Efficacy of a skin protectant textile for the management of skin fold conditions

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INVESTIGATOR ACKNOWLEDGMENT SIGNATURE

- I agree to conduct the study in accordance with the relevant, current protocol and will make changes in the protocol only after notifying the sponsor, except when 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 sponsor, 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 and 21 CFR 812.
- I have read and understood 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.

I have received and reviewed this investigational plan. I will conduct the study as described.

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

DOCUMENT HISTORY

VERSION	DATE	DESCRIPTION
Version 1.0	07-JUN-2022	Initial Release
Version 2.0	13-FEB-2023	1. Update to participant exclusion criteria
Version 3.0	06-MAR-2023	1. Update to participant exclusion criteria 2. Clarification of the last day of study participation 3. Clarification about the schedule of activities
Version 4.0	23-OCT-2023	1. Update to method to photograph target areas 2. Update to details of study population in Synopsis and Section 5

1. PROTOCOL SUMMARY

1.1. Synopsis

Title: Efficacy of a skin protectant textile for the management of skin fold conditions.

Study Description: Chronic irritation at skin-on-skin contact areas such as skin folds may be caused by moisture, heat, friction, lack of air circulation, incontinence, or poor hygiene, and can result in inflammatory conditions. These conditions may be complicated by fungal and/or bacterial infections. Commonly affected areas include the groin, inner thigh, armpits, the areas between the buttocks, the underside of the breasts, or the abdominal panniculi.[1] Signs and symptoms include erythema, crusted or oozing skin, itching, burning, pain, and malodor. Important risk factors include obesity, malnourishment, immobility, and diabetes, with the elderly or bed-ridden individuals and infants being commonly affected.

DriGo-HP™ (formerly known as the "Stay Fresh® Skin Fold Management Textile"; henceforth referred to as "skin protectant textile [SPT]") is used in skin folds to provide moisture management, friction reduction, and odor control. It is made from a soft, thin, smooth polyester textile, which when placed within skin folds helps to wick moisture away from the skin fold. The textile contains up to 0.3% hydrogen peroxide (H_2O_2), which is released slowly over time. This concentration is safe for the skin and prevents growth of common bacteria, including *Escherichia coli* (*E. coli*) and Methicillin-Resistant *Staphylococcus aureus* (MRSA), in the fabric. The reduction in moisture and control of bacterial growth results in odor control in the skin fold. The SPT is intended to be used between skin folds and in other skin-to-skin contact areas, to provide moisture and odor management, and to reduce friction.

This study will evaluate the efficacy of the SPT to manage erythema, maceration, denudation, satellite lesions, pain, itching, burning, moisture, and odor associated with skin folds (henceforth together referred to as "skin fold conditions"). Participants will be patients with skin fold conditions, which will be treated with the SPT. Healthcare providers (HCPs) will apply the SPT to the participants' skin folds and other skin-on-skin contact areas (henceforth referred to as "target area[s]"). An independent licensed clinician with experience in identifying and treating skin fold conditions (henceforth referred to as "third-party clinician"), will use photographs of the target areas to assess the status of erythema, maceration, denudation, and satellite lesions in the target areas when the SPT is first applied (Day 0), and on Days 1, 3, and 5 (or the last day of study participation [ie, fully healed target area(s)]), during SPT changes. The PI or qualified designee will take photographs of the target areas and assess moisture and odor in these areas. Participants will provide their impressions of pain, itching, and burning in the target area(s) on the same days as the skin fold condition photography. In addition, the study will include feedback from the HCPs about the SPT and overall experience of the participants with the SPT.

Phase:	Post-market
Primary Objective:	To evaluate the efficacy of the SPT to improve skin fold conditions.
Secondary Objectives:	1. To gather PI or qualified designee's assessment of moisture control in the target areas. 2. To assess HCP feedback on the SPT. 3. To assess the overall participant experience with the SPT.
Primary Endpoint:	1. Improvement in skin fold conditions such as erythema, maceration, denudation, satellite lesions, odor, pain, itching, and burning over five days of treatment. 1a. Likert scales developed for erythema, maceration, denudation, and satellite lesions. Scoring of the target area(s) done by a third-party clinician using the Likert scale(s) and photographs taken by the PI or qualified designee on Day 0, and on Days 1, 3, and 5, during SPT changes. 1b. Assessment of odor in the target area(s) on Day 0, and on Days 1, 3, and 5, during SPT changes, using a Likert scale. 1c. Participant assessment of discomfort (pain, itching, and burning) using a visual analogue scale (VAS) on Day 0, and on Days 1, 3, and 5, during SPT changes. Participants will also be asked to identify the most prominent type of discomfort in the skin fold: pain, itching, or burning.
Secondary Endpoints:	1. PI or qualified designee survey responses for moisture in the target area(s) on Day 0, and on Days 1, 3, and 5, during SPT changes, using a Likert scale. 2. HCP survey responses on Day 5, regarding their feedback about the SPT, using a VAS. 3. Participant responses on Day 5, regarding their experience with the SPT, using a VAS.
Note:	All endpoint-related activities planned for Day 5 will be carried out for the last day of study participation (ie, fully healed target area[s]) if it occurs before Day 5.
Study Population:	Number of target areas, N = 119. Participants can be the source of up to two target areas, and each target area can have more than one skin fold condition. Per the assessment of the PI or qualified designee, the skin fold conditions of the participants must be anatomically distant enough to allow the participants to make an objective assessment of discomfort (pain, itching, and burning) in each target area. A participant may be re-enrolled using a new participant study identification (ID) number for another set of up to two target areas at a different location. The target areas must be anatomically distant (per the assessment of the PI or qualified designee), as described above.

