NYU Langone Health

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Impact of Promogran Prisma™ on pain of split-thickness skin graft donor sites compared to standard of care alone – a pilot study

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Study Product:	Promogran Prisma™
Study Product Provider:	KCI – An Acelity Company

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STATEMENT OF COMPLIANCE

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), 21 CFR Parts 50, 56, 312, and 812 as applicable, any other applicable US government research regulations, and institutional research policies and procedures. The International Conference on Harmonisation ("ICH") Guideline for Good Clinical Practice ("GCP") (sometimes referred to as "ICH-GCP" or "E6") will be applied only to the extent that it is compatible with FDA and DHHS regulations. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

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LIST OF ABBREVIATIONS

AE	Adverse Event/Adverse Experience
CFR	Code of Federal Regulations
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation

IRB	Institutional Review Board
MOP	Manual of Procedures
N	Number (typically refers to participants)
OHRP	Office for Human Research Protections
PI	Principal Investigator
POD	Postoperative day
SAE	Serious Adverse Event/Serious Adverse Experience
SOC	Standard of Care
STSG	Split Thickness Skin Graft
UP	Unanticipated Problem

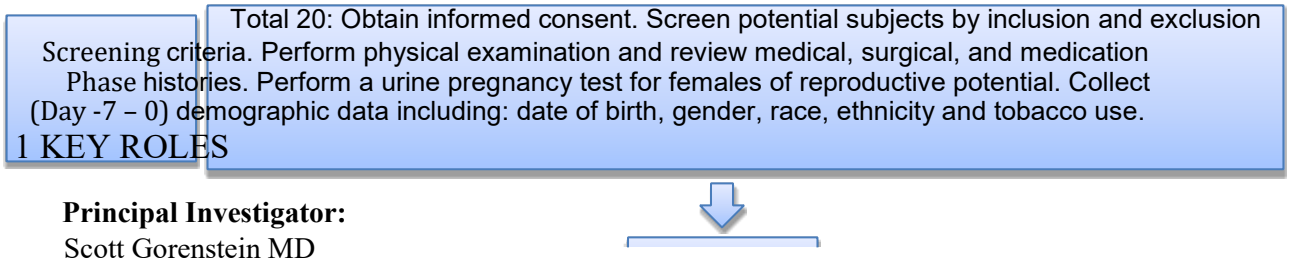
Study number: s19-00437
Version: 3.2

PROTOCOL SUMMARY

Title	Impact of Promogran Prisma™ on pain of split-thickness skin graft donor sites compared to standard of care alone – a pilot study
Short Title	Impact of Prisma on donor site pain
Brief Summary	Twenty patients will be randomized into two groups: control and treatment. The control group will received standard of care (SOC) dressings at the split thickness skin graft (STSG) donor site and the treatment group will receive Promogran in direct contact with the donor site in addition to SOC. SOC at NYU Winthrop Hospital includes, but is not limited to, xeroform or semi-occlusive adhesive dressings. The primary outcome is to assess the feasibility of evaluatingPromogran in addition to SOC for the management of donor-site pain following STSG. The only difference between the two groups is the addition of Prisma in direct contact with the donor site under the SOC dressings in the treatment group.
Objectives	The primary objective of this study is to assess the feasibility of evaluating the use of a composite collagen, silver-oxidized regenerated cellulose matrix compared to the standard of care dressing on donor site pain for patients undergoing split-thickness skin grafting in preparation for a larger study.
Methodology	This is a prospective, randomized, open-label, single-center feasibility study.
Endpoint	The primary endpoint of this feasibility study is to evaluate if using Promogran in addition to SOC is associated with a clinically meaningful difference in pain score (≥2 points on the visual analog pain scale) between the treatment and control arms on postoperative day (POD) 1.
Study Duration	Two years
Participant Duration	Six weeks
Duration of IP administration	One application
Population	Twenty patients; 10 in the intervention group and 10 in the control group. All genders, ≥18 years old, all demographics and geographic locations; scheduled to undergo STSG.
Study Sites	Single site: NYU Winthrop Hospital
Number of participants	20 participants
Study compensation	$70. Two payments of $35 will be given to participants – one at enrollment and one at collection of the 10-day pain diary.
Description of Study Agent/Procedure	Promogran Prisma™ is a composite collagen-silver-oxidized regenerated cellulose dressing that is a sheet applied topically to the STSG donor site.
Reference Therapy	The control group will receive a standard of care dressing on the STSG donor site (i.e., non-adherent dressing)
Key Procedures	Placement of either Prisma or standard of care dressing on the STSG donor site. Record daily pain score of the donor site for 10 days post-grafting. Return to clinic for weekly follow-up visits for 6 weeks.

