the application of the study product and it cannot be reasonably explained by any other known characteristics of the subject's clinical state, environmental or toxic factors, or other modes of therapy administered to the subject. It disappears or decreases upon discontinuation of the study product and reappears on a re-challenge of the study product.

11.3 SERIOUS ADVERSE EVENTS

Definition: An SAE is defined as any adverse experience occurring that results in any of the following outcomes:

1. death
2. immediately life-threatening illness
3. hospitalization (> 24 hours) or prolongation of existing hospitalization
4. a persistent or significant disability
5. a congenital anomaly/birth defect
6. "other" important medical event

These are not anticipated, however, should an SAE occur, the primary investigator (Zoe Diana Draelos, MD) will immediately notify the sponsor. The sponsor will provide instructions as to how to report the SAE to the FDA.

12. STATISTICAL METHODS

The statistical evaluation will be performed by Dermatology Consulting Services. Along with descriptive statistics (means, standard deviations and percentages), investigator and subject ordinal nonparametric data will be analyzed using the Wilcoxon signed rank test. Acne lesion counts will be assessed using a Student t test. Change will be considered significant at a p value of less than or equal to 0.05.

12.1 SAMPLE SIZE RATIONALE

A sample size of 50 study subjects was chosen by the study sponsor.

12.2 SIGNIFICANCE LEVEL

Significance is defined at the $p<0.05$ level based on a two-sided test.

12.3 TOLERABILITY ASSESSMENT

Subjects who discontinue will be queried as to any side effects experienced by the study products. The tolerability endpoint is the investigator-assessed absence of skin irritation from the facial study device at any time during the 12-week study.

12.4 SAFETY ASSESSMENT

Incidence of all adverse events reported during the study will be summarized. Tabulated summaries will include adverse events grouped by relation to study product. The safety endpoint is the absence of significant adverse reactions.

12.5 EFFICACY ASSESSMENT

The efficacy endpoint is the investigator assessed improvement in investigator global assessment (IGA) after 12 weeks of every other day device use as compared to baseline.

13. ETHICS

13.1 INFORMED CONSENT

The principles of Informed Consent, according to FDA Regulations and ICH step 5 guidelines on GCPs, will be followed.

Subjects must provide written informed consent prior to any study procedures being completed. Each subject's signed informed consent must be kept on file by the Investigator for Regulatory Authorities' inspection at any time. A copy of the signed and dated consent form will be given to the subject.

13.2 INSTITUTIONAL REVIEW BOARD (IRB)

The study will be submitted to an IRB selected by Dermatology Consulting Services for approval to insure the safety of the human subjects enrolled in the study.

13.3 SUBJECT CONFIDENTIALITY

All participants are concerned for the individual subject's privacy and, therefore, only a subject identification number and subject initials will identify all subject data. However, in compliance with federal guidelines regarding the monitoring of clinical studies and in fulfillment of his/her obligations to the Sponsor, it is required that the Investigator permit the study monitor and/or FDA representative

to review that portion of the subject's medical record that is directly related to the study. This shall include all study relevant documentation including subject medical histories to verify eligibility, laboratory test result reports to verify transcription accuracy, admission/discharge summaries for hospital stays occurring while the subject is enrolled in the study, and autopsy reports for deaths occurring during the study.

As part of the required content of informed consent, the subject must be informed that his/her medical chart may be reviewed by the sponsor, the Sponsor's authorized representative, or a representative of the FDA. Should access to the medical record require a separate waiver or authorization, it is the investigator's responsibility to obtain such permission from the subject in writing before the subject is entered into the study. All subjects will sign a HIPAA document as part of the informed consent.

14. DOCUMENTATION

14.1 SITE DOCUMENTS REQUIRED FOR INITIATION

Prior to the initiation of the study, the following items must be received:

a) Sponsor approval of study
b) Current curriculum vitae of the Investigators
c) Copy of Principal Investigator's Medical license
d) A signed copy of the protocol Investigator's Agreement page
e) Original Non-Disclosure Agreement
f) Signed Budget Agreement
g) Approved FDA Investigational Device Exemption

14.2 STUDY DOCUMENTS SUPPLIED BY THE SPONSOR

Dermatology Consulting Services will provide all study documents.

14.3 MAINTENANCE AND RETENTION OF RECORDS

The study will be conducted according to Good Clinical Practices as outlined in ICH step 5 guidelines by the Food and Drug Administration. It is the responsibility of the Investigator to maintain a comprehensive and centralized filing system of all relevant documentation.

