Study Title:

A randomized, open-label investigational safety evaluation of the MAP Wound Matrix (TT101) device as a volumetric biomaterial scaffold applied to clean wounds after skin cancer surgery with Mohs micrographic surgery (MMS) compared to control.

Protocol Number:	TT-CLN-004-03
Protocol Version:	A
Issued Date:	July 12, 2024
Investigational Product:	MAP Wound Matrix (TT101)
Study Phase:	A first-in-human, not statistically powered, safety study
Sponsor:	Tempo Therapeutics, Inc.
Address:	3030 Bunker Hill Street, STE 104 San Diego, CA 92109

Contents

List of Abbreviations

Abbreviation	**Definition**
ADE	Adverse device effect
AE	Adverse Event
ASADE	Anticipated Serious Adverse Device Event
BSS	Biological Skin Substitute
BWAT	Bates-Jensen Wound Assessment Tool
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CRF	Case Report Form
CRO	Clinical Research Organization
DSMB	Data Safety Monitoring Board
ECM	Extracellular Matrix
EDC	Electronic Data Capture
EOS	End Of Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
HMM	Hydrogel Microsphere Matrix
HMS	Hydrogel Microsphere Suspension
ICF	Informed Consent Form
IFU	Instructions For Use
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intention To Treat
LI-xlink	Light-Initiated Crosslinking
MAP	Microporous Annealed Particle
MedDRA	Medical Dictionary for Regulatory Activities
MMS	Mohs Micrographic Surgery
PEG	Poly(ethylene glycol)
PI	Principal Investigator
PP	Per Protocol
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SAP	Statistical Analysis Plan
SOC	Standard Of Care
SOG	System Organ Class
SW	Source Worksheet
USADE	Unanticipated Serious Adverse Device Effect

1 Summary

Official Title:	A randomized, open-label, investigational safety evaluation of the MAP Wound Matrix (TT101) device as a volumetric biomaterial scaffold applied to clean wounds after skin cancer surgery with Mohs micrographic surgery (MMS) compared to control.
Short title:	Safety of MAP Wound Matrix in patients with clean surgical wounds.
Document/Protocol Number:	TT-CLN-004-03
Sponsor:	Tempo Therapeutics, Inc.
Investigational Device:	MAP Wound Matrix (TT101 Device)
Proposed Indication for Use:	The MAP Wound Matrix is indicated for the management of full thickness wounds including surgical sites, donor skin graft sites, wound dehiscence, lacerations, and draining wounds. The Device is prescription only. The device. MAP Wound Matrix is intended for the adult population; individuals 22 years or older.
Control treatment	Hydrocolloid dressing (DuoDerm®)
Study Objectives:	The primary objective of the study is to evaluate the safety of MAP Wound Matrix (TT101) when used in the treatment of clean wounds after skin cancer surgery with Mohs micrographic surgery (MMS) compared to control.
Study Hypothesis	The MAP Wound Matrix device can be safely used for the management of clean, acute post-surgical wounds after Mohs Micrographic Surgery (MMS), as measured by the frequency of serious adverse device events (SADE) relative to a control treatment throughout the study.
Study Design overview:	This is a first-in-human, randomized, open-label clinical study evaluating the safety of the MAP Wound Matrix device when applied to full thickness wounds after skin cancer surgery with Mohs micrographic surgery (MMS) subjects. A minimum of thirty (30) subjects scheduled for MMS will be enrolled in the trial. Subjects will undergo skin cancer surgery via MMS at the Treatment visit in the clinic per standard of care. Post-surgery, approximately twenty (20) subjects will receive the MAP Wound Matrix device and approximately ten (10) subjects will receive the standard of care control treatment. Subjects will be randomly assigned to investigational or control treatment in a 2:1 ratio. In the MAP Wound Matrix treatment arm, the MAP Wound Matrix device will be topically applied to the wound immediately following MMS (same

day as MMS procedure) according to the Instructions for Use (IFU) (TT-CLN-004-TT101-IFU). The MAP Wound Matrix device will be in direct contact with the wound bed surface. Prior to applying the MAP Wound Matrix device, the wound must have reached hemostasis as established clinically by the Investigators.

A topical covering will be placed over the MAP Wound Matrix device after application. This will consist of a non-adherent (e.g., Telfa, Adaptic) dressing followed by an adhesive, occlusive dressing (e.g. Tegaderm) per the Investigator's discretion. Additional dressings such as a non-adherent gauze and pressure bandage may be applied in the first week after treatment as deemed necessary by the Investigator. This is in accordance with standard bandaging procedures used for other bioengineered skin substitutes and dermal templates.

In the control treatment arm, a hydrocolloid (DuoDerm) will be topically applied to the wound immediately following MMS (same day as MMS procedure) according to the manufacturer's instructions. The control treated wounds will be dressed with an absorbent dressing (e.g. gauze), at investigator discretion, above the hydrocolloid dressing. The hydrocolloid and optional absorbent dressing will be secured by an occlusive dressing (e.g., Tegaderm). Additional dressings such as a non-adherent gauze and pressure bandage may be applied above the Tegaderm in the first week after treatment as deemed necessary by the Investigator.

Although MAP Wound Matrix is intended to be applied only once, the device may be reapplied one time if (i) the device is observed to have been removed from the wound or (ii) the device has been disturbed in the wound site during the first week after treatment. Subject pain will be assessed after reapplication if it occurs.

If post-application wound site infection is suspected at any point in the study, the MAP Wound Matrix device may be removed by debridement, and the wound tissue further debrided, as deemed medically necessary by the Investigator and in accordance with standard of care procedures for wound site infections. The safety, ease and effectiveness of removal will be evaluated if it occurs. Evaluation of safety in any instance of device removal will include the assessment of wound site bleeding after removal, peri-wound erythema and edema, ability of the wound site infection to be resolved by antibiotic treatment and standard practices, and subsequent wound healing after device removal and infection control. Evaluation of the effectiveness of device removal will be through clinical observation of the wound before and after debridement, as well as the assessment of the amount of residual device remaining in the wound after device removal.

The control dressings will be reapplied every 3-4 days within the first two weeks (by the investigator during follow-up visits and by the subject at home between visits). During week three and onward, the control dressings will be reapplied once weekly by the Investigator during the follow-up visits or the subject at home, until the wound is closed. Each re-

	application of the control will require the dressings to be changed. This is in accordance with standard of care for these patients when using a hydrocolloid dressing.
Study Population:	The study population is subjects aged ≥ 22-years-old scheduled for skin cancer surgery with Mohs micrographic surgery (MMS). Subjects who will be permitted into the study include those who will meet all the inclusion criteria and will have none of the exclusion criteria.
Sample Size	A minimum of 30 adult subjects (20 treated with the MAP Wound Matrix device and 10 treated with control) will be enrolled. To allow for potential loss to follow-up or other drop-out events, additional subjects may be enrolled. No more than 50 subjects will be considered for enrollment.
Safety:	All AEs, of all type and severity, will be collected and reported.
Safety Endpoint	Incidence of serious adverse device effects (SADE) (including delays in wound healing and surgical site infections) in subjects treated with MAP Wound Matrix, compared to the control treatment group. An independent Data Safety Monitoring Board (DSMB) will review all reported AEs, SAEs, and SADEs to determine whether the study should be stopped before enrollment completion due to safety risk. The DSMB will also provide additional perspective (in addition to the PI) regarding whether SAE are related to the investigational device.
Exploratory Endpoints:	Exploratory endpoints include: • Investigator assessment of wound healing (size, depth, edges, undermining, necrotic tissue, exudate, peripheral tissue edema, granulation tissue, and epithelialization) over the follow-up period following MAP Wound Matrix application (using digital imaging and the Bates-Jensen Wound Assessment Tool). • Assessment of the healed wound site using a clinical assessment (investigator and subject) and digital imaging (2D or 3D). • Subject reported pain at the index wound site over the follow-up period following MAP Wound Matrix application, using a Visual Analog Scale (VAS) of 0-10. • Investigator assessment of device embedment and presence in the wound following MAP Wound Matrix application. • Incidence of device removal over the follow-up period following MAP Wound Matrix application. • Investigator assessment of safety, ease and effectiveness of removal over the period following MAP Wound Matrix application,

	if it occurs. The amount of residual device remaining in the wound after device removal will be assessed.
Subject Inclusion Criteria:	To be eligible for trial participation subjects must meet the following inclusion criteria: 1. Willing to undergo the written informed consent process prior to enrollment in this study. 2. At least 22 years of age at screening. 3. Has non-melanoma skin cancer and be scheduled for skin cancer surgery with Mohs micrographic surgery (MMS) on a location suitable for secondary intention healing. 4. Resulting surgical wound after Mohs micrographic surgery (MMS) must be at least 1 cm and no more than 4 cm in diameter (or surface area of at least 0.8 cm^2 and no more than 12.6 cm^2). 5. Resulting surgical wound after MMS must be full thickness. 6. Willing to return for all required follow-up visits. 7. Willing to follow the instructions of the Principal Investigator.
Subject Exclusion Criteria:	Subjects are excluded from this trial if they do not fulfill the inclusion criteria, or if any of the following are observed: 1. Has a confirmed diagnosis of clinically significant peripheral neuropathy. 2. Has uncontrolled Type I or Type II diabetes and HbA1c values greater than 8.0% within the last 6 months. 3. Has a known infection in the area of the Mohs surgery. 4. Has a known allergy to any of the components of the TT101 Device. 5. Is an active daily cigarette smoker. 6. Is pregnant or lactating. 7. Is a woman of child-bearing potential who is unwilling to avoid pregnancy or use an appropriate form of birth control (adequate birth control methods are defined as: topical, oral, implantable, or injectable contraceptives; spermicide in conjunction with a barrier such as a condom or diaphragm; IUD; or surgical sterilization of partner). 8. Has clinical evidence of Peripheral Vascular Disease (PVD) in the form of grade 2 pitting Edema or higher. 9. Has been diagnosed with a surgical or wound site infection within the last 6-months. 10. Has been diagnosed with chronic ulcer or wound within the last 12-months. 11. Has a remote active infection concurrent with having the MMS. 12. Per Investigator's discretion the subject is not appropriate for inclusion in the trial.

Phase:	First-in-human safety study.
Number of Sites Enrolling Participants:	It is anticipated that there will be 3-5 participating sites in the US.
Study Follow-Up Visit:	The following visits are required after the study treatment application. • In-clinic Visits: Visit #3, #4, #6, #8, and #10. • Virtual Visits: Visit #5, #7, and #9. Depending on the type of follow-up visits (in clinic or virtual), assessments will include standard wound care, clinical wound assessment, wound imaging, device assessment, systemic antibiotics (per the Investigator's discretion), monitoring for incidence and severity of treatment emergent AEs and SAEs as well as the incidence of Serious Adverse Device Effects (SADEs). Investigators will be able to schedule additional dressing changes outside of the visit schedule as needed. These will be performed either by the Investigator at the clinic during unscheduled visits or by the subject at his/her home. A two-week confirmation follow-up visit will be scheduled after the first observation of wound closure. Subjects will remain in the study for up to three months following confirmed wound closure. During this follow-up period, optional virtual visits can be conducted monthly. Unscheduled visits may occur during this period to evaluate any subject self-reported adverse events, or as deemed medically necessary by the Investigators. A final in-clinic follow-up visit will occur at the earlier of 3 months after confirmed wound closure or 24 weeks after treatment. At this final visit, the subject's study participation is considered complete. If the wound is not closed and MAP Wound Matrix is clinically present in the wound at Week 24, the Investigator will be instructed to debride the remaining device out of the wound. Figure 1 illustrates an overview of the follow-up visit timeframe and study assessments after MMS and treatment application.
Participant Duration:	It is anticipated that subjects will participate in the study for up to six (6) months.
Study Duration:	The entire study is expected to last for approximately 9-12 months.
Safety Review & Stopping Criteria:	The Data Safety Monitoring Board (DSMB) may recommend that the trial be stopped and evaluated at any time. The trial should also be stopped should there be two Serious Adverse Device Effects (SADEs) in two subjects.

