# An evaluation of the skin protection characteristics of two commercially available skin barrier protectants

Protocol Number MED-2022-DIV71-003

08-AUG-2022
Version 2.0

Prepared by:

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Contents

## INVESTIGATOR ACKNOWLEDGMENT SIGNATURE

- I agree to conduct the study in accordance with the relevant, current protocol and will make changes to the protocol necessary to protect the safety, rights, or welfare of participants.
- I agree to personally conduct and supervise the investigation as described within.
- I agree to inform all participants that the device is being used for the purposes of an investigational study.
- I will ensure that requirements relating to obtaining informed consent in the guidelines for Good Clinical Practices (GCP), and 21 Code of Federal Regulations (CFR) Part 50 and Institutional Review Board (IRB) review and approval in 21 CFR Part 56 are met.
- I agree to report to the IRB and/or Ethics Committee, according to the protocol, adverse experiences that occur during the course of the investigation in accordance with guidelines for GCP, 21 CFR 812, and 21 CFR 312.
- I have read and understand the information in the protocol, including the potential risks.
- I agree to maintain adequate and accurate records in accordance with guidelines for GCP and 21 CFR 812.140 and to make those records available for inspection.
- I will ensure that an IRB compliant with the requirements of guidelines for GCP and 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human participants or others.
- I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in the guidelines for GCP, and the CFR.

| |
|---|
| Principal Investigator (PI) (Print name): |
| Principal Investigator (Signature): |
| Date (DD-MMM-YYYY): |

I have received and reviewed this Investigational Plan. I will conduct the study as described.

## DOCUMENT HISTORY

| VERSION | DATE | DESCRIPTION |
|---|---|---|
| Version 1.0 | 15-JUL-2022 | Initial Release |
| Version 2.0 | 08-AUG-2022 | 1. Change in washout period duration from 18–24 hours to a minimum of 18 hours.<br>2. Change in participant duration from 11 to 13 days.<br>3. Individuals who are able to identify the manufacturer of the skin barrier protectants (SBPs) included in the study added as an exclusion criterion. |

# 1. PROTOCOL SUMMARY

## 1.1. Synopsis

**Title:** An evaluation of the skin protection characteristics of two commercially available skin barrier protectants.

**Study Description:** The skin is the largest organ in the human body serving a myriad of vital functions. In addition to being the organ of touch, heat, and cold, the skin is a physical barrier to microbes and the environment and helps regulate body temperature. There are numerous circumstances in the healthcare environment where supporting the barrier function of the skin is important. For example, skin that is chronically subjected to moisture and chemical stress (eg, fecal and urinary incontinence, high levels of mucus or perspiration) is susceptible to skin breakdown.[1] Treating the affected skin with a barrier would reduce this stress on the skin. Additionally, skin changes naturally with age and elderly patients often have frail skin that can tear easily.[2,3] Treating the periwound area with a skin barrier protectant (SBP) would shore up the frail skin and limit the extension of the tear. The current study will evaluate the duration of wear and durability of two commercially available SBPs: Medline Marathon® XL No Sting Cyanoacrylate Skin Protectant (henceforth referred to as "Marathon®") and 3M™ Cavilon™ Advanced Skin Protectant (henceforth referred to as "Cavilon™"). The presence and deterioration over time of the SBPs will be measured with a Corneometer® CM 825 (henceforth referred to as "Corneometer®"), which is a device that determines skin surface hydration via measurement of skin capacitance. After baseline measurements are taken using the Corneometer®, the volar surface of the forearms (henceforth referred to as "volar forearms") and inner elbows of the participants will be randomized for treatment with the SBPs. A distinct area of each volar forearm of the participants will be left as an untreated control. After the SBPs have dried completely, Corneometer® measurements will be taken again. Thereafter, measurements will be taken daily over a period of seven days with a two-day break over the weekend. The final Corneometer® measurements will be taken on Monday or Tuesday, depending on the date of the participants' first visit (Visit 1). The participants will also complete a survey regarding their experience with the two SBPs on specific days during study participation.

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| **Primary Objective:** | To evaluate and compare the duration of wear and durability of Marathon® and Cavilon™ |
| **Secondary Objective:** | To collect information on the participant experience with the two SBPs |
| **Primary Endpoint:** | 1. Degradation of the SBPs over seven days as measured by the Corneometer®.<br>1a. The breakdown of the SBPs on the volar forearm will reflect the duration of wear of the SBPs.<br>1b. The breakdown of the SBPs on the inner elbow, relative to the volar forearm, will reflect the durability of the SBPs. |
| **Secondary Endpoint:** | Responses to participant surveys |
| **Study Population:** | Number of participants, N = 42; Medline Industries, Limited Partnership (LP) (henceforth referred to as "Medline") employees will be recruited for the study. The employees may be healthcare providers (HCPs) or non-HCPs, but they must be unable to identify the manufacturer of the SBPs included in the study. This will be determined by showing the images of the SBPs to the participants in order to assess whether the participants can recognize either of them. |

**Inclusion Criteria**

Individuals who meet all the following criteria will participate in this study:

- Individuals ≥ 18 years of age

**Exclusion Criteria**

Individuals will not be eligible for the study if ANY of the criteria given below are met:

