Document Title: Study Protocol

Study Title: Surgical Drape with a Releasable Acrylic Adhesive for Atraumatic Negative Pressure Wound Therapy

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PROTOCOL STUDY

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Title: Surgical drape with a releasable acrylic adhesive for atraumatic negative pressure wound therapy.

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Sponsor & Principle-Investigator

Global Biomedical Technologies, LLC

Version: 2.1
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1. NAME AND ADDRESSES OF INVESTIGATORS

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2. INVESTIGATIONAL AGENT

Global Biomedical Technologies, LLC has developed a method to employ a proprietary resin “OGS” (oligo- glycerol sebacate) blended with an acrylic, pressure sensitive adhesive and made into surgical drapes with Comfort Release® innovation: a switchable adhesive. This strong skin bonding adhesive Negative Pressure Wound Therapy (NPWT) drape, when properly triggered, releases with less pain and trauma to the skin. This skin friendly NPWT drape is important to decrease the pain and suffering associated with chronic wounds, as well as to increase compliance for the completion of NPWT. This is especially important for patients with frail, geriatric, or sensitive skin, as well as those patients enduring multiple applications of strong, skin irritating adhesive NPWT drapes.

3. REPORT OF PRIOR INVESTIGATIONS

Global Biomedical Technologies, LLC has not conducted prior clinical IRB supported studies on the new Comfort Release® Drape. The Comfort Release® Drape has undergone non-clinical studies to support its safety features. These studies include an analysis of the adhesive stickiness by-way of peel strength and moisture vapor transmission rate in direct comparison to the Control Drape being used in the study (Data is available upon request). We have done some limited evaluations of the drape S-2747. This is the prototype for our Comfort Release® Drape to be used in the NIH study. We had three nurses apply S-2747 drapes to themselves and other volunteers to evaluate its wearability and easy release, compared to other drapes. The S-2747 drapes performed as indicated with no adverse effects noted. I have attached a folder with our S-2747 drape testing. Appropriate biocompatibility studies, including animal skin sensitization, skin irritation and cytotoxicity will be completed prior to use of the Comfort Release® Drape in this research.

UPMC Presbyterian Hospital study finds preference of Comfort Release® bidirectional, transparent tape compared to the Market Leading transparent tape 3M Transpore™. This study was a product evaluation comparing the use of Comfort Release® bidirectional, transparent tape to the market leading transparent tape used at the UPMC Presbyterian Hospital in Pittsburgh. The 100-patient study included individuals aged 20-84, 59% female and 39% male (2% preferred not to say). The VAT-IV team was responsible for applying the tapes for skin securement and the nursing staff was responsible for removing the tape and completing a corresponding survey. Prior to removing Comfort Release®, tape nurses were queried on prior experiences with patient tape removal including the type of tape most often encountered and how often patients experienced pain, redness, and erythema during the process. Nurses were then instructed to remove the tape by swiping the outside with alcohol prep pads and were asked a series of follow up questions related to the activity. These included patient-centered questions such as their perceived pain during the removal process as well as usability questions such as time spent removing the tape and utility of the tape. Throughout the study, length of tape application time ranged from 24-72 hours depending on the patient. To increase enrollment of patients undergoing phlebotomy on the study, additional facility units were also added. Key study findings were as follows: Nurses demonstrate preference for Comfort Release® tape over 3M Transpore tape and report patients had favorable opinions towards the Comfort Release® tape. Overall conclusions from 100 nursing staff responses: • Nurses overwhelmingly prefer Comfort Release® tape over 3M Transpore tape. Only one nurse from the 100 favored the 3M product. • 98% of nurses surveyed responded that Comfort Release® was as good or better than current dressings. • 90% of nurses reported that Comfort Release® is easy to apply and remove. • Every 9 of 10 nurses indicated that their patient will directly benefit from the use of Comfort Release® Tapes. Comfort Release® tape had a low rate of skin response. Nursing staff report that the incidence of medical adhesive skin injury ranged between 30% and 50% of all patients, using current tape products at

UPMC. However, nursing staff reported the occurrence of medical adhesive skin injury in the 100 test patients was less than 10%. In total,85% of patients tested had no skin response and 3% had only a faint response (measured by erythema). Comfort Release® tape resulted in minimal pain to patients. Nursing staff report that incidence of significant pain (from tape removal) ranged between 40% and 50% of all patients, using current tape products at UPMC (i.e., 3M Transpore tape). In contrast, nursing staff reported the occurrence of significant pain in only 12%of the 100 test patients who used Comfort Release® tape. Critically,71% had no pain and 17% had only minimal pain or an unpleasant sensation.C.2.3 Clinical Surveys demonstrate user satisfaction with Comfort Release®.

Clinical Surveys demonstrate user satisfaction with other Comfort Release® adhesive products.

Nurse Evaluation. A focus group and product evaluation of Comfort Release® was performed by eight nurses of varying levels of experience. All nurses had prior experiences with IV site dressing, and all but one nurse had experience with border dressings and medical tape. Prior to beginning product testing participating nurses were asked a series of questions before being introduced to the Comfort Release® products. Preliminary survey questions found that 89% agreed that trauma to a wound (or surrounding area) often occurs while removing a bandage/dressing (compared to 11% disagree); 78% agreed that removal of bandage is a significant problem in wound care management, and 89% agreed patients complain of pain during dressing/bandage removal. After seeing, testing, and trying our product, 100% of surveyed nurses agreed that Comfort Release® would likely: decrease pain and trauma associated with dressing removal; decrease the frequency of skin tears; and improves patient comfort during dressing removal.

Adult Patient evaluation. A total of n=100 adult patients were recruited to participate in a product evaluation of Comfort Release® bandages over the course of 2-3 days. The primary outcomes of this study were skin sensitivity responses to the bandage and/or IPA), durability of the bandage, and occurrence of adhesive residue. Participants were asked a series of questions before and after wearing sample Comfort Release® bandages during the study period. They were given limited background information and simple label instructions for use. All signed normal consent to participate in the evaluation. None were paid. Of those surveyed, 95% had prior experience with bandages and tapes (compared to 5% disagree); 78%reported that all other bandages fall off with simple bathing (compared to 12% disagree & 10% don't know); and80% agree they are dissatisfied with other bandages and tapes (compared to 20% disagree).After trying the Comfort Release® Bandage, 99% reported Comfort Release® stayed on (90% for full test period of 48 or 72 hours, 9% for 24-36 hours, and 1% less than 12 hours), 88% agreed Comfort Release® easily removed with rubbing alcohol (compared to 9% disagree and 3% details not provided), and 94% agreed Comfort Release® left no glue residue (compared to 6% who reported minimal residue). After seeing, testing, and trying our product, 94% of adult patients agreed they were satisfied with Comfort Release.