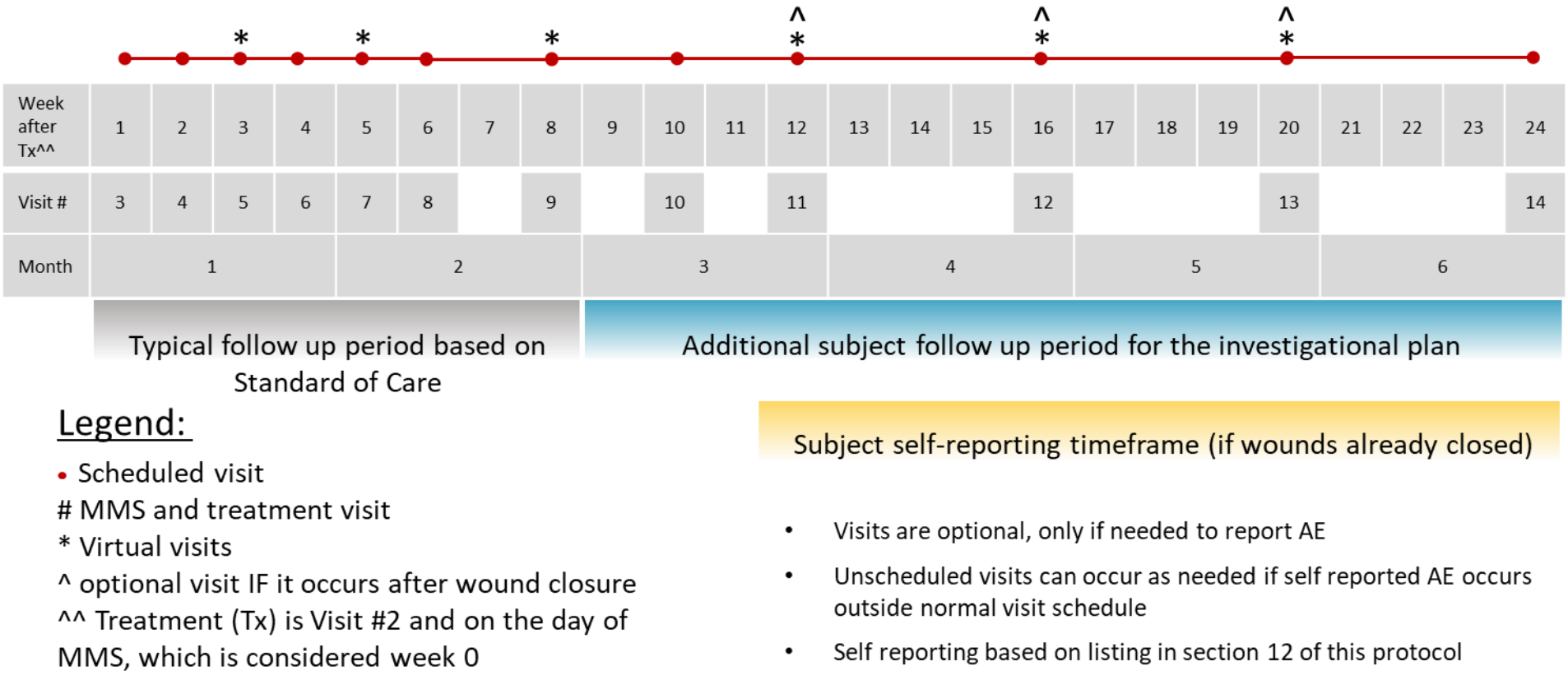

Figure 1: Illustration of visit schedule during the follow-up period after MMS and treatment application to subjects.

2 Introduction

2.1 The Clinical Landscape

Mohs surgery is performed about 850,000 times each year in the United States (US)[1]. Mohs surgery is a highly effective technique for removing cancerous skin lesions, particularly basal cell carcinoma and squamous cell carcinoma; however, the procedure itself creates a wound that requires careful management to optimize healing and minimize complications. The most prevalent complications of post-operative wound management following Mohs micrographic surgery (MMS) are (i) infection and (ii) scarring from dermal atrophy and scar contracture.[2] Maintaining a clean wound environment until the wound is fully closed is crucial to prevent infection, a potential setback in healing. Furthermore, facial defects from scarring following Mohs surgery can cause significant functional, cosmetic, pain, and psychologic issues[3]. Finding the right balance between achieving complete healing and minimizing scarring remains an ongoing challenge.

Currently, there is not a one-size-fits-all approach or a single standard treatment to post-Mohs wound care[2]. To achieve the best outcome, doctors and patients can choose from various treatment options. Ideally, these treatments would promote the return of healthy tissue while minimizing the risk of skin cancer recurrence. The best course of action depends on the specific wound characteristics. Factors like size, anatomical location, patient comfort, and available resources all come into play. Treatment options might include:

- Surgically grafting skin from another area of the body (autologous graft).
- Stitching the wound closed (primary closure).
- Using nearby skin to cover the wound (local flap).
- Tissue reconstruction for more complex closures.
- Letting the wound heal naturally (secondary intention healing or granulation).
- Applying a biological skin substitute (BSS), such as porcine or amnion tissue.

BSS products offer several advantages. Their natural structure promotes the formation of a healthy dermis, and they contain growth factors that can help with healing and fight infection. Studies have shown they can effectively protect wounds, reduce bacteria, control inflammation, and stimulate angiogenesis. However, BSS products are expensive which can be a barrier for some patients, and they may not be covered by all health insurance plans. In addition, they are not always readily available in all healthcare settings and are not suitable for certain types of post-Mohs wounds depending on their size, depth, or location. They must also be applied multiple times over the course of healing to have an effect, and there is always the possibility the body might reject the BSS. Lastly, while BSS products can promote healing, they may not fully replicate the functionality and aesthetic qualities of natural skin in all cases[2].

2.2 Justification for the Design of the Clinical Investigation

Tempo Therapeutics has developed MAP Wound Matrix (TT101), a flowable biomaterial that (i) conforms to the wound shape, (ii) physically integrates with the tissue to enable ‘graft take’, (iii) enables fast granulation tissue to support vascularization, and (iv) maintains the mechanical strength of the scaffold and tissue throughout the healing process to minimize scarring.

MAP Wound Matrix is a concentrated hydrogel microsphere suspension (HMS). The HMS is formulated in

isotonic phosphate buffered saline, pH 7.4 containing Eosin Y, and has properties of a flowable viscous gel. The hydrogel microspheres (HM) are spherical hydrogel particles composed of a water-swollen polymer mesh of poly(ethylene glycol) (PEG) and synthetic peptides. In use, MAP Wound Matrix is flowed into the wound bed as the HMS and then exposed to white light causing a light-initiated crosslinking (LI-xlink) reaction. This LI-xlink reaction covalently links the hydrogel microspheres together to form a stabilized hydrogel microsphere matrix (HMM) in the wound bed. The HMM acts as a scaffold to support wound healing and is bio-absorbed by the body throughout the healing process. MAP Wound Matrix has shown the ability to enable rapid granulation tissue and support vascularization without eliciting a foreign body response against the device and without the need for drugs, cells or biologics[4–6].

This trial is designed as a first-in-human study to evaluate the safety of MAP Wound Matrix (TT101) when used in the treatment of clean wounds after skin cancer surgery with Mohs micrographic surgery (MMS).

The study design is based on previous discussions with FDA, and the knowledge gained during multiple preclinical studies in various animal models that were performed to evaluate the safety and performance of MAP Wound Matrix as a medical device for wound healing therapy. Specifically, the performance of MAP Wound Matrix, as well as safety measures such as local irritation and tissue response, were evaluated in a healthy porcine wound healing study performed under Good Laboratory Practices (GLP). Other preclinical safety studies performed under GLP evaluated local irritation in a rat, sub-chronic systemic toxicity in rat, irritation and sensitization in guinea pig, material mediated pyrogenicity in rabbit, and mutagenicity and cytotoxicity in multiple cell types. The results from these performance and preclinical studies met their defined performance and safety end points and therefore support the biological safety of the MAP Wound Matrix device. Further details and information on these studies can be found in the TT101 Report of Prior Investigations (TT-CLN-004-01).

3 Study Objective

The primary objective of the study is to evaluate the safety of MAP Wound Matrix (TT101) when used in the treatment of clean surgical wounds after skin cancer surgery with Mohs micrographic surgery (MMS) compared to a control.

4 Overview of study design

This study will be conducted according to the following:

- U.S Federal Regulations 21CFR 11, 50, 54, 56, 812, 820
- ISO 14155: 2020 - Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice

The hypothesis under study: It is hypothesized that the MAP Wound Matrix device can be safely used for the management of clean, acute post-surgical wounds after Mohs Micrographic Surgery (MMS) as measured by the frequency of serious or severe adverse events relative to a control treatment throughout the study.

Potentially eligible subjects will be assessed against all inclusion and exclusion criteria, with the exception of resulting wound size, which can only be assessed after MMS is performed at Visit #2. Patients will have the opportunity to evaluate if they would like to participate in the study prior to signing the ICF. Consent will be obtained prior to initiation of any study-specific activities. Subjects will undergo Mohs Micrographic Surgery (MMS). Post-procedure wound assessment will include image capture, size, depth, granulation tissue formation, and wound closure. This will occur after MMS and before treatment

application. The final inclusion/exclusion criterion of the resulting wound size will be assessed after MMS. If patients meet all inclusion criteria and no exclusion criteria, they will be randomized to receive either MAP Wound Matrix treatment or control treatment (DuoDerm). Subjects will undergo investigational device assessment (presence, removal), digital image capture, and additional wound assessment after receiving the treatment but before topical bandage coverings are applied.

5 Study Population

5.1 General Considerations

The study population consists of adult subjects aged ≥ 22-years-old scheduled for skin cancer surgery with Mohs micrographic surgery (MMS). Subjects who will be permitted into the study include those who meet all the inclusion criteria and have none of the exclusion criteria.

A minimum of 30 adult subjects (20 treated with the MAP Wound Matrix device and 10 treated with control) will be enrolled in the study. A minimum of 30 subjects will be randomized to the treatment or control group in a 2:1 ratio with a minimum of 20 subjects will receive the MAP Wound Matrix, and a minimum of 10 subjects will receive DuoDerm (control). To allow for potential loss to follow-up or other drop-out events, more than 30 subjects may be enrolled to the study. No more than 50 subjects may be considered for enrollment.

Exclusion Criteria and Inclusion Criteria of study subjects are detailed in the Study Summary Pages 10-11.

5.2 Screen Failures

Screen failures are defined as potential subjects who are found during the screening visit to not meet all the inclusion and exclusion criteria to participate in the trial. Screen failure information will be collected and captured in EDC to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements, and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

5.3 Strategies for Recruitment and Retention

Potential study subjects will be recruited primarily from the clinical practice of the participating study sites. Investigators will share the inclusion and exclusion criteria with their clinical staff. Any signage or advertising at the clinics relating to this trial will have been previously submitted to, and approved by, the relevant IRB.

Broader advertising through newspaper, radio, fliers, or posters in adjacent healthcare facilities may only be used if prior review and approval is granted by the Sponsor. All such advertising will be submitted to and approved by the relevant IRB prior to use.

All subjects will receive a nominal stipend to offset travel and meal costs for the duration of their participation. The actual amount will depend upon IRB approval, but in no case will it be intended to create an incentive to ignore the risks associated with participation in the trial.

6 Randomization

Randomization will be used to avoid bias in the assignment of treatment to each subject, to increase the likelihood that attributes of the subject are evenly balanced across treatment groups, and to enhance the

validity of statistical comparisons across treatment groups.