- Individuals have skin conditions that might interfere with Corneometer® measurements, including rash, irritation, sunburn, tattoo, birthmark, any other dermal irregularities on the left or right volar forearm or inner elbow.
- Individuals have excessive hair on the left or right volar forearm or inner elbow as determined by study personnel.
- Individuals have a self-reported allergy/sensitivity to ingredients present in either of the SBPs, components of

| | |
|---|---|
| | the soap used for bathing, or the exam gloves and non-toxic marker used in the study.<br>▪ Individuals are pregnant.<br>▪ Individuals whose self-reported activities may affect friction on one arm more than the other (eg, sports like tennis or holding a baby where one arm is used more routinely than the other).<br>▪ Individuals who are able to identify the manufacturer of the SBPs included in the study. |
| **Phase:** | Post-market |
| **Description of Sites/Facilities Enrolling Participants:** | Study visits will be conducted in the Clinical Evaluation Rooms at the Northfield location of Medline. |
| **Description of Study Intervention:** | Completion of informed consent and participant screening will be followed by a washout period of minimum 18 hours (wherein participants will be asked to avoid application of cleansers, lotions, or perfumes to both forearms and inner elbows) prior to the first visit (Visit 1) of the study. During Visit 1, study personnel will confirm that the washout period has been successfully completed. Participants will wash their forearms and inner elbows with a standardized soap and dry them using paper towels for each arm. After the participants' forearms and inner elbows have fully dried, study personnel will use a Corneometer® (which measures skin hydration) to record baseline measurements of the skin within 2-inch x 2-inch squares (starting about two inches above the wrist) marked with a non-toxic marker on the volar forearms and inner elbows of the participants. Thereafter, participants will be randomized to the two SBPs, Marathon® or Cavilon™ (designated SBP). The designated SBP will be applied to the volar forearm and inner elbow "test areas" on the participant's dominant arm (as determined by the participant). The other SBP will be applied to the volar forearm and inner elbow "test areas" on the participant's non-dominant arm. A distinct area of each volar forearm will be used as an "untreated control area". Corneometer® measurements will be taken again on the same day after the SBPs have been left to dry for at least one minute or have fully dried. Thereafter, subsequent measurements will be taken daily over a seven-day period with a two-day break over the weekend. Each participant will commence the study on Monday or Tuesday. This will permit |

daily readings for the first 72 hours, which is the more important window to evaluate SBP wear time. There will be a two-day break in measurements over the weekend, after which Corneometer® measurements will be taken either on Monday, or Monday and Tuesday, depending on the participants' start date. Participants will be allowed to bathe their arms using a standardized soap provided by the study personnel but will be asked to minimize scrubbing and any other abrasion of the volar forearms and inner elbows. In addition, participants will be instructed not to engage in activities, for eg, sports (eg, tennis) or holding a baby that may cause significant abrasion on one arm and not the other. On the last visit of the study (Visit 6), study personnel will take the last set of Corneometer® measurements. In addition, participants will also complete surveys regarding their experience with the SBPs on specific days during study participation.

The Corneometer® measurements will help determine the presence of the SBPs and their deterioration over time. Skin treated with the SBPs will typically have lower readings than untreated skin. As the SBPs break down, the corresponding readings are expected to rise.

**Study Duration:** Up to three months.

**Participant Duration:** Up to 13 days.

## 1.2. Schedule of Activities (SOA)

| Assessments and Activities[#] | Pre-visit Activities | Visit 1 | Visit 2–5 | Visit 6 (Final visit) |
|---|---|---|---|---|
| Informed consent | X | | | |
| Participant Screening | X | | | |
| Demographics | X | | | |
| Participants complete minimum 18 hours washout period | X | | | |
| Participants wash forearms and inner elbows with standardized soap, and dry them using paper towels | | X | | |
| Participant forearms and inner elbows allowed to dry | | X | | |
| Randomization of SBP to be applied to the dominant arm of the participant[§¥] | | X | | |
| Baseline Corneometer® measurements taken | | X | | |
| SBPs applied at the volar forearm and inner elbow test areas according to the Randomization Schedule[§] | | X | | |
| SBPs allowed to dry | | X | | |
| Post-application Corneometer® measurements taken at untreated control areas and test areas | | X | X | X |
| Participants complete surveys regarding experience with the SBPs[¥] | | X | X | X |
| Monitoring for adverse device events | | X | X | X |
| Participant dismissal | | | | X |

[#] Study activities will occur after informed consent has been signed, and the participant has met all the inclusion criteria and none of the exclusion criteria.
[§] Randomization will assign each participant to either Marathon® or Cavilon™ (designated SBP). The designated SBP will be applied to the volar forearm and inner elbow test areas of the participants' dominant arm (as determined by the participant), whereas the other SBP will be applied to the volar forearm and inner elbow test areas of the participants' non-dominant arm.
[¥]The same type of SBP will be applied to the volar forearm and inner elbow test areas.
[£]Participants will complete surveys on Visits 1, 3, and 6.