Statistical Analysis	Proposed sample size (10 patients in each arm, a total of N=20) is obtained from a recruitment and cost feasibility point of view. For the primary endpoint, the pain score at POD 1 will be compared between treatment groups using Wilcoxon rank-sum (Mann-Whitney) test. The secondary endpoint, time from randomization to donor site healing, will be compared between treatment groups using time to event approach via Kaplan-Meier method.

SCHEMATIC OF STUDY DESIGN



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2 INTRODUCTION, BACKGROUND AND RATIONALE

2.1 Background Information and Relevant Literature

Split-thickness skin grafting (STSG) is the mainstay of therapy for the management of wounds that cannot be closed primarily or left open to close by secondary intention. However, the wounds created by STSG are often a source of pain and morbidity to patients. Multiple studies have compared various donor site dressings in attempt to decrease pain and morbidity[1–4]. This study will look specifically at the effect on patient-reported donor site by using of a collagen dressing. The addition of a composite collagen-silver-oxidized regenerated cellulose dressing (Promogran Prisma™) which has been cleared by the FDA(510k) in direct contact with the donor site is hypothesized to decrease pain at the donor site.

2.2 Potential Risks & Benefits

Risks involved with the procedures (i.e. surgical procurement of the STSG, use of advanced wound care therapies included in the SOC at NYU Winthrop Hospital Wound Center) are similar to risks in the standard treatment of wounds of this nature (i.e. infection; allergic reaction; excessive redness, pain, swelling, or blistering). Procurement of the STSG will be performed under sterile conditions in the operating room under monitored supervision and adequate pain control by a trained anesthetist. There is no difference between the treatment and control groups in the way that the STSG is obtained. Standard risks associated with anesthesia will be explained to the patient in detail prior to the operation. Skin grafting can cause localized pain with associated local bleeding that will be controlled in the operating room.

Benefits include decreased pain at the STSG donor site, decreased time to heal, and decreased occurrence of adverse events (e.g. wound infection). Even in the event that no improvement is made to donor site pain or wound healing, information gained from the study will be used to help understanding and improve future treatment options for people undergoing STSG.

3 RESEARCH OBJECTIVES AND PURPOSE OF THE STUDY

The primary purpose of this study is to assess the feasibility of evaluating the use of a composite collagen, silver-oxidized regenerated cellulose matrix compared to the standard of care dressing on donor site pain for patients undergoing split-thickness skin grafting in preparation for a larger study.

4 STUDY DESIGN AND ENDPOINTS

4.1 Study Description

This is a prospective, randomized, single-center feasibility study. Twenty patients will be randomized into two groups: control and treatment. The control group will receive standard of care (SOC) dressings at the STSG donor site and the treatment group will receive Promogran in direct contact with the donor site in addition to SOC. SOC at NYU Winthrop includes, but is not limited to, xeroform or semiocclusive adhesive dressings. Thrombin spray may be used for hemostasis. Patients are routinely followed in the outpatient wound clinic until wound healing occurs. Healing is defined as complete donor site epithelialization without drainage.