Inclusion criteria

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

- Individuals ≥ 18 years of age.
- Individuals who have evidence of one or more of the following skin fold conditions: erythema, maceration, denudation, satellite lesions, pain, itching, burning, moisture, and odor.
- Individuals whose treatment plan permits assessment of the skin fold condition(s) for up to six days.

Exclusion criteria

Individuals who meet any of the following criteria will not be eligible to participate in this study:

- Individuals whose target area(s) are being managed with topical treatments such as antibiotics, antifungals, ointments including skin protectants, anti-itch products, anoperineal dressings or absorbent pads (eg, ARD®).
- Individuals with a known allergy or sensitivity to the ingredients in the SPT, such as the fabric or H_2O_2, as well as the tape that may be used to secure the SPT.
- Individuals who are pregnant or are breastfeeding.

Description of Sites/Facilities Enrolling Participants:	At least one acute care facility (non-intensive care unit [non-ICU]) will be involved in the study. If more than one facility is involved, enrollment will be competitive.
Participant Duration:	Up to six days.

Note:

Two interim analyses will be conducted to confirm that participants being enrolled present a balanced distribution of skin fold conditions.

1.2 Schedule of Activities (SOA)

Assessments and activities[#]	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5/ last day of participation[¥]	Photographic evaluation using the wound camera system
PI or qualified designee obtains informed consent	X						
PI or qualified designee carries out participant screening	X						
As part of screening, PI or qualified designee examines and documents the skin fold conditions to identify potential target area(s)	X						
PI or qualified designee collects applicable demographics and co-morbidities information	X						
PI or qualified designee collects applicable medication information	X	X	X	X	X	X	
PI or qualified designee takes photographs of target areas using the wound camera system	X	X		X		X	
PI or qualified designee assesses skin fold conditions (moisture and odor) in the target area(s)	X	X		X		X	
Participant completes a survey regarding discomfort (pain, itching, and burning) in the target area(s)	X	X		X		X	
Participant identifies the prominent type of discomfort	X	X		X		X	
HCP applies SPT to the target area(s)	X	X	X[§]	X	X[§]		

Assessments and activities[#]	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5/ last day of participation[¥]	Photographic evaluation using the wound camera system
HCP completes a feedback survey regarding their experience with the SPT						X	
Participant completes a survey regarding experience with the SPT						X	
Third-party clinician assesses skin fold conditions such as erythema, maceration, denudation, and satellite lesions							X
Monitoring for adverse events	X	X	X	X	X	X	
Participant dismissal from study activities						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.
[§] SPT will be changed if clinically warranted.

[¥]If the target area(s) heal before Day 5, all activities planned for Day 5 will be carried out on the last day of study participation.

2. INTRODUCTION

2.1. Background & Rationale

Skin acts as a defensive physical barrier against multiple detrimental external forces such as mechanical trauma, noxious irritants, infectious pathogens, and excessive fluids. However, prolonged exposure of the skin to different sources of moisture such as urine or stool, perspiration, wound exudate, secretions including mucus and saliva, and their contents can compromise the integrity of this barrier.[2]

Moisture, in the form of sweat, which gets trapped in the skin folds and other skin-on-skin contact areas due to lack of air circulation, can lead to overhydration and maceration of skin. Maceration increases friction between opposing skin surfaces, which leads to inflammation, presenting initially as minimal erythema of the skin folds.[3] The signs and symptoms of such skin inflammation are gradual in onset, including itching, pain, burning, prickling, or stinging sensations in the intertriginous areas. Initial presentation involves mild erythematous patches mirrored on both sides of the intertriginous areas, but the lesions can quickly progress to exudative erosions, fissures, maceration, or crusts.[4] In addition, development of a secondary cutaneous infection by bacteria or fungi may be suggested by worsening erythema, pustules or vesicles, satellite lesions, or malodor.[5,6,7]

This type of chronic irritation of the intertriginous areas is commonly seen in bed-ridden or elderly individuals, and infants, due to reduced immunity, immobility, and incontinence.[6] Infants are also susceptible to this skin condition as a result of drooling, short neck structure with prominent skin folds, and flexed position.[3,5,8] Obesity and hyperhidrosis are also considered important risk factors, with other predisposing factors being diabetes, urinary or fecal incontinence, poor personal hygiene, malnutrition, immunosuppression, occlusive clothing, and a hot and humid climate.

