PROTOCOL

PROTOCOL TITLE:	A 28-Day, Single-Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages
PROTOCOL NUMBER:	CCSTOH001689
VERSION & DATE:	**Amendment 3: Final Version 4.0, 28 Aug 2019** Amendment 2: Final Version 3.0, 20 Aug 2019 Amendment 1: Final Version 2.0, 12 Aug 2019 Original: Final Version 1.0, 10 Jul 2019
SPONSOR:	Johnson & Johnson Consumer Inc. 199 Grandview Road, Skillman, NJ 08558 USA
STUDY SITE:	[redacted] Thomas J. Stephens & Associates, Inc., Dallas Research Center 1801 N. Glenville Dr., Suite 200 Richardson, Texas 75081 USA [redacted]
PRINCIPAL INVESTIGATOR (PI):	Lily Jiang, Ph.D. Address: Refer to Study Site address
SUB INVESTIGATOR (SUB-I):	[redacted]
STUDY PHYSICIAN/SUB INVESTIGATOR (SUB-I):	[redacted]
STUDY MANAGER (SM):	[redacted]
STUDY DIRECTOR:	Robin Mathew, Ph.D. Address: Refer to Sponsor address
DEPARTMENT HEAD:	[redacted]
HEAD OF CLINICAL RESEARCH:	[redacted]
DESIGNATED PHYSICIAN REPRESENTATIVE (DPR):	[redacted]

The principles of the International Council for Harmonisation (ICH) Guidelines for Good Clinical Practice (GCP E6 (R2)) will be applied to this study.

VERSION TRACKING

VERSION	DATE	STATE	REASON FOR CHANGE	DESCRIPTION OF CHANGE
1	10 Jul 2019	Obsolete	N/A - new protocol	N/A
2	12 Aug 2019	Obsolete	Change the type of reinforcement tape used, correct SAE definition 2, correct question #4 and completion timing for Day 0 of the Self-Assessment Questionnaire, correct Screen Failure language, and clarify a few procedures in section 7 to match the Schedule of Events in Table 2.	See Summary of Changes in Appendix VIII.
3	20 Aug 2019	Obsolete	[redacted]	See Summary of Changes in Appendix IX.
4	28 Aug 2019	Issued	Continue clinical grading of wound healing parameters until Day 16 for all wound sites.	See Summary of Changes in Appendix X.

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SYNOPSIS

<table>
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<tr><td>STUDY PHYSICIAN/SUB-INVESTIGATOR (SUB-I):</td><td>[redacted]</td></tr>
<tr><td>OBJECTIVE</td><td>The objective of this study is to assess the wound healing efficacy (time to complete healing) of different adhesive bandages.</td></tr>
<tr><td>STUDY DESIGN</td><td>Single center, randomized, comparator-controlled, proof-of-principle clinical trial.</td></tr>
<tr><td>STUDY POPULATION</td><td>Healthy subjects who meet the eligibility criteria, including:
Males or females, 25 – 55 years old.
Fitzpatrick Skin Types II-III
Uniform skin color on both volar forearms</td></tr>
<tr><td>SAMPLE SIZE</td><td>A sufficient number of subjects will be screened to enroll as many as 40 qualified subjects to ensure completion of 30 subjects.</td></tr>
<tr><td>INVESTIGATIONAL STUDY MATERIALS</td><td>
<table>
<tr><th>Treatment Code/Identification</th><th>UPC/PR#</th><th>Product type</th></tr>
<tr><td rowspan="3">“Bandage”
A – H
(as randomly assigned by Sponsor)</td><td>[redacted]</td><td>N/A – uncovered wound; Negative Control</td></tr>
<tr><td>[redacted]</td><td>Investigational Product (IP) – [redacted]</td></tr>
<tr><td>[redacted]</td><td>IP – Benchmark Control 1</td></tr>
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	[redacted] IP – Benchmark Control 2 [redacted] IP [redacted] IP [redacted] IP [redacted] IP [redacted] Auxiliary Product
DOSE AND MODE OF APPLICATION	The auxiliary product will be provided to the subjects at Visit 1 to use on their forearms and for all body cleansing in place of their regular body cleanser for the duration of the study. The IPs will be applied to 7 of the 8 wound sites for each subject at Baseline (Day 0) by trained staff according to a preassigned randomization scheme. The last wound site will be left uncovered as an untreated control. IPs* will be removed at the beginning of each study visit from Day 1 (Visit 3) through Day 16 (Visit 18) and replaced** at the end of each study visit from Day 1 (Visit 3) through Day 15 (Visit 17). [redacted] **Wound sites will remain uncovered once completely healed.
STUDY DURATION	The study will be conducted over approximately 5 weeks with visits at Screening (Day -7 to Day -3), daily from Baseline (Day 0) to Day 16, on Day 21, and at the end of the study on Day 28.
METHODOLOGY	• Clinical Grading of Wound Healing Parameters (erythema, edema, epithelial confluence, crusting/scabbing, smoothness, and general wound appearance) • Scarring Assessment [redacted] • TEWL Measurements • [redacted] • Self-Assessment Questionnaire
MEASUREMENT AND/OR EVALUATION SCHEDULE AND ASSOCIATED SUCCESS CRITERIA	The following evaluations will be conducted for each wound site at the indicated time points: • Clinical Grading of Wound Healing Parameters (erythema, edema, epithelial confluence, crusting/scabbing, smoothness,

	and general wound appearance) – Day 0 through Day 16* • Scarring Assessment - Day 0 and Day 28 • [redacted] • TEWL Measurements - Day 0 through Day 14* • [redacted] • Self-Assessment Questionnaire - Day 0 through Day 4 [redacted] Success Criterion: • [redacted]
STATISTICAL METHODS	All statistical analyses will be performed using the Statistical Analysis System (SAS) v9.4 software. The statistical analysis will be performed by the Biostatistics Group at the Sponsor. All collected assessment data will be listed individually for all subjects. The following descriptive statistics will be presented: mean, standard deviation (SD), median, minimum, and maximum. Percentage change from baseline will also be presented. The primary endpoint, time to complete healing, is defined as the time (in days) elapsed from the time of wound creation to 12PM of the day on which the wound is evaluated as "completely healed." Time to complete healing will be analyzed using a survival analysis method. The survival function (cumulative percentage of wounds healed at each time point) will be estimated by the Kaplan-Meier (KM) method for each treatment separately. The median time to complete healing will be derived from the estimated survival function and be compared using the bootstrap re-sampling method.

LIST OF ABBREVIATIONS

Abbreviation	Definition
3D	Three-Dimensional
A.A.S.	Associate of Applied Science
AE	Adverse Event
BLT	Benzocaine/Lidocaine/Tetracaine
cm	Centimeter
cm^2	Centimeter Squared
C.M.L.S.O.	Certified Medical Laser Safety Officer
CRF	Case Report Form
DPR	Designated Physician Representative
EDC	Electronic Data Capture
EIU	Exposure In Utero
Er:YAG	Erbium: Yttrium Aluminum Garnet
f	Focal Length
FDA	US Food and Drug Administration
g	Gram(s)
h	Hour
HIPAA	Health Insurance Portability and Accountability Act
ICD	Informed Consent Document
ICH GCP	International Council for Harmonisation Good Clinical Practice
ID	Identification
IEC	Independent Ethics Committee
IP	Investigational Product
IRB	Institutional Review Board
ITT	Intent-to-Treat
J	Joules
kHz	Kilohertz
KM method	Kaplan-Meier Method
LLC	Limited Liability Company
m^2	Meter Squared
M.D.	Doctor of Medicine
mg	Milligram
mm	Millimeter
nm	Nanometer
[redacted]	[redacted]
Ph.D.	Doctor of Philosophy
PI	Principal Investigator
PQC	Product Quality Complaint
PTAE	Pre-Treatment Adverse Event
SAE	Serious Adverse Event
SD	Standard Deviation
SEM	Standard Error of the Mean
SM	Study Manager
SMF	Site Master File

Abbreviation	Definition
[redacted]	[redacted]
SPF	Sun Protection Factor
TMF	Trial Master File
µm	Micrometer
W	Watt

TABLE OF CONTENTS

1. INTRODUCTION

The primary goal in wound care is to protect the wound from further damage and to facilitate healing by providing the optimal environment that limits infection, inflammation and scarring. Appropriate wound dressings play an important role in providing this necessary protection and may promote restoration of skin barrier function compared to untreated wounds.[1]

Wound healing is a complex process wherein the skin surface and the underlying tissue must go through an intricate process of tissue repair. The dermis of an uncovered wound is relatively more fibroplastic, fibrotic, and scarred compared to occluded wounds, and is likely to be more inflamed and necrotic in early stages of repair. Exudate, the moisture secretion from the wound site, facilitates the healing process, by providing a variety of bioactive mediators such as enzymes, growth factors and hormones. Wound exudate may also aid in limiting inflammation by providing various immune cells with an ideal medium to destroy invading pathogens such as bacteria, foreign bodies and necrotic tissues. However, exudate in an uncovered wound can lead to scab formation, with trapped inflammatory cells, wound debris, and a layer of desiccated dermal tissue. Covering a wound with an occlusive dressing reduces scab formation and may radically alter the pattern of epidermal wound healing.

Another factor that plays an important role in wound healing is the moisture in the wound environment. As early as 1962, Winter et al., provided the first evidence that keeping wounds moist helps them heal faster compared to dry wounds.[2]

As occlusion affects both the epidermis by enhancing epithelial cell migration and the dermis by enhancing dermal collagen synthesis, maintaining a moist environment may promote the restoration of epidermal barrier function and overall wound healing while making dressing changes relatively easier. Moreover, it has been suggested that the scar left by an occlusively dressed wound is more cosmetically acceptable than that left by an uncovered wound.[3]

[redacted]

2. OBJECTIVE

The objective of this study is to assess the wound healing efficacy (time to complete healing) of different adhesive bandages.