4.2 Study Endpoints

The primary aim of this feasibility study is to evaluate if using Promogran in addition to SOC will improve the pain score compared to SOC alone. Specifically, we would like to detect a clinically meaningful difference in pain score (≥2 points on the pain scale) between the treatment and control arms on postoperative day (POD) 1.

Secondary aims include:

1. Describe and compare the percent of patients healed between treatment groups
2. Describe and compare weekly surface area between treatment groups
3. Compare time to complete donor site healing between treatment groups

4. Describe and compare adverse events between groups
5. Describe and compare decreased use of narcotics and other pain medications between groups
6. Describe and compare percent of granulation tissue at the donor site between treatment groups. Granulation will be reported in quartiles (0-25%, 26-50%, 51-75%, and 76-100%).

5 STUDY ENROLLMENT AND WITHDRAWAL

Participants will be recruited from the NYU Winthrop Hospital Wound Care center, inpatient service, and other outpatient surgical services. Consent will be obtained by the principal and sub-investigators of the study.

5.1 Randomization:

Randomization will be performed 1:1 at enrollment. A computer generated randomized block assignment list will be given to the study coordinator. Each block of 2 or 4 subjects will contain an equal number of the two groups: 1) SOC, 2) Promogran+SOC. SAS PROC PLAN will be used to generate this list.

5.2 Inclusion Criteria:

1. Patient ≥18 years of age
2. Male or female
3. Patient scheduled to undergo STSG for any reason
4. Patientis able to provide informed consent and has read and signed the IRB-approved informed consent form.

5.3 Exclusion Criteria:

1. Active infection or history of radiation to the donor site
2. Patient has a known sensitivity to Promogran Prisma™ or silver
3. Elevated INR >3.0
4. Insensate at the donor site
5. Chronic narcotic use (>6 months of daily use)
6. Patient is currently pregnant and/or breastfeeding

The target number of enrolled patients will be 20, with 10 patients in the control and treatment groups, respectively. Patients will be allowed to withdraw consent at any time, with no adverse effect on the care received at NYU Winthrop Hospital.

6 STUDY PROCEDURES AND SCHEDULE

The study will last six weeks. After consent and enrollment, patients in both the control and treatment groups will undergo STSG as scheduled. Promogran will be available in the operating room and applied by the operating surgeon (study or non-study surgeon) directly to the donor site of patients randomized to the treatment group. Patients in the control group will receive SOC dressings per the attending surgeon's clinical judgment. SOC dressings include a primary non-adherent dressing, a secondary gauze and transparent film or tape. The only difference between the two groups is the addition of Prisma in direct contact with the STSG donor site under the primary dressing in the treatment group.

Pain will be patient-reported using the visual analogue/Wong-Baker pain rating scale (VAS), which is reported on a scale from 0-10. Pain will be measured once at each of the following 12 time points: preoperatively, post-operatively (POD 1), and each subsequent postoperative day for ten days. After day 10, pain will be recorded by the assessing clinic provider during the weekly visits, until week six.

Patients will be followed daily while inpatient and weekly while outpatient for six weeks. The number of study visits will be between 6-10. The study visits will be combined with SOC vists and there will

be no study related procedures other than assessing pain at the donor site. Dressings will be changed and wounds assessed according to the standard of care at NYU Winthrop Hospital.

Screening Phase - Week -1 (within 7 days prior to treatment visit)

- Evaluation of eligibility for study inclusion
- Obtain informed consent
- Screening of inclusion/exclusion criteria
- Assign a unique subject identification number (SID).
- Randomize to treatment or control arm
- Perform physical examination and review medical, surgical, and medication histories.
- Perform a urine pregnancy test for females of reproductive potential.
- Collect demographic data including: date of birth, gender, race, ethnicity and tobacco use.
- Give patient pain diary and payment of $35 patient stipend.