# 2. INTRODUCTION

## 2.1. Background & Rationale

Skin acts as a protective barrier against a wide range of external forces. However, the integrity of this barrier can be compromised by a number of factors. Exposure to different sources of moisture such as urine, feces, wound drainage, ostomy fluid, or perspiration affects the outermost layer of the skin, the stratum corneum, leading to overhydration and inflammation of the skin. The resultant moisture-associated skin damage (MASD) can result in skin maceration. Moisture can also increase the coefficient of friction of the skin, and expose the skin to shearing forces.[1] In addition to moisture, repeated use of adhesive tapes and dressings can strip away the outer layer of the skin leading to injuries.[4,5] Furthermore, aging can make the outer layer of the skin thinner, which can make the skin of the elderly more susceptible to exposure to moisture-, friction-, shear-related injuries and skin tears.[2,3]

Cyanoacrylate-based liquid wound dressings are a class of skin barrier protectants (SBPs) that can be used on at-risk skin to prevent or manage damage from minor skin tears or abrasions, as well as moisture-, friction-, and shear-related skin breakdown.[6] These SBPs have a high affinity for moisture. Contact with moisture present in the skin triggers a "chain reaction", which leads to the formation of a polymeric substance that interacts with and adheres to the skin at the molecular level,[6] and protects it from moisture, friction, shear, or other irritants such as adhesives. These SBPs offer multiple advantages. They are solvent-free, which eliminates the stinging sensation associated with solvents.[6] Moreover, absence of a solvent ensures that most of the product remains deposited on the skin where it is applied.[6] The SBPs form a transparent, flexible film when applied to the skin. Therefore, along with ease of application, there is better visualization of the skin to which the SBP is applied.[7] Moreover, these SBPs do not dissolve in water and result in forming a film that is resistant to bodily fluids.[6] Furthermore, since the SBPs bond chemically with the skin, they are removed naturally as the stratum corneum sloughs off.[6,8]

The aim of this study is to evaluate and compare the duration of wear and durability of two commercially available SBPs, Marathon® and Cavilon™, applied to the volar forearms and the inner elbows of the participants per the Randomization Schedule. A Corneometer®, which determines skin hydration through measurement of skin capacitance, will be used to assess the presence of the SBPs and their deterioration over a seven-day period. Participants will also complete surveys regarding their experience with the two SBPs on specific days during study participation.

## 2.2. Study Products

### 2.2.1 Marathon® XL No Sting Cyanoacrylate Skin Protectant (referred to as Marathon®)

Marathon® (#MSC093001XL) is a non-cytotoxic, fast drying liquid barrier film for the protection of damaged or intact skin from the effects of moisture such as urine, feces, digestive juices,

perspiration, and wound drainage. It can be used in areas that are exposed to friction (rubbing) or shear (tearing) from bedding, clothing, shoes, or any material that would rub against the skin. It helps protect skin against irritation caused by adhesive products. Marathon® is applied as a liquid and dries within a minute, adhering to the contours of the skin to form a transparent flexible film. It will wear off naturally, as the skin regenerates. The applicator and packaging are sterilized.

### 2.2.2 3M™ Cavilon™ Advanced Skin Protectant (referred to as Cavilon™)

Cavilon™ (#MMM5050CS) is a polymeric-cyanoacrylate solution intended for the protection of intact or damaged skin. It is effective in conditions where skin is exposed to moisture and caustic irritants such as feces, digestive fluids, wound drainage and urine, frequently or continuously. It can also be used in areas exposed to friction and shear from bedding, clothing, shoes or any other material that would rub against the skin. Upon application to skin, the liquid dries rapidly to form a primary long-lasting waterproof, highly durable film barrier. It is elastomeric, adhering to the contours of the skin and providing a uniform film. The film is transparent and possesses good oxygen and moisture vapor permeability. The polymer-cyanoacrylate is dispersed in a non-stinging solvent. The film is colorless, non-cytotoxic and has a low dermatitis potential. The film adheres to dry, moist or wet skin surfaces and remains intact during conditions of continuous or repeated exposure to moisture or caustic irritants. It will wear off the skin and does not require removal.

## 2.3. Risk/Benefit Profile

2.3.1.Potential Study Risks

This study entails minimum risk to the study participants. The SBPs used in the study are commercially available products that can be used in both home and clinical settings. There may be a minor risk of skin irritation for the participants. In such a case, for Marathon®, a clean tissue can be used before the film formed by the SBP dries. If the film has already dried, petroleum jelly can be used to soften the film, after which the SBP can be removed. In case of Cavilon™, the SBP can be removed using an adhesive remover containing hexamethyldisiloxane (HMDS). The risk to the study personnel is minimal, as they will use an applicator to apply the SBPs to the participants' volar forearms and inner elbows. The risk is further minimized as the study personnel will wear gloves during application of the SBPs.

2.3.2. Potential Study Benefits

The participants will not benefit from the study directly. However, the study will furnish data regarding the duration of wear and durability of the SBPs, as well as participant feedback about the SBPs. This information may help inform clinical use decisions made by HCPs. Furthermore, the SBPs do not require prescription for use and may therefore benefit non-clinically trained consumers. Overall, the results of this study may translate into better care and protection of at-risk skin from moisture-, friction-, shear-, and adhesive-related injuries.

2.3.2. Assessment of Potential Risk/Benefit Profile

Given the minimal risk of this study for the participants, and the potential for future benefit from the study, the risk/benefit profile of the study is acceptable.

