CO-170726100607-SACT

Randomized, Exploratory Study to Evaluate Changes to Skin Microbiome with Tape-stripped Wounds

Compound Name	Adhesive Bandages
Protocol Number	CO-170726100607-SACT
IND / IDE / EudraCT number	Not applicable
Phase	Not Applicable
Version and Date	Amendment 2: 22JAN2018

1. SYNOPSIS

Name of Sponsor/Company:

Johnson & Johnson Consumer Inc. (JJCI)

Active Ingredient(s):

One Investigational product contains 0.8% Benzalkonium Chloride (BZK)

Test Product #4 – [redacted] applied topically

Title of Study:

Randomized, Exploratory Study to Evaluate Changes to Skin Microbiome with Tape-Stripped Wounds

Countries:

United States

Principal Investigator/Site:

Phillip LaStella, MD
TKL Research [redacted]

Phase of development:

N/A (Exploratory Study)

Objective:

The primary objective of this study is to evaluate skin microbiome changes of induced wounds covered with adhesive bandages in comparison to uncovered wounds and intact skin in healthy subjects.

The secondary objective of this study is to evaluate the following for induced wounds covered with adhesive bandages in comparison to uncovered wounds and intact skin: changes in skin barrier function, and skin redness. [redacted]

Methodology:

This single center, 15-day clinical trial is being conducted to assess the changes to the skin microbiome of induced wounds on the back in approximately 35 healthy adult subjects aged 18-55 years, with Fitzpatrick Skin Types I – III. There will be 6 test sites randomly assigned to treatments for each subject. Four of the test sites will be wounded and covered with various marketed adhesive bandages, one test site will be wounded and un-covered (positive control) and one test site will remain intact and un-covered (negative control). Following a screening visit (3-14 days prior to Visit 2) and a 3-day washout period, subjects will be assessed at Baseline (Day 0), Days 1 – 7 and Day 14; subjects will also return to the study site daily for bandage changes.

The following assessments will be performed by trained study staff at Baseline (Day 0), Days 1-7, and Day 14:

- Microbiome [redacted]: Swabs will be used to collect bacteria[redacted] from the test site surfaces. A total of 2 swabs will be taken per test site per timepoint.
- Trans Epidermal Water Loss (TEWL; tewameter): Noninvasively measures water evaporation from the skin, which is a measure of skin barrier function. These measurements will be done three times for each test site.
- [redacted]
- Skin pH (Skin pH Meter PH905): Noninvasively measures skin surface pH. [redacted]
- Diffuse Reflectance Spectroscopy (DRS): Noninvasively measures redness by oxy-, deoxy-hemoglobin, and melanin levels in the skin. Five repetitive spectra acquisition will be implemented for each test site.
- [redacted]

A randomization code will designate which wound will receive the appropriate treatment. Study bandages will be changed daily (by study staff on each day of the

study Days 1 -14). Subjects will report back to the study facility for daily bandage changes (Days 1-14) and for assessments on Days 1-7 and 14. Adverse events will be monitored throughout the study.
Number of subjects (planned): A sufficient number of subjects will be screened, approximately 35 subjects will be randomized to ensure completion of at least 30 subjects
Diagnosis and main criteria for inclusion: Adults aged 18-55 who meet the inclusion criteria and none of the exclusion criteria, which include generally healthy male or female subjects with Fitzpatrick skin types I-III and who agree to the requirements of the study, will be eligible for the study.
Study product, dosage and mode of administration: Test Product #1 [redacted] applied topically Test Product #2 [redacted] applied topically Test Product #3 [redacted] applied topically Test Product #4 – [redacted] applied topically
Reference therapy (comparator or placebo control), dosage and mode of administration: Positive Control – Wounded, uncovered skin Negative Control – Intact, uncovered skin
Duration of treatment: 2 weeks (14 days)

Criteria for evaluation:

Efficacy Endpoints:

- Predominant microflora based on the following criteria:
  - Microbial Community Richness on the back at Baseline (Day 0), Days 1-7, and Day 14, based on the total number of different bacterial taxa detected in the sample.
  - Microbial Community Diversity on the back at Baseline (Day 0), Days 1-7, and Day 14 based on the Shannon Index.
  - Microbial Community Evenness on the back at Baseline (Day 0), Days 1-7, and Day 14 based on Pielou's evenness index.
- Skin barrier function as assessed by mean TEWL measurements of all test sites at Baseline (Day 0), Days 1-7 and Day 14
- Redness as assessed by mean DRS measurements of oxy-, deoxy-hemoglobin, and melanin levels at all test sites at Baseline (Day 0), Days 1-7 and Day 14

[redacted]

Safety Assessments:

Adverse events will be monitored throughout the study.

Statistical methods:

Statistical Analysis Population

Efficacy data will be evaluated for all intent-to-treat (ITT) subjects who received induced wounds and started the treatment procedure. Adverse events will be summarized for all subjects who received induced wounds.

Statistical Analysis Plan

The skin microflora [redacted] data will be analyzed and reported independently by external partners.

The TEWL measurements, [redacted], and DRS measurements will be analyzed by the sponsor and will be summarized at each assessment time point for each test site.

The within product comparison will be performed using the paired t-test to compare the values of each product at each post baseline time point with its own baseline value.

The between product comparison will be performed based on the change from baseline (post baseline value minus baseline value). The change from baseline of each product will be analyzed using mixed effect ANCOVA model at each post baseline time point. The ANCOVA model will include the product as the factor and the baseline value as the covariate. The model will include the subject as a random effect to incorporate the within subject correlation. The adjusted mean of each product from the ANCOVA model will be compared between the test products and the negative control, between the test products and the positive control, and between the negative control and the positive control.

2. SCHEDULE OF ACTIVITIES

Table 1: Time and Events Schedule

Activity	Visit 1 Screening 3-14 days prior to V2	Visit 2 Baseline Day 0	Visits 3-9 Days 1-7	Visits 10 – 15 Days 8- 13	Visit 16 Day 14 End of Study	Follow-up Visit (if needed)
Informed Consent	X					
Medical History and Demographics	X					
Prior and Concomitant Medications/Non-Drug Therapies	X	X	X	X	X	X
Inclusion/Exclusion Criteria	X	X				
Urine pregnancy testing on women of childbearing potential	X					
Back skin assessment	X	X				
Adverse Event Review	X	X	X	X	X	X
Dispense Body Wash Product	X					
Randomization		X				
Test site cleansing		X				
Test site identification with template		X				
Acclimation		X	X	X	X	X
Wounding		X				
Swab Sampling		X	X		X	
TEWL		X	X		X	
[redacted]		X				
[redacted]						
[redacted]						
DRS		X	X		X	
Bandage application		X	X	X		

Subject Verbal & Written instructions	X	X	X	X		
Tape dispensing		X				
Bandage removal			X	X	X	
Collect Body Wash					X	

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4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

The following abbreviations and specialist terms are used in this study protocol.

Table 2: Abbreviations and Specialist Terms

Abbreviation or Specialist Term	Explanation
AE	Adverse Event
BZK	Benzalkonium Chloride
CRF	Case Report Form
DO	Doctor of Osteopathy
DRS	Diffuse Reflectance Spectroscopy
EDC	Electronic Data Capture
EIU	Exposure In Utero
GCP	Good Clinical Practice
ICH	International Council for Harmonisation
IP	Investigational Product
IRB	Institutional Review Board
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
PI	Principal Investigator
PQC	Product Quality Complaint
SAE	Serious Adverse Event
TEWL	Trans Epidermal Water Loss

5. ETHICS

5.1. Institutional Review Board/Ethics Committee (IRB/EC)

It is the responsibility of the Investigator to have prospective approval of the study protocol, protocol amendments, informed consent forms, and other relevant documents, e.g., advertisements, if applicable, from the IRB/EC. All correspondence with the IRB/EC should be retained in the Investigator File (Site Master File). Copies of IRB/EC approvals obtained by the Investigator should be forwarded to the Sponsor.

The only circumstance in which a protocol amendment may be initiated before IRB/EC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the Investigator must notify the IRB/EC and the Sponsor in writing within 5 working days after implementation.