Subjects will be randomized to receive either MAP Wound Matrix treatment or control treatment (DuoDerm) on a 2:1 basis. This randomization will occur at the Treatment Visit.

7 Investigational Product and Comparators

7.1 Investigational product: MAP Wound Matrix device (TT101)

7.1.1 Formulation

The MAP Wound Matrix is a topical, flowable mechanically stabilized porous moist wound matrix device that is applied directly to an open wound to fill the volume of the wound defect. The device contains only synthetic components and consists of poly(ethylene glycol) (PEG)-based polymer and synthetic peptides with sequences derived from collagen and extracellular matrix (ECM). After application, the device is exposed to white light to crosslink the matrix in situ, forming a mechanical scaffold. Over time as the surrounding tissue grows into the scaffold, the device degrades. Further details on MAP Wound Matrix can be found in the Report of Prior Investigations (TT-CLN-004-01).

7.1.2 Shipping, handling, and storage conditions

The investigational MAP Wound Matrix device will be shipped in a validated Thermosafe temperature shipping unit and maintained at +2-8°C. The MAP Wound Matrix product will be stored at +2-8°C and used prior to the expiration date printed on the product box, as specified in the IFU (TT-CLN-004-TT101-IFU) and in accordance with Good Clinical Practice and regulatory requirements, as applicable. Product access will be limited to authorized trial personnel.

7.1.3 Wound preparation and MAP Wound Matrix treatment application

Wound preparation: The MAP Wound Matrix device will be applied to an acute, clean, surgical wound . Wound hemostasis must be achieved prior to applying the MAP Wound Matrix device to the wound bed. Prior to application, the wound surface will be cleansed using sterile saline or a non-ionic cleanser or a hypochlorous solution followed by extensive sterile saline or sterile water flush to the wound. All wound preparation procedures are in accordance with standard care. Each vial of the device is single use only. The vials cannot be reused, and any residual material must be discarded after use.

Note: Per the MAP Wound Matrix IFU (TT-CLN-004-TT101-IFU), antiseptic agents including hydrogen peroxide, acetic acid, chlorhexidine, povidone/iodine, and cetrimide may be used but must be rinsed with sterile saline or water prior to MAP Wound Matrix application. Antiseptic agents may not be used after MAP Wound Matrix application. Topical antimicrobials are prohibited.

MAP Wound Matrix application: The MAP Wound Matrix device will be applied in accordance with the MAP Wound Matrix IFU. A training on how to use and apply the MAP Wound Matrix device will be provided to the Investigators and necessary study personnel. Briefly, the Investigator or delegate opens the light-protective foil pouch, removes the product vial, and then flips up the vial cap to expose the rubber stopper. The Investigator then collects the contents of the vial using a standard sterile syringe and blunt fill needle. The blunt fill needle is provided with the device kit; a standard sterile 3-mL syringe is recommended, but not supplied. The MAP Wound Matrix is then flowed into the wound. After the MAP Wound Matrix is deployed into the wound bed, the Investigator uses a lighting unit specified in the IFU to expose the device to white light (TT-CLN-004-TT101-IFU). The Philips Burton Super Exam LED (SELED), a medical electrical LED-based exam light or luminaire (Class I) that conforms to the IEC 60601-2-41 standard is specified for use. During this light exposure, the device undergoes a light-initiated crosslinking

(LI-xlink) reaction where the hydrogel microspheres covalently link together to form a hydrogel microsphere matrix (HMM) in the wound.

Dressing for MAP Wound Matrix-treated wounds: After light exposure, the wound will be bandaged using a non-adherent (e.g., Telfa, Adaptic) dressing followed by an adhesive, occlusive dressing (e.g. Tegaderm) per the Investigator's discretion. Within the first week after surgery, additional dressings such as a non-adherent gauze and pressure bandage may be applied, as deemed necessary by the Investigator. The dressings will be changed at each follow-up visit until the wound is closed. Additional wound dressing changes may be required as deemed necessary by the Investigator. The additional dressing changes will be performed either by the Investigator at the clinic during unscheduled visits, or by the subject at his/her home.

7.1.4 Dose, route, and duration of administration

Potential re-application of MAP Wound Matrix: The application of MAP Wound Matrix will occur immediately after Mohs surgery (Visit #2) once hemostasis has been achieved. While MAP Wound Matrix is intended to be used only once, the device may be reapplied one time if (i) the device is observed to have been removed from the wound or (ii) the device has been disturbed in the wound site during the first week of post-operative application of MAP Wound Matrix. Therefore, the device may be reapplied at Visit #3, but no longer from Visit #4 onward. If the device is reapplied, subject pain at the wound site will be assessed prior to re-application, during re-application, and within 30 minutes after re-application.

If MAP Wound Matrix must be removed: During patient follow-up after treatment application, the wound will be monitored for complications and adverse events at each visit. If post-application wound site infection is suspected at any point in the study, the MAP Wound Matrix device may be removed using sharp debridement, and the wound further debrided, as deemed medically necessary by the Investigator and in accordance with standard of care procedures for wound site infections. The safety, ease and effectiveness of removal will be evaluated if it occurs. Evaluation of safety in any instance of device removal will assess wound site bleeding after removal, peri-wound erythema and edema, the ability of the wound site infection to be resolved by antibiotic treatment and standard practices, and subsequent wound healing after device removal and infection control. Evaluation of the effectiveness of device removal will be through clinical observation of the wound before and after debridement to remove the device if it is deemed medically necessary, as well as the assessment of the amount of residual device remaining in the wound after device removal. MAP Wound Matrix will not be re-applied in this case.

7.1.5 Prior investigations

Please see the Report of Prior Investigations (TT-CLN-004-01) provided separately.

7.2 Control: Hydrocolloid dressing (DuoDerm)

7.2.1 Formulation

The control consists of a hydrocolloid (DuoDerm) that covers the entire open surface of the wound maintaining a moist wound healing environment.

7.2.2 Shipping, handling, and storage conditions

DuoDerm will be stored as specified in the manufacturer's IFU.

7.2.3 Preparation

Wound preparation: DuoDerm will be applied to an acute, clean, surgical wound. Wound hemostasis must be achieved prior to applying the control to the wound bed. Prior to application, the wound surface

will be cleansed using sterile saline or a non-ionic cleanser or a hypochlorous solution followed by extensive sterile saline or sterile water flush to the wound. All wound preparation procedures are in accordance with standard care.

Control application: Once the wound is prepared for control application, DuoDerm will be applied to cover the whole surface of the wound in accordance with manufacturer's IFU, Good Clinical Practice and regulatory requirements, as applicable.

Dressing for control-treated wounds: In addition to the DuoDerm hydrocolloid dressing, the control treated wounds will be dressed with an absorbent dressing (e.g. gauze), at investigator discretion, above the hydrocolloid dressing. The hydrocolloid and optional absorbent dressing will be secured by an occlusive dressing (e.g. Tegaderm). Additional dressings such as a non-adherent gauze and pressure bandage may be applied above the Tegaderm in the first week after treatment as deemed necessary by the Investigator. At each dressing change, the wound will be cleansed after removing the DuoDerm dressing and prior to application of a new DuoDerm dressing.

7.2.4 Dose, route, and duration of administration

The application of the DuoDerm control will occur immediately after Mohs surgery (Visit #2) once hemostasis has been achieved.

The control dressings will be reapplied every 3-4 days within the first two weeks (by the investigator during follow-up visits and by the subject at home between visits). During week three and onward, the control dressings will be reapplied once weekly by the Investigator during the follow-up visits or the subject at home, until the wound is closed. Each re-application of the control will require the dressings to be changed. This is in accordance with standard of care for these patients when using a hydrocolloid dressing[7,8].

Dressing changes will be performed either by the Investigator at the clinic during scheduled or unscheduled visits, or by the subject at his/her home, and will be recorded on the study CRFs.

7.3 Investigational Product Dispensation and Accountability

All study devices must be kept in a securely locked area at the clinical sites in compliance with all applicable FDA regulations and stored according to the storage conditions on the product labelling. The Investigator, or designated study site personnel, who verify the receipt of the devices must complete the Device Acknowledgment Form.

The Investigator will be responsible for ensuring the records adequately document the disposition of all MAP Wound Matrix investigational product received by the site for the trial. Documentation includes review of shipment papers to confirm accurate receipt, and disposition of all products received by the site. Any product used on a trial subject should be documented both in the subject record and on the product accountability log. At the end of the study, any unused product and/or product past expiration will be returned to the Sponsor, according to the investigational product accountability procedure provided to the study site.

7.4 Concomitant Medications and Procedures

In this study, the term Concomitant Medication is inclusive of all medications and therapies.

The following is excluded throughout the entire study after application of the investigational or control treatment:

- Topical antibiotics

- Powdered collagen dressings (e.g., Cellerate®), formulated collagen dressings (e.g., Excellagen®)
- Hyaluronic acid products (e.g., Hyalomatrix®)
- Revascularization procedures (e.g., endoscopic perforator surgery, superficial venous ablation, endovenous laser ablation, valvuloplasty, free flap transfer with microvascular anastomoses)
- Growth factors
- Tissue products containing growth factors (e.g., Oasis®), living skin, cellular products (e.g., Apligraf®, Dermagraft®), amniotic membrane and umbilical cord product (e.g., Epifix®).
- Split-thickness skin graft (STSG)
- Acellular dermal substitutes: Integra®, Omingraft®, Primatrix®, PurePly®
- Silver-containing products (e.g., Aquacel Ag®, Mepilex Ag®, Acticoat®)
- Collagen dressings (e.g., Integra Omnigraft®, Promogran Prisma®, Puracol®, Fibracol®)

7.4.1 Documentation of Concomitant Medications and Procedures

Documentation will be captured in the Case Report Form (CRF) at each visit as outlined in the Schedule of Events (Appendix A).

8 Study Evaluations

8.1 Study Procedures

Each subject who enters Screening will be assigned a subject ID number for traceability. The subject ID will consist of a 2-digit site number and a 3-digit subject identification code (i.e., 01-001, etc.).

8.2 Study Visit Requirements (See Appendix A – Schedule of Events)

8.2.1 Screening Visit (Visit #1)

The following procedures will be performed at this visit:

1. Inclusion/Exclusion criteria will be reviewed to determine subject eligibility.
2. Informed consent.
3. Demographics (date of birth, sex/gender, ethnicity, and race).
4. Medical History (including procedures up to 30 days prior to Screening Visit).
5. Concomitant Medication Assessment.
6. Physical examination, including vital signs (i.e., heart and respiratory rates, blood pressure, and temperature while subject is seated) and collect height and weight.
7. Laboratory tests (e.g., CBC, HbA1c). IF subjects have a documented history of type I or type II diabetes, HbA1c laboratory tests will be drawn. Otherwise, laboratory tests are performed only as needed per the Investigator's discretion.
8. Pregnancy test for women of childbearing potential.

Activities of Visit #1 can occur on the same day as Visit #2 or on different days.

8.2.2 MMS and Treatment Visit (Visit #2)

The following procedures will be performed at this visit or **ALL** subjects:

1. Physical examination, including vital signs (i.e., heart and respiratory rates, blood pressure, and temperature while subject is seated) and collect height and weight.
2. Pregnancy testing will be repeated at Visit #2 only if greater than 6 days have elapsed from Visit #1.
3. Mohs Micrographic Surgery (MMS).
4. Wound assessment, after MMS and hemostasis. Wound assessment will include clinical evaluation (edges, undermining, necrotic tissue, exudate, skin color surrounding wound, peripheral tissue edema, granulation tissue, and epithelialization) and wound size measurement (surface area and depth) using a sterile ruler.
5. Enrollment.
6. Subject identification code assignment.
7. Randomization.
8. Baseline wound photo using digital imaging.