## 3. OBJECTIVES AND ENDPOINTS

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS |
|---|---|---|
| **Primary** | | |
| To evaluate and compare the duration of wear and durability of Marathon® and Cavilon™ | Degradation of the SBPs over seven days as measured by the Corneometer®.<br>1a. The breakdown of the SBPs on the volar forearm will reflect the duration of wear of the SBPs.<br>1b. The breakdown of the SBPs on the inner elbow, relative to the volar forearm, will reflect the durability of the SBPs. | This endpoint will be an objective measurement of the deterioration of the SBPs, and in turn, the skin protection they offer over time. |
| **Secondary** | | |
| To collect information on the participant experience with the two SBPs | Responses to participant surveys | This endpoint evaluates the participants' experience with the SBPs. |

## 4. STUDY DESIGN

### 4.1. Overall Design

This is a randomized, single-blind study, which will evaluate and compare the duration of wear and durability of two commercially available SBPs, Marathon® and Cavilon™. The presence of the SBPs and their deterioration over time will be measured using a Corneometer®, which measures skin hydration.

During a washout period of minimum 18 hours prior to the first visit (Visit 1), participants will be asked to avoid application of cleansers, lotions, or perfumes to both forearms and inner elbows. During Visit 1, study personnel will confirm that the participants have successfully completed the washout period. Participants will then wash their forearms and inner elbows with a standardized soap and dry them using paper towels for each arm. After the participants' forearms and inner elbows have dried completely, study personnel will mark 2-inch x 2-inch squares with a non-toxic marker on the participants' volar forearms and inner elbows (starting about two inches above the

wrist), and baseline Corneometer® measurements will be taken. Per the Randomization Schedule, each participant will be assigned to either Marathon® or Cavilon™ (designated SBP). The designated SBP will be applied to the volar forearm and inner elbow "test areas" on the participants' dominant arm (as determined by the participant). The other SBP will be applied to the volar forearm and inner elbow "test areas" on the participants' non-dominant arm. A distinct area of each volar forearm of the participants will be used as an "untreated control area" for the test areas on that forearm. To assess baseline skin hydration, study personnel will use the Corneometer® to take the average of five initial measurements of skin capacitance and the standard deviation of the measurements, for each of the untreated control areas and the volar forearm and inner elbow test areas. After the baseline measurements have been recorded, the study personnel will apply the two SBPs, Marathon® and Cavilon™, according to the Randomization Schedule to test areas on the participants' volar forearm and the inner elbow. After the SBPs have been left to dry for at least one minute or have dried completely, Corneometer® measurements will be repeated in the untreated control areas and the volar forearm and inner elbow test areas in a manner similar to the baseline measurements. Thereafter, daily Corneometer® measurements will be taken over a seven-day period with a two-day break over the weekend. During the study period, participants will be allowed to bathe their arms using a standardized soap provided by the study personnel but will be instructed to minimize scrubbing or any other abrasion of the skin of the volar forearms and inner elbows. In addition, participants will be instructed not to engage in activities, for eg, sports (eg, tennis) or holding a baby that may cause significant abrasion on one arm and not the other. On the last day of the study (Visit 6), study personnel will take the last set of Corneometer® measurements. In addition, participants will complete surveys regarding their experience with the two SBPs on specific days during study participation.

Note:

1. Skin treated with the SBPs will typically have lower measurements than untreated skin. As the SBP breaks down, the corresponding measurements are expected to rise.

2. Each participant will commence the study on Monday or Tuesday, which will permit daily readings for the first 72 hours, which is the more important window to evaluate SBP wear time. There will be a two-day break over the weekend, after which study personnel will take Corneometer® measurements either on Monday, or Monday and Tuesday, depending on the participant's start date.

### 4.2. End of Study Definition

The study will be considered complete after the participants are dismissed from the study on completion of all study-related activities, and a Clinical Study Report approved by Clinical Affairs has been issued.

## 5. STUDY POPULATION

### 5.1. Inclusion Criteria

Individuals who meet all the following criteria will participate in this study:

- Individuals ≥ 18 years of age

### 5.2. Exclusion Criteria

Individuals will not be eligible for the study if ANY of the criteria given below are met:

- Individuals have skin conditions that might interfere with Corneometer® measurements, including rash, irritation, sunburn, tattoo, birthmark, any other dermal irregularities on the left or right volar forearm or inner elbow.
- Individuals have excessive hair on the left or right volar forearm or inner elbow as determined by study personnel.
- Individuals have a self-reported allergy/sensitivity to ingredients present in either of the SBPs, components of the soap used for bathing, or the exam gloves and non-toxic marker used in the study.
- Individuals are pregnant.
- Individuals whose self-reported activities may affect friction on one arm more than the other (eg, sports like tennis or holding a baby where one arm is used more routinely than the other).
- Individuals who are able to identify the manufacturer of the SBPs included in the study.

### 5.3. Strategies for Recruitment and Retention

Participants will be recruited from an internal database of Medline employees who have previously participated in studies conducted by Medline, and/or have agreed to be contacted for future studies, as well as via advertisement(s). Potential participants will be screened and enrolled until a total of 42 participants with complete data are obtained.

### 5.4 Early Withdrawal and Replacement

Participants will be discontinued or withdrawn from study participation at any time if either the participants or the study personnel feel that it is not in the participants' best interest to continue participation.

Participation in the study may end at several critical points:

- Participant withdraws from the study for any reason.
- Participant is not compliant with study procedures.
- Participant presents with adverse event(s) such that in the opinion of the PI it is in the best interest of the participant to discontinue study participation.
- Protocol violation requiring discontinuation of use of the study product(s).