Treatment Phase - Day 0

- Ensure subject remains eligible prior to study product application.
- Confirm negative urine pregnancy test for females of reproductive potential prior to initial product application.
- Application of Prisma to STSG donor site for patients in the treatment group Record STSG donor site length and width
- Records all pain medications used in postoperative recovery room on POD 0

Follow-Up – Day 1 to 10

- Daily record of pain level in pain journal with the initial record once during 8am to 12pm and prior to each pain medication use
- Record time of any pain medication use
- Record pain of both donor and recipient STSG site

Follow-Up - Weeks 1 to 6 (6 week duration with 1 visit per week)

- Evaluation and record of STSG donor site – photography, length, width
- Record pain level of donor site
- Record any adverse events
- Collection of pain diary and second payment of $35 stipend.

7 ASSESSMENT OF SAFETY

7.1 Adverse Events

Adverse Events (AEs) will be captured from the time the subject is randomized into the study. An AE is defined as follows:

- Any adverse change in the subject's medical status when compared with the subject's baseline condition, whether or not the event is related to the device or a procedure; or
- An exacerbation (either in frequency or severity) in a subject's pre-existing condition.

7.2 Classification of an Adverse Event

Known sequelae, judged by the Investigator to be associated with target wound procedures (e.g., pain or bleeding associated with STSG harvest) and/or the course of normal wound healing (e.g., slough or mild exudate) should not be recorded as an AE unless: 1) an additional treatment/procedure is required (e.g., use of a concomitant medication); or 2) the frequency, severity and/or duration deviates from the expected course. These include but are not limited to:

- Infection/sepsis
- Worsening of wound bed/failure to heal
- Increased chronic inflammation
- Allergic reaction

- Unexplained fever or chills
- Death
- Neurologic symptoms such as light headedness, headache
- Gastrointestinal symptoms including nausea and vomiting

An AE or suspected adverse reaction is considered "serious" if, in the view of either the Investigator 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
- 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 patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
Unanticipated adverse device effect is any serious adverse effect on health or safety, any lifethreatening 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 application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

The Investigator will be asked to assess the severity of the AE using the following categories:

- Mild: Events require minimal or no treatment and do not interfere with the participant's daily activities.
- Moderate: Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- Severe: Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.

7.3 Relationship to Study Agent

For all collected AEs, the clinician who examines and evaluates the participant will determine the AE's causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- Definitely Related: The relationship of the AE and the study device or the study procedure can definitely be established.

- Probably Related: While a clear relationship to the study device or to the study procedure cannot be established, the AE is associated with an expected AE or there is no other medical condition or intervention, which could explain the occurrence of such an event.

- Possibly Related: There is no clear relationship between the AE and the study device or study procedure; however, one cannot definitely conclude that there is no relationship.

- Unrelated Related: There is no relationship between the AE and the study device or study procedure. This may include but is not limited to the incident being an expected outcome of a

previously existing or concurrent disease, concomitant medication or procedure the subject experienced.

7.4 Expectedness

The PI will be responsible for determining whether an AE is expected or unexpected. An AE 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 agent.

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate RF. Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. UPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

All unresolved adverse events should be followed by the investigator until the events are resolved, the subject is lost to follow-up, or the adverse event is otherwise explained. At the last scheduled visit, the investigator should instruct each subject to report any subsequent event(s) that the subject, or the subject's personal physician, believes might reasonably be related to participation in this study. The investigator should notify the study sponsor of any death or adverse event occurring at any time after a subject has discontinued or terminated study participation that may reasonably be related to this study. The sponsor should also be notified if the investigator should become aware of the development of cancer or of a congenital anomaly in a subsequently conceived offspring of a subject that has participated in this study.

7.5 Unanticipated Problem Reporting

Incidents or events that meet the OHRP criteria for UPs require the creation and completion of an UP report form. It is the site investigator's responsibility to report UPs to their IRB and to the DCC/study sponsor. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are SAEs will be reported to the IRB and to the DCC/study sponsor within 5 business days of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and to the DCC/study sponsor within 5 business days of the investigator becoming aware of the problem.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within<insert timeline in accordance with policy> of the IR's receipt of the report of the problem from the investigator.