The following procedures will be performed as soon as possible after Mohs surgery (Visit #2) , enrollment, randomization, and once hemostasis has been achieved:

1. Wound cleansing if deemed medically necessary by the Investigator. Cleansing will be performed using sterile saline, a non-ionic cleanser, or a hypochlorous solution followed by extensive sterile saline or sterile water flush to the wound.
    a. **Note**: Per the MAP Wound Matrix IFU (TT-CLN-004-TT101-IFU), antiseptic agents including hydrogen peroxide, acetic acid, chlorhexidine, povidone/iodine, and cetrimide may be used but must be rinsed with sterile saline or water prior to MAP Wound Matrix application. Antiseptic agents may not be used after MAP Wound Matrix application. Topical antimicrobials are prohibited.
2. **For MAP Wound Matrix subjects:**
    a. MAP Wound Matrix treatment will be applied in accordance with the device IFU (TT-CLN-004-TT101-IFU) as described in section 8.1.3. Briefly, the device is collected from the supplied vial into the supplied syringe, flowed topically into the wound, and exposed to light using the Philips Burton Super Exam LED (SELED) medical exam light specified in the IFU. Light exposure crosslinks the product into a stable matrix in the wound bed.
    b. An additional Digital Wound Image after device application.
    c. After MAP Wound Matrix treatment application, the wound will be bandaged using a non-adherent (e.g., Telfa, Adaptic) dressing followed by an adhesive, occlusive dressing (e.g. Tegaderm). A pressure dressing, including a non-adherent gauze and pressure bandage, will be applied above the occlusive dressing per the Investigator's discretion.
3. **For control subjects:**
    a. DuoDerm will be applied to cover the whole surface of the wound in accordance with manufacturer's IFU.

b. After control DuoDerm application, the control treated wounds will be dressed with an absorbent dressing (e.g. gauze), at investigator discretion, above the hydrocolloid dressing. The hydrocolloid and optional absorbent dressing will be secured by an occlusive dressing (e.g. Tegaderm). Additional dressings such as a non-adherent gauze and pressure bandage may be applied above the Tegaderm per investigator discretion..

4. **In ALL study subjects:** systemic antibiotics will be used, if deemed necessary by the Investigator, as a prophylactic measure against wound site infection, or to resolve baseline infection following standard practice at the site and recommendations from the Infectious Diseases Society of America (IDSA) guidelines when necessary.
5. **In ALL study subjects:** Adverse Event Recording will be performed.
6. **In ALL study subjects:** Pain will be assessed at wound site using 0-10 Visual Analog Scale.

8.2.3 Follow-up Visits #3 – 10

- Weekly follow-up visits will occur for the first six weeks after treatment, and three bi-weekly visits at Weeks 8, 10, and 12.

The following will be performed at the in-clinic visits (Visits 3, 4, 6, 8, 10):

1. Concomitant Medication Assessment.
2. Physical examination, including vital signs (i.e., heart and respiratory rates, blood pressure, and temperature while subject is seated) and collect height and weight.
3. Adverse Event recording.
4. Subject reported pain at the index wound site following MAP Wound Matrix application, using a Visual Analog Scale (VAS) of 0-10 Note: VAS measured before wound dressing manipulation, during manipulation, and 10-20 minutes after IF there was pain level of 5 or greater before or during manipulation.
5. Wound Assessment
   a) Bandage exudate assessment including a semi-quantitative evaluation of the exudate amount in the bandage, in order to assess the drainage state of the wound.
   b) Debridement (as needed) **Note**: Subjects treated with MAP Wound Matrix: debridement will NOT remove MAP Wound Matrix device components unless deemed medically necessary by the Investigator. MAP Wound Matrix may be reapplied during the first week after application if the device has been found to be disrupted or dislocated during the first dressing change (Visit #3). If the device is reapplied at Visit #3, a pain assessment will be performed on the subject at the site of the device application within 15 minutes of completing the light-initiated crosslinking reaction.
   c) Wound assessment including clinical evaluation (edges, undermining, necrotic tissue, exudate, skin color surrounding the wound, peripheral tissue edema, granulation tissue, and epithelialization) and wound size measurement (surface area and depth) with digital imaging and by investigator using a sterile ruler.
6. Investigational device assessment
   a) Presence of the device in the wound bed (when possible).

b) Incidence of device **removal**: unintentionally (e.g., during a dressing change) or intentionally (e.g., the wound needs to be debrided, the wound is infected).

c) Safety of intentional device removal (when applicable).

d) Efficacy and ease of intentional device removal (when applicable). The amount of residual device remaining in the wound after device removal will be assessed.

7. Wound dressing change until the wound is closed**.**

The following will be performed at the virtual visits (Visits 5, 7, 9):

1. Concomitant Medication Assessment.
2. Adverse Event recording.
3. Subject reported pain at the index wound site following MAP Wound Matrix application, using a Visual Analog Scale (VAS) of 0-10.

- A two-week follow-up visit will be scheduled after the first observation of wound closure for confirmation assessment by the Investigator. This wound closure confirmation visit may occur as an unscheduled visit if it is not one of the scheduled follow-up visits.

8.2.4 Follow-up Visits #11 – 13 (In-Clinic or Virtual Visits)

- Subjects will remain in the study for up to three months following confirmed wound closure, and unscheduled visits may occur during this period to evaluate any subject self-reported adverse events or as deemed medically necessary by the Investigators.

The following will be performed at the in-clinic visits:

1. Concomitant Medication Assessment.
2. Physical examination, including vital signs (i.e., heart and respiratory rates, blood pressure, and temperature while subject is seated) and collect height and weight.
3. Adverse Event recording.
4. Subject reported pain at the index wound site following MAP Wound Matrix application, using a Visual Analog Scale (VAS) of 0-10
5. Wound Assessment

a) Debridement (as needed) **Note**: Subjects treated with MAP Wound Matrix: debridement will NOT remove MAP Wound Matrix device components unless deemed medically necessary by the Investigator. MAP Wound Matrix may be reapplied during the first week after application if the device has been found to be disrupted or dislocated during the first dressing change (Visit #3). If the device is reapplied at Visit #3, a pain assessment will be performed on the subject at the site of the device application within 15 minutes of completing the light-initiated crosslinking reaction.

b) Wound assessment including clinical evaluation (edges, undermining, necrotic tissue, exudate, skin color surrounding the wound, peripheral tissue edema, granulation tissue, and epithelialization) and wound size measurement (surface area and depth) with digital imaging and by investigator using a sterile ruler.

6. Investigational device assessment
    a) Presence of the device in the wound bed (when possible).
    b) Incidence of device removal: unintentionally (e.g., during a dressing change) or intentionally (e.g., the wound needs to be debrided, the wound is infected).
    c) Safety of intentional device removal (when applicable).
    d) Efficacy and ease of intentional device removal (when applicable). The amount of residual device remaining in the wound after device removal will be assessed.
7. Wound dressing change until the wound is closed**.**

The following will be performed at the virtual visits:

1. Concomitant Medication Assessment.
2. Adverse Event recording.
3. Subject reported pain at the index wound site following MAP Wound Matrix application, using a Visual Analog Scale (VAS) of 0-10.

8.2.5 Final Visit #14

- A final in-clinic follow-up visit will occur at the earlier of (i) the end of the three-month timeframe after confirmed wound closure or (ii) 24 weeks after treatment application, at which point the subject's study participation will be considered complete.

General subject assessment

1. Concomitant Medication Assessment.
2. Physical examination, including vital signs (i.e., heart and respiratory rates, blood pressure, and temperature while subject is seated) and collect height and weight. **Note**: only at in person visits, not at virtual visits.
3. Adverse event recording.

Device and Wound Assessment

4. Debridement (as needed) **Note**: Subjects treated with MAP Wound Matrix: If the wound is not closed and MAP Wound Matrix is clinically present in the wound at Week 24, the Investigator will be instructed to debride the remaining device out of the wound.
5. Wound assessment including clinical evaluation (edges, undermining, necrotic tissue, exudate, skin color surround wound, peripheral tissue edema, granulation tissue, and epithelialization) and wound size measurement (surface area and depth) using a sterile ruler.
6. Investigational device assessment including:
    - Presence of the device in the wound bed (when possible).
    - Incidence of device removal: unintentionally (e.g., during a dressing change) or intentionally (e.g., the wound needs to be debrided, the wound is infected).
    - Safety of intentional device removal (when applicable).
    - Efficacy and ease of intentional device removal (when applicable). The amount of residual

device remaining in the wound after device removal will be assessed.

7. Clinical assessment of the wound scar, if the wound confirmation visit has occurred.
8. Digital photography of the wound site.

8.2.6 Reporting and recording data

All the assessments performed during all visits will be recorded in EDC as well as on the source documents. In addition to the activities described above, the Investigator will acknowledge that the data entries for all the pages contained in the subject's case record are accurate, complete, and compatible with the source documents. In addition, the Principal Investigator will acknowledge that all the entries within the Subject's case record were made by him/her or a person under his/her direct supervision whose name has been documented on the Statement of Investigator/delegation of responsibilities form.

8.2.7 Unscheduled Visits

Unscheduled visits may be conducted at the discretion of the Investigator or if the subjects have any self-reported adverse events that require medical assessments. They may occur in-clinic or virtually via videoconferencing. All obtained information should be recorded in the source documents and on the Unscheduled Visit CRF. The purpose of these potential visits may be for additional wound bandage changes and/or monitoring. If unscheduled bandage changes occur, wound assessment should be recorded in the Unscheduled Visit CRF.

8.2.8 Study-Specific Testing and Procedures

Wound imaging. Wounds will be imaged for documentation and analysis at each in-clinic visit. Wound imaging will be performed such that a sterile ruler is placed in the field of view to enable proper scaling of images for post-hoc analysis. Usage of a software application (e.g., SWIFT, Ekare, Tissue Analytics) or computer aided device (e.g., Enspectra Health, Vivascope, Spectral AI) may be employed to analyze wound images for wound area and granulation assessment. For analysis of fully healed wounds digital imaging (e.g., SWIFT, Ekare, Tissue Analytics), or 3D imaging (e.g., Canfield Vectra H1 H2 or M3) can be employed for exploratory data capture using minimally invasive approaches.

Wound evaluation. Wound healing including size, depth, edges (e.g., well defined, fibrotic, scarred, or hyperkeratotic), undermining, necrotic tissue, exudate, skin color surrounding wound, peripheral tissue edema, peripheral tissue induration, granulation tissue, and epithelialization will be assessed using the Bates-Jensen Wound Assessment Tool (BWAT). This will be performed by the Investigator based on visual and tactile assessment of the wound, and from photographs captured with a digital camera. Wound size will be measured using a sterile ruler. To reduce bias, the DSMB will independently review the photographs, in a blinded fashion, to provide an independent assessment of wound healing. A scar assessment scale such as POSAS 3.0 may be used to evaluate the healed wound at the final (EOS) visit.

Each wound healing criterion (size, depth, edges, undermining, necrotic tissue, exudate, skin color surrounding the wound, peripheral tissue edema, peripheral tissue induration, granulation tissue, and epithelialization) will be scored according to the Bates-Jensen Wound Assessment Tool (BWAT), then the total score will be calculated by adding each individual criterion score. The higher the total score, the more severe the wound status. Wound healing status will be assessed as follows:

- Score $\leq$ 13, the wound is regenerated and completely healed.
- 13 < Score $\leq$ 60, the wound is healing.
- Score > 60, the wound is degenerated.

Delay in wound healing. Wound healing will be considered delayed if:

- The wound healing status has a BWAT score > 60 at any point over the follow-up study period or
- Any increase in the BWAT score is observed and considered significant by the Investigator. In this case, the Investigator must assess whether it is related to the device. Upon review of study data, the DSMB will also assess if delays in wound healing are related to the device.