Based on the above reasons, if any participant withdraws from the study or is dismissed, another participant will be recruited such that the total number of participants who complete the study will be 42. If a participant is being replaced, the randomization sequence associated with the replaced participant will be used for the new participant.

# 6. STUDY PROCEDURES AND ASSESSMENTS

## 6.1. Informed Consent and Screening

### 6.1.1. Informed Consent

The study visits will take place in a Clinical Evaluation Room (henceforth referred to as "study room") at Medline. The study personnel will obtain written informed consent from the participant either in the study room or over a video conference call with the participant. Written consent must be obtained from all participants and documented on an Informed Consent Form (ICF) that has received approval from an IRB/Ethics Committee. The signed ICF must be written in accordance with GCP and Good Documentation Practices (GDP) and must comply with all elements required by United States (US) Food and Drug Administration (FDA) 21 CFR 50.25 and International Conference on Harmonisation (ICH) 4.8, state and local regulations, and additional elements relevant to specific study situations (including a statement that Medline and relevant authorities have access to participant records). A copy of the signed consent will be given to each participant.

### 6.1.2 Verification and Eligibility

Following informed consent, the participants will undergo screening based on the inclusion/exclusion criteria detailed in Sections 5.1 and 5.2. Study personnel will verify participant eligibility in the study room at Medline, or over a video conference call with the participant. Thereafter, participants will receive a unique screening number that will be recorded in the Participant Screening Form (PSF). The reason for participant exclusion will also be documented in this form.

Potential participants who satisfy all inclusion/exclusion criteria for the study will be enrolled in the study and will be assigned a randomization sequence according to the Randomization Schedule. Participants will receive unique participant identification (ID) numbers based on the order in which they are enrolled after being screened. Demographic information of the participants will be documented in the PSF. Self-reported skin tone (or phototype) of the participants will be documented in the CRF. The Randomization Schedule, Case Report Forms (CRFs), PSF, and other study-related documents will be provided separately to the study personnel.

### 6.1.3. Washout Period

Following study enrollment, participants will be instructed to adhere to a minimum 18 hours washout period, during which they must avoid application of any perfumes, or moisturizing, skin hydrating, or body cleansing products to both forearms and inner elbows. Participants will also be instructed to return for Visits 1 through 6 wearing clothing that allows exposure of their volar forearms and inner elbows.

## 6.2. Visit 1

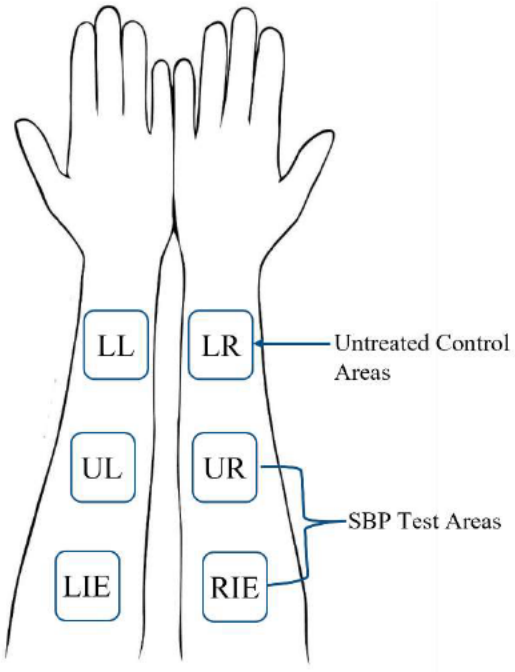
### 6.2.1

Participants will be asked to self-report their skin phototype based on the Fitzpatrick skin phototype classification (scale I-VI)[9], and the response will be documented in the CRF by the study personnel.

### 6.2.2 Randomization of Target Areas

Study personnel will confirm that the washout period of minimum 18 hours prior to Visit 1, has been successfully completed. Participants will wash their forearms and inner elbows with a standardized soap and use paper towels to dry each arm. After the participants' forearms and inner elbows are fully dried, they will be randomized according to the Randomization Schedule.

**Figure 6.2.2. Randomization of Untreated Control Areas and Test Areas on the Volar Forearms and Inner Elbows**




| Figure 6.2.2. Key | |
|---|---|
| LL | Lower left |
| UL | Upper Left |
| LR | Lower Right |
| UR | Upper Right |
| LIE | Left Inner Elbow |
| RIE | Right Inner Elbow |

Note: The inner elbow test areas will receive the same SBP as the one applied to the test area of the same arm

Randomization will assign each participant to either Marathon® or Cavilon™ (designated SBP). The designated SBP will be applied to the volar forearm and inner elbow "test areas" of the participant's dominant arm, as determined by the participant. The other SBP will be applied to the volar forearm and inner elbow "test areas" of the participant's non-dominant arm. The SBP applied to the volar forearm and inner elbow test areas of a particular arm will be the same. Randomization will provide an equal probability for an SBP to be assigned to either the dominant or non-dominant arm. A distinct area on a particular volar forearm of the participant will be used as an "untreated control area" for the test areas on the same forearm.