5.2. Regulatory Authority(ies)

Before initiating the clinical trial, the Sponsor [or the Sponsor and the investigator, if required by the applicable regulatory requirement(s)] should submit any required application(s) to the appropriate authority(ies) for review, acceptance, and/or permission [as required by the applicable regulatory requirement(s)] to begin the trial. Any notification/submission should be dated and contain sufficient information to identify the protocol.

Amendments to the protocol that are considered as substantial, i.e. are likely to have an impact on the safety of the trial subjects, to change the interpretation of the scientific documents in support of the conduct of the trial, or if they are otherwise significant, must be reviewed and approved by the appropriate authority(ies).

5.3. Ethical Conduct of the Study

The study will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice guidelines (ICH E6), and applicable local regulatory requirements and laws.

5.4. Subject Information and Consent

All parties will ensure protection of subject personal data and will not include subject names or subject initials on any forms, reports, publications, or in any other disclosures. Each subject will be assigned a study number that is used in the Case Report Form (CRF) in lieu of the subject's name. In case of data transfer, the Sponsor will maintain high standards of confidentiality and protection of subject personal data.

The informed consent form must be agreed to by the Sponsor and the IRB/EC and must be in compliance with ICH E6, Good Clinical Practice (GCP), local regulatory requirements, and legal requirements.

The Investigator must ensure that each study subject is fully informed about the nature and objectives of the study and possible risks associated with participation. The Investigator, or

a person designated by the Investigator, will obtain written informed consent from each subject before any study-specific activity is performed. The informed consent form used in this study, and any changes made during the course of the study, must be prospectively approved by both the IRB/EC and the Sponsor before use. The Investigator will retain the original of each subject's signed consent form. A copy of the signed and dated consent form will be provided to subjects.

6. STUDY ADMINISTRATIVE STRUCTURE

Details on the administrative structure of the study (e.g., Principal Investigator (PI)/study site personnel, the Sponsor's study team, and the external service providers) will be included in a study contact list. The study contact list will also include contact information for the Sponsor, Investigator, Monitor, Clinical, and Bioanalytical Laboratories, and IRB/EC, as well as the names and titles of the persons authorized to sign the protocol and protocol amendments, for the Sponsor. This list will be maintained in the site's and sponsor's study master files throughout the study for inclusion in the trial master file.

7. INTRODUCTION

7.1. Background

The skin is colonized by diverse microorganisms, and the genetic contributions of these microorganisms is collectively referred to as the skin microbiome. These microorganisms, in combination with mammalian cells of the host produce a diverse array [redacted], which are unique chemical fingerprints left behind by specific cellular processes, important for normal cell function. The microorganisms and metabolic processes exist in a dynamic equilibrium and are believed to contribute to acute wound healing. However, when the skin is compromised (i.e. a wound occurs), adverse organisms can also colonize [redacted] profiles can shift in the wound leading to impaired or prolonged healing [1,2]. Thus, characterizing the skin microbiome [redacted] during the wound healing process is critical to understanding their role in wound repair.

7.2. Rationale

This exploratory study is being conducted to characterize the microbial load and diversity of the skin microbiome [redacted] of induced wounds in relation to specific skin properties, and after treatment with various adhesive bandages to further establish the role of microorganisms in wound healing.

8. STUDY OBJECTIVES AND ENDPOINTS

The primary objective of this study is to evaluate skin microbiome changes of induced wounds covered with adhesive bandages in comparison to uncovered wounds and intact skin in healthy subjects.

The secondary objective of this study is to evaluate the following for induced wounds covered with adhesive bandages in comparison to uncovered wounds and intact skin: changes in skin barrier function, and skin redness [redacted]

8.1 Endpoints

- Predominant microflora based on the following criteria:
  - Microbial Community Richness on the back at Baseline (Day 0), Days 1-7, and Day 14, based on the total number of different bacterial taxa detected in the sample.
  - Microbial Community Diversity on the back at Baseline (Day 0), Days 1-7, and Day 14 based on the Shannon Index.
  - Microbial Community Evenness on the back at Baseline (Day 0), Days 1-7, and Day 14 based on Pielou's evenness index.
- Skin barrier function as assessed by mean TEWL measurements of all test sites at Baseline (Day 0), Days 1-7 and Day 14.
- Redness as assessed by mean DRS measurements of oxy-, deoxy-hemoglobin, and melanin levels at all test sites at Baseline (Day 0), Days 1-7 and Day 14.

[redacted]

9. INVESTIGATIONAL PLAN

9.1. Overall Study Design and Plan

This single center, 15-day clinical trial is being conducted to assess the changes to the skin microbiome of induced wounds on the backs of approximately 35 healthy adult subjects aged 18-55 years, with Fitzpatrick Skin Types I – III. There will be 6 test sites randomly assigned to treatments for each subject. Four of the test sites will be wounded and covered with various marketed adhesive bandages, one test site will be wounded and un-covered (positive control) and one test site will remain intact and un-covered (negative control). Following a screening visit (Day -3 to -14) and a 3-day washout period, subjects will be assessed at Baseline (Day 0), Days 1 – 7 and Day 14; subjects will also return to the study site daily for bandage changes.

<u>The following assessments will be performed by trained study staff at Baseline (Day 0), Days 1-7, and Day 14:</u>

- Microbiome [redacted] Sampling: Swabs will be used to collect bacteria [redacted] from the skin surface. A total of 2 swabs will be taken per site per timepoint.
- Trans Epidermal Water Loss (TEWL; tewameter): Noninvasively measures water evaporation from the skin, which is a measure of skin barrier function. These measurements will be done three times for each test site.
- [redacted]
- Diffuse Reflectance Spectroscopy (DRS): Noninvasively measures redness by oxy-, deoxy-hemoglobin, and melanin levels in the skin. Five repetitive spectra acquisition will be implemented for each test site.
- [redacted]

A randomization code will designate which test site will receive the appropriate treatment. Study bandages will be changed daily (by study staff on each day of the study Days 1 -14).

Subjects will report back to the study facility for daily bandage changes (Days 1-14) and for assessments on Days 1-7 and 14.

Adverse events will be monitored throughout the study.

9.2. Selection of Study Population

The following eligibility criteria are designed to select subjects for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be considered when deciding whether this protocol is suitable for a particular subject. No waivers to inclusion or exclusion criteria will be permitted.

9.2.1. Subject Inclusion Criteria

Each subject must meet all of the following inclusion criteria (and none of the exclusion criteria) to be eligible for enrollment into the study:

1. Adults aged 18 to 55 years of age.
2. Fitzpatrick skin types I to III.
3. Must be able to comprehend and follow the requirements of the study (including availability on scheduled visit dates) based upon research site personnel's assessment;
4. Must be able to read and understand the local language;
5. Must be able to provide a signed and dated informed consent form and photographic release form prior to any study-related procedures;
6. Avoid excessive sun exposure (including tanning beds), and to commit to all follow up visits for the duration of the study (up to the Follow-Up Visit if needed) as per the Investigator's discretion if their wounds are not healed at Day 14;
7. Willing to refrain from topical product use on the back for the duration of the study. Topical products that should not be used include moisturizers, lotions, creams, sunscreens, oils, tanners;
8. Subjects must agree not to immerse their bandages in water for the duration of the study. Subjects will only be allowed to shower during the study (no swimming, baths, hot tubs, etc.).;
9. Individuals who are generally in good health as determined by the investigator or designee, based on medical history reported by the subject;
10. Subjects must be willing to sign a photographic release form, which will allow the study sponsor to use and distribute the photos/images for education and information purposes, general and/or professional advertising, publicity and promotional purposes, including distribution to the media, and in publication of the scientific work. All subject identities will remain confidential;

11. Male and female subjects with reproductive potential who agree to practice a medically acceptable form of birth control (described in section 11.11) during the study Females must have used such birth control for at least 3 months prior to the Screening Visit 1and for 30 days following the last application of investigational product.