Device assessment. The presence of the MAP Wound Matrix in the wound bed will be clinically assessed by the Investigator when possible. As the wound heals, the wound may be covered with scab (not anticipated), eschar (not anticipated), or new tissue (anticipated) that may interfere with the direct observation of the device. At each follow-up visit, the dressings in direct contact with the wound will be visually examined to assess if the device has been unintentionally removed. If (i) the device is observed to have been removed from the wound or (ii) the device has been disturbed in the wound site during the first week of post-operative application, then the device may be reapplied one time at Visit #3. If the device is reapplied at visit #3, patient pain at the wound size will be evaluated within 15 minutes of completing the light-initiated crosslinking reaction.

If post-application wound site infection is suspected at any point in the study (see below for infection assessment), the MAP Wound Matrix device may be removed using sharp debridement as deemed medically necessary. The safety and effectiveness of removal will be evaluated if it occurs. Evaluation of safety in any instance of device removal will assess wound site bleeding after removal, peri-wound erythema and edema, ability of the wound site infection to be resolved by antibiotic treatment and standard practices, and subsequent wound healing after device removal and infection control. Evaluation of the effectiveness of device removal will be through clinical observation of the wound before and after debridement to remove the device if it is deemed medically necessary, as well as the assessment of the amount of residual device remaining in the wound after device removal.

The incidence of device removal, either unintentionally or intentionally, will be recorded.

Assessment of wound infection. The Investigator will clinically assess wound infection (e.g., expanding erythema, pain out of proportion to the wound, purulent discharge, or foul odor) at each follow-up visit as part of the assessment of Adverse Events. If any wound infection is observed, the standard of care will be immediately provided, which consists of debriding the wound of all non-viable tissue (including foreign materials), obtaining tissue cultures or bacterial swab at the time of debridement, and instituting frequent dressing changes for close monitoring of the wound in addition to the administration of antimicrobial therapy. Tissue culture is the preferred method for infection assessment, however if tissue is unavailable and a bacterial swab is the only method appropriate, then the Investigator will use the Levine method for taking a bacterial swab to reduce potential false-positive results. The Investigator must assess whether the infection is related to the device. Upon review of study data, the DSMB will also assess if wound infections are related to the device.

Wound care. Over the normal course of healing, scab (heme crust) may form on the wounds. If scab/heme crust is observed on the wounds during a visit, the investigator may gently remove the scab/heme crust using soft debridement and/or soaking the scab/heme crust in saline solution to soften the scab/heme crust before removing. The investigator will use standard care practice to treat and remove the scab/heme crust if it is observed during a visit. Eschar is not anticipated to form in relation to the device, however if eschar is observed during a visit the investigator may remove the eschar using sharp debridement as necessary, per standard of care.

8.3 Procedures for handling biological samples

8.3.1 Laboratory tests

All laboratory investigations will be performed at a local accredited clinical laboratory. The volume of blood to be taken will be determined according to the standard practices for each type of test. The normal reference ranges must be provided to Sponsor. Laboratory accreditation certificates must be verified.

8.4 Study Intervention Discontinuation and Participant Withdrawal

8.4.1 Participant Discontinuation or Withdrawal

A subject can voluntarily withdraw from the study at any time. The Investigator may also withdraw a subject from the trial at any time if they deem it medically necessary. The reason for discontinuation should be documented and trial staff should attempt to bring the subject in for an End of Study Visit (Visit #14) and perform all applicable assessments, as appropriate.

Subjects may be discontinued from the trial for reasons including but not limited to the following:

- Adverse Event that, per the PI, warrants withdrawal
- Subject voluntary withdrawal of consent
- The Sponsor or Investigator terminates the trial
- The Subject is lost to follow-up
- Product-related > Grade 2 skin or systemic allergic reaction (CTCAE criteria).
- MMS-related complications (i.e., life-threatening, infection-related sepsis complications)
- Subject not eligible based on study eligibility criteria
- Subject death

In the event of a subject's withdrawal, the Investigator will promptly notify the medical monitor and will make every effort to complete all procedures per the End of Study (EOS) Visit. The EOS CRFs will be completed, and the date, time, and reason for withdrawal will be documented in the eCRF and the subject's source document. Even if subjects have been removed from the trial, if an adverse event remains ongoing, Investigators should follow up with subjects as per their standard medical practice. Investigators must also report this information to the local IRB as defined by their institution's policies and procedures.

8.4.2 Lost to Follow-up

If a subject is lost to follow-up, a minimum of three documented contact attempts, including one certified letter, should be in the records. If there is no contact made by the subject after sending the certified letter, the next of kin and the physician responsible for managing the subject's health should be contacted to obtain information about the subject's current health status.

9 Risk-Benefit Analysis

Details of potential risks and benefits can be found in the Report of Prior Investigations (TT-CLN-004-01). The informed consent form will also describe the potential risks to the subjects.

10 Statistical Methods and Data Analysis

10.1 Sample Size Determination

The clinical study is not statistically powered. The sample size for this study has been established based on FDA's recommendations (response letter from FDA dated November 2, 2023, to the De Novo application: DEN220068-S002). A minimum of 30 adult subjects (20 treated with the MAP Wound Matrix device and 10 treated with control) will be enrolled. No more subjects will be enrolled than the number needed to complete all study visits with 30 subjects (20 treated with the MAP Wound Matrix device and 10 treated with control). To allow for potential loss to follow-up or other drop-out events, additional subjects may need to be enrolled. No more than 50 subjects may be considered for enrollment.

10.2 Data Analysis

10.2.1 Analysis Sets

- *Intention-to-treat Population*: The ITT population will consist of all enrolled subjects. The ITT population is the primary population and will be used to conduct all analyses on primary endpoints.
- *Per Protocol Population*: The Per Protocol (PP) population is a subset of subjects in the ITT and is the secondary population. The PP population will be defined as all qualified and treated subjects meeting inclusion and exclusion criteria and completing the study treatment as planned in the protocol, with no major protocol deviations during the follow-up period. Major protocol deviations will be determined by the trial clinical team prior to database lock. Subjects found to have major protocol deviations will be excluded from the PP population.

For all study participants, the following subject demographic and baseline data will be collected and reported to enable analysis of their effects on safety and effectiveness outcomes:

- Age
- Sex/Gender
- Ethnicity
- Race
- Medical history
- Disease diagnosis, severity, and prior treatment
- Physical examinations

Endpoints may be reported by subgroup when the size of the subgroup allows as follows:

- Male vs. female
- By race based on combined categories of American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White
- By age group
- Use of systemic antibiotics

10.3 Primary endpoint

10.3.1 Variables and Criteria

Incidence of serious adverse device effects (SADE) (including delays in wound healing and surgical site infections) in subjects treated with MAP Wound Matrix, compared to the control treatment group.

10.3.2 Methods of Analysis

Safety measures will be reported as summary statistics during treatment. Adverse events will be coded using the version of MedDRA available at the start of the trial. Each AE will be counted once for each subject unless it resolves and recurs, in which case it may appear as multiple AEs. Severity, frequency, and relationship of AEs to study intervention will be presented by System Organ Class (SOC) and preferred term groupings.

AE listings will be provided for deaths, SAEs, AEs leading to discontinuation, ADEs related to the wound, and SADEs. AE listings will include severity and relationship to test article, as well as actions taken.

AE tables will be provided summarizing AEs, UADEs, ASADEs, SADEs, SAEs.

The categorical data will be summarized descriptively by frequencies along with associated percentages for each group.

The incidence of all types of AEs will be tracked throughout the post-treatment study period. The incidence rates of SADEs for the MAP Wound Matrix treatment group and the control treatment group will be compared using an exact statistical comparison test such as a normal-theory exact test for two sample inference of incident rates or a Fisher's exact test. This testing will inform if the SADE incidence rate for MAP Wound Matrix treatment group is significantly different than that of the control treatment group.

10.4 Exploratory Endpoints

10.4.1 Variables and Criteria

Exploratory endpoints include:

- Investigator assessment of wound healing (size, depth, edges, undermining, necrotic tissue, exudate, peripheral tissue edema, granulation tissue, and epithelialization) following MAP Wound Matrix application (using digital imaging and the Bates-Jensen Wound Assessment Tool).
- Assessment of the healed wound site using a clinical assessment (investigator and subject) and digital imaging (2D or 3D).
- Subject reported pain at the index wound site following MAP Wound Matrix application, using a Visual Analog Scale (VAS) of 0-10.
- Investigator assessment of device embedment and presence in the wound following MAP Wound Matrix application.
- Incidence of device removal following MAP Wound Matrix application.
- Investigator assessment of safety and effectiveness of device removal following MAP Wound Matrix application if it occurs. The amount of residual device remaining in the wound after device removal will be assessed.

10.4.2 Methods of Analysis

Wound imaging and investigator assessment using the BWAT will be utilized to assess exploratory endpoints associated with wound healing.

When analyzing the exploratory endpoints, all continuous data will be expressed as mean and 95%

Confidence Intervals, whereas categorical variables will be expressed as frequency and percentages. Although not statistically powered, a p value less than 0.05 may be considered statistically significant when comparing any data.

Continuous demographic variables, such as age, will be summarized for the population with descriptive statistics (number, mean, median, SD, minimum and maximum value, and 95% two-sided confidence limits) and compared between groups with a two-sample t-test. Categorical demographic variables, such as sex, will be summarized as a proportion of the ITT population and compared between treatments by use of a two-tailed Fisher's exact test. The distribution of values by variable will be analyzed using a Shapiro-Wilk test. In instances that do not have normal distributions, a non-parametric procedure will be used to compare the baseline values between treatment groups.

10.5 Handling of Missing Data

If missing values are identified upon eCRF review either during Study Monitor site visits or at final site closeout visits, an effort will be made by the study staff to review the subjects' medical records. If the values are not available in the original charts, then these data will remain as missing in analyses. Any missing data will be noted and statements regarding missing data will be included in analysis and communications about study results. No methods for imputing missing data will be used.

10.6 Health Economics

Data such as the number of bandage dressings will be collected.

11 Adverse Events

All AEs should be recorded from the time of informed consent through completion of Visit #10. The Investigator should use his/her discretion in ordering additional tests as necessary to monitor the resolution of such events. Event outcome at resolution, or at the time of the Final Study Visit, will be recorded. In the event an AE is ongoing at the time of the EOS Visit, the Investigator should record the AE outcome as ongoing and continue to follow up outside of the trial per their standard of care.

All AE definitions, their seriousness and their device relatedness are interpreted per ISO14155:2020.

11.1 Definitions

11.1.1 Adverse Event (AE)

Adverse Event is defined as any untoward medical occurrence in a subject associated with the investigational use of a device in humans, whether or not considered device related. It can be any unfavorable and/or unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of a device, whether or not considered related to the device. Only abnormal laboratory values that are deemed clinically significant by the Investigator will be classified as adverse events.

11.1.2 Adverse Device Effect (ADE)

Adverse event related to the use of an investigational medical device.

Note: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. Note 3: This includes 'comparator' if the comparator is a medical device.

11.1.3 Serious Adverse Event (SAE)

Serious Adverse Event is defined as any AE that results in any of the following outcomes:

- Death.
- A life-threatening adverse experience.
- In-patient hospitalization or prolongation of existing hospitalization.
- A permanent/persistent or significant disability/incapacity, 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 subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

11.1.4 Serious Adverse Device Effect (SADE)

Serious adverse device effect (SADE) is defined as an ADE that has resulted in any of the consequences characteristic of a serious adverse event. This includes:

- **Adverse tissue reaction**, whereby a SADE is determined by the Investigator and the DSMB.
- **Infection**, whereby a SADE is defined as a wound infection that cannot be resolved with debridement to remove of all devitalized tissue and foreign materials with initiation of antibiotic therapy.
- **Delay in wound healing** as defined in section 8.2.8, whereby SADE is determined by the Investigator and the DSMB.
- **Failure of device integration**, whereby SADE is determined by the Investigator and the DSMB.
- **Toxicity**, whereby SADE is determined by the Investigator and the DSMB.