7.6 Reporting Procedures – Notifying the Study Sponsor

The study clinician will complete a SAE Form within the following timelines:

- All deaths and immediately life-threatening events, whether related or unrelated, will be recorded on the SAE Form and submitted to the DCC/study sponsor within 24 hours of site awareness. See Section 1, Key Roles for contact information.
- Other SAEs regardless of relationship will be submitted to the DCC/study sponsor within 72 hours of site awareness.

All SAEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the adherence to be stable. Other supporting documentation of the event may be requested by the DCC/study sponsor and should be provided as soon as possible.

As a follow-up to the initial report, within the following 48 hours of awareness of the event, the investigator shall provide further information, as applicable, on the unanticipated event or the unanticipated problem in the form of a written narrative. This should include a copy of the completed Unanticipated Problem form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing unanticipated adverse effects shall be provided promptly to the study sponsor.

8 Clinical Monitoring

Clinical site monitoring will be conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with Good Clinical Practice (GCP), and with applicable regulatory requirement(s).

Data safety monitoring will be done by the Clinical Research Coordinator. Events that will be monitored are infection at donor site, increasing pain at donor site, and allergic reaction to dressing. Monitoring will occur on a weekly basis once patients are enrolled. There are no predefined stopping points and reviews will be disseminated at the weekly research meeting.

9 STATISTICAL CONSIDERATION

9.1Sample Size

A pilot study is limited in terms of statistical power due to its small sample size. As a result, no formal power computation was carried out. Proposed sample size (10 patients in each arm, a total of N=20) is obtained from a recruitment and cost feasibility point of view. The main aim of the study is to determine feasibility of the intervention, recruitment, randomization, retention a priori to a large full scale randomized clinical trial. No inferential decision will be made based on p-values; however the direction and size of the effect of the intervention on the outcomes observed will be critical for designing future randomized controlled trial where efficacy of the intervention will be determined.

9.2 Statistical Analysis Plan

Data will be summarized using descriptive statistics such as mean (standard deviation), median (Interquartile Range) based on the distribution of the continuous variables. Categorical variables will be presented as count (percentage).

9.3 Primary endpoint

Reducing pain at POD 1 was thought to be clinically important. Hence, the pain score at POD 1 will be compared between treatment groups using Wilcoxon rank-sum (Mann-Whitney) test. For demographic and other clinical covariates, we will test whether baseline characteristics are well balanced between two groups. If a baseline variable is not balanced or correlated with outcome ($r>0.30$), we will develop an ANCOVA model for POD 1 pain score and include it as a covariate in addition to baseline pain score and treatment groups.

9.4 Secondary endpoints

Time from randomization to donor site healing will be compared between treatment groups using time to event approach via Kaplan-Meier (KM) method. The log-rank test will be used to compare the KM curves. Adverse events will be summarized between groups using counts and percentages. Percent of patients healed, percent use of narcotics and other pain medication (ie amount of medication used) and percent of granulation will be compared between groups using Fisher's exact test.

All analyses will be performed using SAS version 9.4 for Windows (SAS Institute Inc.). Nominal P< values will be presented.

10 SOURCE DOCUMENTS AND ACCESS TO SOURCE DATA/DOCUMENTS

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial. It is acceptable to use CRFs as source documents. If this is the case, it should be stated in this section what data will be collected on CRFs and what data will be collected from other sources.

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write "N/D". If the item is not applicable to the individual case, write "N/A". All entries should be printed legibly in black ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.

Access to study records will be limited to IRB-approved members of the study team. The investigator will permit study-related monitoring, audits, and inspections by the IRB/EC, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

11 ETHICS/PROTECTIONI OF HUMAN SUBJECTS

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

Consent forms describing in detail the study agent, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study product. The informed consent is submitted with this protocol.