Child Patient Evaluation. Comfort Release® Bandages were also tested in a group of n=100 children at a pediatric medical practice. Each of our 100 child participants and their consenting adults were asked to provide answers about their experience with other adhesive products and with the results of using Comfort Release samples. All consenting adults signed a written consent, and each child received an incentive to participate. Of those surveyed, 94% had prior experience with bandages and tapes (compared to 6% disagree),81% agree that all other bandages fall off too easily (compared to 19% disagree), 93% agree that all other bandages fall off with simple bathing (compared to 7% disagree), and 84% agree all other bandages are painful to remove(compared to 16% disagree).86% of children had Comfort Release® bandages on for the full test period — all of which easily removed their bandages with alcohol — 86% of children easily removed their Comfort Release® bandages with rubbing alcohol(compared to 14% that did need the alcohol), 86% removed Comfort Release® with no glue residue left on skin(compared to 14% with minor residue left after bandage removal), and 94% agreed Comfort Release® was not painful to remove (compared to 6% reporting slight discomfort). After seeing, testing, and trying our product, 94%of children and their parents agree they would purchase Comfort Release®

4. INVESTIGATIONAL PLAN

4.1. PURPOSE

NPWT is commonly used for the management of more than 100 indications, including chronic wounds, acute open wounds, burns, and post operative sites. An estimated 6.5 million patients suffer from chronic wounds and an estimated 48 million inpatient surgeries are performed each year in the US[3,4]. NPWT involves covering a wound with an airtight dressing, sealed by adhesive, and applying sub-atmospheric pressure via a vacuum device. Strong adhesives are typically required for NPWT drapes. Exudate can leak with weaker adhesives, tainting peri-wound skin, causing loss of drape adherence, subsequently leading to the potential for macerated tissue, increased wound size, and slower or reduced healing. However, strong adhesives substantially increase the risk for medical adhesive-associated skin injuries (MARSI) during drape removal/changes. Drape removal can cause epidermal layers to separate and/or detach from the dermis, resulting in skin tears and moisture-associated skin damage, and skin irritation. Studies show the type of drape used correlates with acute pain during dressing changes and injury to the peri-wound tissue, in turn delaying the wound healing process. Previous attempts to develop a product with strong adhesion and easy removability have fallen short. Silicone adhesives have poor skin adherence and are expensive, thus requiring stronger adhering acrylic sealing strips or other acrylic components to mitigate leaks. Addressing this unmet need, Global Biomedical Technologies has developed an adhesive acrylic NPWT drape incorporating innovative ester oligomers that release from the skin with the addition of isopropyl alcohol. This painless adhesive technology, "Comfort Release®," has proven high patient satisfaction with low incidence of MARSI. This project will confirm the superior functionality and acceptability of Comport Release® NPWT drapes against the market leader (V.A.C. drape by KCI Technologies, Inc.) in both single-use and serial-use NPWT applications. The data obtained from this Direct to Phase II project is expected to support a 510K FDA clearance.

The proposed research aims to provide the clinical validation and data needed for a510K FDA clearance. If successful, the knowledge gained as a result of this trial can bring to market a novel surgical drape for wound therapy that has strong potential to be pain-free and atraumatic and will help facilitate wound healing. This can potentially contribute to improved patient outcomes. Given that there are minimal risks in this trial we find them reasonable to obtain the knowledge and clinical data needed bring this drape to pursue FDA clearance and bring this novel NPWT drape to market.

Aim 1: Compare performance of Comfort Release® drapes with control V.A.C. drapes in **single-use NPWT** applications in a randomized controlled trial. Single use negative pressure wound therapy is used after post-surgical procedures.

Aim 2: Compare performance of Comfort Release® drapes with control V.A.C. drapes in **serial-use NPWT** applications in a randomized controlled trial. Serial use negative pressure wound therapy is used with patients with chronic wounds.

4.1.1 PRIMARY EFFECTIVENESS ENDPOINT

Primary effectiveness will be determined by patient improvement and satisfaction and by product acceptance by the clinicians involved in the study.

Measurements between Comfort Release® test drape and the control drape used in the clinical study should demonstrate a:

1) Decrease incidence of medical adhesive-related skin irritation and injuries following drape removal.

2) Decrease amount patient discomfort and pain during the drape removal.

3) Decrease use of medications for anxiety and pain and stress related to drape removal.

4) Maintaining a seal with a leak incidence rate that is as low or lower than the control drape.

Type	Name	Time Frame	Brief Description
Primary	Skin irritation	At time of drape removal	At time of removal, clinicians will assess associated skin irritation and injuries by using the MARSI classification scale.
Primary	Medical Adhesive-Related Skin Injury (MARSI)	At time of drape removal	Participating clinicians will be trained (led by Denise Anderson, RN, WCC) on how to identify and measure MARSI across presentations (erythema lasting more than 30 minutes, skin tears, skin stripping, folliculitis, maceration, tension/injury blister, allergic contact dermatitis, and irritant contact dermatitis). All incidences of MARSI will be recorded.
Primary	Pain	At time of drape removal	Clinicians will ask patients to assess pain using the Indiana Polyclinic Combined Pain Scale.
Primary	Treatment compliance	Duration of study	Instances of patients prematurely stopping treatment will be recorded.
Primary	Narcotic/pain medication use	Duration of study	Patient use of narcotics, pain and stress-reducing medications prescribed to patients undergoing the dressing removal will be recorded throughout the duration of the study.
Primary	Leak rate	Duration of study	During the NPWT application, clinicians will be instructed to record any incidence of leaks (as alerted by vacuum pump machine) that occur as a result of unsealed adhesive.

4.1.2 SAFETY ENDPOINTS

Completion of the Negative Pressure Therapy treatment plan as established by ordering physician.

Treatment and resolution of any medical adhesive related skin injuries from the drape removal in both control and study patients.

4.1.3 SECONDARY EFFECTIVENESS ENDPOINT

Secondary effectiveness will be determined by healthcare professionals use of both drapes.

Use of Comfort Release® drape will be compared to control drape use in the clinical study and should demonstrate:

1) Clinician acceptability of the Comfort Release® drape.

2) Less time to remove the Comfort Release® NPWT drape and the economic value of less clinician time spent in the drape removal activity.

3) Measurement of patient rate drop-out (or refusal) to continue and finish their NPWT therapy prescribed by treating their physician

4.2 PROTOCOL

Negative pressure wound therapy (NPWT) is a common primary or adjunctive treatment approach for more than 100 indications, including chronic complex wounds that are potentially non-healing, and acute open wounds that are infected or subject to swelling, severe burns, and post operative care. Despite demonstrated benefits of NPWT, the technology faces challenges regarding the adhesive sealant component of the system as the strong adhesive required to establish and maintain an airtight seal for successful implementation of NPWT substantially increases the chances for mechanical injury. Addressing this, Global Biomedical Technologies will compare Comfort Release® NPWT drape with an innovative “switchable adhesive” technology for painless and trauma free removal with the standard KCI V.A.C.® drape in post-surgical wound patients. The types of post-op wounds that receive NPWT that are eligible for this study include adult acute wounds and incisions, as well as chronic wounds and burns.

50% of participants have the new drape	50% of participants have the standard drape
Both groups: KCl V.A.C ® Negative Pressure Wound Therapy pump and Kit.	
Comfort Release® Drape	KCl V.A.C.® Drape
Dressing removal: Tab on the side of the drape is lifted and rubbing alcohol is applied to skin/drape to decrease adhesive bond and remove the drape gently from the skin.	Dressing removal: Drape is pulled from skin as gently as possible, per standard care.
Both groups: Using a standard number scale, rate pain or discomfort, if any during drape removal.	
Both groups: Any pain or anxiety medicine received is recorded (if given)	
Both groups: Clinician will record any skin changes, including skin, redness or swelling, as a result of wearing the drape.	
Both groups: Anyone who finishes NPWT earlier than prescribed will be asked to answer a few questions: Early Exit questionnaire.	