9.2.2. Subject Exclusion Criteria

1. Excessively hairy back, acne, scars and pigmentation or nevi that could interfere with evaluations or study procedures;
2. Subjects with known allergies or sensitivities to ingredients contained in the Test Products or washout product;
3. Suspected alcohol or substance abuse (e.g., amphetamines, benzodiazepines, cocaine, marijuana, opiates);
4. Pregnant or Lactating, or planning on becoming pregnant;
5. Known allergies or sensitivities to anesthetics, adhesive bandages, wound treatment products or tapes;
6. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study;
7. Participation in any other clinical study within 30 days of Visit 1;
8. Subjects who have a health condition and/or pre-existing or dormant dermatologic conditions (e.g., psoriasis, rosacea, rashes, active herpetic lesions, or severe excoriations, etc.) or who have clinically active bacterial, fungal, or viral skin infections or those who are susceptible to cutaneous infections that could interfere with the outcome of the study or be deemed inappropriate for study participation as determined by the Investigator or designee;
9. Subjects who report using prescription or OTC medication (oral or topical) that can make skin more sensitive or influence the skin (i.e. antibiotics, hormones, insulin, etc.) within 6 weeks prior to entry into the study;
10. Subjects receiving topical and/or inhaled medications that may alter or compromise the bleeding/healing process (i.e. oral corticosteroids, immunosuppressive agents, anti coagulants, antiplatelet drugs, cytotoxic agents, continuous aspirin therapy or chemotherapy, daily medication for chronic asthma), within 30 days prior to study initiation, or as per the Investigator's judgment.Subjects viewed by the Investigator or designee as not being able to complete the study;
11. Individuals with a history of immunosuppression/immune deficiency disorders (Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Scleroderma, chronic connective tissue disorders, Poly Arteritis Nodosa) (including HIV infection or AIDS) or currently using immunosuppressive medications (e.g., azathioprine,

belimumab, cyclophosphamide, Enbrel, Imuran, Humira, mycophenolate mofetil, methotrexate, prednisone, Remicade, Stelara.), and/or radiation as determined by study documentation;

12. Individuals with any planned surgeries and/or invasive medical procedures during the study;
13. Subjects with a known history of keloid or hypertrophic scar formation;
14. Subjects diagnosed with any blood clotting disorder;
15. Hyperthyroidism or hypothyroidism or with active or recently treated (within 1 year) skin cancer, or those in poor nutritional status;
16. Subjects taking oral Vitamin A derivatives such as Accutane, isotretinon, or using retinoic acid in the past 1 year or using topical Vitamin A derivatives in the 3 weeks prior to study start;
17. Subjects with clinically infected skin lesions;
18. Subjects with cracked or excoriated skin, or other skin problems that would, in the opinion of the Investigator, increase their risk or interfere with study evaluations (i.e. active psoriasis anywhere on the body, seborrheic dermatitis, atopic dermatitis, or other skin dermatoses, etc);
19. Diabetes mellitus that cannot be controlled by diet alone (i.e. requires systemic medications for control);
20. Subjects with friable skin, at the discretion of the Investigator;

9.2.3. Subject Withdrawal Criteria

Subjects have the right to withdraw from the study at any time for any reason. The Investigator and/or the Sponsor may terminate a subject from the study and/or follow-up in the event of any of the following:

- Medical reasons considered significant by the subject, Investigator and/or the Sponsor, which may include an adverse event, inter-current illness or medical reasons unrelated to the study
- Nonmedical reasons (e.g., subject request or noncompliance with the treatment procedure as determined by the investigator, the Sponsor and/or subject)
- Pregnancy
- Serious eligibility or on-study violation of the protocol
- Unanticipated event or situation that could result in inadequately characterized pharmacokinetic profile such as missed blood sample collections
- Administrative or other reasons

Should a subject decide to withdraw from the study at any point, all efforts should be made to complete all end of study assessments (if subject cannot come to study site, a telephone call to collect information could be performed). In case of questions surrounding the circumstances that a subject needs to be withdrawn from the study (e.g., protocol deviation), the Sponsor, or the Sponsor representative should be consulted. The reason for withdrawal should be documented in the subject's source document and on the Subject Disposition Electronic Data Capture (EDC) page. If a subject does not return for a scheduled visit, three documented attempts will be made to contact the subject via:

1. Documented phone call (date, time, person completing the call, result)
2. Regular mail
3. Certified letter/return receipt (if service is available)

If the subject withdraws from the study and also withdraws consent for disclosure of future information, no further evaluations will be performed and no additional data will be collected. The Sponsor may retain and continue to use any data collected before such withdrawal of consent.

10. INVESTIGATIONAL PRODUCT MATERIALS AND MANAGEMENT

10.1. Investigational Products

10.2. Description of Investigational Products

Table 3 Investigational Products

Investigational Product	[redacted]
Dosage Form	Bandage - 1 x 2.5 in - pad size 7/16 in by 1 1/16 in
UPC Number	[redacted]
Route of Administration	Topical
Physical Description	Adhesive bandage
Manufacturer	[redacted]
[redacted]	[redacted]
Investigational Product	[redacted]
Dosage Form	Bandage – ¾ x 3 in - pad size 6/8 in by 13/16 in

UPC Number	[redacted]
Route of Administration	Topical
Physical Description	Adhesive Bandage
Manufacturer	[redacted]
[redacted]	[redacted]
Investigational Product	[redacted]
Dosage Form	Bandage – 7/8 x 2 ¾ in - pad size 7/16 in by 1 in
UPC Number	[redacted]
Route of Administration	Topical
Physical Description	Adhesive Bandage
Manufacturer	[redacted]
[redacted]	[redacted]
Investigational Product	[redacted]
Dosage Form	Bandage – ¾ x 3 in –Pad size: 10mm x 25mm
UPC Number	[redacted]
Route of Administration	Topical
Physical Description	Medicated Adhesive Bandage
Manufacturer	[redacted]

Table 4 Auxilliary & Ancillary Products

Product Name:	[redacted]
UPC Number	[redacted]
Dosage Form:	N/A
Directions for Use:	Refer to commercial product label
Route of Administration:	Topical
Physical Description:	Clear amber viscous liquid
Manufacturer:	[redacted]
Product Name:	[redacted]

UPC Number	[redacted]
Dosage Form:	Tape
Directions for Use:	Apply as needed to secure Investigational Products. Do not cover padstock area of the test products
Route of Administration:	Topical
Physical Description:	White adhesive coated tape
Manufacturer:	[redacted]

10.3. Investigational Product Packaging and Labeling

Investigational product will be packaged by Johnson and Johnson. The investigational product will be stored in a secure area at room temperature.

Study product label will be affixed to the outer container of all investigational products. The label will contain the following information:

- Protocol Number
- Site Identification
- Treatment Code
- 24-Hour Emergency Phone Number
- Directions for Use
- For Investigational Use
- Warnings
- Net Contents
- Storage Conditions

10.4. Method of Assigning Subjects to Treatment Groups

As subjects sign a consent form, each subject will be sequentially issued a subject ID. The subject ID is an eight-digit number, beginning with the four-digit site ID "1001" and the remainder of the numerals assigned in ascending numerical order beginning with 1001, 1002, 1003, etc.

At the baseline visit, each qualified subject will be assigned a unique randomization number (e.g., 1 to 35) which determines the bandage assignment sequences. The assigned treatment will be carried out on the same wound site for Days 0 through 14. Once a randomization number has been assigned to a subject, it cannot be reassigned to another subject in that part. The assignments of the treatments and control will be based on the randomization scheme devised by the Quantitative Sciences Department at the Sponsor.

10.5. Study Product Storage and Accountability

The Investigator, or a designated study staff will ensure that investigational product is stored in a secured area under room temperature of approximately 68 °F to 77 °F (20 °C to 25 °C), in accordance with applicable regulatory requirements.

The Investigator must maintain adequate records documenting the receipt, use, loss, or other disposition of the investigational product on an investigational product accountability log. The log must identify the investigational product and account for its disposition on a subject-by-subject basis, including specific dates. The log must be signed by the individual who dispensed, and copies must be provided to the Sponsor.

At the end of the study, the Sponsor will provide instructions for the disposition of investigational product as well as any containers used for dispensation of investigational product.

10.6. Administration of the Investigational Product

All investigational products will be administered at the site by trained study staff. Study staff will apply each bandage according to the randomization schedule and protocol. Subjects will not apply products at home. All used bandages will be discarded at the study site.