### 6.2.3 Application of Skin Barrier Protectants (SBPs) and Corneometer® Measurements

Study personnel will draw 2-inch x 2-inch squares on the participants' forearms for each untreated control area and each test area using a non-toxic marker, such that three squares are marked on each volar forearm and inner elbow taken together. The lower squares on the volar forearms (LL and LR) will be marked about two inches above each wrist and will be used as untreated control areas. The upper squares on the volar forearms (UL and UR) will be used as test areas. The squares marked on the inner elbows of the participants (LIE and RIE) will be used as test areas as well. Refer to Figure 6.2.2 for details.

To measure baseline skin hydration, study personnel will use the Corneometer® to take the average of five measurements of skin capacitance and the standard deviation of the measurements for both the left and right forearm within each of the untreated control areas and volar forearm and inner elbow test areas. The Corneometer® measurements will be recorded in the CRF.

After the baseline measurements have been taken, study personnel will apply a thin layer of either Marathon ® or Cavilon ™ (per the Randomization Schedule), such that the SBP covers the participants' skin within the border of the volar forearm and inner elbow test area squares. Each volar forearm will also include a 2-inch x 2-inch untreated control area square where no SBP will be applied. The participants will not be informed about the type of SBP applied to the volar forearm and inner elbow test areas. The participants will be instructed not to leave the study room, and that their forearms must remain exposed such that no article of clothing comes in contact with their forearms and inner elbows.

After the SBPs have been left to dry for at least one minute or have dried fully, Corneometer® measurements will be repeated in a manner similar to the baseline measurements, for each of the two untreated control areas and four test areas. The average of the Corneometer® measurements and the standard deviation of the measurements will be recorded in the CRF.

Participants will be dismissed from the study room and will be instructed to return the next day (within a 24 ± 4 hours window) for Visit 2.

### 6.3. Visit 2 through 5

#### 6.3.1 Corneometer® Measurements

The participants will return for daily visits except the weekend. For Visits 2 through 4, participants will be instructed to come to the study room within a 24 ± 4 hours window from the previous day's visit.

During Visit 2 through Visit 5, the average of five Corneometer® measurements of skin capacitance and the standard deviation of the measurements will be taken for each of the untreated control areas and test areas on each volar forearm and inner elbow of the participants. The average of the Corneometer® measurements and the standard deviation of the measurements will be recorded in the CRF.

Note: During the period from Visits 1 through 6, participants will be allowed to bathe their arms using a standardized soap provided by the study personnel and will be asked to minimize scrubbing or any other abrasion of the treated skin. In addition, participants will be instructed not to engage in activities, for eg, sports (eg, tennis) or holding a baby that may cause significant abrasion on one arm and not the other.

### 6.4. Visit 6 – Final Visit

#### 6.4.1 Corneometer® Measurements

The study personnel will take the last set of the Corneometer® measurements (as detailed in Section 6.3.1) and record them in the CRF.

### 6.5. Administration of Survey

Participants will complete surveys on Visits 1, 3, and 6, regarding their experience with the two SBPs.

### 6.6. Participant Dismissal

After completion of all study activities, participants will be dismissed from the study.

Note: Each participant will commence the study on Monday or Tuesday, which will permit daily readings for the first 72 hours, which is the more important window to evaluate SBP wear time. There will be a two-day break over the weekend, after which study personnel will take Corneometer® measurements either on Monday, or Monday and Tuesday, depending on the participant's start date.

# 7. ADVERSE DEVICE EVENTS (ADEs)

## 7.1. Definition of ADE

Adverse event related to the use of an investigational medical device resulting from insufficiencies or inadequacies in the instructions for use, the deployment, installation, the operation, or any malfunction of the investigational medical device or from error in use.

## 7.2. Definition of Serious Adverse Device Event (SADE)

The SADE is the adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event (SAE).

The FDA definition of a SAE will be used in this study: An AE or suspected adverse reaction is considered "serious" if, in the view of the investigator, it results in any of the following outcomes:

- Death
- A life-threatening adverse event
- Inpatient hospitalization or prolongation of existing hospitalization
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions or,
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. All SADEs will be reported to the reviewing IRB as necessary according to their rules.

## 7.3. Definition of Unanticipated Adverse Device Effect (UADE)

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

## 7.4. Severity of ADE

- **Grade 1:** Mild; asymptomatic or mild symptoms; clinical or diagnostic observation only; intervention not indicated.
- **Grade 2:** Moderate; minimal, local or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living.
- **Grade 3:** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting activities of daily living involving self-care.

- **Grade 4:** Life threatening consequences; urgent intervention indicated.
- **Grade 5:** Death related to ADE.

### 7.5. Relatedness of ADE and SADE

- **Unrelated:** This category applies to those ADEs, which after careful consideration, are clearly and incontrovertibly due to extraneous causes (disease, environment, etc.)
- **Possible:** This category applies to those ADEs for which, after careful medical consideration at the time they are evaluated, a connection with the Investigational Product administration appears unlikely but cannot be ruled out with certainty.
- **Probable:** This category applies to those ADEs, which after careful medical consideration at the time they are evaluated, are felt with a high degree of certainty to be related to the Investigational Product.
- **Definite:** This category applies to those ADEs, which after careful consideration, are clearly and incontrovertibly due to the Investigational Product.