11.1.5 Anticipated Serious Adverse Device Effect (ASADE)

Serious adverse device effect (ASADE) is defined as an effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report. ASADEs are identified as potential risks in the Report of Prior Investigations (TT-CLN-004-01).

11.1.6 Unanticipated Serious Adverse Device Effect (USADE)

Unanticipated Serious Adverse Device Effect (USADE) is defined as 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 any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

11.2 Safety Monitoring

An independent Data Safety Monitoring Board (DSMB) will be comprised of three voting members who are board certified dermatologists or plastic surgeons, and a non-voting member who is a Statistician. The DSMB will monitor the safety of all study subjects. It will be charged with the following responsibilities:

- Monitors and review safety data throughout the study.
- Monitors the data to assess compliance with the protocol for safety and administrative reasons.

- Provides recommendations to the Sponsor to continue the study without modification, to modify the protocol or informed consent documents, or to temporarily stop enrollment in all or some of the study centers. If the DSMB recommends any protocol changes, these changes will be approved by the IRB and FDA prior to implementation.
- Review, in blinded fashion, the photographs of the wounds to provide an independent assessment of wound healing.

The DSMB will operate under a written, detailed charter.

11.3 Stopping Rules

The DSMB may recommend that the trial be stopped based on any relevant safety data at any time.

The trial will also be stopped should there be:

- One (1) Serious Adverse Device Effect reported in two different subjects.

11.4 Reporting Procedures for all Adverse Events

At each visit, the subject will be evaluated by the Investigator for Adverse Events. After review with the subject by the study site personnel, all Adverse Events will be documented in the subject's source document and on the appropriate CRF pages. The following attributes must be documented:

- Description of event
- Date of onset
- Date of resolution
- Duration
- Seriousness
- Severity
- Relationship to the study device and/or procedure
- Action(s) taken
- Outcome(s)
- Attending physician treating event

If the Adverse Event is of such severity in the Investigator's judgment that it warrants withdrawal from the study, the subject should be withdrawn, and a termination assessment performed (End of Study (EOS) CRFs completed). The subject should be given appropriate care under medical supervision until symptoms resolve.

11.4.1 Relationship

The relationship of an AE to the study device or procedure must be determined using the following classification:

- **None:** The adverse Event is not associated with the study device or procedure.
- **Possible:** This causal relationship is assigned when the Adverse Event:
    - Follows a reasonable temporal sequence from device use or procedure, but

- Could have been produced by the subject's clinical state or other modes of therapy administered to the subject.

- **Probable:** This causal relationship is assigned when the Adverse Event:
  - Follows a reasonable temporal sequence from device use or procedure; and
  - Cannot be reasonably explained by known characteristics of the study subject's clinical state or other modes of therapy administered to the subject.

11.5 Serious Adverse Event Reporting

All serious adverse events will be reported to Sponsor or designee as soon as possible and in no event later than 10 working days of Investigator becoming aware of the event. Safety reports should be submitted to the IRB in accordance with the IRB and institution's policy. The Investigator must notify his/her IRB and the Sponsor of all Serious Adverse Device Effects (SADE) occurring at the site, and reports received from the Sponsor or its designee.

The Sponsor must report all SADEs to the FDA and to all reviewing IRBs and participating investigators within 10 working days.

11.6 Deaths

Deaths which must be reported to the sponsor/designee include all deaths while participating in the study.

For all deaths, copies of available autopsy reports and relevant medical reports should be sent to the Sponsor or its designee with the subject's name masked (except for the first initials of the first and last name), and the subject ID.

11.7 Withdrawals for Adverse Events

All Adverse Events which result in the subject's withdrawal from the study must be reported immediately by telephone to the Sponsor or its designee.

The Investigator may be asked to provide detailed follow-up information. The Sponsor or its designee will determine the reportability of the event on a case-by-case basis and will report to the appropriate regulatory authorities and participating investigators, if applicable.

11.8 Measures to Assure Subject's Safety

The Investigator will be responsible for monitoring the safety of subjects who enter this study and for documenting and reporting all Adverse Events to the Sponsor.

The Investigator will be responsible for the appropriate medical care of the subjects during the study in connection with protocol procedures for his/her site. The Investigator will remain responsible for providing any appropriate health care options after a subject's completion or discontinuation from the study due to adverse events.

A DSMB will also independently review the safety information and make recommendations if the study should be paused or terminated early due to potential safety risk.

11.9 Device Failures

A device failure is defined as inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies include use errors, and inadequate labeling.

If a device failure occurs with MAP Wound Matrix device, a Device Failure Form must be completed and submitted to the contact listed for the Sponsor in section 13 of this document. Upon receipt of the form, instructions will be given on handling/returning of the defective device. Any device issues will be documented, tabulated, and evaluated by the Sponsor to determine whether corrective action is needed to prevent recurrence of the problem. Device failure may or may not also cause or contribute to AE/SAE/SADE.

12 Regulatory Obligations

12.1 Informed Consent

The Informed Consent Form will be prepared in accordance with FDA 21CFR50. The Informed Consent Form will be used to explain in simple terms, before the subject is entered into the study, the possible risks and benefits to the subject. The Informed Consent Form will contain a statement that the consent is freely given, that the subject is aware of the risks and benefits of entering the study, and that the subject is free to withdraw from the study at any time.

The Informed Consent Form will need to be reviewed and approved by the Sponsor or its designee prior to the Investigator submitting the form to its IRB for review and approval. All appropriate bills/ legislative actions are to be considered and the Informed Consent Form amended, as appropriate (e.g. California Bill of Rights is to be on the forefront of the Informed Consent Form if study conducted in California).

Subjects will be given as much time as needed to read the form, ask questions of the interviewer, and to discuss the study with others before making a decision. Prior to a subject's participation in the study, the written Informed Consent Form will be signed and personally dated by the subject and witnessed by the person who conducted the Informed Consent Form discussion.

Based on the recommendation of the Investigator the Sponsor will provide a certified translation of the ICF.

Only authorized trial staff should obtain consent and the most currently approved IRB consent form must be used. The Investigator is required to report any failure to obtain subject consent to the IRB and the Sponsor within 5 working days of such an event.

Note: The Investigator must document acquisition of the written Informed Consent Form in the subject's medical records, and the subject must be given a copy of the Informed Consent Form document prior to enrollment into the study.

12.2 Institutional Review Boards/Ethics Committees

Prior to the start of the study the Investigator will provide the Sponsor or its designee with documentation that the IRB has reviewed and approved the protocol, the Informed Consent Form, or recruiting documents. Additional documentation may be submitted pending applicable local requirements. Each Investigator must provide at least the following documentation:

- IRB approval of the protocol
- IRB approval of the Informed Consent Form
- IRB annual (or other frequency – i.e., quarterly, semiannually according to the local IRB standard operating procedure) renewal approval of the study
- IRB approval of any revision to the Informed Consent Form or amendments to the protocol

No changes will be made to the protocol or informed consent form without appropriate approval from the IRB, the Sponsor and/or the regulatory agencies.

12.3 Regulatory Considerations

This study will be conducted in accordance with the Good Clinical Practice (GCP) guidelines and applicable regulatory requirements including but not limited to:

- FDA Regulations on Investigational Device Exemption (21 CFR 812),
- FDA Regulations on research with human beings (21 CFR 50 and 56),
- ISO 14155:2020 for Good Clinical Practices
- Privacy Rule (45 CFR 160 and 164) of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

12.4 Data Management

12.4.1 Electronic Data Capture (EDC)

Clinical data (including adverse events (AEs) and concomitant medications) and clinical laboratory data will be entered into EDC, a 21 CFR Part 11-compliant data capture system. The EDC data system will include password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data may be entered into EDC directly from the source documents.

12.4.2 Data Collection

During the trial, the Investigator will maintain adequate records for the trial. Individual subject files should be maintained in addition to the eCRFs. These files should include visit dates (including date of enrollment), name or initials of the subject, date of birth, medical history, physical examinations administered, concomitant treatment, records detailing the progress of the trial for each subject, evidence that subject met the inclusion/exclusion criteria, original signed and dated informed consent forms, investigational product disposition records, correspondence with the IRB, AE/SAE reports, and information regarding subject discontinuation and completion of the trial. These files constitute “source data” and must be signed and dated by the study research personnel who recorded the data. All entries in the eCRFs must be backed up by source data. The eCRFs must be kept in order and up-to-date so that they reflect the latest observations on the subjects enrolled in the study.

All paper source documentation should be completed using a pen and must be legible. Errors should be corrected by a single line through the error, and the correction written in ink initialed and dated by the Investigator or a member of the study site personnel, authorized by the Principal Investigator. Where information is not applicable, “N/A” should be inserted.

eCRFs and all other documents/data sent to the Sponsor will not contain identifying study subject information. Each subject will be assigned a unique subject identification code that reflects the site number and subject number.

12.5 Study Monitoring and Auditing

Protocol compliance by the Investigator and site staff will be monitored by routine site visits conducted by the Sponsor or designee as outlined in a separate detailed monitoring plan. The study monitor will be trained and have the scientific and clinical knowledge needed to monitor the study appropriately. Monitoring will occur as frequently as needed to assure proper conduct of the protocol.

Tempo Therapeutics, Inc. or its designee shall implement and maintain quality assurance procedures with written standard operating procedures to ensure the trial is conducted and data are generated, documented, and reported in compliance with the protocol, GCP, and applicable regulatory requirements.

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants 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), ISO 14155:2020, and with applicable regulatory requirement(s).

The clinical monitor will periodically inspect all CRFs, trial documents, and research facilities associated with this trial at mutually convenient times during and after the completion of the trial. The monitoring visits provide the Sponsor with the opportunity to evaluate the trial's progress; verify the accuracy and completeness of CRFs; ensure that all protocol requirements, applicable FDA regulations, and Investigator's obligations are being fulfilled; and resolve any inconsistencies in the trial records. This includes inspection of all documents and records that are required to be maintained by the Investigator, including but not limited to medical records (office, clinic, or hospital) for the subjects in this trial.

The Clinical Monitoring Plan contains more complete details about monitoring this trial and the specific duties of the study monitors.

12.5.1 Confidentiality of Subject Records

The clinical study will comply with the HIPAA Privacy Act. All information and data sent to the Sponsor or designees in reference to any subject's participation in this investigation will be considered confidential by the Sponsor and designees. The Investigator will take the appropriate measures at the Sponsor's instruction to protect all subjects' privacy. Subject's identifying information will be replaced with the subject's study identifier on CRFs, case reports, and other information provided to the Sponsor, IRB or FDA. The investigational sites are not to provide to the Sponsor/designee information such as subject's telephone numbers, home address, identification numbers such as social security or passport numbers, etc. Care must be taken by site research personnel when communicating with representatives from the Sponsor/designees in the form of telephone or electronic correspondence to ensure information that may disclose a subject's identity is not provided.

Documents associated with the study that are not intended to be submitted to the Sponsor/designee (e.g., signed Informed Consent Forms, source documents) must be kept in strict confidence by the Investigator. Only authorized Sponsor personnel or designee, regulatory authority inspectors, as well as the study site personnel will have access to these confidential files. Authorized regulatory authority inspectors will be allowed to review all records pertinent to this Investigation.

12.5.2 Records Retention

The Investigator must maintain all records pertaining to this study for the maximum period of time permitted by the hospital, institution or private practice, or as specified below. The study monitor must be informed if, for any reason, the Investigator wishes to assign the custody of the files to someone else, remove them to another location or is unable to retain them for the specified period.