Management of such skin fold conditions typically focuses on removal of predisposing factors, including minimizing moisture and friction in the involved areas. This is followed by topical or systemic antimicrobial (antibacterial or antifungal) agents as well as low-potency corticosteroids if required.[5,7] Preventive measures are important as they may help not only with management of current skin fold conditions, but also to avoid future episodes.[6,7]

This study will evaluate the efficacy of a skin protectant textile (SPT) to manage skin fold conditions in participants over a five-day treatment period. Healthcare providers (HCPs) will apply the SPT to the target area(s) of the participants. As part of the participant screening process, the PI or qualified designee will examine and document the skin fold conditions to identify potential target area(s) before the SPT is first applied (Day 0) to these area(s). The PI or qualified designee will also take photographs of the target areas on Day 0, and on Days 1, 3, and 5 (or the last day of study participation [ie, fully healed target area(s)]), during SPT changes. These photographs will be used by a third-party clinician to assess the status of erythema, maceration, denudation, and satellite lesions in the target areas. The PI or qualified designee will assess moisture and odor, and participants will appraise discomfort (pain, itching, and burning) in the target area(s) on the same days as the target area photography. The study will also include HCP feedback regarding their experience with the SPT, and a survey about overall experience of the participants with the SPT.

2.2. DriGo-HP™ (referred to as "Skin Protectant Textile [SPT]")

DriGo-HP™ (formerly known as the "Stay Fresh® Skin Fold Management Textile" [#MSCWH219S]; referred to as "Skin Protectant Textile [SPT]") is designed for use in skin-to-skin contact areas. It is made of a soft, thin, smooth polyester fabric that helps manage moisture, reduce friction, and provide comfort

and odor control. It is designed to wick moisture away from the skin fold and keep it dry. The moisture from the skin fold is translocated towards the external edge of the fabric where it is dispersed by evaporation.

In addition, the SPT uses a unique, patented technology where hydrogen peroxide (H_2O_2) is encapsulated in a binder leading to its slow release over time when exposed to moisture. H_2O_2 is a known germicidal agent, which prevents the growth of bacteria such as *Escherichia coli* (*E. coli*) and Methicillin-Resistant *Staphylococcus aureus* (MRSA) in the textile throughout the duration of the product's use. H_2O_2 is used in the product at a concentration no greater than 0.3%, released slowly over time. SPT can be left in place for up to five days, depending on soiling, odor, amount of moisture, and condition of the skin.

2.3. Risk/Benefit Profile

2.3.1. Potential Study Risks

The participant may experience an allergic reaction to the fabric of the SPT, H_2O_2, or the tape used to secure the SPT. To minimize participant risk, screening will be done for any known allergy or sensitivity to these components. Furthermore, the participants will be under the care of a physician who will take timely measures to address and mitigate any adverse reactions should they occur. The PI or qualified designee and the HCPs will be at minimal risk during the study. Care of skin fold conditions is a conventional task in these clinical settings; the SPT is a commercially available product; and the PI or qualified designee and the HCPs will be wearing gloves as they make assessments for moisture or odor of the target areas, or during application of the SPT to the target areas of the participants, respectively.

2.3.2. Potential Study Benefits

The participants may benefit from faster resolution of their skin fold conditions, which may lead to enhanced level of comfort. Furthermore, HCP feedback and participant survey may help enhance understanding as regards experience with the SPT. No prescription is required to use the SPT; therefore, the study data may also benefit non-clinically trained consumers who may be able to use the SPT to treat skin fold conditions. The PI or qualified designee and HCPs will not benefit from the study directly.

2.3.3. Assessment of Potential Risk/Benefit Profile

The use of this currently marketed SPT presents minimal risk to the participants, the PI or qualified designee and the HCPs while offering the potential for benefit to the participants enrolled in the study. Therefore, the risk-benefit profile for the study is acceptable.

3. OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINT(S)
Primary		
To evaluate the efficacy of SPT to improve skin fold conditions.	1. Improvement in skin fold conditions such as erythema, maceration,	1a. This endpoint addresses the objective

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINT(S)
	denudation, satellite lesions, odor, pain, itching, and burning over five days of treatment. 1a. Likert scales developed for erythema, maceration, denudation, and satellite lesions. Scoring of the target area(s) done by a third-party clinician using the Likert scale(s) and photographs taken by the PI or qualified designee on Day 0, and on Days 1, 3, and 5, during SPT changes. 1b. Assessment of odor in the target area(s) on Day 0, and on Days 1, 3, and 5, during SPT changes, using a Likert scale. 1c. Participant assessment of discomfort (pain, itching, and burning) assessment using a VAS on Day 0, and on Days 1, 3, and 5, during SPT changes. Participants will also be asked to identify the most prominent type of discomfort in the skin fold: pain, itching, or burning.	assessment of erythema, maceration, denudation, and satellite lesions by a third-party clinician. 1b. This endpoint evaluates the assessment of odor, which may be an indicator of infection, in the target areas during the use of SPT. 1c. This endpoint addresses the participants' perception of discomfort in the target area(s), while also evaluating which symptom, pain, itching, or burning is the most prominent over the duration of SPT use.
Secondary		
1. To gather PI or qualified designee's assessment of moisture control in the target areas. 2. To assess HCP feedback on the SPT. 3. To assess the overall participant experience with the SPT.	1. PI or qualified designee survey responses for moisture in the target area(s) on Day 0, and on Days 1, 3, and 5, during SPT changes, using a Likert scale. 2. HCP survey responses on Day 5 regarding feedback about the SPT, using a VAS. 3. Participant responses on Day 5 regarding their experience with the SPT, using a VAS.	1. This endpoint evaluates the assessment of moisture present in the target areas during the use of the SPT. 2. This endpoint evaluates HCPs' feedback about the SPT and may influence their future use of the SPT in clinical practice. 3. This endpoint evaluates participants'

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINT(S)
		experience with the SPT.
Note: All endpoint-related activities planned for Day 5 will be carried out for the last day of study participation (ie, fully healed target area[s]) if it occurs before Day 5.		

4. STUDY DESIGN

4.1. Overall Design

This is a prospective unblinded study in which the effectiveness of the SPT in the management of participants with skin fold conditions such as erythema, maceration, denudation, satellite lesions, pain, itching, burning, moisture, and odor will be evaluated. As part of the screening process, the PI or qualified designee will examine and document the skin fold conditions to identify potential target area(s) prior to application of the SPT to these areas (Day 0). The PI or qualified designee will take photographs of the target areas using a wound camera system once the participants are enrolled in the study (Day 0). The HCPs will apply the SPT to the target area(s) of the participants as described in the Instructions for Use (IFU). The PI or qualified designee will again take photographs of the target areas using the wound camera system on Days 1, 3, and 5 (or the last day of study participation [ie, fully healed target area(s)]), during SPT changes. On days when the target areas are photographed, the PI or qualified designee will also assess moisture and odor using Likert scales, and participants will provide their impressions of pain, itching, and burning in the target area(s) using a VAS survey. Participants will also be asked to identify the most prominent type of discomfort during this assessment. On Day 5 or the last day of study participation (ie, fully healed target area[s]), as applicable, VAS surveys will be used for the following: (1) HCP feedback about the SPT, and (2) Overall participant experience with the SPT. After the participants are dismissed from the study, a third-party clinician will score the status of erythema, maceration, denudation, and satellite lesions in the target areas using the photographs taken by the PI or qualified designee and the Likert scales developed for the study.

4.2. End of Study Definition

The study will be considered complete after the participants are dismissed upon completion of all study-related activities, the third-party clinician has assessed 119 target areas, and a Clinical Study Report approved by the Clinical Affairs Director has been issued.

5. STUDY POPULATION

Participants can be the source of up to two target areas, and each target area can have more than one skin fold condition. Per the assessment of the PI or qualified designee, the skin fold conditions of the participants must be anatomically distant enough to allow the participants to make an objective assessment of discomfort (pain, itching, and burning) in each target area. A participant may be re-enrolled using a new participant study identification (ID) number for another set of up to two target areas at a different location. The target areas must be anatomically distant (per the assessment of the PI or qualified designee), as described above.

5.1. Inclusion Criteria

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

- Individuals ≥ 18 years of age.
- Individuals who have evidence of one or more of the following skin fold conditions: erythema, maceration, denudation, satellite lesions, pain, itching, burning, moisture, and odor.
- Individuals whose treatment plan permits assessment of the skin fold condition(s) for up to six days.

5.2. Exclusion Criteria

Individuals who meet any of the following criteria will not be eligible to participate in this study:

- Individuals whose target area(s) are being managed with topical treatments such as antibiotics, antifungals, ointments including skin protectants, anti-itch products, anoperineal dressings or absorbent pads (eg, ARD®).
- Individuals with a known allergy or sensitivity to the ingredients in the SPT, such as the fabric or H_2O_2, as well as the tape that may be used to secure the SPT.
- Individuals who are pregnant or are breastfeeding.