10.7. Blinding and Unblinding

Due to the nature of the study, it is not feasible to reliably blind the investigational product or to conceal the identity of the treatment assignments from study subjects or all study personnel (e.g. those involved in dispensing and providing instructions on use of the assigned investigational product, reviewing subject diaries for completeness, reviewing investigational product compliance and reviewing subject-reported adverse events). Staff responsible for product accountability and dispensing will not complete any assessments or sampling. Subjects will be instructed not to disclose information about their assigned study treatments to the clinician or study staff completing any of the assessments, or to discuss any other information that may reveal the treatment assignment. While staff completing the assessments will not know the treatment assignments to each site, due to the nature of this study, it is not possible to completely blind the assessors as one site is unwounded/untreated, and the other sites may have adhesive residue generally indicating the test sites assigned to a bandage.

The randomization scheme will be used by the Johnson & Johnson Consumer's Clinical and Consumer Packaging Operations Department to generate the subject specific single disclosure envelopes. The site clinical study coordinator will receive one package containing individual subject specific disclosure envelopes indicating treatment decode for each randomization number. Identification of the treatment assignments to each site for a subject may be revealed in the event of a serious adverse event by opening the single

subject specific envelope that displays the subject's randomization number. In such an instance, the Investigator will, if circumstances and time permit, contact the Sponsor prior to breaking the code. The date and reason for such unblinding must be described on the subject's source document. Upon completion of the study, all subject specific disclosure envelopes must be returned to the study monitor who will return them to the sponsor.

Treatment assignments should only be revealed when required and only for the subject in question. The Investigator must notify the Sponsor, when circumstances and time permit, prior to unblinding of any subject. Expectedness of serious and related adverse events should be assessed using the Safety Attestation letter and/or, for marketed products, the locally approved labeling.

If there is a medical emergency and the Investigator deems it necessary to know the subject's study treatment urgently for the subject's proper medical care, the Investigator may break the treatment code immediately, and then contact the Study Director or designee as soon as possible afterward. If in the opinion of the Investigator it is necessary to break the treatment code and circumstances allow, the Investigator will first contact the Study Director or designee for consultation about breaking the study blind.

10.8. Product Quality Complaints

A Product Quality Complaint (PQC) for a non-marketed product 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. This does not include effectiveness, preference, or performance measures, which will be reviewed in aggregate at appropriate intervals.

A PQC for a marketed product is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of a product after it is released for distribution.

Any PQC discovered during the initial inventory should follow the instructions provided on the receipt letter; no PQC form should be filed for issues identified when opening or unpacking a shipment. Subsequently, any observation of a PQC requires immediate notification to the study manager via a completed PQC form and telephone call. The Investigator or designee should complete, sign, and forward a copy of the PQC form to the Sponsor. Contact information will be provided.

In addition, PQC information must be noted on the investigational product accountability log or equivalent in the comments field. A Sponsor representative may assist in answering questions related to this process. To aid in the initial conversation and understanding of a PQC, the site staff may be asked to photograph the issue and send it to the Study Manager.

11. STUDY PROCEDURES

11.1. Visit 1 /Screening (3-14 days prior to V2)

Prior to their screening visit, potential subjects will be pre-screened over the telephone by the initial inclusion and exclusion criteria. Subjects who meet the pre-screening eligibility, will be given an appointment time for their screening visit. The screening visit can occur upto 14 days prior to the Baseline Visit. Subjects will be clearly instructed when to begin the wash-out period.

The following procedures will be performed at Visit 1 (Screening):

- Obtain informed consent – Study personnel will conduct the informed consent form (ICF) discussion with the subject and address any questions or concerns related to the study procedures. Subjects who agree to participate will sign the ICF before any study-related procedures are performed. Subjects will be given a copy of their signed ICF;
- Collect demographic information;
- Obtain significant medical history and prior medication history (including medication use within the last 28 days);
- Ensure that the subject meets the inclusion and none of the exclusion criteria;
- Trained study personnel will examine the subject's back to determine if the subject meets the study entrance criteria;
- Females determined to be of child-bearing potential will have a urine pregnancy test(dipstick). This test must be negative to continue in the study;
- Subjects who meet all study entrance criteria will be provided written and verbal instructions for a 3 day wash-out period [redacted]. They will also use this body wash for the remainder of the study;
- An appointment time for the Baseline Visit (Day 0) will be provided,

11.2. Visit 2 / Baseline Visit/ Day 0

Subjects will return to the clinic following the 3 day wash-out period. The following study procedures will be performed:

- Update any changes in medical history or prior medications and non-drug therapies and confirm subject eligibility
- Assess for adverse events since last visit
- Trained study personnel will examine the subject's back again to ensure subject still meets the study entrance criteria;

- Eligible subjects will be assigned a randomization number which will specify which test sites will be wounded and the treatment assignments for each site.
- Subjects will acclimate in the test facility for at least 15 minutes in a temperature controlled setting of 68-75°F.
- Six test sites will be identified on the back.
- 5 test sites will be wounded using a tape-stripping method as described in Section 11.8, five uniform wounds will be created by the trained study staff on the subjects back according to the randomization schedule.
- Four of the test sites will be wounded and covered with various marketed adhesive bandages (treatment groups); one test site will be wounded and un-covered (positive control) and one test site will remain intact and un-covered (negative control).
- The following assessments will completed on each test site, in the order below:
  - [redacted]
  - Trans Epidermal Water Loss (TEWL; tewameter): Noninvasively measures water evaporation from the skin, which is a measure of skin barrier function. These measurements will be done three times for each test site.
  - [redacted]
  - [redacted]
  - Diffuse Reflectance Spectroscopy (DRS): Noninvasively measures redness by oxy-, deoxy-hemoglobin, and melanin levels in the skin. Five repetitive spectra acquisition will be implemented for each test site.
  - Microbiome[redacted] sampling: Swabs will be used to collect bacteria[redacted] from the test site surface. A total of 2 swabs will be taken per test site, plus control swabs.
- Bandages will be placed on the wounds according to the randomization schedule.
- Subjects will be provided written and verbal instructions.
- Subjects will be informed of their next appointment.

- Subjects will report back to the study facility for daily bandage changes (Days 1-14) and for assessments on Days 1-7 and 14. All clinic visits will be at approximately the same time.

11.3. Visits 3 -9 / Days 1-7

Subjects will be required to report to the study site at approximately the same time each visit. day for all visits. The following procedures will be completed:

- Update any changes in medical history or concomitant medications and non-drug therapies.
- Assess for adverse events since last visit.
- Subjects will acclimate in the test facility for at least 15 minutes in a temperature controlled setting of 68-75°F.
- Bandages will be removed prior to assessments.
- Wound assessments outlined at visit 2 will also be completed at these visits in the order listed below:
  - [redacted]
  - Trans Epidermal Water Loss (TEWL; tewameter): Noninvasively measures water evaporation from the skin, which is a measure of skin barrier function. These measurements will be done three times for each test site.
  - [redacted]
  - [redacted]
  - Diffuse Reflectance Spectroscopy (DRS): Noninvasively measures redness by oxy-, deoxy-hemoglobin, and melanin levels of the skin. Five repetitive spectra acquisition will be implemented for each test site.
  - Microbiome [redacted] sampling: Swabs will be used to collect bacteria [redacted] from the test site surface. A total of 2 swabs will be taken per site, plus control swabs, per time point.
  - A new bandage will be applied to each site as applicable.

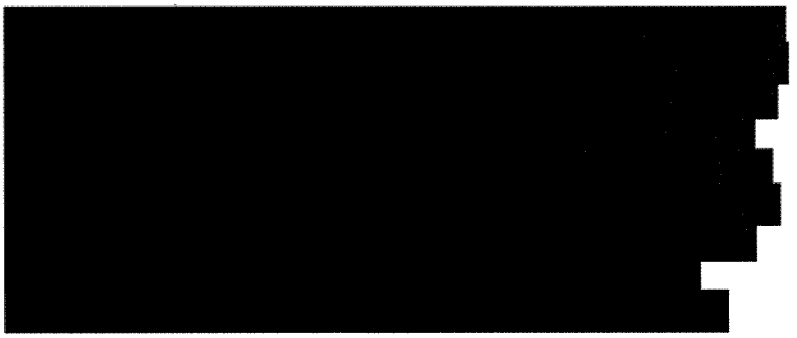
- Subjects will be provided written and verbal instruction.
- Subjects will be informed of their next appointment.