In Aim 1, we will evaluate drape performance in post-surgical single-use NPWT, where the approach will be used to treat surgical sites (e.g. skin closures and skin grafts), a common occurrence at both study sites.

Aim 1: Compare performance of Comfort Release® drapes with V.A.C. drapes in **single-use NPWT** applications in a randomized controlled trial. Post-surgical patients (n=200) with prescribed NPWT, will be enrolled at Weill Cornell under PI. Dr. Robert Winchell and at Columbia Presbyterian hospital under co-Principal Investigator Dr. Jarrod Bogue for single-use NPWT. Patients will be randomized to a single use control (V.A.C. drape) or intervention (Comfort Release® drape). All other components of the NPWT device including but not limited to the pump, tubing, foam or dressing insert and will be identical.

Aim1 Testing Protocol

1) measurement of medical adhesive-related skin irritation and injuries, as measured by the Medical Adhesive-Related Skin Injury (MARSI) classification scale.
2) measurement of pain, as measured by the Indiana Polyclinic Combined Pain Scale.
3) measurement of the use of medications for pain and stress related to dressing removal.
4) measurement of the effectiveness in maintaining seal (leak incidence rate).
5) measure clinician acceptability of the Comfort Release® drape.
6) measurement of patient drop-out from the prescribed length of the NPWT therapy prescribed by treating physician.

In Aim 2, we will evaluate the drape for serial-use NPWT; this course of treatment is commonly used at Weill Cornell for numerous types of wounds including burns, pressure ulcers, fasciotomy sites, and other post-traumatic indications.

Aim 2: Compare performance of Comfort Release® drapes with V.A.C. drapes in serial-use NPWT applications in a randomized controlled trial. Chronic wound patients (n=100) with prescribed NPWT will be enrolled at Weill Cornell Medical Center under Principal Investigator Dr. Robert Winchell. All patients will undergo 3 NPWT drape changes per week. Patients will be randomized to control (V.A.C. drape.) or intervention (Comfort Release® drape) for the duration of their study enrollment. All other components of the NPWT device including but not limited to the pump, tubing, foam or dressing insert will be identical.

Aim 2 Testing Protocol

1) measurement of medical adhesive-related skin irritation and injuries, as measured by the Medical Adhesive-Related Skin Injury (MARSI) classification scale.
2) measurement of pain, as measured by the Indiana Polyclinic Combined Pain Scale.
3) measurement of the use of medications for pain and stress related to dressing removal.
4) measurement of the effectiveness in maintaining seal (leak incidence rate).
5) measure clinician acceptability of the Comfort Release® drape.
6) measurement of the time to remove the NPWT drape and any economic value through change in nursing time spent in the activity.
7) measurement of patient drop-out from the prescribed length of the NPWT therapy prescribed by treating physician.

Clinicians, including nurses, physicians, residents, and physician assistants, will be trained to use the investigational drape and record data on patient reactions to the Comfort Release® Drape and the KCI V.A.C.® Drape. If nurses participate, they will be incentivized to engage in this training and data collection. Clinicians will be asked to evaluate the ease of learning and using the new drape. Training on using the Comfort Release® Drape and rating and skin injuries according to the Medical Adhesive-Related Skin Injury (MARSI) classification scale will be provided through online videos and, if needed, on-site sessions

Comfort Release® Drape applies to the skin like most standard NPWT drape, with the exception of a tab that remains attached to the drape on the patient's skin. The tab assists in the removal of the drape at the time of dressing removal. Comfort Release® removal is different than other drapes because of the IPA needed to break the adhesive bond from the skin.

A detailed step by step device instruction is in the PDF below or refer to GB141-A IFU.

(Please see the attached PDF of GB141-A – Pouch Label)

Aim 1
Initial Visit

Step 1) Compare inclusion/exclusion criteria to find eligible participants and record them on the case report.

Inclusion Criteria:
1. 18 years or older post-surgical inpatients with a plan of treatment using NPWT
2. Able to communicate and consent to participation in the study
3. Access to V.A.C. by KCI drape and NPWT kits
4. Able to report pain level using a pain scale.

Exclusion Criteria:
1. History of known hypersensitivity to acrylic adhesives
2. History of known hypersensitivity to isopropyl alcohol
3. NPWT treatment within past 3 months
4. The patient is expected to be unconscious during the drape removal/change
5. Under the age of 18 years 6. Unable to give consent, including language barrier, unless an interpreter is readily available.

Step 2) Willing participants sign consent, is witnessed, and in a timely matter is signed by PI.

Step 3) Subject is assigned an identification code number. Date, subject initials, ID, DOB, gender at birth, ethnicity, eligibility, medications, and health history are recorded on case report forms.

Step 4) The Site PI or a designated individual will email the Program Coordinator, Denise Anderson, RN, WCC at: danderson@comfortrelease.com, to receive the next subject ID number from the sponsor's randomized list.

In the case of a delayed response or for after-hours surgeries, the Site PI or designee may text Denise Anderson at (352) 397-8810 to receive the subject ID. Denise Anderson will then send a follow-up email that includes a screenshot of the text with the ID number for documentation purposes.

Randomized subject ID numbers beginning with 1-XXXX are control participants (KCI V.A.C.® drape), and randomized subject ID numbers beginning with 0-XXXX are study participants (Comfort Release® drape).

a. Randomize patients- 1/2 of the patients to receive KCI drape and 1/2 to receive Comfort Release drape.

0-XXXX= Study drape (Comfort Release®)
1-XXXX = Control drape (KCI®)

Step 5) Fill in the information and answer questions regarding drape application:
1. Record wound location and measurements.
2. Which drape was applied?
3. Was the drape easy to apply?
4. Were the drape application instructions easy to follow?

Drape Removal Visit*

Step 1) Answer drape removal questions:
a. Which drape was removed?
b. Was the drape easy to remove?
c. Were the drape removal instructions easy to follow?
d. Using the Indiana Polyclinic Combined Pain Scale (below), Ask the participant to score the amount of pain during drape removal.
Step 2). Assess and score the periwound skin using the MARSI classification scale (below).
Step 3) Answer the following questions:
a. Was pain or anxiety medication given to the participant due to pain or discomfort experienced during drape removal?
b. Did the drape maintain an effective seal during the course of use?
c. Use the additional notes section to explain any issues with the drape maintaining a seal or for any other treatment complications.
e. Is the patient dropping out of the prescribed treatment?
f. Please specify in the comments section the reason for the subject dropping out of treatment or put unknown.

*In the rare event that a second application of NPWT is used, the metrics from the second application will be measured, and the participant will remain in the study.

Aim 2
Initial Visit

Step 1) Compare inclusion/exclusion criteria to find eligible participants and record them on the case report.

Inclusion Criteria:
1. 18 years or older post-surgical inpatients with a plan of treatment using NPWT
2. Able to communicate and consent to participation in the study
3. Access to V.A.C. by KCI drape and NPWT kits
4. Able to report pain level using a pain scale.