3. STUDY DESIGN

This is a single center, randomized, comparator-controlled, proof-of-principle clinical trial. The target population is 25- to 55-year-old males and females of Fitzpatrick skin types II-III who have uniform skin color on both volar forearms. A sufficient number of subjects will be screened and enrolled to ensure completion of at least 30 subjects.

At Screening (Visit 1; 3 to 7 days prior to Baseline), subjects will be provided with an auxiliary cleanser to use on their forearms and for all body cleansing in place of their regular body cleanser for the duration of the study.

At Baseline (Visit 2), a Sciton Er:YAG 2940 laser will be used to induce eight partial-thickness (i.e. minor) wounds on the subjects' forearms (four per arm).[4] The wounds created by this method heal by the migration of epidermal cells from the dermal appendages located in the wound's base (dermal islands) and/or wound borders, and mimic minor wounds similar to real life scraped skin, typically healing in at less than 14 days if left untreated, based on the Site's previous experience.

Each wound site will be [redacted] and assessed at pre-specified intervals by clinical grading of wound healing parameters (until Day 16), [redacted] In addition, subjects will assess the wound sites via questionnaire from Day 0 to Day 4, [redacted]

Between Baseline and Day 16, each wound site will be subjected to one of eight randomly-assigned treatments (see section 6) until day of complete healing. Treatments include an adhesive bandage that is considered the [redacted] a marketed adhesive bandage benchmark control, a non-marketed adhesive bandage benchmark control, four non-marketed adhesive bandages, and no treatment (uncovered, negative control). [redacted] Once a wound site has completely healed, bandage changes will be discontinued and the wound will be left uncovered.

All wound sites will be uncovered from Day 16 to Day 28, at which point subjects will return for a scar assessment of each wound site[5], and [redacted]

See section 7 for detailed procedures.

4. SUBJECT SELECTION AND ENROLLMENT

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

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

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

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

4.1. INFORMED CONSENT

The ICD must be read by the subject and explained to the subject by the PI or designee.

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

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

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

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

4.2. STUDY POPULATION

The PI must ensure that an individual meets all the inclusion criteria and none of the exclusion criteria to be included in the study. Waivers to inclusion or exclusion criteria are not permitted. In addition, the PI or designee must ensure that the subject remains eligible through the entire study conduct.

The initial verification of eligibility, including review of medical history and concomitant medications, may be conducted by a non-medically qualified individual (PI or designee).

The eligibility must then be reviewed and confirmed by a medically qualified individual (the Study Physician) before enrollment. The medically qualified individual is not required to review the eligibility information if the potential subject is screen-failed by the non-medically qualified staff.

4.2.1. Inclusion Criteria

a) Male or female

b) 25 to 55 years old

c) Fitzpatrick Skin Type II or III (see Appendix I)

d) Uniform skin color on both volar forearms.

e) Generally in good health based on medical history reported by the subject.

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

g) Individual has signed the Consent for Photograph Release and ICD including Health Insurance Portability and Accountability Act (HIPAA) disclosure.

h) Has access to a computer or phone with internet access and the ability to complete online questionnaires.

i) Willing to have temporary (semi-permanent) dot-tattoos applied to the volar forearms.

j) Willing to undergo topical anesthetic and laser wound treatment on the volar forearms.

k) Intends to complete the study and is willing and able to follow all study instructions (see section 4.2.3).

4.2.2. Exclusion Criteria

a) Has known allergies, hypersensitivity, or adverse reactions to anesthetics, adhesive bandages, latex, wound treatment products, or any component/ingredient present in the IPs/auxiliary/ancillary products.

b) Has a known history of a blood-clotting disorder, keloid formation, or a cardiovascular, hepatic, or renal disease.

c) Presents with a skin condition that would, in the opinion of the PI or Study Physician, confound the study results, increase risk to the subject, or interfere with study evaluations (e.g., active psoriasis, seborrheic dermatitis, atopic dermatitis, skin dermatoses, keloids, hypertrophic scars, cracked/excoriated skin, acne scars, pigmentation, friable skin, or clinically infected skin lesions).

d) Has excessive hair or tattoos on either volar forearm.

e) Has a known history of severe systemic immune system disorders such as Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Scleroderma, chronic connective tissue disorders, Poly Arteritis Nodosa, or immunodeficiency, including HIV infection.

f) Has self-reported Type 1 or Type 2 diabetes or is taking insulin or another anti-diabetic medication.

g) Has self-reported uncontrolled chronic diseases such as hypertension, hyperthyroidism, hypothyroidism, or active or recently treated (within 1 year) skin cancer.

h) Is taking a medication that would mask an Adverse Event (AE), confound the study results, or alter or compromise the bleeding/healing process including:

- Antibiotics, corticosteroids, immunosuppressive agents, anti-coagulants, antiplatelet drugs, cytotoxic agents, continuous aspirin therapy, chemotherapy, or daily medications for chronic asthma, within 1 month before Visit 1.*
- Non-steroidal anti-inflammatory drugs or steroidal drugs within 5 days before Visit 1.* Low dose aspirin (81 mg per day) is allowed.
- Antihistamines within 2 weeks before Visit 1.*

* If an individual is taking one of these medication types, the individual is not considered eligible at screening. However, if a subject begins using one of these medications during the study, the Study Physician should be consulted to consider the impact of the specific medication on subject safety and/or the study results as described in section 0 (“Concurrent/Concomitant Medication”).

i) Is self-reported to be pregnant or planning to become pregnant during the study.

j) Has taken/used (oral or topical) vitamin A derivatives such as Accutane, isotretinoin, or retinoic acid within the past 1 year.

k) Has used topical leave-on products on the volar forearms within 1 week prior to Visit 1.

l) Is participating or has participated in 1) any clinical trial involving a topical or systemic investigational drug within 30 days prior to Visit 1 or 2) any other clinical study within 10 days prior to Visit 1.

m) Has a body mass index (BMI) above 35 on the BMI scale (see Appendix II), based on the subject's self-reported height and weight.

n) Is self-reported to be an alcohol or drug abuser.

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

p) Either is or lives with someone who is a current employee of any company that makes or markets adhesive bandages or first aid products.

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

4.2.3. Subject Responsibilities

During the study, the subject should follow the instructions below:

- Use the provided cleanser on your forearms and body for the duration of the study in place of your normal body cleanser. Do not use any other products on your forearms during the study. For the rest of the body, continue using your normal skincare products; do not start using any new products/brands.
- Do not wet or put your forearms in water for the duration of the study (i.e., swimming, baths, hot tubs, etc.). Only showering is acceptable.
- Do not shower within 2 hours before a visit.
- Do not expose the test sites to sunlight or use tanning booths/beds during the study.
- Wear long sleeves when going outdoors and for the first 12 hours after each tattoo application (ink may transfer to other skin locations).
- Avoid touching/scratching the test sites.
- Leave the test products (the bandages) on your forearms – only the study site should remove or apply them. If the bandages become loose between clinic visits, you may use the provided tape to secure the bandage; apply the tape only on the adhesive parts of the bandage (not on the pad or middle of the bandage).
- If any test product (bandage) falls off, record the date and time that the bandage fell off and report that information at your next visit. Do not try to reapply any bandage if it falls off. Please bring the bandage that has fallen off to your next visit.
- Whenever possible, inform the study team before you start using any new medication.
- Avoid pregnancy by continuing to use a medically acceptable contraception method, if applicable.
- Attend all study visits at the scheduled time and date.
- Do not start any other studies during this study.

4.3. CONCURRENT PRODUCTS

Subjects should use only the provided auxiliary cleanser on their forearms and body in place of their normal body cleanser. They should not use any other products on their forearms during the study (other than the auxiliary product and IPs). For the rest of their body, they should continue using their normal skincare products and not start using any new products/brands.

4.4. CONCURRENT/CONCOMITANT MEDICATION

If a subject is taking any medication during the course of the study and/or within 4 weeks prior to the study, it must be recorded. The minimum information that is required is the name of the medication.

If this medication is linked to the treatment of an IP-related or study-related AE, the dose and duration of the treatment should be specified.

Medications excluded are indicated in the section "Exclusion Criteria"*;* if a subject begins using an excluded medication during the study, the Study Physician must consider whether it will impact the subject's safety and/or confound study results and document the decision. In case of impact, the subject should be discontinued.

4.5. SCREEN FAILURE

All individuals who sign the ICD and withdraw their consent for participation in the study or fail to meet at least one of the eligibility criteria during the initial evaluation will be considered a "screen failure" and their data will be entered in the Electronic Data Capture (EDC) system and the AEs will be included in the final report.

5. SAMPLE SIZE

A sufficient number of subjects will be screened to enroll as many as 40 subjects to ensure completion of at least 30 subjects.

If the final sample size is smaller than expected, a protocol deviation should be recorded and communicated to the Sponsor.

6. INVESTIGATIONAL STUDY MATERIALS

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

6.1. IDENTITY OF INVESTIGATIONAL STUDY MATERIALS

The following IPs and auxiliary product will be provided under authorization of the Sponsor:

Table 1. IP and Auxiliary Product List/Study Treatments

Treatment Code/Identification	UPC/PR #	Product type	Regulatory Class in USA
"Bandage" A – H (as randomly assigned by Sponsor)	[redacted]	N/A - uncovered wound; Negative Control	N/A
	[redacted]	IP – [redacted]	[redacted]
	[redacted]	IP – Benchmark Control 1	[redacted]
	[redacted]	IP – Benchmark Control 2	[redacted]
	[redacted]	IP	[redacted]
	[redacted]	IP	[redacted]
	[redacted]	IP	[redacted]
	[redacted]	IP	[redacted]
[redacted]	[redacted]	Auxiliary Product	Cosmetic

A letter of non-significant risk, which outlines the safety of the IPs, will be provided to the IRB and the PI and filed in the SMF.