11.4. Visits 10-15/Days 8-13

- Update any changes in medical history or concomitant medications and non-drug therapies.
- Assess for adverse events since last visit.
- Each bandage will be removed and replaced with a new bandage, one test site at a time.
- Written and verbal instructions will be provided.
- Subjects will be informed of their next appointment.

11.5. Final Visit 16/Day 14

- Update any changes in medical history or concomitant medications and non-drug therapies
- Assess for adverse events since last visit
- Subjects will acclimate in the test facility for at least 15 minutes in a temperature controlled setting of 68-75°F
- Bandages will be removed prior to assessments.
- Wound assessments outlined at visit 2 will also be completed at this visit in the order listed below:
  - [redacted]
  - Trans Epidermal Water Loss (TEWL; tewameter): Noninvasively measures water evaporation from the skin, which is a measure of skin barrier function. These measurements will be done three times for each test site.
  - [redacted]

- 
- Diffuse Reflectance Spectroscopy (DRS): Noninvasively measures redness by oxy-, deoxy-hemoglobin, and melanin levels in the skin. Five repetitive spectra acquisition will be implemented for each test site.
- Microbiome [redacted] sampling: Swabs will be used to collect bacteria [redacted] from the skin surface. A total of 2 swabs will be taken per site, plus control swabs.

- Subject Disposition

11.6. Randomization

Subjects who meet the eligibility criteria, will be randomized during Visit 2. The Sponsor will be responsible for the generation of the randomization schedule and products will be packaged according to this randomization schedule.

11.7. Unscheduled/ Follow-up Visit

Subjects may be scheduled for a follow-up visit, as determined to be necessary by the Investigator. The Investigator will provide any applicable post-study wound care treatment as needed. All follow-up information will be documented as applicable.

If a subject experiences an adverse event that is deemed to have a causal relationship to the trial procedures, when the subject either completes or discontinues participation in the study, he/she must return to the site for a follow-up visit until the event is stabilized at a level acceptable to the Investigator.

11.8. Procedures for Tape-stripping, Bandage Application and Bandage Removal

See appendix 1 for diagram for test site numbers.

11.8.1. Site Selection

Six test sites will be identified by the investigative staff and numbered from 1 to 6. The selected sites will be free from nevi or other skin conditions. Using a template and permanent marker, six (6) test areas will be marked at least 2" – 3" apart from each other

on the back on each subject. Test sites will be positioned side by side on a rectangular design so that three are made on each side of the spine. The test sites will be located paraspinally with three test sites on each side of the mid back below the shoulder blades.. Enough space will be left between the test sites so that the bandages can be placed over the wounds without an overlap. If the subject is female, the test sites will be positioned below the bra line.

The randomization schedule will detail the treatment assignments for each test site. Tape Stripping Procedure & Preparation

- The subjects will rest in a prone position (front or ventral surface downward) for the wounding procedure. Instruments used will be sterile. The Investigator or trained clinician creating the wounds as well as assisting staff will wear gloves. Test sites may be re-marked as needed.
- All test sites will be cleaned with an alcohol wipe prior to wounding. NOTE: the test site randomly assigned to be intact (unwounded) and untreated will not be wiped with alcohol.
- Superficial irritation will be created by a tape stripping method to obtain a glistening layer using 3M tape or similar ,(3M St. Paul, MN, USA) for sequential stripping of the epidermis of the test site.
- Strips may be pre-cut and placed on release paper.
- Approximately a 1 cm x 1 cm wound will be created on each of the designated test sites.
- The technician will place the tape on the test site, press it down, rub firmly within the test site marks, and remove the strip with a strong and quick stroke.
- This process will be repeated until a clear glistening layer will be visualized upon removal of the strip. The number of strippings necessary to reach the glistening layer varies among subjects and depends upon the thickness and looseness of the subject's stratum corneum layer.
- The number of strips used per site will be recorded in the source document.

11.8.2. Bandage Application and Removal

Trained personnel will apply/re-apply the bandages to the subjects according to the randomization schedule. Subjects will be placed in a seated or prone position during the bandage application process.

All staff applying test products will wear gloves. Test products will not be applied if wounds show signs of infection, excessive redness, pain, or swelling. Each individual test product is for a single use and will not be reused. Each product will be placed on the designated test site, ensuring that the pad stock covers the wound, adhesive tabs should not directly contact the wound. To prevent tape irritation to the surrounding skin, trained personnel will rotate the bandages in a wheel-like fashion with each application so that

adhesive is not continuously applied to the same area of skin, while also ensuring that the padstock covers the wound completely. Reinforcement tape may be applied to each bandage (covering only the adhesive portions of the bandage, not the central portion containing the pad) to ensure that bandages will remain in place until the next visit, only as needed. Subjects will also be provided a roll of tape to take home for use in case bandages become loose between clinic visits.

Only trained personnel will remove and replace bandages during scheduled visits by gently lifting one corner of the bandage with upward force until one side is completely detached. The other side will be removed in the same manner. Bandages will be removed preserving the intact wound condition as best as possible. All used bandages and tapes will be discarded in a biohazard water container.

If a bandage falls off at home, subjects will be instructed to report the date and time that the bandage fell off and report that information at their next visit. Bandages will not be replaced at home if they fall off. Subjects will be instructed to retain any bandages that have fallen off and bring them to their next appointment.

11.9. Subject Acclimation

Subjects will acclimate in the test facility for at least 15 minutes in a temperature controlled setting of 68-75°F prior to assessments and swabbing. All bioinstrument assessments and swabbing will be completed in a temperature controlled setting of 68-75 F and 35-65 Relative Humidity. Temperature and humidity from the assessment area will be recorded daily during study visits.

11.10. Life Style Guidelines

Subjects will be requested not to immerse the bandages in water (i.e. no baths, swimming, hot tubs, etc.). Subjects will only be allowed to shower during the study using the provided [redacted] WASH. Subjects will be instructed to shower the night prior to their clinic visits to allow the bandages sufficient time to dry prior to removal/evaluations. Subjects should not apply lotions, creams, perfumes, or other topical products to their back during the study, to keep the back as clean as possible.

11.11. Contraception for females

Female subjects with reproductive potential must agree to practice a medically acceptable form of birth control during the study.Females must have used such birth control for at least 3 months prior to the Screening visit and for 30 days following the last application of investigational product.

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

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

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

11.12. Contraception for Males

Male participants will be informed about potential risks of the study medication for embryos and fetuses.

Male subjects are instructed to prevent their partner from becoming pregnant from the first application of investigational product. Information about effective means of birth control (hormonal contraception, intrauterine devices, vasectomy, sexual abstinence) will be provided, and discussed as appropriate with individual subjects.

11.13. Prior and Concomitant Medications

Any medications taken before the first application of investigational product will be defined as a prior medication. Medications taken after the first application of investigational product until after discharge from the study will be defined as concomitant medications.

Female subjects who are using hormonal contraceptives will continue with their prescribed medication. The investigator should approve medication that may be required due to unexpected illness during the study. The usage must be reported to the sponsor and recorded on the case report forms.

Subjects will abstain from using prescription or nonprescription drugs, and dietary/herbal supplements in accordance with the inclusion or exclusion criteria. All concomitant medication taken during the study must be recorded with indication, dose, start and stop times, and dates of administration. All subjects will be questioned about concomitant medication upon admission for each study period.

11.14. Treatment Compliance

The packaging of investigational product will be managed by the Sponsor according to applicable regulatory requirements.

The designated personnel will dispense the investigational product following the procedures set out in the study protocol. The investigator will be responsible for assuring the retrieval of all investigational products from subjects, if the investigational product were to accidentally come off at a location other than the clinical site.

The investigator will maintain accurate and adequate records including dates of receipt and return of investigational product shipments, and quantities received from the Sponsor as well as dates and amounts dispensed. The Investigational Product Accountability Log will be used to record this information.

Compliance of study subjects will be monitored by by a visual inspection of the bandages to ensure they are being treated in the appropriate fashion (i.e. the subject is not swimming or using a hot tub, etc.).

11.15. Rescue Therapy

Subjects may be withdrawn from the study at their request or at the discretion of the Investigator if they experience excessive pain, discomfort, signs of infection, or excessive bleeding. In addition, the following therapies may be provided at the discretion of the Investigator: Acetaminophen, topical or systemic antimicrobial therapy, topical lidocaine, and/or pressure or topical aluminum chloride solution in the case of excessive bleeding.