Exclusion Criteria:
1. History of known hypersensitivity to acrylic adhesives
2. History of known hypersensitivity to isopropyl alcohol
3. NPWT treatment within past 3 months
4 The patient is expected to be unconscious during multiple drape removals/changes
5. Under the age of 18 years
6. Unable to give consent, including language barrier, unless an interpreter is readily available.

Step 2) Willing participants sign consent, is witnessed, and in a timely matter is signed by PI.

Step 3) Subject is assigned an identification code number. Date of evaluation, subject initials, ID, DOB, gender, ethnicity questions, and eligibility evaluation are recorded on case report form.

Step 4) The Site PI or a designated individual will email the Program Coordinator, Denise Anderson, RN, WCC at: danderson@comfortrelease.com, to receive the next subject ID number from the sponsor's randomized list.

In the case of a delayed response or for after-hours surgeries, the Site PI or designee may text Denise Anderson at (352) 397-8810 to receive the subject ID. Denise Anderson will then send a follow-up email that includes a screenshot of the text with the ID number for documentation purposes.

Randomized subject ID numbers beginning with 1-XXXX are control participants (KCI V.A.C.® drape), and randomized subject ID numbers beginning with 0-XXXX are study participants (Comfort Release® drape).

a. Randomize patients- 1/2 of the patients to receive KCI drape and 1/2 to receive Comfort Release drape.

0-XXXX= Study drape (Comfort Release®)
1-XXXX = Control drape (KCI®)

Step 5) Fill in the information and answer questions regarding drape application:

1. Record wound location and measurements.
2. Which drape was applied?
3. Was the drape easy to apply?
4. Were the drape application instructions easy to follow?

Drape Removal Visit

Step 1) Record the time taken (in minutes) for drape removal and put in the case report.
Step 2) Answer drape removal questions:

a. Which drape was removed?
b. Was the drape easy to remove?
c. Were the drape removal instructions easy to follow?
d. Using the Indiana Polyclinic Combined Pain Scale (below), ask the participant to score the amount of pain during drape removal.

Step 3) Assess and score the periwound skin using the MARSI classification scale (below) If skin injury is found, re-assess in 30 minutes.
Step 4) Answer the following questions:

a. Was pain or anxiety medication given to the participant for pain or discomfort experienced due to drape removal?

b. Did the drape maintain an effective seal during the course of use?

c. Use the additional notes section to explain any issues with the drape maintaining a seal or for any other treatment complications.

d. Is the patient dropping out of the prescribed treatment?

e. Please specify in the comments section the reason for the subject dropping out of treatment or put unknown.

Indiana Polyclinic Combined Pain Scale

Indiana Polyclinic Combined Pain Scale

Rate your pain according to the following scale

		Examples	
0	**No Pain**	No pain	0
1	**Unpleasant Sensation** - An occasional uncomfortable feeling. Almost no limit to function	Mild skin irritation	1
2	**Minimal** - Pain frequently brought to one's attention but acceptable. Able to engage in pleasures of life with some interference. Causes to avoid rigorous activities.	Small bruise	2
3	**Mild** - Tolerable, but unsettling and on one's mind. Interferes with pleasures of life. Stops some productive activities.	Scraped knee, Jammed finger	3
4	**Mild to Moderate** - Only short intervals of comfortable function; sometimes interrupts Activities of Daily Living, such as bathing and clothing and regularly prevents involvement in many tasks outside of the home. Decrease in job performance.	Major bruise, Ankle sprain	4
5	**Moderate** - Pain constantly on one's mind; decrease in concentration, job performance and noticeably decreased enjoyment of life. Frequent missed work / time off. Cannot perform normal tasks without an increase in pain.	Moderate toothache, Headache for days	5
6	**Moderate to Severe** - Significant limitations of Activities of Daily Living; productive activity/work is nearly impossible. Hard to do anything, but think of pain and ER visit.	Day after major surgery pain	6
7	**Severe** - Difficulty doing more than basic chores; pain prevents productive activity. Frequent crying; pain is impossible to tolerate for long period of time without going to the ER.	Stabbed with a knife, Broken leg	7
8	**Debilitating** - Causes uncontrollable moaning and distress and completely impairs productive activity. Cannot be still, can't maintain a reasonable conversation. It is impossible to "put on a good face." Emergency medical attention is required.	Natural childbirth, Small kidney stone	8
9	**Agonizing** - Individual cannot function; uncontrolled screaming and tearfulness. Emergency medical attention is required and hospitalization is recommended.	Arm burning in a fire, Large kidney stone	9
10	**Worst Imaginable** - Paralyzing; person is in and out of consciousness and near death as a result of the pain. Emergency medical attention ***and*** hospitalization are required.	Being torn apart while still alive	10

Medical Adhesive-Related Skin Injury (MARSI) classification scale

MARSI Classification Form.

Instructions for Use:

- **Initial Evaluation**: Clinicians assess the skin under the drape immediately after drape removal and check the appropriate box based on the severity of each skin injury.
- **30-Minute Evaluation**: For any score above 0, reassess after 30 minutes, and record the findings in the appropriate column.

Skin Injury Type	Initial Evaluation (0–4)	30-Minute Evaluation (0–4)
1. Erythema (Redness)	0 = No redness ☐1 = Very slight redness ☐2 = Well-defined redness ☐3 = Moderate ☐ 4 = Severe redness ☐	0 = No redness ☐1 = Very slight redness ☐2 = Well-defined redness ☐3 = Moderate ☐ 4 = Severe redness ☐
2. Skin Stripping	0 = No stripping ☐1 = Very slight stripping ☐2 = Partial epidermal loss ☐3 = Full-thickness ☐ 4 = Severe stripping ☐	0 = No stripping ☐1 = Very slight stripping ☐2 = Partial epidermal loss ☐3 = Full-thickness ☐ 4 = Severe stripping ☐
3. Tension Blisters	0 = No blisters ☐1 = Very small blister ☐2 = Small blister ☐3 = Large blister ☐4 = Severe blister ☐	0 = No blisters ☐1 = Very small blister ☐2 = Small blister ☐3 = Large blister ☐4 = Severe blister ☐
4. Maceration	0 = No maceration ☐1 = Very slight softening ☐2 = Mild softening ☐ 3 = Moderate ☐4 = Severe ☐	0 = No maceration ☐1 = Very slight softening ☐2 = Mild softening ☐ 3 = Moderate ☐4 = Severe ☐
5. Contact Dermatitis	0 = No reaction ☐1 = Slight reaction ☐2 = Moderate reaction ☐ 3 = Severe reaction ☐4 = Severe with vesicles ☐	0 = No reaction ☐1 = Slight reaction ☐2 = Moderate reaction ☐3 = Severe reaction ☐4 = Severe with vesicles ☐
6. Folliculitis	0 = No inflammation ☐1 = Mild irritation ☐2 = Moderate irritation ☐3 = Severe inflammation ☐ 4 = Infected ☐	0 = No inflammation ☐1 = Mild irritation ☐2 = Moderate irritation ☐3 = Severe inflammation ☐ 4 = Infected ☐

4.2.1 OVERVIEW

This is a nonblinded study to measure the following, in two randomized groups: ½ of the study patients that have prescribed NPWT will receive the standard of care NPWT KCI V. A. C. drape and ½ of the patients will receive the NPWT Comfort Release drape.