The Ingredient List for the auxiliary product is provided in Appendix IV.

All the investigational study materials will be manufactured according to Good Manufacturing Practices.

6.2. LABELING

The Sponsor will affix a study label to each IP or kit of IP. The study labels will contain (but are not limited to) the following information, consistent with the requirements of 21 CFR 812.5:

- Protocol number
- Treatment Code
- The name and place of business of the distributor (in accordance with 21 CFR 801.1)
- The quantity of the contents
- Caution statement ("CAUTION - Investigational device. Limited by United States law to investigational use").
- All relevant contradictions, hazards, adverse effects, interfering substances or devices, warnings, and precautions for the device that are not captured in the ICD/study instructions.

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

- Protocol number
- "For Participant Use Only"

- Directions
- Study Site Identification
- Site Emergency Contact Information
- Unit #

6.3. STORAGE AND ACCOUNTABILITY

The IPs and auxiliary product for this study will be secured in a room or cabinet that is only accessible to Study Site authorized personnel and kept at room temperature (15 - 30°C or 59 - 86°F), with temperature recorded daily.

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

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

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

At the end of the study, all unused units of the IPs and all units of the auxiliary product (used and/or unused) must be returned to the Sponsor at the following address:

Johnson & Johnson Consumer Inc.
199 Grandview Road
Skillman, NJ 08558 USA
Attn: Clinical Supplies

The Sponsor will provide the return forms.

All used units of the IP will be destroyed by the Site following its standard operating procedures for biohazardous waste. Proof of destruction must be provided to the Sponsor.

6.4. PRODUCT QUALITY COMPLAINTS

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

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

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

PQC information must also be included on the Product Dispensing and Accountability Log (or equivalent).

The SM can provide assistance and answer questions related to this process. To aid in the initial conversation and understanding of a PQC, the Site staff may be asked to photograph the issue and send the photograph to the SM. The SM will coordinate the replacement or return of the affected products, if necessary.

6.5. APPLICATION/USE OF THE INVESTIGATIONAL STUDY MATERIALS

6.5.1. Auxiliary Product

At Screening (Visit 1), subjects will be provided with the auxiliary cleanser to use on their forearms and for all body cleansing in place of their regular body cleanser for the duration of the study. The labeled directions will be as indicated below:

[redacted]

Use this cleanser on your forearms and body in place of your normal body cleanser. Wet your skin with warm water, apply wash with your hand or washcloth, gently lather, and rinse.

Do not use any other products on your forearms for the duration of the study.

See section 4.2.3 and Appendix III for overall study instructions.

6.5.2. IPs

All IP application and removal will be performed at the study site as described below by trained study staff wearing gloves and according to the randomization schedule (see section 6.6). [redacted] Each IP unit is for single use; used bandages will not be re-applied and should be discarded by the Site as described in section 6.3.

IP will be applied by a designated study staff member as follows:

[redacted]

Additional application details for all IPs:

- If a wound shows signs of excessive redness, pain, or swelling or signs of infection (which should be documented as an AE, per section 10.3.2.1), IP will not be applied.
- [redacted] Subjects will also be provided a roll of tape to take home for use in case IPs become loose between clinic visits.
- If an IP falls off at home, subjects will be instructed to report the date and time that the IP fell off and report that information at their next visit. IPs will not be replaced at home if they fall off. Subjects will be instructed to retain any IPs that have fallen off and bring them to their next appointment.
- [redacted]

IP will be removed by a designated study staff member as follows:

[redacted]

6.6. RANDOMIZATION/IP ALLOCATION AND BLINDING

Upon signing the ICD, each subject will be sequentially issued an eight-digit subject ID. The first four digits will be the center ID, 1001, and the next four digits will be a unique subject identifier assigned in ascending numerical order beginning with 1001 (i.e. subject ID 10011001, 10011002, 10011003, etc.).

Qualified subjects will be assigned a randomization number sequentially from the randomization list at the Baseline visit (Visit 2). Once a randomization number has been assigned to a subject, it cannot be reassigned to another subject.

Randomization of the study treatments to the eight wound sites (see section 7.2.3.3; one study treatment per wound site) will be based on a randomization scheme devised by the Biostatistics Group at the Sponsor using assigned treatment codes (A through H). [redacted]

Due to the nature of the IPs and the study design, it is not feasible to fully blind the IPs or to conceal the treatment assignments from study subjects or from all study personnel (i.e. those involved in applying/removing the IPs, IP accountability, or assessing subject compliance). Staff responsible for IP accountability and IP application/removal (hereafter "unblinded staff") will have access to the randomization schedule in order to accurately administer the study treatments. The unblinded staff will not complete any subject evaluations other than the interview for compliance/AEs.

The PI and staff conducting evaluations other than the interview for compliance/AEs (hereafter "blinded staff") will not have access to the randomization schedule, and the IPs will be kept separate from the blinded staff. Subjects will be instructed not to disclose information about their assigned study treatments to blinded staff, or to discuss any other information that may reveal the treatment assignment. [redacted]

The randomization schedule will be used by the Sponsor to generate treatment code-specific disclosure envelopes. In the event that the PI or designee believes an unblinding is necessary and circumstances allow, the PI or designee will contact the SM who will consult with the DPR to determine whether a code break is needed. If there is a medical emergency and the PI or designee deems it necessary to urgently know the treatment assignment for the subject's proper medical care, the PI or designee may break the treatment code immediately by contacting the unblinded designee for relevant randomization information for that subject and opening the relevant treatment code-specific envelope. The time, date, and reason for the unblinding should be noted in the subject's source document and documentation should be provided to the Sponsor. Blinding should only be broken for serious, unexpected, and related AEs, and only for the subject/treatment code in question, or when required by local regulatory authorities.

All disclosure envelopes must be returned to the Sponsor at the conclusion of the study.

7. INVESTIGATIONAL PLAN

7.1. STUDY DURATION

The study will consist of 20 visits over approximately 5 weeks with visits scheduled at Screening (Visit 1, 3 to 7 days prior to Visit 2), Day 0 (Visit 2, Baseline/Pre-Wound and Post-Wound time points), daily on Days 1 through Day 16 (Visit 3 through Visit 18), Day 21 (Visit 19), and Day 28 (Visit 20). A subject's Day 0 through Day 28 study visits should be scheduled at approximately the same time of day for each visit (i.e., morning, afternoon, or evening).

7.2. STUDY PROCEDURES AND EVALUATION SCHEDULE

The table below presents a summary of the study procedures and evaluation schedule.

Table 2. Schedule of Events

Procedures:	**Visit:**	1 Screening	2 Baseline (Pre-Wound)	2 (Post-Wound)	3 & 4	5	6	7, 9, 11, 13, & 15	8, 10, 12, & 14	16	17	18	19	20
	Day:	-7 to -3	0	0	1 & 2	3	4	5, 7, 9, 11 & 13	6, 8, 10 & 12	14	15	16	21	28
ICD with HIPAA disclosure & Photo Release		X												
Demographics, medical history, and conmeds collection		X												
Review of eligibility/enrollment		X												
Dispense auxiliary cleanser & study instructions		X												
Interview for compliance and changes in health/AEs/conmeds			X	X (AEs only)	X	X	X	X	X	X	X	X	X	X
Randomization			X											
[redacted]			X[A]	X[A]	X[A]	X[A]	X[A]	X[A]	X[A]	X[A]	X[A]	X[A]	X[A]	
Test site label application			X	X	X	X	X	X	X	X	X	X	X	X
IP Removal					X[B]	X	X[B]	X	X[B]	X[B]	X	X		
5-min acclimation			X	X	X[B]	X	X[B]	X	X[B]	X[B]	X	X		X
Clinical grading of wound healing parameters			X	X	X[B]	X	X[B]	X	X[B]	X[B]	X	X		
Scarring assessment			X											X
[redacted]			X	X	X[B]	X	X[B]	X	X[B]	X[B]	X	X	X	X
[redacted]			X	X	X[B]	X	X[B]	X	X[B]	X[B]				
TEWL measurements			X	X	X[B]	X	X[B]	X	X[B]	X[B]				
[redacted]			X		X[D]									X
BLT cream application (30 min prior to wounding)			X											
Test site cleaning and wounding			X											
IP application[E]				X	X[B]	X	X[B]	X	X[B]	X[B]	X			
Subject self-assessment questionnaire				X[C]	X	X	X							
Collect auxiliary product														X

[redacted]

[C]Assessment will be completed remotely approximately 3-4 hours after BLT cream application once numbness is gone.
[D]At time of complete healing for a particular wound site.
[E]Completely healed wound sites will be left uncovered for the remainder of the study.

7.2.1. Pre-Screening

Potential subjects will be pre-screened using IRB-approved materials. Subjects who meet the pre-screening eligibility criteria will be given an appointment time for their screening visit.

7.2.2. Visit 1/Screening (3 to 7 days prior to Visit 2)

7.2.2.1. Informed Consent

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

7.2.2.2. Demographics, Medical History, Concomitant Medications, BMI, and Review of Eligibility

The demographics, medical history, and concomitant medications of each candidate subject will be collected and reviewed.

BMI will be calculated using the subject's self-reported height and weight and the Body Mass Index Table (Appendix II).

All of the eligibility requirements of the study will also be reviewed to assess each candidate subject's eligibility, according to the inclusion/exclusion criteria. As part of this review, trained study personnel will examine the subject's volar forearms to determine if the subject meets the eligibility criteria.

The Study Physician will review the above information (medical history, concomitant medications, and eligibility review) to confirm the eligibility of each subject prior to their enrollment in the study as described in section 4.2.

7.2.2.3. Distribution of Auxiliary Cleanser

Enrolled subjects will be provided with a unit of the auxiliary cleanser along with written and verbal study instructions (Appendix III).