11.16. End-of-Study Procedures

End of study is defined as the subject's last day of study participation due to study completion or early withdrawal/termination. Assessment of adverse events, collection of study materials and subject disposition should be completed.

12. ASSESSMENTS

Study staff will be trained by the sponsor on the use of all equipment, as well as the swabbing procedure. A separate document will detailed step by step instructions for equipment operation and swabbing.

[redacted]

12.1.2. Transepidermal Water Loss

This assessment will be performed by trained study staff at Days 0,1-7, and 14 for each test site.

Transepidermal water loss (TEWL) measurements are performed in many laboratories and discussed in the literature as a method to characterize barrier function of the stratum corneum (SC) [8]. There are various types of instruments which measure TEWL. All instruments contain relative humidity and temperature sensors and measure flux density (g/m2h) through the SC. It is a open-chamber instrument which measures water vapor flux through a chamber, calculating TEWL values based on changes in relative humidity of the chamber, with a range of 3-200 g/m^{2}h.

TEWL readings will be done in triplicate and each reading will be recorded on the source document.

[redacted]

12.1.5. Diffuse Rflectance Spectroscopy (DRS)

This assessment will be performed by trained study staff at Days 0, 1-7 and 14 for each test site. DRS is a non-invasive diagnostic tool that uses an optical fiber probe to deliver and collect light after multiple scattering and absorption events in the skin. The probe is a bifurcated fiber bundle and one of its legs is used for delivery of light and the other leg is used for collection of light that is remitted from the skin. The distal end of the probe consists of randomized fiber bundle from both legs. Analysis of the reflectance spectrum provides information on skin redness by measuring the levels of skin chromophores such as oxy-hemoglobin, deoxy-hemoglobin, and melanin.

A transparent membrane will be placed over each test site so the probe will not directly contact the skin. Five repetitive spectra acquisition will be implemented for each wound test site for each time point.

For DRS measurements, the site will provide the DRS readings to Sponsor who will derive the DRS meansurements. These measurement will be exported into an macro-enabled audit-trail excel workbook and provided to Quantitative Sciences department for analysis.

12.1.6. Skin Microbiome[redacted] Sampling

Non-invasive collection of the skin microbiome[redacted] is conducted by swabbing a polyester-tipped applicator, that has been wetted by 0.85% saline, across a defined test site for thirty seconds. Two test swabs will be collected from each test site at each time point.

Two control swabs must be collected at the beginning of each day that subjects are sampled.

Collected swabs will be sent to RTL Genomics for microbial DNA extraction, sequencing and analysis. [redacted]

The results of the microbiome[redacted] sampling will be analyzed and summarized in a report which will be appended to the clinical study report.

12.2. Safety Assessment

At the Screening visit (Visit 1), the Investigator will perform an examination to make sure the subject has generally healthy skin and is eligible to participate in the study. Any skin abnormalities, condition, or exam finding that was present at the time of examining the

subject's back (e.g., tattoos, bruising, mechanical trauma, etc.) which does not exclude the subject and has not worsened during the course of the study will be considered medical history and not captured as an AE in subsequent exams.

Expected reactions (e.g. bleeding, pain, itching, etc.) related to the tape stripping procedure, normal healing process, and adhesive bandage application and removal will not be captured as adverse events unless there is exacerbation of these reactions as judged by Investigator. These reactions will be documented on the case report form." The Investigator is to report all directly observed adverse events and all adverse events spontaneously reported by the study subject. In addition, each study subject will be questioned about adverse events. The Investigator's assessment of causality must be provided for all adverse events.

13. ADVERSE EVENT REPORTING

13.1. Introduction

All observed or volunteered/spontaneously reported Adverse Events (AEs) regardless of treatment group or suspected causal relationship to the investigational product(s) will be reported as described in the following sections. For all AEs, the Investigator or medically qualified individual (MD/DO) must pursue and obtain information adequate both to determine the outcome of the AE and to assess whether it meets the criteria for classification as a Serious Adverse Event (SAE) requiring immediate notification (within 24 hours) to the Sponsor or its designated representative. For all AEs, sufficient information should be obtained by the Investigator or medically qualified individual to try to determine causality. The Investigator is required to assess causality. For AEs with a suspected causal relationship to the investigational product, follow-up by the Investigator or medically qualified individual is required until the event or its sequelae resolve or stabilize at a level acceptable to the Investigator, and the Sponsor concurs with that assessment.

13.2. Reporting Period

All AEs, whether serious or non-serious, observed or spontaneously reported, beginning from the time the informed consent is signed and dated, are collected on the source document. AEs of randomized subjects will be entered in EDC while screen failure subjects will not. Subject's participation in the clinical trial begins at signing the informed consent. All AEs are recorded even if the AE occurs prior to the subject's participating in any study-related procedure and/or receiving IP or investigational device. Nonserious AEs will be reported through the subject's last study visit (or termination if the subject terminates early from the study for any reason). Spontaneous reports of SAEs will be collected through and including 30 calendar days after administration of the subject's last dose or exposure to IP.

SAEs require immediate notification to the Sponsor or its designated representative. Any SAE occurring any time after the reporting period (30 calendar days post IP exposure or last dose) must be promptly reported if a causal relationship to study product is suspected.

13.3. Definition of an Adverse Event

An AE is any untoward medical occurrence in a subject after they have signed an informed consent for a trial involving an IP or medical device. Any AE that occurs after the signing of the informed consent, until first usage of IP, will be considered non-treatment emergent and cannot (by virtue of time of occurrence) have a causal relationship with the IP.

The event does not need to have a suspected causal relationship with the investigational product. An AE can therefore be any unfavorable and unintended sign, symptom, disease or injury temporally associated with the use of an investigational product, whether or not related to the investigational product. Examples of adverse events 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.

Additionally, they may include the signs or symptoms resulting from

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

13.4. Abnormal Test Findings

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

- Test result is associated with accompanying symptoms, and/or
- Test result requires additional diagnostic testing or medical/surgical intervention beyond ordering a repeat test, and/or
- Test result leads to a discontinuation from the study, significant additional concomitant treatment, or other therapy, and/or
- Test result is considered to be an adverse event by the medically qualified Investigator or the Sponsor.

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

13.5. Serious Adverse Events (SAE)

An AE or suspected adverse reaction is considered "serious" for a device study if, in the view of either the Investigator (physician) or the Sponsor, it results in any of the following outcomes:

- 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 medicinal product (medically significant)

13.6. Hospitalization

Adverse events reported from clinical studies associated with hospitalization or prolonging hospitalization are considered serious. Any initial admission (even if less than 24 hours) to a healthcare facility meets these criteria. Admission also includes transfer within the hospital to an acute/intensive care unit (e.g., from the psychiatric wing to a medical floor, medical floor to a coronary care unit, neurological floor to a tuberculosis unit). Hospitalization does not include the following:

- Rehabilitation facilities,
- Hospice facilities,
- Respite care (e.g., caregiver relief),
- Skilled nursing facilities,
- Nursing homes,
- Emergency room visits (unless the reason for the emergency room visit meets one of the other outcomes in the definition of serious), and/or
- Same day surgeries (as outpatient/same day/ambulatory procedures)

Hospitalization or prolongation of hospitalization in the absence of a precipitating, clinical AE is not in itself a SAE. Examples include:

- Admission for treatment of a pre-existing condition not associated with the development of a new AE or with a worsening of the pre-existing condition (e.g., for work-up of persistent pre-treatment lab abnormality),
- Social admission (e.g., subject has no place to sleep),
- Administrative admission (e.g., for yearly physical exam),
- Protocol-specified admission during a clinical study (e.g., for a procedure required by the study protocol),
- Optional admission not associated with a precipitating clinical AE (e.g., or elective cosmetic surgery),

Pre-planned treatments or surgical procedures should be noted in the baseline documentation for the entire protocol and/or for the individual subject.

- Diagnostic and therapeutic non-invasive and invasive procedures, such as surgery, should not be reported as AEs. However, the medical condition for which the procedure was performed should be reported if it meets the definition of an AE. For example, an acute appendicitis that begins during the AE reporting period should be reported as the AE and the resulting appendectomy should be recorded as treatment of the AE.