Skin irritation and skin injury: At time of removal, clinicians will assess associated skin irritation and injuries using the MARSI classification scoring system. Briefly, the clinician will utilize the four-point scoring system for 1) erythema, (scale ranks from no erythema (0) to severe erythema (4). Participating clinicians will be trained (led by Clinical Research Coordinator, Denise Anderson, RN, WCC) on how to identify and measure MARSI across presentations (erythema lasting more than 30 minutes, skin

stripping, folliculitis, maceration, tension/injury blister, allergic contact dermatitis and irritant contact dermatitis). All incidences of MARSI will be recorded.

Table: Description of MARSI Injury

Skin Injury Type	Severity (0)	Severity (1)	Severity (2)	Severity (3)	Severity (4)
Erythema (Redness)	No redness: Skin is the normal color without any signs of irritation.	Very slight redness: A faint pinkish hue is visible where the adhesive was applied.	Well-defined redness: A clearly visible red area, but it is confined to the adhesive site and not raised.	Moderate redness: A more intense red color, possibly extending slightly beyond the adhesive area and may feel warm to the touch.	Severe redness: Deep, bright red color covering a larger area, possibly accompanied by swelling.
Skin Stripping	No stripping: Skin is intact with no visible damage.	Very slight stripping: A very small patch of skin appears slightly abraded, but no underlying tissue is visible.	Partial epidermal loss: A noticeable area where the top layer of skin has peeled away, exposing a raw surface.	Full-thickness stripping: Complete removal of the skin's upper layers over a small area, possibly with some bleeding.	Severe stripping: Extensive stripping over a larger area, leaving deep, raw, and potentially bleeding tissue exposed.
Tension Blisters	No blisters: No blisters present on the skin.	Very small blister: A tiny, clear fluid-filled blister less than 5mm in diameter.	Small blister: A slightly larger blister, between 5mm and 10mm, but still intact.	Large blister: A sizable blister larger than 10mm, possibly painful and starting to rupture.	Severe blister: Multiple or very large blisters that have ruptured, leaving raw, painful skin exposed.
Maceration	No maceration: Skin appears dry and healthy without any signs of moisture damage.	Very slight softening: The skin appears slightly softened with a faint whitish hue, indicating mild moisture exposure.	Mild softening: The skin is moderately softened, and a larger area has a white, waterlogged appearance.	Moderate maceration: The skin is soft, swollen, and white, showing more severe effects of moisture damage.	Severe maceration: The skin is severely softened, white, and may be peeling or breaking down, with signs of potential infection.
Contact Dermatitis	No reaction: No visible signs of a reaction; the skin appears healthy.	Slight reaction: A small area shows slight redness or itching, but no blistering or swelling.	Moderate reaction: More widespread redness, itching, and slight swelling, but no severe skin changes.	Severe reaction: Redness, swelling, and possibly small blisters, with pronounced itching or discomfort.	Severe with vesicles: Severe swelling, redness, and the presence of multiple fluid-filled vesicles (small blisters) over the affected area.

Folliculitis	No inflammation: Hair follicles are normal, with no signs of irritation.	Mild irritation: Hair follicles appear slightly red or irritated but no swelling or pus.	Moderate irritation: The follicles are visibly inflamed, with moderate redness and possibly a small amount of pus.	Severe inflammation: The area is very red and swollen, with larger amounts of pus visible around multiple hair follicles.	Infected: Severe redness, swelling, and infection, with significant pus, possibly extending deeper into the skin.

Pain: Taking repeated measures of pain is best practice for pain intensity measurement. Immediately prior to adhesive removal clinicians will ask patients to assess pain using the Indiana Polyclinic Combined Pain Scale and record a baseline pain measure. This will then be repeated during and immediately after adhesive removal. This ten-point scale provides criteria for each score, ranging from "No pain" (0) to "Worst Imaginable – Paralyzing; person is in and out of consciousness and near death as a result of the pain. Emergency medical attention and hospitalization are required".

Treatment compliance: Patient treatment plan adherence is a known challenge with NPWT. In this study we will assess patient compliance to the prescribed NPWT. Instances of patients prematurely stopping treatment will be recorded.

Medication use: Patient use of narcotics, pain, and stress reducing medications prescribed to patients undergoing the dressing removal will be recorded throughout the duration of the study. These data will be used to assess any differences in usage between the two treatment groups.

Leak rate: During the NPWT application clinicians will be instructed to record any incidence of leaks (as alerted by vacuum pump machine) that occur as a result unsealed adhesive. With any leak, the clinicians will record steps to remediate the leak (e.g., applying additional adhesive strips).
and homogenous variance will be assessed visually using plots of the model residuals.

Clinician acceptability Questions provided to clinician at each dressing removal.

Economic Analysis: Using collected data from serial-use application participants (patient chart data, clinical surveys), we will perform an economic analysis to evaluate the potential for time added value with Comfort Release® drapes compared to standard of care. Variables that will be included in the analysis include clinician time; cost of materials; medication use cost; and length of treatment period.

4.2.2 SAMPLE SIZE DETERMINATION

Sample Size Justification for Aim1, single-use NPWT:
Sample sizes of 100 patients per randomization group (n=50 patients per randomization group from each of two hospital facilities) will allow for a standardized mean difference

of 0.4between the treatment groups to be considered statistically significant at an $\alpha = 0.05$ level with 80% power. An effect size of $d = 0.4$ is considered a moderate effect size and would translate to a mean difference of 1 unit on the MARSI classification scoring system assuming a within group standard deviation of 2.5; and a mean difference of 4 units on the Indiana Polyclinic Combined Pain Scale assuming a within group standard deviation of 10.

Sample Size Justification for Aim2, multi-use NPWT:
Sample sizes of 50 patients per randomization group (from a single hospital facility) will allow for an overall standardized mean difference of $d = 0.6$ between the treatment groups to be considered statistically significant at an $\alpha = 0.05$ level with 80% power. An effect size of 0.6 is considered a moderate effect size and would translate to a mean difference of 1.5 units on the MARSI classification scoring system assuming a within group standard deviation of 2.5; and a mean difference of 6 units on the Indiana Polyclinic Combined Pain Scale assuming a within group standard deviation of 10. We expect a larger effect size in Aim 2 patients than patients than the Aim 1 patients because the rate of MARSI is much higher in serial-use NPWT applications.

4.2.2.1 STATISTICAL METHODS

Statistical Analysis:
For single-use NPWT, measures of skin irritation, injuries, and pain will be analyzed using linear models to compare Comfort Release® drapes with VAC drapes while controlling for gender, age,
hospital facility, and other relevant patient comorbidities. All hypothesis tests will be two-sided and p-values <0.05 will be considered statistically significant. Model assumptions of normality and homogenous variance will be assessed visually using plots of the model residuals.

For serial-use NPWT, measures of skin irritation and injuries and pain collected repeatedly after each drape change will be analyzed using linear mixed models to compare Comfort Release® drapes with V.A.C. drapes. Fixed effects will include treatment group (intervention vs. control), time, an interaction between treatment group and time, gender, age, and other relevant patient comorbidities. Models will include a random effect of the patient id to control for the repeated measurements taken on patients over time. All hypothesis tests will be two-sided and p-values <0.05 will be considered statistically significant. Model assumptions of normality and homogenous variance will be assessed visually using plots of the model residuals.