Study records are subject to inspection by the Sponsor or its designee, FDA, and other Regulatory Agencies. Study files, all CRFs, documentation notebooks and source documents must be maintained in a fire safe environment and must be retained for a minimum of two years after the study has ended or until the records are no longer required to support the regulatory submissions, whichever is longer. These documents may be retained for a longer period however, if required by the applicable local laws.

Each clinical location will need to keep the following up to date at all times:

- A copy of the protocol
- IRB approval and correspondence
- Signed and dated recent (within 2 years from the Site Qualification Visit) Investigator and Sub-Investigator Curriculum Vitae
- Device Handling, Storage and Shipping Instructions
- Monitoring Visit Log
- Clinical Memoranda
- Study Correspondence
- Copies of all Reports

Each eCRF will be signed by the authorized individual who recorded the required information. Adverse Event Forms and Study Termination Forms are to be signed by Principal Investigator.

Federal law (21 CFR part 812) and GCP (ISO 14155:2020 requires that all investigational medical devices be strictly controlled. Therefore, the Device Accountability Logs will be maintained at each study site. These logs will list all investigational devices received including product number, lot number, date received, ID of the subject receiving treatment from the device, device usage date and/or return date. Study site personnel will sign the log each time a device is received, used, or returned.

13 Contact Details

Sponsor's Contacts
Westbrook Weaver, PhD
Chief Executive Officer
westbrook@tempothera.com

Andrea Quach
Director of Clinical Operations
andrea.quach@tempothera.com

14 References

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APPENDIX A. SCHEDULE OF EVENTS

Procedure	Visit 1 (Screening)	Visit 2 +/-2 days (Treatment)	Visit 3 +/-2 days	Visit 4 +/-2 days	Visit 5 +/-2 days	Visit 6 +/-2 days	Visit 7 +/-2 days	Visit 8 +/-3 days	Visit 9 +/-3 days	Visit 10[a] +/-3 days	Visit 11[a] +/-3 days	Visit 12[a] +/-3 days	Visit 13[a] +/-3 days	Visit 14 +/-3 days	Unscheduled Visit[b]
		Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 8	Week 10	Week 12	Week 16	Week 20	Week 24	
In Clinic Visit Required[i]	X	X	X	X		X		X		X				X[h]	
Virtual Visit					X		X		X		X	X	X		X
Inclusion/Exclusion	X														
Informed consent	X														
Demographics	X														
Medical history	X														
Concomitant medication	X		X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination		X	X	X		X		X		X				X	
Laboratory assessment[c]	X														
Pregnancy test[d]	X[j]	X[j]													
Surgical Mohs procedure		X													
Debridement (as needed)			X	X		X		X		X				X	X
Wound photo		X	X	X		X		X		X				X	X
Wound assessment			X	X		X		X		X				X	X
Subject identification code assignment		X													
Randomization		X													
Application of MAP Wound Matrix, if randomized to the treatment arm		X													
Removal of MAP Wound Matrix if clinically visible and wound is not healed														X	
Application of DuoDerm, if randomized to the Control arm[g]		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Bandaging per SOC[e]			X	X		X		X		X					
AE assessments			X	X	X	X	X	X	X	X	X	X	X	X	X
Pain at wound site[k]			X	X	X	X	X	X	X	X	X	X	X	X	X
Investigational device assessment			X	X		X		X		X				X	X
POSAS scar assessments															X

Footnotes for table are found on the following page

Footnotes for Schedule of Visits table:

a) Optional virtual may occur after confirmed wound closure and/or at the Investigator's discretion if deemed medically necessary.

b) Unscheduled virtual or in-clinic visits may occur to assess any AE related to wound healing.

c) IF subjects have a documented history of type I or type II diabetes, HbA1c laboratory tests will be drawn. Otherwise, laboratory tests are performed only as needed per the Investigator's discretion.

d) For women of childbearing potential.

e) Until wound closure.

f) Evaluating the presence of the MAP Wound Matrix in the wound bed (when possible) and assessment of incidence of device removal (unintentional removal during a dressing change for instance or intentional removal because it was deemed necessary to debride the wound for instance). The safety and effectiveness of removal will be evaluated if it occurs. The amount of residual device remaining in the wound after device removal will be assessed.

g) DuoDerm will be reapplied once a week by either the subject at his/her home or by the Investigator during the follow-up visits until the wound is closed.

h) If MAP Wound Matrix is clinically present in the wound at Week 24, the Investigator will be instructed to debride the remaining device out of the wound.

i) Wound imaging will be performed such that a sterile ruler is placed in the field of view to enable proper scaling of images for post-hoc analysis. Usage of a software application (e.g., SWIFT, Ekare, Tissue Analytics) or computer aided device (e.g., Enspectra Health, Vivoscope, Spectral AI) may be employed to analyze wound images for wound area and granulation assessment. For analysis of fully healed wounds digital imaging (SWIFT, Ekare, Tissue Analytics), or 3D imaging (e.g., Canfield Vectra H1 H2 or M3) can be employed for exploratory data capture using minimally invasive approaches.

j) Pregnancy testing will be repeated at visit #2 only if greater than 6 days have elapsed from Visit #1.

k) **At the in-clinic visits (Visits 3, 4, 6, 8, 10):** VAS measured before wound dressing manipulation, during manipulation, and 10-20 minutes after IF there was pain level of 5 or greater before or during manipulation. If the device is reapplied, subject pain at the wound site will be assessed prior to re-application, during re-application, and within 30 minutes after re-application.

APPENDIX B. BATES-JENSEN WOUND ASSESSMENT TOOL

BATES-JENSEN WOUND ASSESSMENT TOOL
Instructions for use

General Guidelines:

Fill out the attached rating sheet to assess a wound's status after reading the definitions and methods of assessment described below. Evaluate once a week and whenever a change occurs in the wound. Rate according to each item by picking the response that best describes the wound and entering that score in the item score column for the appropriate date. When you have rated the wound on all items, determine the total score by adding together the 13-item scores. The HIGHER the total score, the more severe the wound status. Plot total score on the Wound Status Continuum to determine progress.

Specific Instructions:

1. **Size**: Use ruler to measure the longest and widest aspect of the wound surface in centimeters; multiply length x width.

2. **Depth**: Pick the depth, thickness, most appropriate to the wound using these additional descriptions:
   - 1 = tissues damaged but no break in skin surface.
   - 2 = superficial, abrasion, blister or shallow crater. Even with, &/or elevated above skin surface (e.g., hyperplasia).
   - 3 = deep crater with or without undermining of adjacent tissue.
   - 4 = visualization of tissue layers not possible due to necrosis.
   - 5 = supporting structures include tendon, joint capsule.

3. **Edges**: Use this guide:

Indistinct, diffuse	=	unable to clearly distinguish wound outline.
Attached	=	even or flush with wound base, no sides or walls present; flat.
Not attached	=	sides or walls are present; floor or base of wound is deeper than edge.
Rolled under, thickened	=	soft to firm and flexible to touch.
Hyperkeratosis	=	callous-like tissue formation around wound & at edges.
Fibrotic, scarred	=	hard, rigid to touch.

4. **Undermining**: Assess by inserting a cotton tipped applicator under the wound edge; advance it as far as it will go without using undue force; raise the tip of the applicator so it may be seen or felt on the surface of the skin; mark the surface with a pen; measure the distance from the mark on the skin to the edge of the wound. Continue process around the wound. Then use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved.

5. **Necrotic Tissue Type**: Pick the type of necrotic tissue that is predominant in the wound according to color, consistency and adherence using this guide:

White/gray non-viable tissue	=	may appear prior to wound opening; skin surface is white or gray.
Non-adherent, yellow slough	=	thin, mucinous substance; scattered throughout wound bed; easily separated from wound tissue.
Loosely adherent, yellow slough	=	thick, stringy, clumps of debris; attached to wound tissue.
Adherent, soft, black eschar	=	soggy tissue; strongly attached to tissue in center or base of wound.
Firmly adherent, hard/black eschar	=	firm, crusty tissue; strongly attached to wound base and edges (like a hard scab).

6. **Necrotic Tissue Amount**: Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved.

7. **Exudate Type**: Some dressings interact with wound drainage to produce a gel or trap liquid. Before assessing exudate type, gently cleanse wound with normal saline or water. Pick the exudate type that is predominant in the wound according to color and consistency, using this guide:

Bloody	=	thin, bright red
Serosanguineous	=	thin, watery pale red to pink
Serous	=	thin, watery, clear
Purulent	=	thin or thick, opaque tan to yellow
Foul purulent	=	thick, opaque yellow to green with offensive odor

8. **Exudate Amount**: Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to determine percent of dressing involved with exudate. Use this guide:

None	=	wound tissues dry.
Scant	=	wound tissues moist; no measurable exudate.
Small	=	wound tissues wet; moisture evenly distributed in wound; drainage involves ≤ 25% dressing.
Moderate	=	wound tissues saturated; drainage may or may not be evenly distributed in wound; drainage involves > 25% to ≤ 75% dressing.
Large	=	wound tissues bathed in fluid; drainage freely expressed; may or may not be evenly distributed in wound; drainage involves > 75% of dressing.

9. **Skin Color Surrounding Wound**: Assess tissues within 4cm of wound edge. Dark-skinned persons show the colors "bright red" and "dark red" as a deepening of normal ethnic skin color or a purple hue. As healing occurs in dark-skinned persons, the new skin is pink and may never darken.

10. **Peripheral Tissue Edema & Induration**: Assess tissues within 4cm of wound edge. Non-pitting edema appears as skin that is shiny and taut. Identify pitting edema by firmly pressing a finger down into the tissues and waiting for 5 seconds, on release of pressure, tissues fail to resume previous position and an indentation appears. Induration is abnormal firmness of tissues with margins. Assess by gently pinching the tissues. Induration results in an inability to pinch the tissues. Use a transparent metric measuring guide to determine how far edema or induration extends beyond wound.

11. **Granulation Tissue**: Granulation tissue is the growth of small blood vessels and connective tissue to fill in full thickness wounds. Tissue is healthy when bright, beefy red, shiny and granular with a velvety appearance. Poor vascular supply appears as pale pink or blanched to dull, dusky red color.

12. **Epithelialization**: Epithelialization is the process of epidermal resurfacing and appears as pink or red skin. In partial thickness wounds it can occur throughout the wound bed as well as from the wound edges. In full thickness wounds it occurs from the edges only. Use a transparent metric measuring guide with concentric circles divided into 4 (25%) pie-shaped quadrants to help determine percent of wound involved and to measure the distance the epithelial tissue extends into the wound.

BATES-JENSEN WOUND ASSESSMENT TOOL

Complete the rating sheet to assess wound status. Evaluate each item by picking the response that best describes the wound and entering the score in the item score column for the appropriate date.

Location: Anatomic site. Circle, identify right **(R)** or left **(L)** and use **"X"** to mark site on body diagrams:

____ Sacrum & coccyx ____ Lateral ankle
____ Trochanter ____ Medial ankle
____ Ischial tuberosity ____ Heel Other Site

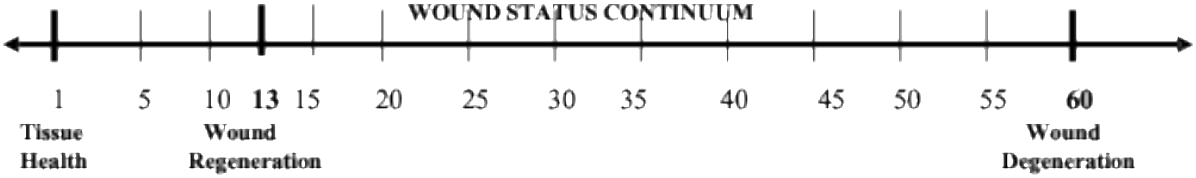
Shape: Overall wound pattern; assess by observing perimeter and depth.