7.2.3. Visit 2/Baseline (Day 0) – Pre-Wound Time Point

Subjects will return to the clinic for Visit 2. The following study procedures will be performed at the Baseline/Pre-Wound time point:

7.2.3.1. Interview for Compliance, Changes in Health/ConMeds, and AEs

Subjects will be interviewed for compliance with study instructions and for any changes in their health or concomitant medications. Any AEs will be recorded.

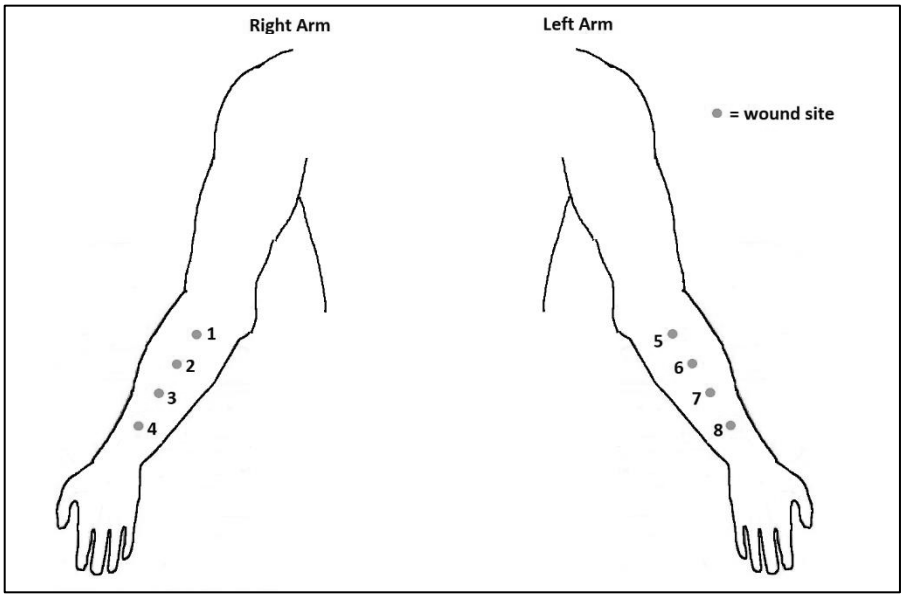
7.2.3.2. Randomization

A unique randomization number will be assigned to each subject as described in section 6.6.

7.2.3.3. Identification of Test Sites and Application of Temporary (Semi-Permanent) Dot-Tattoos and Test Site Labels

Eight test sites (i.e. wound sites) will be identified on the volar forearms, four on each forearm, as shown in Figure 6.

Figure 6. Wound Site Placement



Going from the elbow to the wrist, the test sites on the right volar forearm will be designated test sites 1, 2, 3, and 4, and those on the left volar forearm will be designated test sites 5, 6, 7, and 8. The test sites will be spaced such that the wounds (see section 7.2.4.3.) will be created at least 4.0 cm apart so that the IPs will not overlap when applied.

[redacted]

7.2.3.4. Acclimation

Subjects will acclimate in a controlled environment with the relative humidity maintained at 35-60% and temperature maintained at 19-22°C in the test facility for at least 5 minutes before further evaluations are performed.

7.2.3.5. Clinical Grading of Wound Healing Parameters

After the acclimation period is complete, clinical grading of each test site will be performed by the PI or designee for each parameter listed below:

- Erythema
  0 = none/absent
  1 = mild
  2 = moderate
  3 = marked
  4 = severe

- Edema
  0 = none/absent
  1 = mild
  2 = moderate
  3 = marked
  4 = severe

- Epithelial Confluence
  0 = none, no epithelial coverage
  1 = slight (up to 30%)
  2 = moderate (31-60%)
  3 = extensive (61-90%)
  4 = almost complete or complete (91-100%), covered with a full layer of new epithelial growth

- Crusting/Scabbing
  0 = none
  1 = slight (up to 30%)
  2 = moderate (31%-60%)
  3 = extensive (61%- 90%)
  4 = almost complete or complete (91%-100%)

- Smoothness
  0 = rough, uneven wound
  1 = mild smoothness
  2 = moderate smoothness
  3 = extensive smoothness
  4 = complete smooth, even wound

- General Wound Appearance
  0 = Poor
  1 = Fair
  2 = Good
  3 = Very good
  4 = Excellent

Half-point grading will be allowed.

7.2.3.6. Scarring Assessment

A scarring assessment of each test site will be performed by the PI or designee using the Manchester Scar Scale[5] as follows:

- Color
  1 = Perfect
  2 = Slight mismatch with surrounding skin
  3 = Obvious mismatch with surrounding skin
  4 = Gross mismatch with surrounding skin

- Finish (matte versus shiny)
  1 = Matte
  2 = Shiny

- Contour
  1 = Flush with surrounding skin
  2 = Slightly proud/indented
  3 = Hypertrophic
  4 = Keloid

- Distortion
  1 = None
  2 = Mild
  3 = Moderate
  4 = Severe

- Texture
  1 = Normal
  2 = Just palpable
  3 = Firm
  4 = Hard

7.2.3.7. Instrumental Assessments

[redacted]

[redacted]

[redacted]

[redacted]

7.2.3.7.3. Trans-Epidermal Water Loss (TEWL) Measurements

TEWL measurements will be performed on each test site as described in section 7.5.3.

[redacted]

[redacted]

7.2.4. Visit 2/Baseline (Day 0) – Wound Creation

7.2.4.1. Benzocaine/Lidocaine/Tetracaine Cream Application

Anhydrous numbing Benzocaine/Lidocaine/Tetracaine (BLT) cream (20%/8%/8%) will be topically applied as a thick layer (approximately 2 cm x 2 cm area) at each test site, approximately 30 minutes prior to wounding procedure.

7.2.4.2. Wound Site Cleaning

The subjects' forearms will be cleaned with alcohol wipes after the cream application before the wounding procedure is performed.

7.2.4.3. Wounding Procedure with Er:YAG 2940 Laser (Sciton, Palo Alto, CA, USA)

A certified laser specialist will create 8 uniform wounds on the volar forearms of each subject at the designated wound sites (see section 7.2.3.3) using a Sciton Er:YAG 2940 laser.

- The wounds will be induced with erbium at an energy setting of 12.2 J/cm2
- Number of passes: 3 passes of ~50µm depth per pass
- Each wound will be a circle, 6 mm in diameter
- The wound sites will be at least 4 cm apart, as indicated in section 7.2.3.3.

7.2.5. Visit 2/Baseline (Day 0) – Post-Wound Time Point

7.2.5.1. Clinical/Instrumental Evaluations

After wound creation, the following evaluations will be completed on each test site in the order below:

- Clinical grading of wound healing parameters, as described in section 7.2.3.5.
- [redacted]
- [redacted]
- TEWL Measurements, as described in section 7.2.3.7.3

7.2.5.2. IP Application

After completion of the clinical grading and instrumental evaluations, IPs will be applied to the randomly assigned test sites, as described in section 6. The untreated test site will remain uncovered.

Subjects will be reminded of the study instructions (Appendix III).

7.2.5.3. Self-Assessment Questionnaire

Subjects will be asked to remotely complete a self-assessment questionnaire (see Appendix VI) approximately 3-4 hours after the BLT cream application, when numbness is gone.

7.2.6. Visits 3-16 (Days 1-14)

The following procedures will be completed:

- Subjects will be interviewed for any changes in their medical history or concomitant medications since the last visit. Any AEs will be recorded.
- [redacted]
- Test site labels will be applied as described in section 7.2.3.3.
- [redacted]
- Subjects will acclimate as described in section 7.2.3.4.
- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.
  - Instrumental measurements, as described in section 7.2.3.7.
  - [redacted]
- The designated IP will be applied to each test site per the randomization schedule.[i]
- At Visits 3-6: Subjects will complete the self-assessment questionnaire at the study site (Appendix VI) after the IP application.

7.2.7. Visit 17–18 (Day 15–16)

The following procedures will be completed:

- Subjects will be interviewed for any changes in their medical history or concomitant medications since the last visit. Any AEs will be recorded.
- [redacted]
- Test site labels will be applied as described in section 7.2.3.3.
- All IPs will be removed from the wound sites prior to acclimation.
- Subjects will acclimate as described in section 7.2.3.4.
- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.
  - [redacted]

[i] Completely healed wound sites will be left uncovered for the remainder of the study.

- At Visit 17: The designated IP will be applied to each test site per the randomization schedule.[ii]
- At Visit 18: Subjects will be reminded of the study instructions. Wound sites will remain uncovered for the remainder of the study.

7.2.8. Visit 19 (Day 21)

The following procedures will be completed:

- Subjects will be interviewed for any changes in their medical history or concomitant medications since the last visit. Any AEs will be recorded.
- [redacted]

7.2.9. Visit 20 (Day 28)

The following procedures will be completed:

- Subjects will be interviewed for any changes in their medical history or concomitant medications since the last visit. Any AEs will be recorded.
- Test site labels will be applied as described in section 7.2.3.3.
- Subjects will acclimate as described in section 7.2.3.4.
- After the acclimation period, the following evaluations will be conducted for each test site:
  - Scar assessment, as described in section 7.2.3.6
  - [redacted]
- The auxiliary cleanser will be collected.

[redacted]

[ii] Completely healed wound sites will be left uncovered for the remainder of the study.

[redacted]

[redacted]

7.4. SUBJECT COMPLIANCE METRICS

Compliance of study subjects will be monitored by a visual inspection of the IPs and interview to ensure that the subjects are complying with the study instructions.

Any missed subject visits or other noncompliance will be documented as a protocol deviation.

7.5. STUDY INSTRUMENTS

[redacted]

[redacted]

7.5.3. TEWL Measurements (Tewameter TM300 or TM330T; Courage + Khazaka, Köln, Germany)

TEWL, the passive transfer of water through the stratum corneum, will be measured for each wound site at Visit 2 Baseline/Pre-Wound time point, Visit 2 Post-Wound time point, and Visits 3-16 using the Tewameter TM300 or TM330T (Courage + Khazaka electronic GmbH, Köln, Germany). The same instrument (Tewameter TM300 or TM330T) that is used at Day 0 for one subject will be used for all subsequent measurements.