5.3. Strategies for Recruitment and Retention

The PI at the study site will recruit potential participants from the current patient population being treated at the facility who satisfy the inclusion/exclusion criteria. The PI will inform the participants that they are free to withdraw from the study at any time and that it will not affect their treatment in any way. For this study, advertisements of any kind or a database to look up potential participants will not be used.

Retention will ideally be managed by targeting participants who are anticipated to require at least five days of SPT treatment.

5.4 Early Withdrawal and Replacement

Participants whose skin fold conditions are healed prior to Day 5 will be considered to have complete data.

Participation in the study may end at several critical points:

- Participant withdraws from the study for any reason, including when the target area(s) have not healed but the participant is discharged due to resolution of the medical condition for which the participant was hospitalized.
- 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, additional participant(s) will be recruited such that the total number of target areas included in the study will be 119.

6. STUDY PROCEDURES AND ASSESSMENTS

6.1. Informed consent and screening (Day 0)

6.1.1 Informed Consent

The PI or qualified designee will obtain written informed consent from all participants. Written informed consent must be documented on an Informed Consent form (ICF) that has received approval by an IRB/Ethics Committee. The ICF must be written in adherence to 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 Industries, Limited Partnership [LP], henceforth referred to as "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, and will receive a unique screening number that will be recorded in the Participant Screening Form (PSF). The PI or qualified designee will examine potential target area(s) of the participants and document the skin fold conditions such as erythema, maceration, denudation, or satellite lesions in the PSF. As part of this process, the PI or qualified designee will obtain a medical history of the participants' target area(s) and document concomitant medications such as pain medications, systemic antimicrobials, systemic steroids, and topical treatments being administered to the target areas.

Potential participants who satisfy all inclusion/exclusion criteria for the study will be enrolled and will receive unique participant study 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. Case Report Forms (CRFs), PSF, and other study-related documents will be provided separately to the PI or qualified designee, and the HCPs.

Note: A participant may be re-enrolled using a new participant study ID number for another set of up to two target areas at a different location.

6.2. Evaluation of the Study Product

6.2.1 Initial Assessment (Day 0)

6.2.1.1. Photographic Documentation to Assist Third-Party Clinician in Assessment of Erythema, Maceration, Denudation, or Satellite Lesions in Target Areas

The PI or qualified designee will photograph the skin fold conditions in the target area(s) using the wound camera system.

6.2.1.2. Assessment of moisture and odor in the target areas

The PI or qualified designee will assess moisture and odor in the individual target area(s) of the participants using study-specific Likert scales developed for these parameters.

6.2.1.3 Assessment of discomfort in the target areas

Participants will assess discomfort (pain, itching, and burning) in the target areas using a VAS survey. They will be asked to mark a point on the VAS using a pen such that the point reflects their perception of discomfort. The PI or qualified designee will measure the distance between the start of the line (the left side of line) and the point marked by the participants, using a calibrated ruler. The measured value will be recorded in the survey.

Participants will also be asked to identify the most prominent type of discomfort in the target area: pain, itching, or burning. The response will be recorded in the CRF.

6.2.1.4. Application of SPT on Day 0

The HCPs will apply the SPT to the target area(s) of the participants per the IFU.

6.2.2. Assessments on Days 1, 3, and 5 (or Last Day of Study Participation [ie, healed target area(s)])

6.2.2.1 Assessments

The HCPs will remove the SPT from the target areas and perform the assessments as detailed in Section 6.2.1.1–6.2.1.3 will be performed. Any additional care of the target areas given by the HCPs will be documented in the CRF.

6.2.2.2. Application of SPT

After performing the assessments and care in Section 6.2.2.1, the HCPs will apply a fresh SPT to the target area(s).

Note: On Days 2 and 4, the PI or qualified designee may examine the target areas, but no study-related assessments will be performed, unless it is the last day of study participation. The SPT in the target areas may be changed per assessment by the PI or qualified designee. This may also occur on Days 1, 3, and 5 in addition to the scheduled application of the SPT.

6.2.3. Additional Study Activities on Day 5 (or Last Day of Study Participation [ie, fully healed target area(s)])

6.2.3.1 Feedback about the SPT

HCPs will complete a survey providing their feedback about the SPT using a VAS.

6.2.3.2. Assessment of experience with SPT

Participants will complete a survey regarding their overall experience with the SPT using a VAS.

6.3. End of participant activity

The HCPs will remove the SPT from the target areas of the participants after all study activities have been completed. Thereafter, the participants will be dismissed from the study.

If the skin fold conditions in the target area(s) of any participant resolve before Day 5, the last day of study participation will occur on that day (earlier than Day 5). All activities planned for Day 5 should be carried out on the last day of study participation in order for participants to have complete data.