Investigators will be instructed to retain all study records required by the sponsor, as well as the regulations, in a secure and safe facility with limited access. Regulations require retention for a period of at least two years after last marketing approval and notification from the sponsor. These regulatory documents should be retained for a longer period if required by local regulatory requirements.

Archiving of data - Copies of all pertinent records will be retained by the investigator for at least two years following final approval of the drug and/or notification from the sponsor. These records include documents pertaining to the receipt and return of drug supplies, IRB, Informed Consent, as well as final signed case report forms. No documents shall be transferred from the site or destroyed without first notifying the sponsor. The sponsor will archive the data for the lifetime of the product.

14.3.1 CASE REPORT FORMS (CRF)

CRFs for individual subjects will be provided and completed by Dermatology Consulting Services, as appropriate. CRFs must be legible and complete.

A CRF must be completed and signed by the investigator for each subject enrolled, including those removed from the study for any reason. The reason for removal must be noted on the study conclusion CRF by the investigator for each subject. CRFs must be kept current to reflect the subject's status at each phase during the course of the study. Subjects are not to be identified on CRFs by name; appropriately coded identification and the subject's initials must be used. The investigator must keep a separate log of the subject's names and addresses.

The research site will maintain the following documents:

1. Subject Screening Log: This log will reflect the reason any subject screened for the study was found to be ineligible.
2. Study Personnel Signature Log: This log will contain all site personnel along with their responsibilities and signatures. This log will be maintained at the site throughout the study.
3. Monitoring Log: This log will contain the date and purpose of all monitoring visits by the Sponsor.
4. Enrollment Log: This log will contain subject initials and start and end dates for all subjects enrolled.
5. Product Inventory / Packing Slip Log: This log will reflect the total amount of study product shipped to the site and received and signed for by the Investigator.
6. Product Accountability Log: This log will reflect the total amount of study product dispensed to and returned by each subject.

14.3.2 MONITORING

A Sponsor appointed representative, if desired will monitor the study.

14.4 PRIMARY SOURCE DOCUMENTS

Dermatology Consulting Services will not maintain source documents for this study. Final case report forms (CRFs) will be maintained as study documentation.

14.5 PROTOCOL MODIFICATION

The procedures defined in the protocol and in the CRF will be carefully reviewed to ensure that all parties involved with the study fully understand the protocol. In order to ensure the validity of the data, no deviations from the protocol may be made unless the issue is broad enough to warrant revision of the protocol. Such revisions must be submitted to and have approval in writing from the Sponsor and the IRB prior to implementation.

14.6 AUDITS/INSPECTIONS

During the course of the study and/or after it has been completed, one or more site visits may be undertaken by auditors as authorized representatives of the Sponsor.

15. USE OF INFORMATION AND PUBLICATION

15.1 CONFIDENTIAL INFORMATION

All information supplied by the Sponsor in connection with this study and not previously published, is considered confidential information. This information includes, but is not limited to, the clinical protocol, case report forms, and other scientific data. Any data collected during the study is considered confidential. This confidential information shall remain the sole property of the Sponsor, shall not be disclosed to others without written consent of the Sponsor, and shall not be used except in the performance of the study.

The information developed during the conduct of this clinical study is also considered confidential, and will be used by the Sponsor in connection with the development of the study product. The information may be disclosed as deemed necessary by Sponsor. To allow the use of the information derived from this clinical study, the investigator is obliged to provide the Sponsor with complete test results and all data developed in this study. The information obtained during this study may be made available to other investigators who are conducting similar studies with express written consent/agreement from sponsor.

Should the investigator wish to publish the results of this study, the investigator agrees to provide the Sponsor with a manuscript for review 60 (sixty) days prior to submission for publication. The Sponsor retains the right to delete from the manuscript confidential information and to prevent publication or modify its timing.

In the event the Sponsor chooses to publish the data from this study a copy will be provided to the investigator at least 30 days prior to the expected date of submission to the intended publisher.

INVESTIGATOR'S AGREEMENT

I have carefully read the foregoing protocol and agree that it contains all the necessary information for conducting this study safely. I will conduct this study in strict accordance with this protocol, Good Clinical Practices, and local regulatory guidelines, and will attempt to complete the study within the time designated. I will provide copies of the protocol and all other information relating to pre-clinical and prior clinical experience submitted by the Sponsor to all personnel responsible to me who participate in the study. I will discuss this information with them to assure that they are adequately informed regarding the study product and conduct of the study. I agree to keep records on all subject information (case report forms, shipment and drug return forms and all other information collected during the study) in accordance with FDA regulations.

_____ _____

Principal Investigator's Signature Date