The measurement of water evaporation is based on the diffusion principle in an open chamber and the density gradient is measured indirectly by two pairs of sensors located inside the hollow cylindrical probe. Data are analyzed by a microprocessor and reported in $g/m^2/h$. A decrease in TEWL values reflects a decrease in the rate of water loss of the skin.

Duplicate 30-second measurements will be taken for each wound site; if the TEWL reading is not stable within 30 seconds, the measurement should be expanded to 60 seconds. A sterile metal adaptor ring (C+K Catalog # Z00812) will be mounted on the measuring head of the probe. The metal adaptor ring will be cleaned with an ethanol wipe between wound sites on the same subject and allowed to completely air dry before each reading. The metal adaptor rings will be thoroughly cleaned and autoclaved between subjects.

7.6. SUBJECT COMPLETION/WITHDRAWAL

7.6.1. Subject Completion

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

7.6.2. Subject Discontinuation

When an individual who has signed the ICD is not included in the study or discontinues/is discontinued prior to completing the study, the reason is to be documented on the Screening and Enrollment Log (or equivalent) and in the final study report. Reasons for subject discontinuation may include:

- Screen Failure (i.e. fails to meet inclusion/exclusion criteria or chooses not to participate)
- Participant is determined to be ineligible after enrollment
- Subject's choice to withdraw
- Investigator terminated (e.g. noncompliance, etc.)
- AE/SAE (must be reported in accordance with the reporting requirements defined in the AE/SAE section "Adverse Event Reporting").
- Lost to follow-up
- Protocol Violation
- Lack of efficacy
- Study terminated by sponsor
- Death
- Pregnancy
- Other

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

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

Additional subjects may be enrolled in the study to compensate for early subject withdrawal.

8. STATISTICAL ANALYSIS METHODS

The analyses will be based on the Intent-to-Treat (ITT) principle, i.e., all subjects who received laser-induced wounds and started the study treatments will be included in the analysis.

8.1. SAMPLE SIZE DETERMINATION

As this is a proof-of-principle study to estimate the effect size, and no prior data are available on these endpoints from previously conducted studies of similar study design on these prototypes, a sample size of 40 with a target completion of at least 30 subjects should provide a reliable estimation of the effect size.

8.2. DATA ANALYSIS

The Biostatistics Group at the Sponsor will be responsible for the statistical analysis of the primary and secondary endpoints. Summary statistics will be provided at each time point for the primary and secondary efficacy and safety assessments. For continuous variables, descriptive summaries will include number of subjects, mean, standard deviation, median, minimum and maximum values. Distributions of categorical variables will be summarized by presenting the number and percent of subjects in each response category.

8.3. ENDPOINTS

8.3.1. Primary Endpoints

The primary endpoint of the study will be "Time to Complete Healing" defined as the time (in days) elapsed from the time of wound creation to 12 PM of the day on which the composite healing score (calculated from the clinical grading of wound healing parameters, as defined below) first meets the complete healing criterion of being at least a score of 8. If a composite healing score does not meet the complete healing criterion by Day 16, the time to complete healing will be censored at the last day on which the composite healing score is available.

The composite healing score will be calculated from the clinical grading of wound healing parameters as follows:

> Composite Healing Score = [general wound appearance score + smoothness score + epithelial confluence score] – [erythema score + edema score + crusting/scabbing score]

The composite healing score on a 25-point scale (-12 thru +12) is indicative of the extent of wound healing and will be calculated for each wound site at each evaluation day.

Time to complete healing will be analyzed using a survival analysis method. The survival function (cumulative percentage of wounds healed at each time point) will be estimated by the Kaplan-Meier method for each treatment separately. The median time to complete healing will be derived from the estimated survival functions and be compared using the bootstrap re-sampling method.

8.3.2. Secondary Endpoints

The secondary endpoints for this study are the change from baseline* to each applicable time point (see Table 2) for the following parameters:

- Change from baseline* to each applicable time point (see Table 2) for the following parameters:
    - TEWL measurements
    - Clinical Grading of Wound Healing – Erythema

  - Clinical Grading of Wound Healing – Edema
  - Subject self-assessment questions 1, 3, and 5.
  - Composite Scar Score – calculated as the sum of the individual parameters on the Manchester Scar Scale (Color, Finish, Contour, Distortion and Texture). Composite Scare Scores range from 5 to 18, with 5 representing clinically best scars and 18 representing clinically worst scars.
- Subject self-assessment questions 2 and 4 at each applicable time point.

*Baseline is considered the Day 0 Pre-Wound time point for all endpoints except the subject self-assessment questions. For the subject self-assessment questions, baseline is considered the Day 0 Post-Wound time point.

TEWL measurements, erythema, edema, the composite scar score, and self-assessment questions 1, 3, and 5 will be analyzed within-treatment and between-treatment. The within-treatment comparison will be performed at each post-baseline time point by comparing the post-baseline scores with the baseline score within each treatment using the paired t-test. The between-treatment comparison will be performed by comparing the change from baseline between treatments using a mixed effect analysis of covariance (ANCOVA) model. The ANCOVA model will include the treatment as the factor and the baseline value as the covariate. The model will include subject as a random effect to incorporate the within-subject correlation.

Self-assessment questions 2 and 4 will be summarized by frequency distribution for each treatment at each collection time point.

8.3.3. Exploratory Endpoints

[redacted]

8.4. AE ANALYSIS

All subjects who have IP applied at least once will be included in the safety analysis. All AEs reported during the AE reporting period will be listed by subject number. The number of subjects experiencing AEs will be presented by body system, preferred term, and treatment (if assessed as related to a particular IP). The latest version of the Medical Dictionary for Regulatory Activities (MedDRA) will be used as the adverse event classification system.

9. SUCCESS CRITERIA

[redacted]

10. MANAGEMENT OF INTERCURRENT EVENTS

10.1. AMENDMENTS TO THE PROTOCOL

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

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

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

10.2. PROTOCOL DEVIATIONS

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

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

10.3. ADVERSE EVENT REPORTING

10.3.1. Introduction

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

10.3.2. Definitions

10.3.2.1. Adverse Event (AE)

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

severity/frequency of a baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

Examples of AEs include but are not limited to:

- Abnormal test findings,
- Clinically important symptoms and signs,
- Changes in physical examination findings,
- Hypersensitivity, and
- Progression/worsening of underlying disease.

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

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

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

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

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

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

Expected Events

Expected mild reactions (e.g. bleeding, pain, itching, etc.) related to the laser wounding procedure, normal healing process, and IP removal will not be captured as AEs unless there is exacerbation (moderate or severe) of these reactions as judged by the PI or designee. All reactions will be documented in the source documents.

Pre-Treatment AE (PTAE)

A PTAE is defined as any AE present prior to the initiation of the treatment/administration of IP.

10.3.2.2. Serious Adverse Event (SAE)

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

Definition 1:

The event fulfills at least one of the following criteria:

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

Definition 2:

- the event involves subject contact with a device AND
- the event results in:
    - Death
    - Serious injury, which means an injury or illness that:
        - Is life-threatening (immediate risk of death)
        - Results in permanent impairment of a body function or permanent damage to a body structure, or
        - Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure (*permanent means irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage*).
    - Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
    - A malfunction that the device (or similar device marketed by the same manufacturer or importer) would be likely to cause death or similar injury if the malfunction were to recur.
    - Any suspected transmission of any infectious agent via a product (medically significant).

10.3.2.3. Severity

The severity of all AEs must be assessed by the Study Physician.

The severity classifications are:

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

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

10.3.2.4. Causality Assessment

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

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

10.3.3. Procedures for Reporting AEs

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

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

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

All AEs, regardless of seriousness, severity, or presumed relationship to study procedures, must be recorded using medical terminology. Whenever possible, diagnoses should be given when signs and symptoms are due to a common etiology (e.g., cough, runny nose, sneezing, sore throat, and head

congestion should be reported as "upper respiratory infection"). The Study Physician must record or confirm their opinion concerning the seriousness, severity, and relationship of the AE to the study. All measures required for AE management must be recorded and reported according to Sponsor instructions.

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

Tabulation of AEs

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

- Pre-Treatment AEs (PTAEs)
- Expected AEs
- AEs related to the product(s)/study
- AEs not related to the product(s)/study
- SAEs related to the product(s)/study
- SAEs not related to the product(s)/study

Additional Reporting Procedures

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

If a **SAE** occurs, in addition to the above reporting procedures, the Site will **immediately** upon SAE awareness notify the SM or designee by telephone or encrypted email (see contact information in Appendix VII and on front page).

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

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

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

The PI may be requested by the Sponsor to obtain specific additional follow-up information or more detailed information in an expedited fashion. In general, this will include a description of the SAE in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as concomitant medications and illnesses, must be provided.

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

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

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

10.3.4. Monitoring and Resolution of AEs

10.3.4.1. Non-Serious AEs

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

10.3.4.2. Serious AEs (SAEs)

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

10.3.4.3. Resolution

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

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

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

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

10.3.5. Pregnancy Reporting and Exposure In Utero (EIU)

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

Pregnancies occurring in subjects classified as screen failures do not require follow-up unless the screening procedures could have had an effect on the pregnancy outcome or the screen failure was detected after the study procedures or application/use of the investigational study material(s) was already started.

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

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

- For initial notification, complete and send securely the "*Pregnancy Notification and Update Form*" to the SM or designee within 24 hours of awareness.
- Provide any updates using the "*Pregnancy Notification and Update Form."*
- Follow-up with the subject to determine the pregnancy outcome. At the end of the pregnancy, complete and send securely the "*End of Pregnancy Collection Form*" within 24 hours from when the information becomes available.