Note: Should the PI or qualified designee determine that continued treatment of the skin fold condition(s) beyond five days is necessary, such treatment must be administered per hospital procedures and using materials from hospital inventory. Study materials must be reserved for up to six days of participant enrollment.

6.4 Scoring of erythema, maceration, denudation, and satellite lesions in the target areas

After the participants have been dismissed from the study, a third-party clinician will score the skin fold conditions such as erythema, maceration, denudation, and satellite lesions in the participants' target area(s) using photographs taken by the PI or qualified designee and Likert scale(s) developed for the study.

For each participant, the photographs for each type of skin fold condition for Days 0, 1, 3, and 5 (or the last day of study participation [ie, fully healed target area(s)]) will be bundled and provided (in the order in which the photographs are taken) to the third-party clinician.

7. ADVERSE DEVICE EVENTS (ADEs)

7.1. Definition of ADE

An ADE is the adverse event related to the use of an investigational medical device resulting from insufficiencies or inadequacies in the IFU, the deployment, the 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 either the PI or sponsor, 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 Medline, regardless of potential relationship to the study product(s). SADEs will be reported to the reviewing IRB as necessary according to their reporting requirements.

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 the participants.

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 study product(s).
- **Definite:** This category applies to those ADEs, which after careful consideration, are clearly and incontrovertibly due to the study product(s).

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 qualified designee 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 will require documentation of onset and duration of each episode.

Non-serious ADEs will be reported to the study sponsor on a monthly basis for review or as agreed upon with the study sponsor, and reported to the IRB per IRB reporting requirements.

7.8. SADE and UADE reporting

The PI shall complete an SADE form (provided by Medline) and submit to the study sponsor as soon as possible, but in no event later than 48 hours after the PI first learns of the effect. The PI will be responsible for reporting the event to the IRB, if applicable, per the IRB's reporting requirements. The sponsor is

responsible for conducting an evaluation of the SADE, and shall report the results to the FDA and to all reviewing IRBs, if applicable, within 10 working days after the sponsor first receives notice of the effect. Thereafter, the sponsor 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 or the Medline Director of Clinical Operations:

Name: Julie A. Miller, Director Clinical Operations, RN, BSN, CCRA
Phone: 630-418-6891
E-mail: clinicaloperations@medline.com

8. STATISTICAL CONSIDERATIONS

8.1. Sample Size Determination

The sample size of 119 skin fold conditions was selected to detect a minimal clinically significant difference of 10 in the VAS pain scale between days of SPT changes with an estimated standard deviation of 30 and a Bonferonni adjusted α of α = .0083 at 80% power, using the "Paired Wilcoxon Signed-Rank Test" procedure in PASS 2021 Power Analysis and Sample Size Software (2021). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass). It is noted that participants may have skin folds with independent skin fold conditions. One participant may be the source of, at most, two skin fold conditions for the purposes of this study. The candidate skin fold conditions must be, in the assessment of the PI or qualified designee, anatomically distant enough to permit objective assessment of discomfort (pain, itching, and burning) in each target area by the participant. In the event that a participant withdraws from the study, additional participants will be enrolled to achieve a final number of 119 target areas with complete data and until adequate power for analysis has been reached.

8.2. Randomization

No randomization is planned at this time.

8.3. Populations for Analyses

The analyses will be performed on the intent-to-treat population, which consists of all participants who were qualified for entry criteria and adhered to the protocol, meaning completing five days of treatment with complete data on assessment of skin fold conditions, as well as responses on discomfort and overall experience with the SPT.

No per protocol, safety, or other analysis 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. Interim Analysis

Two interim analyses will be performed at 34% and 67% completion, testing for early efficacy or futility, using t-score boundaries that follow O'Brien-Fleming Analog alpha and beta spending rules. Assuming that the two interim analyses will occur after approximately 40 (1/3 of 119 total target areas) and 80 (2/3) target

areas have been assessed and adjudicated, the nominal alpha levels to reject the null hypotheses for efficacy are as follows in the table below.

Analysis Order	Number of Target Areas	Nominal critical point (Z-value)	Alpha level
1	40	-4.42	0.00000
2	80	-3.09	0.00122
Final	119	- 2.406	0.00804

Futility analyses are planned to be conducted to coincide in timing with the tentative interim analyses. The formal criterion for determination of futility is that at each interim look, if the condition power (defined as the probability of rejecting the null hypothesis at the final analysis given the data accumulated so far and under the assumption that the alternative hypothesis under the original design is true) falls below 20%, then the trial will be considered for stopping.

An interim monitoring tool, the most current version of PASS software will be used to estimate the conditional power.

8.6. Endpoints

8.6.1. Primary Endpoints

1. Improvement in skinfold conditions such as erythema, maceration, denudation, and satellite lesions, which will be rated on Likert scales by a third-party clinician using photographs taken by the PI or qualified designee on Days 0, and Days 1, 3, and 5 (or last day of study participation [ie, fully healed target area(s)]) during SPT changes.