4.2.2.1.1 SUBJECT POPULATION FOR ANALYSIS

Aim1.

Post-surgical inpatient participants (n=200) prescribed NPWT by the treating physician will enroll in this study. Any patient meeting the inclusion criteria of: patient is 18 years or older, scheduled for non-emergency surgery; a plan of treatment using NPWT; access to V.A.C. by KCI drape and NPWT kits; patient ability to verbally communicate are eligible. Exclusion criteria include known hypersensitivity to acrylic adhesives; known hypersensitivity to isopropyl alcohol; NPWT treatment within past 3 months, unconscious patient during the expected time of the drape removal/change; under the age of 18 years; unable to give consent; and language barrier, unless interpreter is readily available.

Aim2.

Chronic wound patients (n=100) prescribed NPWT will be enrolled in this study for inpatient serial use NPWT applications. Inclusion criteria are: patient is 18 years or older, NPWT recommended by the treating physician; a plan of treatment using NPWT; access to VAC by KCI drape and NPWT kits; patient ability to verbally communicate. Exclusion criteria include known hypersensitivity to acrylic adhesives; known hypersensitivity to isopropyl alcohol; NPWT treatment within past 3 months, unconscious patient during the expected time of the drape removal/change; under the age of 18 years; unable to give consent; and language barrier, unless interpreter is readily available.

4.2.2.1.2 PRIMARY ANALYSIS METHOD

For single -use NPWT:

To demonstrate that compared to market leader (VAC NPWT drapes), patients with the Comfort Release® drapes have statistically significant (α=0.05): 1) decreased medical adhesive-related skin irritation and injuries, as measured by the MARSI scoring system, 2) lower experience of pain, as measured by the Indiana Polyclinic Combined Pain Scale, 3) decreased use of medications for pain and stress related to dressing removal, 4) demonstrate equivalent or improved effectiveness in maintaining seal compared to control (leak incidence rate), and 5) establish clinician acceptability of the Comfort Release® drape: average questionnaire scores >4.

For serial-use NPWT, measures of skin irritation and injuries and pain collected repeatedly after each drape change will be analyzed using linear mixed models to compare Comfort Release® drapes with V.A.C. drapes. Fixed effects will include treatment group (intervention vs. control), time, an interaction between treatment group and time, gender, age, and other relevant patient comorbidities. Models will include a random effect of the patient id to control for the repeated measurements taken on patients over time. All hypothesis tests will be two-sided and p-values <0.05 will be considered statistically significant. Model assumptions of normality and homogenous variance will be assessed visually using plots of the model residuals.

In Aim 2 (serial-use NPWT) the methodology is to demonstrate that compared to VAC NPWT drapes, patients with Comfort Release® drapes have statistically significant (α=0.05): 1) decreased medical adhesive-related skin irritation and injuries, as measured by the MARSI scoring system, 16 2) lower experience of pain, as measured by the Indiana Polyclinic Combined Pain Scale,17 3) improved compliance to the full duration of treatment as prescribed by clinician, 4) decreased use of medication for pain and stress related to dressing removal, 5) demonstrate equivalent or better effectiveness in maintaining seal compared to control (leak incidence rate), 6) demonstrate clinician acceptability (questionnaire score >4) 7) demonstrate the ability of Comfort Release® drape to reduce nursing time by at least 20% compared to VAC drape; and 8) demonstrate significant time added economic value compared to VAC drape through economic analysis.

4.2.2.1.3 IMPUTATION METHOD WHEN HANDLING MISSING DATA IN THE PRIMARY ANALYSIS

Imputation is the process of replacing the missing date with estimated value based on other available information. Instead of deleting any patient that has missing information, the current study approach preserves all cases by replacing the missing data with a probable value estimated by other available information on the same patient with other drape changes. This will allow each patient's data to be analyzed using standard statistical techniques.

4.2.2.1.4 JUSTIFICATION OF ZERO SUPERIORITY MARGIN

The aim of demonstrating superiority of the Comfort Release® drape showing that the product is 'superior' to the V.A. C. drape, which is the current standard treatment used in both medical centers. The data from these trials are assessed for statistical significance That is, do the data show a difference between the drapes. The Comfort Release® product can be shown to be superior if results are statistically significant. This does not necessarily mean that the findings have clinical relevance. Statistical significance is a mathematical confirmation that the sample size is adequate to sufficiently determine if the data shows that a visible effect exists within the sample. Superiority is shown statistically when the difference between the mean of the new treatment drape and the mean of the standard treatment drape is not equal to zero within a

95% two-sided confidence interval. The difference between their means are different statistically to a significance of 5% (p=0.05).

4.2.3 ENROLLMENT

Post-surgical patients (n=200) will be enrolled at Weill Cornell under PI. Dr. Robert Winchell and at Columbia Presbyterian hospital under co-investigator Dr. Jarrod Bogue for single-use NPWT. Patients will be randomized to control (V.A.C. drape) or intervention (Comfort Release® drape).

Chronic wound patients (n=100) will be enrolled at Weill Cornell Medical Center under Principal Investigator Dr. Robert Winchell. Patients will be randomized to control (V.A.C. drape) or intervention (Comfort Release® drape).

4.2.4 STUDY DURATION

Post-surgical patients (n=200) enrolled at Weill Cornell under PI. Dr. Robert Winchell and at Columbia Presbyterian hospital under co-investigator Dr. Jarrod Bogue will occur over one year with interim checkpoints every 3 months to evaluate technical process and enrollment. For the treatment to be effective, the applied NPWT must maintain a strong adhesive seal for the duration of the treatment (1-7days).

Chronic wound patients (n=100) will be enrolled at Weill Cornell Medical Center under Principal Investigator Dr. Robert Winchell over two years.

4.2.5 INCLUSION CRITERIA

Inclusion of Individuals Across the Lifespan
Adults of all age ranges will be included in this study. Children will not be included as 1) we would like to test our novel drape technology in adults first and 2) there are no pediatric or neonatal guidelines for negative pressure wound therapy.

Inclusion of Women and Minorities
Women and minorities will be represented in this study. We will make our best effort to recruit across all races and ethnicities and aim to have a study population that is representative of the demographics of the United States, however actual study enrollment may be limited due to the available patients.

Inclusion criteria for Aim 1 are:

1. patient is 18 years or older,
2. scheduled for non-emergency surgery,
3. NPWT recommended by the treating physician;
4. a plan of treatment using NPWT;
5. access to V.A.C. by KCI drape and NPWT kits;
6. patient ability to communicate pain using a scale.

Inclusion criteria for Aim 2 are:

1. patient is 18 years or older,
2. NPWT recommended by the treating physician;
3. a plan of treatment using NPWT;
4. access to VAC by KCI drape and NPWT kits;
5. patient ability to communicate pain using a scale.

4.2.6 EXCLUSION CRITERIA

Exclusion criteria for Aim 1include:

1. known hypersensitivity to acrylic adhesives;
2. known hypersensitivity to isopropyl alcohol;
3. NPWT treatment within past 3 months,
4. The patient is expected to be unconscious during the drape removal/change;
5. unable to give consent; and language barrier, unless an interpreter is readily available.