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

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

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

11. ETHICAL CONSIDERATIONS

11.1. SUBMISSION TO INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE

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

Details of the IRB/IEC for this study are located in Appendix VII.

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

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

12. DATA HANDLING AND RECORD KEEPING

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

The following source data will be captured on paper source documents:

- ICD, HIPAA Disclosure, and Photograph Release
- Inclusion/Exclusion Criteria
- BMI
- Medical History
- Concomitant Medications
- Investigational Study Materials Accountability Information
- Protocol Deviations

Subject self-assessment questionnaires will be completed using Qualtrics (Provo, UT), an online survey platform. If needed, subjects may complete these questionnaires on paper and the Site will enter the information into Qualtrics or Medidata Rave.

The following data will be captured directly in the Sponsor's EDC system:

- Demographics
- Fitzpatrick Skin Type Classification
- Randomization
- Clinical Grading of Wound Healing Parameters
    - Erythema score
    - Edema score
    - Epithelial confluence score
    - Crusting/scabbing score
    - Smoothness score
    - General wound appearance score
- Manchester Scar Scale
    - Color score
    - Finish (matte versus shiny) score
    - Contour score
    - Distortion score
    - Texture score
- TEWL Measurements
- Adverse Events
- Subject Disposition

In the rare event that the electronic system is not functioning, the study will continue and the assessments will be captured on a paper source documents and entered into the system once it is functional.

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

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

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

All data entered into the EDC system and Qualtrics will be sent to the Sponsor's Quantitative Sciences Department for statistical analysis. All final data recorded in the EDC system will be kept by the Sponsor and at the clinical site.

The Study Site shall maintain and archive the SMF for 2 years from the time the final report is issued.

The Sponsor must be notified before the disposal of any study record, even if retention requirements are met.

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

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

13. STUDY MONITORING, QUALITY CONTROL, AND QUALITY ASSURANCE

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

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

Any contact concerning this study should be made with the SM or designee (see contact information on the front page or in Appendix VII).

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

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

14. SPONSOR DISCONTINUATION CRITERIA

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

15. FINAL REPORT

The draft report will be prepared by Thomas J. Stephens and Associates.

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

16. CONFIDENTIALITY

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

17. PUBLICATION

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

18. BIBLIOGRAPHIC REFERENCES

1) Mancini AJ, Sookdeo-Drost S, Madison KC, Smoller BR, Lane AT. Semipermeable dressings improve epidermal barrier function in premature infants. Pediatr Res., 36(3):306-14, 1994.

2) Winter GD. Formation of the scab and the rate of epithelization of superficial wounds in the skin of the young domestic pig. Nature. 193:293-4, 1962.

3) Winter G.D. Some factors affecting skin and wound healing. J Tissue Viability. 16(2):20-3, 2006.

4) Trookman NS, Rizer RL, Weber T. Treatment of minor wounds from dermatologic procedures: a comparison of three topical wound care ointments using a laser wound model. J Am Acad Dermatol., 64(3 Suppl): S8-15, 2011.

5) Fearmonti R, Bond J, Erdmann D, Levinson H. A review of scar scales and scar measuring devices. Eplasty, 10: e43, 2010.

6) NIH Publication No. 98-4083 (1998, September). Adapted from Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report. Retrieved from URL. https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi_tbl.htm. 22 May 2019.

7) Easy.Ink™ Semi-Permanent Tattoo Freehand Ink – Full Kit. 2019. Retrieved from https://easy.ink/collections/freehand-ink/products/freehand-ink-full-kit.

8) Buckenmaier CC, Galloway KT, Polomano RC, McDuffie M, Kwon N, Gallagher RM. Preliminary validation of the Defense and Veterans Pain Rating Scale (DVPRS) in a military population. Pain Medicine, 14(1):110-23, 2013.

[Remainder of Page Intentionally Left Blank]

19. PROTOCOL SIGNATURE PAGE

[redacted]

[redacted]

20. PRINCIPAL INVESTIGATOR RESPONSIBILITY STATEMENT

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

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

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

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

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

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

Signature and Date:

21. APPENDICES

Appendix I. Fitzpatrick Skin Type Classification

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

Skin Type	Characteristics
I	Always burns easily, never tans (sensitive)
II	Always burns easily, tans minimally (sensitive)
III	Burns moderately, tans gradually (light brown) (normal)
IV	Burns minimally, always tans well (moderate brown) (normal)
V	Rarely burns, tans profusely (dark brown) (insensitive)
VI	Never burns, deeply pigmented (insensitive)

This study will only be enrolling Fitzpatrick Skin Types II – III.

Appendix II. Body Mass Index Table[6]

Body Mass Index Table

	Normal						Overweight					Obese										Extreme Obesity																				
BMI	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
Height (inches)	Body Weight (pounds)																																								
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167	172	177	181	186	191	196	201	205	210	215	220	224	229	234	239	244	248	253	258
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173	178	183	188	193	198	203	208	212	217	222	227	232	237	242	247	252	257	262	267
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179	184	189	194	199	204	209	215	220	225	230	235	240	245	250	255	261	266	271	276
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185	190	195	201	206	211	217	222	227	232	238	243	248	254	259	264	269	275	280	285
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191	196	202	207	213	218	224	229	235	240	246	251	256	262	267	273	278	284	289	295
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197	203	208	214	220	225	231	237	242	248	254	259	265	270	278	282	287	293	299	304
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204	209	215	221	227	232	238	244	250	256	262	267	273	279	285	291	296	302	308	314
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234	240	246	252	258	264	270	276	282	288	294	300	306	312	318	324
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216	223	229	235	241	247	253	260	266	272	278	284	291	297	303	309	315	322	328	334
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223	230	236	242	249	255	261	268	274	280	287	293	299	306	312	319	325	331	338	344
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230	236	243	249	256	262	269	276	282	289	295	302	308	315	322	328	335	341	348	354
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236	243	250	257	263	270	277	284	291	297	304	311	318	324	331	338	345	351	358	365
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243	250	257	264	271	278	285	292	299	306	313	320	327	334	341	348	355	362	369	376
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250	257	265	272	279	286	293	301	308	315	322	329	338	343	351	358	365	372	379	386
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258	265	272	279	287	294	302	309	316	324	331	338	346	353	361	368	375	383	390	397
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265	272	280	288	295	302	310	318	325	333	340	348	355	363	371	378	386	393	401	408
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272	280	287	295	303	311	319	326	334	342	350	358	365	373	381	389	396	404	412	420
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279	287	295	303	311	319	327	335	343	351	359	367	375	383	391	399	407	415	423	431
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287	295	304	312	320	328	336	344	353	361	369	377	385	394	402	410	418	426	435	443

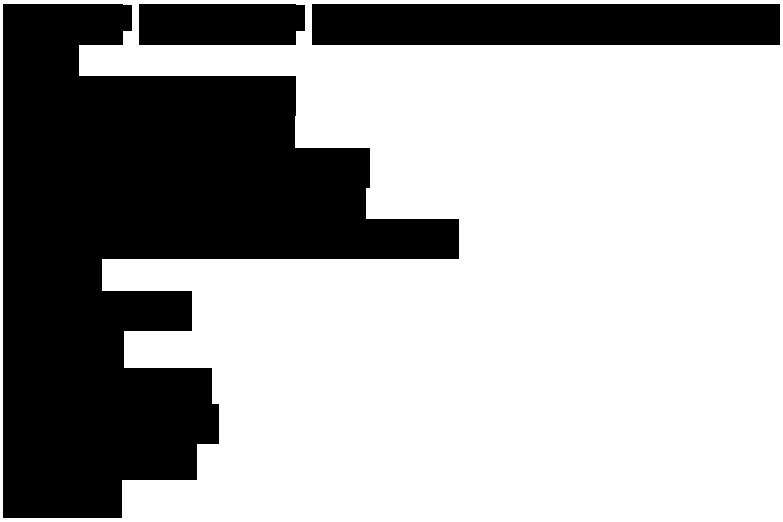
Source: Adapted from *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report.*

Appendix III. Subject Instructions

During the study, please follow the instructions below:

- Use the provided cleanser on your forearms and body for the duration of the study in place of your normal body cleanser. Do not use any other products on your forearms during the study. For the rest of the body, continue using your normal skincare products; do not start using any new products/brands.
- Do not wet or put your forearms in water for the duration of the study (i.e., swimming, baths, hot tubs, etc.). Only showering is acceptable.
- Do not shower within 2 hours before a visit.
- Do not expose the test sites to sunlight or use tanning booths/beds during the study.
- Wear long sleeves when going outdoors and for the first 12 hours after each tattoo application (ink may transfer to other skin locations).
- Avoid touching/scratching the test sites.
- Leave the test products (the bandages) on your forearms – only the study site should remove or apply them. If the bandages become loose between clinic visits, you may use the provided tape to secure the bandage; apply the tape only on the adhesive parts of the bandage (not on the pad or middle of the bandage).
- If any test product (bandage) falls off, record the date and time that the bandage fell off and report that information at your next visit. Do not try to reapply any bandage if it falls off. Please bring the bandage that has fallen off to your next visit.
- Whenever possible, inform the study team before you start using any new medication.
- Avoid pregnancy by continuing to use a medically acceptable contraception method, if applicable.
- Attend all study visits at the scheduled time and date.
- Do not start any other studies during this study.