13.7. Resolution

The Investigator will be required to assess the outcome of the AE for investigational product as one of the following:

- Resolved,
- Not Resolved,
- Fatal,
- Resolved with sequelae,
- Resolving, or
- Unknown (lost to follow up)

Any causally-related AEs unresolved upon completion of the last study visit will be followed up by the study staff until the event or its sequelae resolve or stabilize at a level acceptable to the Investigator and recorded on the CRF.

13.8. Severity Assessment

The severity of AEs will be assessed by the Investigator or medically qualified individual (MD/DO) using the following general categorical descriptors:

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

13.9. Causality Assessment

The Investigator's or medically qualified individual (MD/DO) assessment of causality for investigational product (i.e., relationship to investigational product) must be provided for all AEs (serious and nonserious). An Investigator's causality assessment is the determination

of whether there exists a reasonable possibility that the investigational product caused or contributed to an AE.

- Not Related - An AE that is not related to the use of the drug
- Doubtful - An AE for which an alternative explanation is more likely, e.g., concomitant drug(s), concomitant disease(s), or the relationship in time suggests that a causal relationship to investigational product is unlikely.
- Possible - An AE that might be due to the use of the drug. An alternative explanation, e.g., concomitant drug(s), concomitant disease(s), is inconclusive. The relationship in time is reasonable; therefore, the causal relationship to investigational product cannot be excluded.
- Probable - An AE that might be due to the use of the drug. The relationship in time is suggestive (e.g., confirmed by dechallenge) and an alternative explanation is less likely, e.g., concomitant drug(s), concomitant disease(s).
- Very Likely - An AE that is listed as a possible adverse reaction and cannot be reasonably explained by an alternative explanation, e.g., concomitant drug(s), concomitant disease(s). The relationship in time is very suggestive (e.g., it is confirmed by dechallenge and rechallenge) for a causal relationship to the drug.

If the Investigator determines a SAE is associated with study procedures, the Investigator must record this suspected causal relationship in the source documents and CRF, as appropriate, and report such an assessment in accordance with the SAE reporting requirements, if applicable.

13.10. Exposure In Utero (EIU)

For investigational products within clinical studies and for marketed products, an exposure *in utero* EIU occurs if

- a woman is exposed to the investigational product at any time between her last menses before conception through the delivery of the baby.
- there is a possibility of intrauterine exposure to drug via semen from the male partner who is taking the investigational product at the time of conception, thereby possibly exposing the fetus to the product.

If any study subject or study subject's partner becomes or is found to be pregnant during the study subject's participation, the Investigator must report the pregnancy to the Sponsor on a Pregnancy Notification Form (to be provided by the Sponsor when applicable). In addition, the Investigator must submit information regarding environmental exposure to a Sponsor product in a pregnant woman (e.g., a nurse reports that she is pregnant and has been exposed to a cytotoxic product by inhalation or spillage) using the Pregnancy Notification Form. This must be done irrespective of whether an adverse event has occurred and notification must

occur within 24 hours of awareness of the pregnancy. Initial notification via telephone to the Sponsor's study team contact must occur immediately upon the Investigator site's awareness of the pregnancy. The Pregnancy Notification Form must then be sent to the Sponsor within 24 hours of the site's awareness. The information submitted should include the anticipated date of delivery (see below for information related to induced termination of pregnancy).

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

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

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

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

13.11. Withdrawal Due to Serious Adverse Events

When a subject withdraws due to a SAE, the SAEs must be reported in accordance with the reporting requirements defined below.

13.12. Eliciting Adverse Event Information

The Investigator is to report all directly observed AEs and all AEs spontaneously reported by the study subject. In addition, each study subject will be questioned about AEs.

13.13. Reporting Requirements

Each AE is to be assessed to determine if it meets the criteria for a SAE. If a SAE occurs, expedited reporting will follow local and international regulations, as appropriate.

For ransomized subjects, all AEs will be reported on the AE source document and then entered into the EDC system. A Clinical Serious Adverse Event (SAE) Report Form must be completed if the event is considered to be serious. It should be noted that this Clinical SAE Report Form for collection of SAE information is not the same as the AE page(s) of the CRF. Where the same data are collected, the forms must be completed in a consistent manner. For example, the same AE term should be used on both forms. Adverse events should be reported using concise medical terminology on the CRFs as well as on the form for collection of SAE information.

13.14. Serious Adverse Event Reporting Requirements

If a SAE occurs, the Sponsor is to be initially notified by telephone immediately upon awareness of the event by the Investigator's site. Within 24 hours of the Investigator site's awareness of the event, the study site must send the Sponsor the Clinical SAE Report Form. This timeframe also applies to additional new information (follow-up) on previously forwarded SAE reports as well as to the initial and follow-up reporting of EIU cases. In the rare event that the Investigator's site does not become aware of the occurrence of a SAE immediately (e.g., if an outpatient study subject initially seeks treatment elsewhere), the Investigator's site is to report the event immediately after learning of it as described and document the time of the study site's first awareness of the adverse event.

For all SAEs, the Investigator is obligated to pursue and provide information to the Sponsor in accordance with the timeframes for reporting specified above. In addition, an Investigator may be requested by the Sponsor to obtain specific additional follow-up information in an expedited fashion. This information may be more detailed than that captured on the adverse event case report form. In general, this will include a description of the adverse event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as concomitant medications and illnesses must be provided. In the case of a subject death, a summary of available autopsy findings (if available) and death certificate should be collected if permission is obtained from the subject's family. For a hospitalization, a copy of the hospital discharge summary should be requested. If obtained, these documents (with subject's personal identifiers redacted) should be submitted as soon as possible to the Sponsor or its designated representative.

Appropriate SAE forms will be provided to the study site at the initiation of the study. Upon notification of an SAE at the study site, the Investigator or designated study site staff should

call and speak to their Sponsor's study team contact immediately to initially notify them of the SAE.

Within 24 hours of awareness of the event, the Investigator or designated study site staff:

- complete the Clinical SAE Report Form ([provided by the Sponsor] with as much information as possible, however at a minimum, the subject identification number, name of product, SAE, and name of reporter are required);
- ensures the Investigator signs the Clinical SAE Report Form before sending to the Sponsor;
- scans and send via secure email the Clinical SAE Report Form to the Sponsor contacts.
-

13.15. Special Situations

This category of AEs is required for studies involving medicinal investigational products.

Special Situations (SS): Safety events that may not meet the definition of an AE; however, are required to be collected to meet Health Authority requirements. Examples include:

- Overdose of a J&J medicinal product
- Pregnancy exposure (maternal and paternal) to a J&J medicinal product
- Exposure to a J&J product from breastfeeding
- Suspected abuse/misuse of a J&J medicinal product
- Inadvertent or accidental exposure to a J&J medicinal product (including occupational exposure).
- Any failure of expected pharmacological action (i.e., lack of effect) of a J&J product.
- Unexpected therapeutic or clinical benefit from use of a J&J product.

- Medication error involving a J&J medicinal product with or without patient/consumer exposure to the J&J product, (e.g., product name confusion) OR that caused an unintended effect or could cause an intended effect (e.g. adult medicine given to a young child).
- Suspected transmission of an infectious agent via a J&J product.

[redacted]

All nonserious adverse events are to be reported on the adverse event CRFs and will be submitted to the Sponsor.

14. STATISTICS

The Sponsor will be responsible for the data management and statistical analyses of this study. The skin microbiome [redacted] data will be analyzed and reported independently by external partners. The imaging data will be analyzed by the sponsor.
Sample Size Determination

The sample size of this exploratory study is not based on the statistical power consideration.

14.1. Analysis Populations

The efficacy analysis will be based on the Intent-to-treat (ITT) principle, i.e., all subjects who received induced wounds and started the bandage or no treatment will be included in the analysis.

The safety analysis will be based on all subjects who received induced wounds.

14.2. EfficacyAnalysis

The analysis of the predominant microflora will be performed by Research and Testing Laboratories, LLC (external partner).

TEWL [redacted] and DRS are measured at Baseline, Days 1-7 and Day 14. The triplicate values at each assessment time point will be averaged as the final response value, with the exception of the DRS which will have 5 replicates at each timepoint.

The final response values of TEWL and DRS will be summarized at each assessment time point by the assigned test products.