Exclusion criteria for Aim 2 includes:

1. known hypersensitivity to acrylic adhesives;
2. known hypersensitivity to isopropyl alcohol;
3. NPWT treatment within past 3 months,
4. The patient is expected to be unconscious during multiple drape removals/ changes;
5. unable to give consent;
6. and language barrier, unless interpreter is readily available.

4.2.7 PRIOR AND CONCOMITANT THERAPY

Patients with NPWT within the previous 3 months of possible study are excluded. Any other concomitant therapy that study patient might be receiving is allowed as determined by the treating physician.

4.2.8 TREATMENT REGIMEN

Negative pressure wound therapy as ordered by treating physician.

Control patients using the KCI V.A.C. drape will use the facilities standard operating procedures for the drape application and removal, established at the medical centers.

Study patients receiving the alternate Comfort Release® drape will have the following directions for use by the clinicians in the study:

Application of the Comfort Release® drape:
Step 1. Cut and place the drape to cover foam or dressing, with an additional 1"-2" overlap onto intact peri-wound skin. Maintain at least one edge with a portion of the blue #2 tab.

Step 2. Remove layer #1 to expose the adhesive. Place the adhesive side down over wound dressing/foam pad and adjacent skin. Smooth the drape over the skin to prevent creasing.

Step 3. Remove layer #2. Next, to remove the blue #3 handling tab(s), hold the drape side of the perforation steady with one hand. Then use your other hand to pull and remove the blue tab #3 along the perforation line. A small portion of the tab remains on the drape (to assist with drape removal). Pat down to assure a good seal.

Step 4. Follow facility protocol and manufacturer's directions to complete the application of the NPWT device

Removal of the Comfort Release® drape:

Step 1 Lift and swipe under the residual drape tab with alcohol prep pads or alcohol swab sticks, until the drape lifts easily from the skin. Continue to wet the underside of the drape, where it meets the skin.

Step 2 Use additional alcohol prep pads or alcohol swab sticks, as needed, to keep the underside edge of the drape wet, to loosen the drape from the skin.

Step 3 Carefully remove all the foam/dressing pieces from the wound bed. Note the number of pieces removed per facility protocol.

Step 4 Discard the used drape and foam/dressing pieces per facility protocol.

4.2.9 POSTOPERATIVE REGIMEN

SAME CARE AS IS STANDARD FOR NPWT.

4.2.10 CASE REPORT FORMS

See attachments for:

- Aim 1 Training Protocol Manual with Case Report Forms
    - Eligibility
    - Demographics & Medical History
    - Participant Consent Forms (CUIMC-ICF or WCU-ICF)
    - Concomitant Medication Log
    - Drape Application Directions and Questions
    - Drape Removal Concomitant Medication Log
    - Drape Removal Directions and Questions
    - Drape Removal Pain Assessment
    - Drape Removal Skin assessment
    - Drape Re-Application Directions and Questions (use only if more than one drape application is needed)
    - Early NPWT Discontinuation (Early Exit Questionnaire)
- Aim 2 Training Protocol Manual with Case Report Forms
    - Eligibility
    - Demographics & Medical History
    - Concomitant Medication Log
    - Drape Application Directions and Questions
    - Drape Removal Concomitant Medication Log
    - Drape Removal Directions and Questions
    - Drape Removal Pain Assessment
    - Drape Removal Skin Assessment
    - Drape Re-Application Directions and Questions
    - Early NPWT Discontinuation (Early Exit Questionnaire)

4.3 RISK ANALYSIS

Comfort Release® technology has been successfully commercialized in acute and advanced wound care products including bandages, tapes and dressings.

Prior to usage in this study, the Comfort Release® drape has undergone rigorous internal quality testing to ensure its utility for study applications. These tests were used to determine the optimal formulation of the switchable adhesive in the drape. For example, groups of volunteers have already worn the new Comfort Release® drape material and followed directions for successful removal (Data available, upon requested).

In addition, in the unlikely event that product performance milestones are not met, we can modify our prototype by implementing a change in formulation of adhesive and polymer used in its manufacture; these decisions will be dependent on the observed issue. We have already engineered several adhesive formulations that could be easily implemented

if a change is needed. Further, if our enrollment target is not reached, we may need to extend the study length beyond two years.

Risk of the Comfort Release Drape:
Subjects may experience discomfort, pain, irritation, or skin injury with the use of the Comfort Release® drape. Subjects will not participate in this study if you have known sensitivity to acrylic adhesive on the skin.
As with any NPWT drape on the market, the airtight seal on your NPWT may leak air even when the Comfort Release® drape is applied correctly.

Risks of Rubbing Alcohol:
Anyone with known sensitivity to rubbing alcohol on the skin should not participate in this study.
Rubbing alcohol or our standard acrylic adhesives may irritate the skin of some individuals.

Unknown Risks
There may be other risks of taking part in this research study that we don't know about. Subjects will be told if we learn about other risks that can affect their participation in the study.

Discomfort with Questionnaires
The exit questionnaire completed if subjects withdraw from the study can make them uncomfortable. Subjects do not need to answer any questions that they are not comfortable with.

Privacy
To protect subjects' confidentiality, all subjects' data will be assigned numerical study identifiers or "codes." No identifiable information will be provided to GLOBAL BIOMEDICAL TECHNOLOGIES, LLC. Before subject data are shared, the study doctor and staff will replace any information that could directly identify a subject (such as name, address, and contact information) with a generic code which the sponsor cannot link to that subject's identity to protect the confidentiality of the data.

4.4 DESCRIPTION OF DEVICE

This Direct-to-Phase II project will advance an adhesive acrylic NPWT drape incorporating novel OGS resin with pressure sensitive acrylic that releases from the skin with the addition of alcohols. This patented Comfort Release® drape is applied to intact skin surrounding the wound bed packed with sponge or gauze. At removal, isopropyl alcohol is applied to the adhesive interface over intact skin. This painless adhesive technology exhibits high patient satisfaction and decreased nursing time in bandage and

tape applications. This project will demonstrate a) the equivalence of performance; and b) the reduction of MARSI and pain of Comfort Release® NPWT drapes against the market leader, V.A.C. drape (KCI Technologies, Inc.).

4.5 MONITORING PLAN

Our team comprises experienced wound care professionals and clinicians from multiple specialties at Weill Cornell and Columbia Presbyterian Hospitals. This team is highly knowledgeable in the use of NPWT for chronic wound and post-surgical applications and is well-equipped to quickly recognize and address complications specifically related to NPWT.

The monitoring plan prioritizes collecting data relevant to the study objectives. Adverse event (AE) monitoring will focus on events occurring within 1 hour of device removal and deemed related to the removal procedure or the device itself.

4.5.1 PRIMARY SAFETY ENDPOINTS

The primary safety endpoints for this study are:

- The occurrence of adverse events directly related to the removal of the device, recorded within 1 hour post-removal.
- Adverse events will be assessed for severity and attribution (e.g., definite, probable, possible, unlikely, or unrelated). Only events classified as definite, probable, or possible within the specified timeframe will be included in the study's analysis.
- This streamlined data collection process ensures the study focuses on device-specific safety outcomes while excluding unrelated events.

4.5.2 DEFINITIONS

Attribution: The determination of whether an AE is related to a medical treatment or procedure.