Appendix IV. Ingredient Listing



Appendix V. Temporary (Semi-Permanent) Dot-Tattoo Procedure[7]

How to Apply:

1) Wear gloves throughout the dot-tattoo procedure.
2) Shake the bottle to make sure the ink is uniformly mixed.
3) Unscrew lid to ink bottle and place tip on bottle.
4) Squeeze out a small amount of ink onto a paper towel to get the air out of the tip. (Wipe the tip regularly to keep it clean and avoid clogging).
5) Squeeze a small amount of ink (~1mm thick) onto the desired location (a template may be used).
    a. **First application:** apply dot-tattoos to the skin adjacent to the wound sites (ideally equidistant between the wound sites). The tattoos must be [redacted] but should be placed so as not to interfere with evaluations.
    b. **Subsequent applications:** apply dot-tattoos to the skin adjacent to the previous dot-tattoos (e.g. may alternate between two locations for each wound site). In all instances, the tattoos [redacted] but should be placed so as not to interfere with evaluations.
6) Let ink sit on skin for a minimum of 30 minutes. Note: the tattoo will not be visible for a few hours once the ink is removed, so all evaluations should be complete prior to ink removal (especially at Visit 2 [Baseline]) to ensure consistent identification of wound sites and visibility of tattoos [redacted]
7) Use a moist paper towel to carefully remove ink once all evaluations are complete.
8) Tattoo will appear a few hours after ink removal.
9) Subjects should be reminded to wear long sleeves for 12 hours after tattoo applications to prevent transfer of ink to other skin locations.

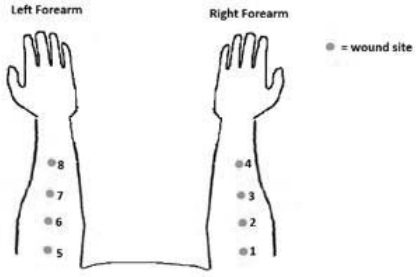
Storage: Refer to package instructions.

Appendix VI. Subject Self-Assessment Questionnaire (Day 0 through Day 4)

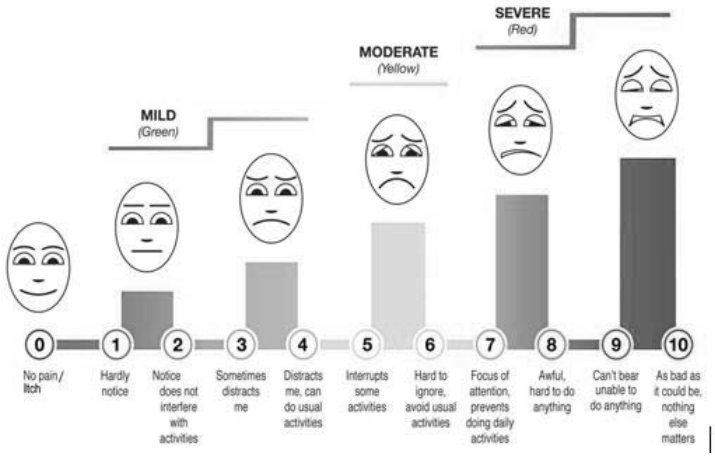
<*Additional Day 0 Instructions:* Please complete this questionnaire as soon as the numbness is gone (this will be around 3-4 hours after the numbing cream was applied).>

Please answer the following questions for each wound on your forearms. Focus on each wound itself (not the surrounding skin that might also be covered by a bandage). The wound sites are numbered as shown in Picture 1. Some of the questions will use the scale in Picture 2.

Picture 1. Wound Site Numbering



Picture 2. Scale for Answering Questions 1, 3, and 5



Note: If you cannot provide an answer for a specific wound site because you cannot distinguish the pain/itch sensation from neighboring wounds, choose "Cannot Distinguish" or enter an X.

	Wound Site (see Picture 1 above)							
Question	1	2	3	4	5	6	7	8
1) With your arm resting by your side, how painful/sore is each wound site? Use the scale in Picture 2.								
2) Is the pain (described in #1) brief (**B**), periodic (**P**), or constant (**C**)?								
3) With your arm in normal motion, how painful/sore is each wound site? Use the scale in Picture 2.								
4) Is the pain (described in #3) brief (**B**), periodic (**P**), or constant (**C**)?								
5) How itchy is each wound site? Use the scale in Picture 2.								

[8] Buckenmaier CC, Galloway KT, Polomano RC, McDuffie M, Kwon N, Gallagher RM. Preliminary validation of the Defense and Veterans Pain Rating Scale (DVPRS) in a military population. Pain Medicine. 2013 Jan 1;14(1):110-23.

Appendix VII. Contact Information

SPONSOR:	Johnson & Johnson Consumer Inc. 199 Grandview Road Skillman, NJ 08558
STUDY SITE:	[redacted] Thomas J. Stephens & Associates, Inc. Dallas Research Center 1801 N. Glenville Dr., Suite 200 Richardson, Texas 75081 USA [redacted]
STUDY MANAGER:	[redacted]
STUDY DIRECTOR:	Robin Mathew, Ph.D. Address: Refer to Sponsor address [redacted]
DEPARTMENT HEAD:	[redacted]
HEAD OF CLINICAL RESEARCH:	[redacted]
DESIGNATED PHYSICIAN REPRESENTATIVE:	[redacted]
STATISTICIAN:	[redacted]
STUDY MONITIOR:	[redacted]
PRINCIPAL INVESTIGATOR:	Lily Jiang, Ph.D. 1801 N. Glenville Dr., Suite 200, Richardson, Texas 75081 USA [redacted]

STUDY PHYSICIAN: [redacted]

SUB-INVESTIGATOR: [redacted]

IRB/IEC: [redacted]

Appendix VIII. Summary of Changes – Amendment 1

CLINICAL PROTOCOL CCSTOH001689 AMENDMENT 1

A 28-Day, Single-Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages

SUMMARY OF CHANGES

Study Product Name:	N/A
Protocol Number:	CCSTOH001689
IND/IDE/Eudra CT:	N/A
Phase:	N/A
Sponsor:	Johnson & Johnson Consumer, Inc.
Version and Date	Amendment 1: Final Version 2.0, 12 Aug 2019 Original: Final Version 1.0, 10 Jul 2019

1. REASONS FOR THE AMENDMENT TO THE FINAL PROTOCOL

Sections of protocol CCSTOH001689, "A 28-Day, Single Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages", dated July 10, 2019 (Final Version 1.0), have been revised to change the type of reinforcement tape used, correct SAE definition 2, correct question #4 and completion timing for Day 0 of the Self-Assessment Questionnaire, correct Screen Failure language, and clarify a few procedures in section 7 to match the Schedule of Events in Table 2.

2. PROTOCOL SECTIONS REVISED

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

- The "Deleted" section represents the original text in Protocol # CCSTOH001689, Final Version 1.0, dated July 10, 2019, that was deleted for Final Version 2.0, dated August 12, 2019.
- The "Changed From" section represents original text in Protocol # CCSTOH001689, Final Version 1.0, dated July 10, 2019, that was changed to new text in Final Version 2.0, dated August 12, 2019. The revised text is indicated in the "Changed To" section.
- The "Added" section represents new text in Protocol # CCSTOH001689, Final Version 2.0, dated August 12, 2019.

2.1. Screen Failure (Section 4.5)

Changed From:

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

Changed To:

All individuals who sign the ICD and withdraw their consent for participation in the study or fail to meet at least one of the eligibility criteria during the initial evaluation will be considered a "screen failure" and their data will be entered in the Electronic Data Capture (EDC) system and the AEs will be included in the final report.

2.2. Additional application details for all IPs (Section 6.5.2)

Changed From:

[redacted]

Changed To:

[redacted]

2.3. Study Procedures and Evaluation Schedule (Section 7.2, Table 2)

Changed From:

[C]Assessment will be completed remotely approximately 2-4 hours after BLT cream application once numbness is gone.

Changed To:

[C]Assessment will be completed remotely approximately 3-4 hours after BLT cream application once numbness is gone.

2.4. Self-Assessment Questionnaire (Section 7.2.5.3)

Changed From:

2-4 hours

Changed To:

3-4 hours

2.5. Visit 17-18 (Day 15-16) (Section 7.2.7)

Changed From:

- Subjects will be reminded of the study instructions. Wound sites will remain uncovered for the remainder of the study.

Changed To:

- At Visit 17: The designated IP will be applied to each test site per the randomization schedule.
- At Visit 18: Subjects will be reminded of the study instructions. Wound sites will remain uncovered for the remainder of the study.

[redacted]

Changed From:

Visits 3-19

Changed To:

Visits 3-20

2.7. Serious Adverse Event (SAE) Definition 2 (Section 10.3.2.2)

Added:

- A malfunction that the device (or similar device marketed by the same manufacturer or importer) would be likely to cause death or similar injury if the malfunction were to recur.

Deleted:

- Congenital anomaly/birth defect

2.8. Subject Self-Assessment Questionnaire (Day 0 through Day 4) (Appendix VI)

Changed Form:

<*Additional Day 0 Instructions:* Please complete this questionnaire as soon as the numbness is gone (this will be around 2-4 hours after the numbing cream was applied).>

…

4) is the pain (described in #4) brief (**B**), periodic (**P**), or constant (**C**)?

Changed To:

<*Additional Day 0 Instructions:* Please complete this questionnaire as soon as the numbness is gone (this will be around 3-4 hours after the numbing cream was applied).>

…

4) Is the pain (described in #3) brief (**B**), periodic (**P**), or constant (**C**)?

Appendix IX. Summary of Changes – Amendment 2

CLINICAL PROTOCOL CCSTOH001689 AMENDMENT 2

A 28-Day, Single-Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages

SUMMARY OF CHANGES

Study Product Name:	N/A
Protocol Number:	CCSTOH001689
IND/IDE/Eudra CT:	N/A
Phase:	N/A
Sponsor:	Johnson & Johnson Consumer, Inc.
Version and Date	Amendment 2: Final Version 3.0, 20 Aug 2019 Amendment 1: Final Version 2.0, 12 Aug 2019 Original: Final Version 1.0, 10 Jul 2019

1. REASONS FOR THE AMENDMENT TO THE FINAL PROTOCOL

Sections of protocol CCSTOH001689, "A 28-Day, Single Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages", dated August 12, 2019 (Final Version 2.0), [redacted]

2. PROTOCOL SECTIONS REVISED

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

- The "Deleted" section represents the original text in Protocol # CCSTOH001689, Final Version 2.0, dated August 12, 2019, that was deleted for Final Version 3.0, dated August 20, 2019.
- The "Changed From" section represents original text in Protocol # CCSTOH001689, Final Version 2.0, dated August 12, 2019, that was changed to new text in Final Version 3.0, dated August 20, 2019. The revised text is indicated in the "Changed To" section.
- The "Added" section represents new text in Protocol # CCSTOH001689, Final Version 3.0, dated August 20, 2019.