### 7.6. Expectedness

The PI will be responsible for determining whether an ADE or SADE is expected or unexpected. An ADE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

### 7.7. ADE Reporting

The ADEs will be recorded on the ADE form (provided by Medline) by the study personnel and reviewed by the PI. Changes in the severity of an ADE will be documented to allow an assessment of the duration of the event at each level of severity. Changes in severity will necessitate a new CRF to document the new level of severity. ADEs characterized as intermittent require documentation of onset and duration of each episode.

Non-serious ADEs are to be reported to the IRB per IRB reporting requirements.

### 7.8. Serious Adverse Event Reporting or SADE and UADE Reporting

The SADEs and UADEs will be recorded on the SADE form (provided by Medline) by the study personnel and reviewed by the PI. The study personnel or the PI shall submit the completed SADE form to Medline as soon as possible, but in no event later than 48 hours after the PI first learns of the effect. The study personnel or the PI will be responsible for reporting the event to the IRB per the IRB's reporting requirements, and to the FDA if applicable. Thereafter, the study personnel or the PI shall submit additional reports concerning the effect as the FDA requests.

The PI shall complete an SADE Form and submit the form to the IRB as soon as possible, but in no event later than 48 hours after the PI first learns of the event. The PI will be responsible for reporting the event to the IRB per the IRB's reporting requirements, and the FDA if applicable. Thereafter, the PI shall submit any additional reports concerning the event as the FDA requests.

The PI shall complete a SADE Form no later than 48 hours after first learning about the effect. The PI shall report the SADE to the reviewing IRB, if applicable, according to their reporting requirements. The PI, who is responsible for conducting an evaluation of the SADE, shall report the results of such evaluation to the FDA and to all reviewing IRBs if applicable within 10 working days. Thereafter, the PI shall submit such additional reports concerning the effect as FDA requests.

For questions regarding this process or the event, you may contact your Medline Clinical Designee:

Name: Gregory Gomez, MSN, MPH, Clinical Affairs Director
Phone: 224-931-1541
E-mail: clinicaloperations@medline.com

## 8. STATISTICAL CONSIDERATIONS

### 8.1. Sample Size Determination

A sample size of 42 was elected for a superiority margin of at least 15 arbitrary capacitance units (A.C.U)[10] as measured by the Corneometer® with an estimated mean of pair differences of 17.5 and the standard deviation of 5.05, given the 80% power at Bonferonni adjusted significance level of $\alpha = .0125$. Internal evaluation SBP data was used as a starting point, and PASS- Paired T-Tests for Superiority by a Margin procedure was utilized for the sample size estimation (PASS 2021 Power Analysis and Sample Size Software (2021). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass).

### 8.2. Randomization

This is a single-blind study, with participants blinded to the SBPs that are applied to them. Due to the primary focus on durability of the SBPs, randomization will target dominant versus non-dominant arms, not left versus right. Participants will be randomized to either Marathon® or Cavilon™, and this SBP will be applied to their dominant arm, as defined by the participant. This ensures an equal probability of Marathon® and Cavilon™ on both dominant and non-dominant arms. If a participant has incomplete data, the participant will be replaced such that the randomization sequence of the replaced participant will be assigned to the new participant.

### 8.3. Populations for Analyses

The analyses will be performed on the intent to treat (ITT) population which consists of all participants who have complete data for all time points and have completed the survey for the secondary endpoint.

No per protocol, safety, or other analyses groups are planned.

### 8.4. Protocol Deviations

The list of protocol deviations will be compiled prior to database lock. All deviations will be reviewed and decisions for handling each of the deviations will be made prior to the start of data analysis.

### 8.5. Demographics, Variables and Covariates

Age will be collected as a continuous measure, with all participants being ≥18 years of age. Age strata will be defined as stratum 1: 18–25 years old, stratum 2: 26–41 years old, stratum 3: 42–57 years old, stratum 4: 58–67 years old, stratum 5: 68–76 years old, stratum 6: 77–94 years old, 95+ years old. Age will be considered for secondary analysis.

Sex will be collected as a categorical variable: 0=male, 1=female, and 2=other. Sex will be considered for secondary analysis.

Left or right arm will also be documented for each SBP as will the information about which arm is the dominant arm. Dominant arm and left or right arm will be considered for secondary analysis.

Participants will be asked to complete a Fitzpatrick skin phototype assessment (scale I-VI). Skin phototype assessment will be considered for secondary analysis and primarily for the secondary endpoint for questions regarding the ability to visually see the SBP(s) on the skin.

### 8.6. Derived Variables

The difference between volar forearm and inner elbow measurements will be calculated for each timepoint.

Degradation Rate will be calculated as = $(C_o - C_t) / C_o$, where $C_o$ is the original Corneometer® measurement value and $C_t$ is the Corneometer® measurement at a given follow-up timepoint. We will be looking to see when the degradation rate reaches 50%.

### 8.7. Handling of Missing Values

All missing data will be quantified in the final report and possible biases for any missing data will be reported.

### 8.8. Statistical Analysis

Statistical analyses will be conducted in SAS® software, Version 9.4 or higher of the SAS System for Windows (Copyright © 2013 SAS Institute Inc.) or other appropriate statistical software. $P < .05$ will be considered statistically significant.

All continuous variables will be summarized for the full sample and by SBP group using the following descriptive statistics: (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size)

of observed levels will be reported for all categorical measures. 95% confidence intervals will be calculated for all means.