ATTRIBUTION CATEGORIES DESCRIPTION

- **Definite:** The adverse event *is clearly related* to the investigational agent
- **Probable:** The adverse event *is likely related* to the investigational agent
- **Possible:** The adverse event *may be related* to the investigational agent
- **Unlikely:** The adverse event *is doubtfully related* to the investigational agent
- **Unrelated:** The adverse event *is clearly NOT related* to the investigational agent
- **Adverse Event (AE):** Any adverse experience that occurs within 1 hour of device removal and is deemed related to the device or procedure.

Disability: A substantial disruption of a person's ability to conduct normal life functions.

Life-threatening Adverse Event: Any adverse device experience that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred (i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death).

Serious Adverse Event (SAE): Any adverse device experience, related to the research intervention that results in any of the following outcomes: death, a life-threatening adverse device experience, inpatient hospitalization or prolongation of existing hospitalization, any 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 a serious adverse device experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Unexpected Adverse Event: Any adverse device experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. "Unexpected" as used in this definition refers to an adverse device experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the device.

4.5.3 RECORDING OF ADVERSE EVENTS

Only adverse events occurring within 1 hour of device removal and deemed related to the removal procedure or device will be recorded. Events unrelated to the device or study intervention will not be collected. Documentation will be based on patient testimonials and investigator evaluation.

4.5.4 REPORTING OF SERIOUS ADVERSE EVENTS

The following events, occurring within 1 hour of device removal and related to the procedure or device, will be reported:

- Moderate and Severe Events – Events that are Unexpected and Possibly, Probably, or Definitely Related/Associated with the device removal.
- ALL Life Threatening or Disabling Events Related to Device Removal
- ALL Fatal Events – When the event occurs within 1 hour of device removal and is related to the procedure or device.

4.5.4.1 STUDY SPONSOR NOTIFICATION BY INVESTIGATOR

All adverse events will be recorded and sent to the Sponsor.

4.5.4.2 IRB NOTIFICATION BY INVESTIGATOR

Reports of all unexpected problems (UPs) (including follow-up information) must be submitted to the IRB within 7 days.

4.5.5 UNBLINDING PROCEDURES

This is an unblinded study both for both study patients and all healthcare professionals involved in the care of a study patient.

4.5.6 STOPPING RULES

NPWT is stopped by the treating clinician.

The patient (in either group) has a known reaction or develops or experiences a hypersensitivity or allergic reaction to the acrylic adhesive in the drape or a reaction to common isopropyl alcohol (rubbing alcohol).

4.5.7 INTERNAL DATA AND SAFETY MONITORING BOARD

Internal data review and safety every 3 months:

That compared to VAC NPWT drapes, patients with Comfort Release® drapes have statistically significant (α=0.05): 1) decreased medical adhesive-related skin irritation and injuries, as measured by the MARSI scoring system, 2) lower experience of pain, as measured by the Indiana Polyclinic Combined Pain Scale, 3) improved compliance to the full duration of treatment as prescribed by clinician, 4) decreased use of medication for pain and stress related to dressing removal, 5) demonstrate equivalent or better effectiveness in maintaining seal compared to control (leak incidence rate), 6) demonstrate clinician acceptability (questionnaire score >4) 7) demonstrate the ability of Comfort Release® drape to reduce nursing time by at least 20% compared to VAC drape; and 8) demonstrate significant time added economic value compared to VAC drape through economic analysis.

4.5.8 INDEPENDENT DATA AND SAFETY MONITORING BOARD

Independent data review will be conducted every 3 months.

That compared to VAC NPWT drapes, patients with Comfort Release® drapes have statistically significant (α=0.05): 1) decreased medical adhesive-related skin irritation and injuries, as measured by the MARSI scoring system, 2) lower experience of pain, as measured by the Indiana Polyclinic Combined Pain Scale, 3) improved compliance to the full duration of treatment as prescribed by clinician, 4) decreased use of medication for pain and stress related to dressing removal, 5) demonstrate equivalent or better effectiveness in maintaining seal compared to control (leak incidence rate), 6) demonstrate clinician acceptability (questionnaire score >4) 7) demonstrate the ability of Comfort Release® drape to reduce nursing time by at least 20% compared to VAC drape; and 8) demonstrate significant time added economic value compared to VAC drape through economic analysis.

5. MANUFACTURING INFORMATION

Global Biomedical Technologies has already gained a presence in the adhesive acute and advanced wound care market, so a logical transition would be to develop Comfort Release® drapes for NPWT in specific medical markets for both post-surgical and chronic wound patient use. Global Biomedical Technologies has developed an adhesive acrylic NPWT drape (Made in the USA) that incorporates innovative ester oligomers that release from the skin via the application of isopropyl alcohol. The underlying technology is a pressure sensitive bioengineered medical adhesive made with oligo (glycerol sebacate) and polyacrylate. This painless adhesive technology, “Comfort Release®,” has

been demonstrated to result in high patient satisfaction and decreased nursing time in bandage and tape applications.

Successful completion of this project is expected to yield the data needed to support a 510K FDA clearance.

Global Biomedical Technologies is FDA registered as a medical device manufacturer for both Class I and Class II devices.

9. NAME AND ADDRESS OF THE INVESTIGATIONAL INSTITUTION

Columbia University Medical Center
622 West 168th Street
New York, NY 10032
(P) 212-305-2500

10. FINANCIAL CLAIMS

10.1 FUNDING SOURCE

This project is funded by a Direct Phase II clinical study by the NIH.
NIH Score: 20

10.2 CONFLICT OF INTEREST

Dr. Jason Spector and Dr. Yadong Wang, both faculty at Weill Cornell are listed consultants to the NIH grant and have minority ownership in Global Biomedical Technologies, LLC. Neither will be involved in the clinical study.

10.3 SUBJECT STIPENDS OR PAYMENTS

Patients will receive no payments for participating in the study from the Sponsor.

11. ENVIRONMENTAL ASSESSMENT

Per Device Advice on the CDRH Web site,
http://www.fda.gov/cdrh/devadvice/ide/application.shtml, an environmental assessment

as required under 21 CFR 25.40 or a claim for categorical exclusion under 21 CFR 25.30 or 25.34 is no longer required.

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15. ATTACHMENTS

- Efficacy of Comfort Release Sacral Bordered Foam Dressings, 2023
- Prototype drape testing (S-2747)
- GB141-A IFU
- Aim 1 Case Report Forms
    - Demographic and Medical History
    - Eligibility Criteria
    - Initial Concomitant Medication Log
    - Initial Drape Application Directions and Questions
    - Drape Removal Concomitant Medication Log
    - Drape Removal Directions and Questions
    - Drape Removal Pain Assessment
    - Drape Removal Skin Assessment
    - Drape Re-Application Directions and Questions
    - Early NPWT Discontinuation – Early Exit Questionnaire
- Aim 2 Training Protocol Manual with Case Report Forms
    - Demographic and Medical History
    - Eligibility Criteria
    - Initial Concomitant Medication Log
    - Drape Application Directions and Questions
    - Drape Removal Concomitant Medication Log
    - Drape Removal Directions and Questions
    - Drape Removal Pain Assessment
    - Drape Removal Skin Assessment
    - Drape Re-Application Directions and Questions
    - Early NPWT Discontinuation – Early Exit Questionnaire