2.1. Synopsis (Dose and Mode of Application)

Added:

**Wound sites will remain uncovered once completely healed.

2.2. Synopsis (Measurement and/or Evaluation Schedule)

Changed From:

The following evaluations will be conducted for each wound site at the indicated time points:

- Clinical Grading of Wound Healing Parameters (erythema, edema, epithelial confluence, crusting/scabbing, smoothness, and general wound appearance) – Day 0 through Day 16*
- Scarring Assessment - Day 0 and Day 28
- [redacted]
- [redacted]
- TEWL Measurements - Day 0 through Day 14*
- [redacted]
- Self-Assessment Questionnaire - Day 0 through Day 4

[redacted]

Changed To:

The following evaluations will be conducted for each wound site at the indicated time points:

- Clinical Grading of Wound Healing Parameters (erythema, edema, epithelial confluence, crusting/scabbing, smoothness, and general wound appearance) – Day 0 through Day 16* (or until completely healed, if earlier)
- Scarring Assessment - Day 0 and Day 28
- [redacted]
- [redacted]
- TEWL Measurements - Day 0 through Day 14*
- [redacted]
- Self-Assessment Questionnaire - Day 0 through Day 4

[redacted]

2.3. Study Design (Section 3.0)

Changed From:

[redacted]

Between Baseline and Day 16, each wound site will be subjected to one of eight randomly-assigned treatments (see section 6). Treatments include an adhesive bandage that is considered the [redacted] a marketed adhesive bandage benchmark control, a non-marketed adhesive bandage benchmark control, four non-marketed adhesive bandages, and no treatment (uncovered, negative control). [redacted]

Changed To:

[redacted] and TEWL (until Day 14). In addition, subjects will assess the wound sites via questionnaire from Day 0 to Day 4, [redacted]

Between Baseline and Day 16, each wound site will be subjected to one of eight randomly-assigned treatments (see section 6) until day of complete healing. Treatments include an adhesive bandage that is

considered the [redacted], a marketed adhesive bandage benchmark control, a non-marketed adhesive bandage benchmark control, four non-marketed adhesive bandages, and no treatment (uncovered, negative control). [redacted] Once a wound site has completely healed, bandage changes will be discontinued and the wound will be left uncovered.

2.4. IPs (Section 6.5.2)

Changed From:

All IP application and removal will be performed at the study site as described below by trained study staff wearing gloves and according to the randomization schedule (see section 6.6). [redacted] Each IP unit is for single use; used bandages will not be re-applied and should be discarded by the Site as described in section 6.3.

…

[redacted]

Changed To:

All IP application and removal will be performed at the study site as described below by trained study staff wearing gloves and according to the randomization schedule (see section 6.6). [redacted] Each IP unit is for single use; used bandages will not be re-applied and should be discarded by the Site as described in section 6.3.

...

[redacted]

Added:

[redacted]

[redacted]

2.5. Study Procedures and Evaluation Schedule (Section 7.2)

Note: formatting change made in Table 2 to add footnotes to "Clinical grading of wound healing parameters" and "IP application" rows. [redacted]

Changed From:

[D]Healed test sites only.

Changed To:

[D] At time of complete healing for a particular wound site.
[E]Clinical grading of wound healing parameters will be performed for a particular test site only until time of complete healing.
[F]Completely healed wound sites will be left uncovered for the remainder of the study

2.6. Identification of Test Sites and Application of Temporary (Semi-Permanent) Dot-Tattoos and Test Site Labels (Section 7.2.3.3)

Changed From:

Eight test sites (i.e. wound sites) will be identified on the volar forearms, four on each forearm, as shown in Figure 5.

Figure 5. Wound Site Placement

Changed To:

Eight test sites (i.e. wound sites) will be identified on the volar forearms, four on each forearm, as shown in Figure 6.

Figure 6. Wound Site Placement

2.7. Visits 3-16 (Day 1-14) (Section 7.2.6)

Changed From:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.
  - Instrumental measurements, as described in section 7.2.3.7.
- The designated IP will be applied to each test site per the randomization schedule.

Changed To:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.[i]
  - Instrumental measurements, as described in section 7.2.3.7.
  - [redacted]
- The designated IP will be applied to each test site per the randomization schedule.[ii]

[i] Clinical grading of wound healing parameters will be performed for a particular test site only until time of complete healing

[ii] Completely healed wound sites will be left uncovered for the remainder of the study.

2.8. Visit 17-18 (Day 15-16) (Section 7.2.7)

Changed From:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.
  - [redacted]
- At Visit 17: The designated IP will be applied to each test site per the randomization schedule.

Changed To:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.[i]
  - [redacted]
  - [redacted]
- At Visit 17: The designated IP will be applied to each test site per the randomization schedule.[ii]

[i] Clinical grading of wound healing parameters will be performed for a particular test site only until time of complete healing

[ii] Completely healed wound sites will be left uncovered for the remainder of the study.

2.9. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Appendix X. Summary of Changes – Amendment 3

CLINICAL PROTOCOL CCSTOH001689 AMENDMENT 3

A 28-Day, Single-Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages

SUMMARY OF CHANGES

Study Product Name:	N/A
Protocol Number:	CCSTOH001689
IND/IDE/Eudra CT:	N/A
Phase:	N/A
Sponsor:	Johnson & Johnson Consumer, Inc.
Version and Date	Amendment 3: Final Version 4.0, 28 Aug 2019 Amendment 2: Final Version 3.0, 20 Aug 2019 Amendment 1: Final Version 2.0, 12 Aug 2019 Original: Final Version 1.0, 10 Jul 2019

1. REASONS FOR THE AMENDMENT TO THE FINAL PROTOCOL

Sections of protocol CCSTOH001689, "A 28-Day, Single Center, Randomized, Comparator-Controlled, Proof-of-Principle Study to Assess Wound Healing Efficacies of Different Adhesive Bandages", dated August 20, 2019 (Final Version 3.0), have been revised to continue the clinical grading of wound healing parameters until Day 16 for all wound sites.

2. PROTOCOL SECTIONS REVISED

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

- The "Changed From" section represents original text in Protocol # CCSTOH001689, Final Version 3.0, dated August 20, 2019, that was changed to new text in Final Version 4.0, dated August 28, 2019. The revised text is indicated in the "Changed To" section.

2.1. Synopsis (Measurement and/or Evaluation Schedule)

Changed From:

- Clinical Grading of Wound Healing Parameters (erythema, edema, epithelial confluence, crusting/scabbing, smoothness, and general wound appearance) – Day 0 through Day 16* (or until completely healed, if earlier)

Changed To:

- Clinical Grading of Wound Healing Parameters (erythema, edema, epithelial confluence, crusting/scabbing, smoothness, and general wound appearance) – Day 0 through Day 16*

2.2. Study Design (Section 3.0)

Changed From:

Each wound site will be photographed (at all time points) and assessed at pre-specified intervals by clinical grading of wound healing parameters (until Day 16 or completely healed, if earlier), [redacted] and TEWL (until Day 14). In addition, subjects will assess the wound sites via questionnaire from Day 0 to Day 4, and [redacted]

Changed To:

Each wound site will be photographed (at all time points) and assessed at pre-specified intervals by clinical grading of wound healing parameters (until Day 16), [redacted] and TEWL (until Day 14). In addition, subjects will assess the wound sites via questionnaire from Day 0 to Day 4, [redacted]

2.3. Study Procedures and Evaluation Schedule (Section 7.2)

Note: formatting change were made in Table 2 to remove the footnote from the "Clinical grading of wound healing parameters" row and to change the footnote on the "IP application" row from F to E.

Changed From:

[E]Clinical grading of wound healing parameters will be performed for a particular test site only until time of complete healing.
[F]Completely healed wound sites will be left uncovered for the remainder of the study

Changed To:

[E]Completely healed wound sites will be left uncovered for the remainder of the study.

2.4. Visits 3-16 (Day 1-14) (Section 7.2.6)

Changed From:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.[i]
  - Instrumental measurements, as described in section 7.2.3.7.
  - [redacted]
- The designated IP will be applied to each test site per the randomization schedule.[ii]

[i] Clinical grading of wound healing parameters will be performed for a particular test site only until time of complete healing
[ii] Completely healed wound sites will be left uncovered for the remainder of the study.

Changed To:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.
  - Instrumental measurements, as described in section 7.2.3.7.
  - [redacted]
- The designated IP will be applied to each test site per the randomization schedule.[i]

[i] Completely healed wound sites will be left uncovered for the remainder of the study.

2.5. Visit 17-18 (Day 15-16) (Section 7.2.7)

Changed From:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.[i]
  - [redacted]

- [redacted]
- At Visit 17: The designated IP will be applied to each test site per the randomization schedule.[ii]

[i] Clinical grading of wound healing parameters will be performed for a particular test site only until time of complete healing
[ii] Completely healed wound sites will be left uncovered for the remainder of the study.

Changed To:

- After the acclimation period, the following evaluations will be conducted for each test site:
  - Clinical Grading of Wound Healing Parameters, as described in section 7.2.3.5.
  - [redacted]
- At Visit 17: The designated IP will be applied to each test site per the randomization schedule.[ii]

[ii] Completely healed wound sites will be left uncovered for the remainder of the study.