Circle and date appropriate description:

____ Irregular ____ Linear or elongated
____ Round/oval ____ Bowl/boat
____ Square/rectangle ____ Butterfly Other Shape

Item	Assessment	Date Score	Date Score	Date Score
1. Size	1 = Length x width <4 sq cm 2 = Length x width 4--<16 sq cm 3 = Length x width 16.1--<36 sq cm 4 = Length x width 36.1--<80 sq cm 5 = Length x width >80 sq cm			
2. Depth	1 = Non-blanchable erythema on intact skin 2 = Partial thickness skin loss involving epidermis &/or dermis 3 = Full thickness skin loss involving damage or necrosis of subcutaneous tissue; may extend down to but not through underlying fascia; &/or mixed partial & full thickness &/or tissue layers obscured by granulation tissue 4 = Obscured by necrosis 5 = Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone or supporting structures			
3. Edges	1 = Indistinct, diffuse, none clearly visible 2 = Distinct, outline clearly visible, attached, even with wound base 3 = Well-defined, not attached to wound base 4 = Well-defined, not attached to base, rolled under, thickened 5 = Well-defined, fibrotic, scarred or hyperkeratotic			
4. Under-mining	1 = None present 2 =Undermining < 2 cm in any area 3 = Undermining 2-4 cm involving < 50% wound margins 4 = Undermining 2-4 cm involving > 50% wound margins 5 = Undermining > 4 cm or Tunneling in any area			
5. Necrotic Tissue Type	1 = None visible 2 = White/grey non-viable tissue &/or non-adherent yellow slough 3 = Loosely adherent yellow slough 4 = Adherent, soft, black eschar 5 = Firmly adherent, hard, black eschar			
6. Necrotic Tissue Amount	1 = None visible 2 = < 25% of wound bed covered 3 = 25% to 50% of wound covered 4 = > 50% and < 75% of wound covered 5 = 75% to 100% of wound covered			
7. Exudate Type	1 = None			

Item	Assessment	Date Score	Date Score	Date Score
	2 = Bloody 3 = Serosanguineous: thin, watery, pale red/pink 4 = Serous: thin, watery, clear 5 = Purulent: thin or thick, opaque, tan/yellow, with or without odor			
8. Exudate Amount	1 = None, dry wound 2 = Scant, wound moist but no observable exudate 3 = Small 4 = Moderate 5 = Large			
9. Skin Color Sur-rounding Wound	1 = Pink or normal for ethnic group 2 = Bright red &/or blanches to touch 3 = White or grey pallor or hypopigmented 4 = Dark red or purple &/or non-blanchable 5 = Black or hyperpigmented			
10. Peripheral Tissue Edema	1 = No swelling or edema 2 = Non-pitting edema extends <4 cm around wound 3 = Non-pitting edema extends ≥4 cm around wound 4 = Pitting edema extends < 4 cm around wound 5 = Crepitus and/or pitting edema extends ≥4 cm around wound			
11. Peripheral Tissue Induration	1 = None present 2 = Induration, < 2 cm around wound 3 = Induration 2-4 cm extending < 50% around wound 4 = Induration 2-4 cm extending ≥ 50% around wound 5 = Induration > 4 cm in any area around wound			
12. Granu-lation Tissue	1 = Skin intact or partial thickness wound 2 = Bright, beefy red; 75% to 100% of wound filled &/or tissue overgrowth 3 = Bright, beefy red; < 75% & > 25% of wound filled 4 = Pink, &/or dull, dusky red &/or fills ≤ 25% of wound 5 = No granulation tissue present			
13. Epithe-lializa-tion	1 = 100% wound covered, surface intact 2 = 75% to <100% wound covered &/or epithelial tissue extends >0.5cm into wound bed 3 = 50% to <75% wound covered &/or epithelial tissue extends to <0.5cm into wound bed 4 = 25% to < 50% wound covered 5 = < 25% wound covered			
	TOTAL SCORE			
	SIGNATURE			



Plot the total score on the Wound Status Continuum by putting an **"X"** on the line and the date beneath the line. Plot multiple scores with their dates to see-at-a-glance regeneration or degeneration of the wound.

APPENDIX C. POSAS GENERIC VERSION 3.0 FORM

POSAS

Observer Scale Generic version 3.0

Participant ID .....

Name of the observer: **Date:**

*i This version is used for **all types of scars**, except for linear scars (see Patient Scale, Linear Scar version).*

*We ask you to focus on **one scar** when filling out this questionnaire. In the case of large scars, please **choose a specific part of the scar** to focus on.*

Location of the scar (area):

Cause of this scar:

- ◯ Burns
- ◯ Infection
- ◯ Donor site (split-thickness skin graft)
- ◯ Other type of trauma
- ◯ Piercing
- ◯ Unknown
- ◯ Other:

Does this concern a keloid?

- ◯ Yes
- ◯ No

Date of injury: _____ *(month, day, year)*

	Not	Minimally	Moderately	Severely	Extremely
0 How different is the **overall quality** of the scar compared to unaffected skin?	◯	◯	◯	◯	◯

Continue with the questionnaire

Participant ID

.....

Check the box that best describes your answer for the scar (area) you have chosen.
For additional instructions on how to use this questionnaire, visit www.posas.org/instructions.

Please compare the following characteristics of the scar to unaffected skin.

i With unaffected skin, we refer to the skin before the injury. For a comparison between the scar and unaffected skin, the surrounding skin or skin on the contralateral side may be used, depending on the situation.

	Not	Minimally	Moderately	Severely	Extremely
1 How different is the **pigmentation** of the scar?	○	○	○	○	○
2 How different is the **vascularity** of the scar?	○	○	○	○	○
3 How different is the **surface level** of the scar?	○	○	○	○	○
4 How different is the **surface texture** of the scar?	○	○	○	○	○
5 How **firm** does the scar feel?	○	○	○	○	○
6 How **adhered** is the scar to underlying tissues?	○	○	○	○	○
7 Under how much **tension** is the scar and its adjacent structures, as a result of scar contraction?	○	○	○	○	○

i Scar colour may be lighter (hypopigmentation), darker (hyperpigmentation), or both (mixed) when compared to unaffected skin.

→ Please describe the **pigmentation** of the scar compared to unaffected skin.

○ Hypopigmentation ○ Hyperpigmentation ○ Mixed

→ Please describe the **colour** of the scar caused by **vascularity**.

☐ Pale/White ☐ Pink ☐ Red ☐ Purple (multiple answers possible)

i In scars, the surface texture is often times more irregular (i.e. more bumpy and rough) than unaffected skin. In some cases, the surface of the scar can be overly and abnormally smooth (even smoother than unaffected skin).

→ Please describe the **level** of the scar surface compared to unaffected skin.

○ Elevated ○ Depressed

→ Please describe the **texture** of the scar surface.

○ Irregular ○ Overly smooth

i Firm scar tissue is less supple and flexible, which makes it difficult to pinch.

i In adhered scars, the movement of the skin in relation to the underlying structures is limited, as a result of being either partially or completely fixed to deeper structures.

i The amount of tension on the scar area can be assessed best when the patient's maximum range of motion is actively achieved in a neighbouring joint. Signs of tension include tightness of the skin, tension lines (banding), discolouration (blanching) of skin colour, and a limited range of motion.

Thank you for completing this questionnaire

For more information about the POSAS please visit www.posas.org

POSAS
Patient and Observer Scar Assessment Scale 3.0

POSAS

Patient Scale | Generic version | 3.0

Participant ID

.....

i *Please choose **one scar (area)** and answer all questions with this scar in mind.*

Date: _____ *(month, day, year)*

Where is this scar (area) located? _____

What is the cause of this scar?

- ◯ Burns
- ◯ Infection
- ◯ Donor site (split-thickness skin graft)
- ◯ Accident
- ◯ Piercing
- ◯ Unknown
- ◯ Other: _____

When did you get the scar? _____ *(month, day, year)*

	Very dissatisfied	A little dissatisfied	Neutral	A little satisfied	Very satisfied
0 How **satisfied** are you with the way your scar looks and feels?	◯	◯	◯	◯	◯

Continue with the questionnaire →

Participant ID

Check the box that best describes your answer for the scar (area) you have chosen.
For additional instructions on how to use this questionnaire, visit www.posas.org/instructions.

The following questions are about your scar at this moment

	Not	A little	Moderately	Very	Extremely
1 How different is the **colour** of your scar, compared to your normal skin?	○	○	○	○	○
2 How **shiny** is your scar, compared to your normal skin?	○	○	○	○	○
3 Is your scar **raised** or **sunken**, compared to your normal skin? Please indicate by how much:	○	○	○	○	○
4 Does your scar feel **hard**, compared to your normal skin?	○	○	○	○	○
5 Is the surface of your scar **irregular**, compared to your normal skin?	○	○	○	○	○

i By irregular we mean how the surface looks and feels, for example, 'bumpy', 'lumpy', with ridges, folds or diamond-patterned.

The following questions are about your scar during the last week:

	Not	A little	Moderately	Very	Extremely
6 Is your scar **overly sensitive to touch**?	○	○	○	○	○
7 Is your scar **less sensitive to touch** ("numbness")?	○	○	○	○	○
8 Is your scar **painful**?	○	○	○	○	○
9 Do you experience a **shooting sensation** in your scar?	○	○	○	○	○
10 Do you experience a **burning sensation** in your scar?	○	○	○	○	○
11 Does your scar **itch**?	○	○	○	○	○
12 Do you experience sensations of **tingling** or **"pins and needles"** in your scar?	○	○	○	○	○
13 Do you experience **tightness** in your scar **at rest**?	○	○	○	○	○
14 Does your scar **pull tight with movement**?	○	○	○	○	○
15 Is your scar **fragile**, causing the skin to break down more easily?	○	○	○	○	○
16 If you do not moisturise your scar, does it feel **dry**?	○	○	○	○	○

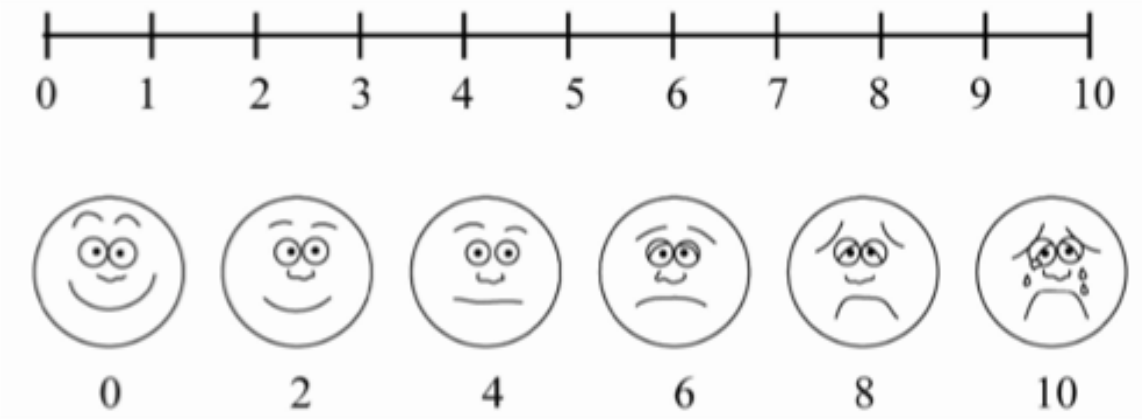
Thank you for completing this questionnaire
For more information about the POSAS please visit www.posas.org

POSAS
Patient and Observer Scar Assessment Scale 3.0

APPENDIX D. SUBJECT PAIN ASSESSMENT AT WOUND SITE USING NUMERIC RATING SCALE (VAS)

On a scale of 0 to 10, with 0 being no pain at all and 10 being the worst pain imaginable, how would you rate your pain RIGHT NOW?

No Pain **Worst Imaginable Pain**



VAS Form