The within product comparison will be performed using the paired t-test to compare the values of each product at each post baseline time point with its own baseline value.

The between products comparison will be performed based on the change from baseline (post baseline value minus baseline value). The change from baseline of each product will be analyzed using mixed effect ANCOVA model at each post baseline time point. The ANCOVA model will include the product as the factor and the baseline value as the covariate. The model will include the subject as a random effect to incorporate the within subject correlation. The adjusted mean of each product from the ANCOVA model will be compared between the test products and the negative control, between the test products and the positive control, and between the negative control and the positive control.

[redacted]

14.3. Subjects Who Use Rescue Therapy or Discontinue

Subjects who use rescue therapy and are not withdrawn from the study will continue to be assessed per protocol and all data points will be included in the analysis. For subjects who discontinue(for any reason) the study early, data points already collected will be included in the analysis.

14.4. Safety Analysis

All subjects who receive at least one dose of study treatment will be included in the safety analysis. All adverse events reported during the adverse-event reporting period will be listed by subject number and treatment. The number of subjects experiencing adverse events will be presented by body system, preferred term, and treatment. The latest version of the Medical Dictionary for Regulatory Activities (MedDRA) will be used as the adverse event classification system.

15. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The Investigator(s)/institution will permit study-related monitoring, audits, IRB/IEC review and regulatory inspection(s) by providing direct access to source data/documents.

15.1. Study Monitoring

Before an investigational site can enter a subject into the study, a representative of the Sponsor will visit the investigational study site to:

- Determine the adequacy of the facilities
- Discuss with the Investigator(s) and other personnel their responsibilities the site's responsibility with regard to protocol adherence as well as the study and monitoring responsibilities of the Sponsor or its representatives. These responsibilities will be documented in a written agreement between the Sponsor and the Investigator.

The site will be fully trained in the protocol during the Initiation visit or web-ex. During the study, a monitor from Sponsor or representative will have regular contacts with the investigational site, for the following:

- Provide information and support to the Investigator(s)
- Confirm that facilities remain acceptable
- Confirm that the investigational team is adhering to the protocol, that data are being accurately recorded in the CRFs, and that IP accountability checks are being performed
- Perform source data verification. This includes a comparison of the data in the CRF with the subject's medical records at the hospital or practice, and other records relevant to the study. This will require direct access to all original records for each subject (e.g., clinic charts).
- Record and report all protocol deviations not previously sent to Sponsor.
- Confirm AEs and SAEs have been properly documented on CRFs and confirm any SAEs have been forwarded to Sponsor and those SAEs that met criteria for reporting have been forwarded to the IRB/IEC.

The monitor will be available between visits if the Investigator(s) or other staff needs information or study-related direction.

15.2. Audits and Inspections

Authorized representative of Johnson & Johnson, a regulatory authority, an Independent Ethics Committee or an Institutional Review Board may visit the site to perform audits or inspectios, including source data verification. The purpose of a Johnson & Johnson audit

or inspection is to systematically and independently examine all study-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol. Good Clinical Practice guidelines of the International Cnference on Harmonization, and any applicable regulatory requirements. The Investigator should contact their study contacts immediately if contacted by a regulatory agency about an inspection.

15.3. Institutional Review Board(IRB)

The Principal Investigator must obtain IRB approval for the investigation. Initial IRB approval, and all materials approved by the IRB for this study include subject consent form and recruitment mateials must be mainted in the Site Master File by the Investigator and made available for inspection.

16. QUALITY CONTROL AND QUALITY ASSURANCE

Authorized representatives of the Sponsor, a regulatory authority, an IEC or an Institutional Review Board may visit the site to perform audits or inspections, including source data verification. The purpose of a Sponsor audit or inspection is to systematically and independently examine all study-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, GCP guidelines of the ICH E6, and any applicable regulatory requirements. The investigator should contact their study contacts immediately if contacted by a regulatory agency about an inspection.

17. DATA HANDLING AND RECORDKEEPING

17.1. Case Report Forms/Electronic Data Record

As used in this protocol, the term case report form (CRF) should be understood to refer to the Electronic Data Capture system.

The EDC system, is the database where pertinent study data is collected such as demography, subject randomization, adverse events, and subject disposition.

Electronic Data Capture pages should be completed for each randomized 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.

All data will be collected on source documents first and the relevant data needed for analysis will be recorded in the Electronic Data Capture (EDC) system except DRS data. The DRS data will be reported into an macro-enabled audit trail Excel worksheet [redacted] be analyzed by external providers and this data will not be entered into the EDC system.

It is the Investigator's responsibility to ensure completion and to review and approve all information captured in the EDC. The subject's data in the EDC system must be electronically signed by the Investigator. These signatures serve to attest that the information contained in the EDC system is true. At all times, the Investigator has final personal responsibility for the accuracy and authenticity of all clinical data entered in the EDC. Subject source documents are the Investigator's subject records maintained at the study site. In cases where the source documents are the hospital or the physician's chart, the information collected in the EDC must match those charts.

All final data recorded in EDC system will be kept by the Sponsor and at the clinical site.

All data recorded on source documents will be kept at the clinical site.

17.2. Inspection of Records

To enable evaluations and/or audits from regulatory authorities or the Sponsor, the investigator agrees to keep records including the identity of all participating subjects (sufficient information to link records, e.g., CRFs and hospital records), all original signed informed consent forms, copies of all CRFs, SAE forms, source documents, and detailed records of treatment disposition. The records should be retained by the investigator according to ICH guidelines, local regulations, or as specified in the Clinical Study Agreement, whichever is longer.

17.3. Retention of Records

The Principal Investigator must maintain all documentation relating to the study for a period of 2 years after the last marketing application approval, or if not approved 2 years following the discontinuance of the test article for investigation. If it becomes necessary for Johnson & Johnson or the Regulatory Authority to review any documentation relating to the study, the Investigator must permit access to such records.

If the investigator relocates, retires, or for any reason withdraws from the study, the Sponsor should be prospectively notified. The study records must be transferred to an acceptable designee, such as another investigator, another institution, or to the Sponsor. The investigator must obtain Sponsor's written permission before disposing of any records, even if retention requirements have been met.

18. SPONSOR DISCONTINUATION CRITERIA

Premature termination of this clinical study may occur because of a regulatory authority decision, change in opinion of the IRB/EC, drug safety problems, or at the discretion of the sponsor. In addition, the Sponsor retains the right to discontinue the study at any time.

If a study is prematurely terminated or discontinued, the Sponsor will promptly notify the investigator. After notification, the investigator must contact all participating subjects within a time period set by the Sponsor (usually two weeks). All study materials must be collected and all CRFs completed to the greatest extent possible.

19. PUBLICATION POLICY

Publication of study results by the Investigator is discussed in the Clinical Study Agreement, as appropriate. Results from this study may be published in the form of oral or written presentations at scientific meetings or as one or more peer-reviewed journal articles. In these cases, no information on individual subjects will be revealed.

20. LIST OF REFERENCES

1. Williams et al (2017). Cutaneous Nod2 Expression Regulates the Skin Microbiome and Wound Healing in a Murine Model. Journal of Investigative Dermatology. Available online June 22, 2017.
2. E.A. Grice, H.H. Kong, S. Conlan, C.B. Deming, J. Davis, A.C. Young, *et al.*Topographical and temporal diversity of the human skin microbiome Science, 324 (5931) (2009), pp. 1190-1192.
3. Pagnoni A, Spineli G, Berger RS, Bowman J, Garreffa S, Snoddy AM. Lack of Burning and Stinging from a Novel First-Aid Formulation Applied to Experimental Wounds. J Cosmet. Sci., 55: 157-162, 2004
4. Fluhr J, Dickel H, Weyher I, et al. Impact of anatomical location on barrier recovery, surface pH, and stratum corneum hydration after acute barrier disruption. Brit J Derm 2001; 146: 770-776.

APPENDIX 1 INSTRUCTIONS FOR USE – TEST SITES

SITE LOCATION AND SELECTION:

VIEW OF SUBJECT'S BACK

HEAD

LEFT SIDE **RIGHT SIDE**

Bra Line for Females

Site 1	**Spine**	**Site 2**
Site 3		**Site 4**
Site5		**Site 6**