Spearman correlation analysis will be used to examine possible associations between the key variables of Marathon® or Cavilon™ use and the Corneometer® measurements at various timepoints with covariates of age, sex, and dominant arm. Additional t-tests or non-parametric tests will be employed to further examine any significant associations found in the correlational analyses between key and covariate measures.

**Analysis of Primary Endpoints**

8.8.1. Primary Endpoints

Degradation of the SBP over seven days as measured by the Corneometer®.

The breakdown of the SBPs on the volar forearm test areas will reflect the duration of wear of the SBPs. Independent sample t-tests or non-parametric equivalent tests will be used to compare mean Marathon® and Cavilon™ Corneometer® values at baseline (Visit 1), Visit 2, Visit 3, Visit 4, Visit 5, and the final Visit 6 for untreated control area and volar forearm test area measurements. Paired-sample t-tests will be used to compare any two data points for a given SBP and location.

The breakdown of the SBP on the inner elbow test area, relative to the corresponding volar forearm test area, will reflect the durability of the products. Derived variables will be created to calculate the difference between the volar forearm test area measurement and the inner elbow test area measurement at baseline (Visit 1), Visit 2, Visit 3, Visit 4, Visit 5, and the final Visit 6. Independent sample t-tests or non-parametric equivalent tests will be used to compare mean Marathon® and Cavilon™ Corneometer® difference values at baseline (Visit 1), Visit 2, Visit 3 and the final Visit 6 on Day 8. Paired-sample t-tests will be used to compare any two data difference points for a given SBP.

Both degradation and durability endpoints will be graphed across time by SBP with and without 95% confidence intervals of the mean.

**Analysis of Secondary Endpoint**

8.8.2. Secondary Endpoint

The secondary objective of this study is to assess the participants' overall experience with Marathon® and Cavilon™. Results from the survey will be reported using the appropriate descriptive statistics for the distribution and scale of the data.

At Visit 1, participants will be asked the following question regarding the SBP on each arm:

1. Is the SBP comfortable? (Likert-like scale)

At Visit 3 and Visit 6, participants will be asked the following questions regarding the SBP on each arm:

1. Do you see the SBP on your skin? (Yes/No)
2. Did the SBP accumulate dirt or debris? (Yes/No)
3. Did the SBP adhere to clothing or any other material? (Yes/No)

Additionally, at Visits 3 and 6, participants will be asked the following questions regarding the SBP on each arm:

1. On which arm (left or right) is it easier to visually determine that the SBP is present?

# 9. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

## 9.1. Regulatory and Ethical Considerations

### 9.1.1. Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by Medline. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party. All study data will be identified with an anonymous participant ID number, and all CRFs and other documents containing data will have the participant ID number and no identifiable information. One master list linking participant ID numbers to participant name and other contact information will be maintained in a secure electronic database by the study personnel in the event identification of a participant is necessary (eg, due to an ADE). This is the only documentation that will link participant name and participant ID number.

Study personnel will ensure all documents for data collection are completed in accordance with GDP in order to ensure accurate interpretation of data. Data will be transferred from paper CRFs to a secure electronic database and analyzed with SAS® 9.4, which will allow for quality checks to identify data that appear inconsistent, incomplete, or inaccurate.

All study records will be maintained for a minimum of two years following study closeout; records will be maintained for a longer period of time as required by IRB or other regulations.

### 9.1.2. Safety Oversight

Safety oversight will consist of monitoring of visit activity, ADEs and SADEs by the PI, who is suitably qualified and experienced to evaluate any ADEs or SADEs. The PI will review all ADEs and SADEs and make any necessary safety determinations or visit activity modification that are in the best interest of the participant as necessary. See also Section 7.0 ADEs for reporting and management requirements.

### 9.1.3. Study Discontinuation

The study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be

provided by the suspending or terminating party to the IRB. If the study is prematurely terminated or suspended, the PI or study personnel will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants as determined by ADE review
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the IRB.

### 9.1.4. Conflict of Interest Policy

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication or any aspect of this trial will be disclosed and managed.

## 9.2. Protocol Deviations

It is the responsibility of the PI and study personnel to use continuous vigilance to identify and report deviations on a routine basis. All deviations must be addressed in study documents and reported to Medline. Protocol deviations must be sent to the reviewing IRB per their policies. The PI is responsible for knowing and adhering to the reviewing IRB requirements.

## 9.3. Abbreviations

| | |
|---|---|
| ADE | Adverse Device Event |
| CFR | Code of Federal Regulations |
| CRF | Case Report Form |
| CRO | Contract Research Organization |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practices |
| GDP | Good Documentation Practices |
| HCP | Healthcare Provider |
| HIPAA | Health Insurance Portability and Accountability Act |

| | |
|---|---|
| HMDS | Hexamethyldisiloxane |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonisation |
| ID | Identification |
| IRB | Institutional Review Board |
| ITT | Intent to Treat |
| LP | Limited Partnership |
| MASD | Moisture-Associated Skin Damage |
| PI | Principal Investigator |
| PSF | Participant Screening Form |
| SAE | Serious Adverse Event |
| SADE | Serious Adverse Device Event |
| SBP | Skin Barrier Protectant |
| SOA | Schedule of Activities |
| UADE | Unanticipated Adverse Device Effect |
| US | United States |

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