2. PI or qualified designee evaluate the odor of the target area(s) using a Likert scale on Days 0, and Days 1, 3, and 5 (or last day of study participation [ie, fully healed target area(s)]) during SPT changes.

3. Participants evaluate the discomfort in their skin fold: pain, itching, or burning using VAS survey on Days 0, and Days 1, 3, and 5 (or last day of study participation [ie, fully healed target area(s)]) during SPT changes, and report the most prominent type of discomfort (pain, itching, or burning) in their target area(s).

8.6.2. Secondary Endpoints

1. PI or qualified designee assess moisture in the target area(s) on Day 0, and on Days 1, 3, and 5 (or last day of study participation [ie, fully healed target area(s)]), during SPT changes, using a Likert scale.

2. HCPs report their feedback about the SPT on Day 5 (or last day of study participation [ie, fully healed target area(s)]), using VAS survey.

3. Participant report their experience with the SPT on Day 5 (or last day of study participation [ie, fully healed target area(s)]), using VAS survey.

8.7. Demographics, Variables and Covariates

Age will be collected as a continuous measure, with all participants being ≥18 years of age. Age will be considered for secondary analysis.

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

Ratings for erythema, maceration, denudation, satellite lesion, odor, and survey responses for moisture in the target areas with skinfold conditions, obtained using Likert scales, will be evaluated as categorical measures. Survey responses for discomfort, HCP feedback and participants' overall experience obtained on a VAS (1–100mm) will be evaluated as continuous measures.

Nominal variables of data collected will include the participant ID, medical history, and concomitant medications. Additional nominal information regarding date, time, and reason for additional SPT changes will be recorded in a log file and this data will be incorporated into supplemental analyses examining if results differ for participants with additional SPT changes.

8.8. Missing Data

All attempts will be made to collect all data per protocol. Any data point that appears to be erroneous or inexplicable based on clinical judgement will be investigated as a possible outlier. In general, values for missing data will not be imputed unless methods of handling missing data are specified in this section or relevant sections.

For the analyses of all primary and secondary objectives, observations with missing clinical ratings (ie, rating of erythema by a third-party clinician) or self-reported ratings (ie, VAS score of participant experience) will be dropped from the analysis of variable of interest.

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

8.9. 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. A p-value of $P < .05$ will be considered statistically significant.

All continuous variables will be summarized 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. In addition, 95% confidence intervals will be calculated for all means.

8.9.1 Analysis of Primary Endpoints

The primary goal of this study is to evaluate the efficacy of the SPT to improve skinfold conditions, including erythema, maceration, denudation, satellite lesions, pain, itching, burning and odor over five days of treatment. Erythema, maceration, denudation, satellite lesions, and odor will be assessed using Likert scales, with "0" being least severe and "4" being most severe. Ordinal mixed models, or other appropriate methods depending on the distribution of data, will be employed to compare the assessment of skin fold

conditions of target areas across five days of treatment, with participants as a random variable and treatment days (Day 0, and Days 1, 3, and 5) as a covariate. Significant omnibus test will be followed by Tukey's post-hoc pairwise comparisons of Day 0 vs Day 1, Day 0 vs Day 3, Day 0 vs Day 5, Day 1 vs Day 3, and Day 3 vs Day 5.

ANOVA/Mixed models, or other appropriate methods depending on the distribution of data, will be conducted to compare VAS scores of discomfort (pain, itching, or burning) reported by participants on Day 0, and Days 1, 3, and 5. Significant omnibus test will be followed by Tukey's post-hoc pairwise comparisons of Day 0 vs Day 1, Day 0 vs Day 3, Day 0 vs Day 5, Day 1 vs Day 3, and Day 3 vs Day 5. In addition, descriptive statistics for the most prominent discomfort in the target area will also be reported in this study.

8.9.2 Analysis of Secondary Endpoints

The secondary objective of this study is to gather PI or qualified designee assessment of moisture control in the target areas, as well as to assess HCP feedback about the SPT and overall participants experience with the SPT.

Moisture level in the target areas, evaluated by the PI or qualified designee using a Likert scale, will be compared across five days of treatment using ordinal mixed models. Appropriate descriptive statistics of moisture level of product, HCP feedback about the SPT, and overall participant experience with the SPT, based on the distribution and scale of the data, will also be reported.

9. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

9.1. Clinical Monitoring

The Clinical Research Associate (CRA) will confirm that the rights and well-being of the participants are protected, and that the reported trial data are accurate, complete, and verifiable from source documents. Moreover, the CRA will confirm that the conduct of the trial by the PI and the site is in compliance with the protocol, GCP, and regulatory requirements as well as any applicable institution, ethical boards, and governmental processes. The first monitoring visit will be scheduled after the first participant has been enrolled. Thereafter, monitoring will occur per the Clinical Monitoring Plan (CMP), if available, or approximately every two months during the study duration or more frequently if:

- The volume or quantity of data is large or there is a backlog of review due to unexpected issues
- The site compliance with the protocol or compliance with expected ICH/GCP and regulatory requirements is lacking or there are continuing unresolved compliance issues
- There are unexpected ADE/SADE or participant safety concerns noted
- There are any unexpected inconsistencies with study product management
- There is a request for more frequent monitoring by the site
- Any mutually agreeable situation as determined by the site(s) and Medline

The frequency of routine monitoring may be increased to a longer interval depending on site enrollment. The CRA(s) will discuss this with Medline's Clinical Affairs Director or Manager, and will inform the PI prior to implementation.

Monitoring activities will include participant eligibility, source data review, CRF completion verification, product accountability, site continued suitability, PI study oversight, compliance, and all general monitoring activities as outlined in FDAs CFR and ICH/GCP guidelines that guide that activity.

Medline may, on occasion, contract with external Contract Research Organizations (CROs) to provide CRA services, and those CRAs are authorized to act on behalf of Medline.

It is expected that the site will be compliant with any institutional SOPs during the execution of the protocol and evidence of that compliance should be readily documented and verifiable by the CRA(s).

The CRA will provide the PI with a detailed follow-up letter after each monitoring visit that will outline the completed monitoring activities as well as any identified areas of concern and the expected/applicable corrections needed. Medline reserves the right to perform audit of the study activities – either routine or for-cause – as needed, and may perform a clinical monitoring audit as well.

9.2. Regulatory and Ethical Considerations

9.2.1. Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the PI, the study staff, and the sponsor. Therefore, 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 without prior written approval of the sponsor. All study data and study records will be managed and stored in accordance with the site's policies on data storage and security. All electronic transmission of data will adhere to Health Insurance Portability and Accountability Act (HIPAA) and any local regulations.

The study monitor, other authorized representatives of the sponsor, representatives of the IRB, and regulatory agencies may inspect all documents and records required to be maintained by the PI, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

A master list linking participant ID numbers to patient name and medical record number will be maintained in a secure database by the PI or paper files in secure cabinet(s). The participants' contact information will be securely stored at each clinical site for internal use during the study. The PI will agree to notify the sponsor of any intent to move or destroy these documents.

9.2.2. Safety Oversight

Safety oversight will consist of monitoring of visit activity, and 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 modifications that are in the best interest of the participant as necessary. See also Section 7 for reporting and management requirements.

9.2.3. 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 PI, sponsor, and the IRB. If the study is prematurely terminated or

suspended, the PI, in collaboration with the sponsor, will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstance(s) that may warrant termination or suspension include, but are not limited to:

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

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and the sponsor and/or the IRB are satisfied.

9.2.4. Study Closeout

Upon completion of the study, Medline and/or its designees will notify the site of closeout-related procedures and will coordinate with the site the return of equipment and/or any unused product. Medline CRA(s) will communicate closely with the PI at that time point and will review all closeout steps and materials. All study data, related study documents, and unused study product, will be returned to the sponsor or as per agreement with the study contract. The site will also notify the IRB that the study has been completed.

9.2.5. Data Handling and Record Keeping

Data collection is the responsibility of the research staff at the site under the supervision of the PI. The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported in the CRFs or any other study activity documentation as part of this study. All the documents should be completed in accordance with GDP to ensure accurate interpretation of data.

Final storage of Medline data will be per ICH/GCP guidelines in a protected access area for the length of the time required.

9.2.6. Conflict of Interest Policy

The independence of the 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 the study will be disclosed and managed.

9.3. Protocol Deviations

It is the responsibility of the PI and qualified designee to use continuous vigilance to identify and report deviations on a routine basis. All deviations must be addressed in the study source documents and reported to Medline. Protocol deviations must be sent to the reviewing IRB per reporting requirements and should be reported to the sponsor in a timely manner. The PI is responsible for knowing and adhering to the reviewing IRB requirements.

9.4. Abbreviations

ADE	Adverse Device Event

CFR	Code of Federal Regulations
CMP	Clinical Monitoring Plan
CRA	Clinical Research Associate
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
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICU	Intensive Care Unit
ID	Identification
IFU	Instructions for Use
IRB	Institutional Review Board
LP	Limited Partnership
MRSA	Methicillin-Resistant *Staphylococcus aureus*
PI	Principal Investigator
PSF	Participant Screening Form
SAE	Serious Adverse Event
SADE	Serious Adverse Device Event
SPT	Skin Protectant Textile
SOA	Schedule of Activities
UADE	Unanticipated Adverse Device Effect
US	United States

VAS	Visual Analogue Scale

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