11.1 Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided to the participants and their families. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the signed informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

A copy of the signed informed consent document will be stored in the subject's research record. The consent process, including the name of the individual obtaining consent, will be thoroughly documented in the subject's research record. Any alteration to the standard consent process (e.g. use of a translator, consent from a legally authorized representative, consent document presented orally, etc.) and the justification for such alteration will likewise be documented.

11.2 Participant and Data Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Study photos will be kept confidential by not including any identifying features (e.g. patient face, tattoo). De-identifies photos will be kept on the secure NYU Winthrop hospital computer network and only accessed by study personnel. Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For

subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

12 DATA HANDLING AND RECORD KEEPING

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. Black ink is required to ensure clarity of reproduced copies. When making changes or corrections, cross out the original entry with a single line, and initial and date the change. DO NOT ERASE, OVERWRITE, OR USE CORRECTION FLUID OR TAPE ON THE ORIGINAL.

Copies of the electronic CRF (eCRF) will be provided for use as source documents and maintained for recording data for each participant enrolled in the study. Data reported in the eCRF derived from source documents should be consistent with the source documents or the discrepancies should be explained and captured in a progress note and maintained in the participant's official electronic study record.

Clinical data (including AEs, concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into a local database kept and maintained at NYU Winthrop Hospital by the Wound Care team. Access to the data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

12.1 Study Records Retention

Study documents will be retained for the longer of 3 years after close-out, 5 years after final reporting/publication, or 2 years after the last approval of a marketing application is approved for the drug for the indication for which it is being investigated or 2 years after the investigation is discontinued and FDA is notified if no application is to be filed or if the application has not been approved for such indication. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

12.2 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH E6:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3 • 5.1 Quality Assurance and Quality Control, section 5.1.1
- 5.20 Noncompliance, sections 5.20.1, and 5.20.2.

It is the responsibility of the site PI/study staff to use continuous vigilance to identify and record deviations within 2 working days of identification of the protocol deviation, or within 2 working days of the scheduled protocol-required activity.

13 References

1. Healy C, Greig AVH, Murphy AD, et al. Prospective randomized controlled trial: Fibrin sealant reduces split skin graft donor-site pain. *Plast Reconstr Surg*. 2013;132(1):139-146. doi:10.1097/PRS.0b013e318299c6f4.

2. Ramesh BA, Jayalakshmi BK, Mohan J. A Comparative Study of Collagen Dressing versus Petrolatum Gauze Dressing in reducing Pain at the Donor Area. *J Cutan Aesthet Surg*. 2017;10(1):18-21. doi:10.4103/JCAS.JCAS_110_16.
3. Sinha S, Schreiner AJ, Biernaskie J, Nickerson D, Gabriel VA. Treating pain on skin graft donor sites: Review and clinical recommendations. doi:10.1097/TA.0000000000001615.
4. García-Salinas AS, Mecott GA, García-Pérez M, et al. Decreased pain in split-thickness skin graft donor sites with the use of a non-adherent polyurethane dressing. *Med Univ*. 2015;17(69):196-202. doi:10.1016/j.rmu.2015.07.001.

14 SCHEDULE OF EVENTS

Activity	**Screening Visit [Day -7-0]**	**Treatment Visit [Day 0]**	**Follow-Up Phase [Day 1-10]**	**FollowUp Visit 1 [Day 7±3]**	**Follow-Up Visit 2 [Day 14±3]**	**Follow-Up Visit 3 [Day 28±3]**	**Follow-Up Visit 4 [Day 35±3]**	**Follow-Up Visit 5 [Day 42 ±3]**	**Final Visit 6 [Day 49 ±3]**
Informed Consent	X								
Eligibility Assessment	X								
Significant Medical, Surgical, Medication History	X								
Baseline demographics: gender, age, height, weight	X								
Pain score at STSG donor site	X	X	X	X	X	X	X	X	X
Randomization		X							
Application of Promogran Prisma™, for intervention group		X							
STSG donor site evaluation and management (SOC dressing, photography, length, width, assessment of appearance)				X	X	X	X	X	X
Closure assessment				X	X	X	X	X	X