An Acelity Company

THE MANAGEMENT OF CLOSED SURGICAL INCISIONS RESULTING FROM INCISIONAL HERNIA REPAIR AND/OR FUNCTIONAL PANNICULECTOMY USING THE PREVENA™ CUSTOMIZABLE™ DRESSING

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Protocol Agreement Page

I confirm that I have read the protocol entitled: "**The Management of Closed Surgical Incisions Resulting from Incisional Hernia Repair and/or Functional Panniculectomy Using Prevena™ Customizable™ Dressing**" dated December 20, 2016 (Version 8.0). I understand the protocol and agree to conduct the study according to the procedures therein in accordance with the Federal Drug Administration (FDA) Code of Federal Regulations (CFR) as well as the International Conference on Harmonisation (ICH) principles of Good Clinical Practice (GCP).

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Signature:_____ Date:_____
Principal Investigator

1 Introduction

1.1 Background

In the United States (US), obesity has reached epidemic proportions, as the number of citizens with a body mass index (BMI) over 30 kg/m^2 amounts to more than a third of the population. Of this obese demographic, morbidly obese individuals, grade 2 (BMI 35≥40) and grade 3 (BMI ≥40), make up more than a 20% of the total number[1]. Additionally, the most recent national data on obesity prevalence among U.S. adults, adolescents, and children show that almost 17% of children and adolescents were obese in 2009–2010. A study by the *Centers for Disease Control and Prevention* (CDC) predicts that obesity rates in the United States will reach up to 42 percent of the population by the year 2030. More than 10 percent will be classified as "morbidly obese," which is 100 pounds or more over a healthy weight range. If these predictions come true, health care costs in the U.S. will increase by well over half a trillion dollars[2].

Bariatric surgery and subsequent weight loss are intended to significantly improve the health of the morbidly obese patient. However, as these patients lose large amounts of weight they are almost always left with excessive folds of skin that cannot be reduced through diet and exercise alone. This is especially evident in the abdomen where the hanging panniculus is almost uniformly present in this patient population.[3] While a patient's BMI can decrease dramatically due to massive weight loss, the residual hanging skin can often lead to long term health problems.

Patients who have undergone massive weight loss, often present with body contour deformities involving a panniculus weighing from <15 to 50 lbs or greater. Symptoms vary among patients and are related to the degree of redundancy and weight of the panniculus. Without effective treatment, panniculitis, cellulitis, interatriginous dermatitis, or folliculitis may occur, which adversely affect patients quality of life. Blistering, abscess formation, gangrene, back pain, abdominal fascial laxity, and cosmetic deformity are also found in individuals with heavier panniculi. Odor resulting from hygiene problems caused by an excessive amount of hanging skin can also affect quality of life.[4] Surgery to remove the panniculus and restore a more normal abdominal contour is often the only effective option to resolve these various maladies.

It is no surprise then that body-contouring procedures following massive weight loss continue to increase in number as more patients undergo bariatric surgical procedures. These patients will often have redundant skin and subcutaneous tissue in both the horizontal and vertical vectors.[5] Abdominal contour deformities represent the most common complaint among massive weight

loss patients presenting for plastic surgery. According to the American Society of Plastic Surgeons, abdominoplasty is the fifth most common cosmetic surgical procedure.

While similar to abdominoplasty, a panniculectomy is the surgical removal of the panniculus and is commonly performed after the patient presents with weight loss achieved through bariatric surgery, diet, and exercise, and, in a minor subset of cases, at the time of bariatric surgery. Additional procedures such as hernia repair, abdominal muscle tightening, and skin reduction of back, chest, or legs are also often performed at the time of the abdominoplasty/panniculectomy [6] Recently, Gurunluoglu *et al*, suggested classification of a patient's panniculus may aid in informing surgeons about practical surgical guidelines that can be used during the removal.[7] Patients who have successfully lost massive amounts of weight and maintained that weight for a minimum of 3 months are candidates for body contouring surgery. Many aspects of the panniculus need to be evaluated as the anterior redundancy may be composed of both vertical and horizontal components, particularly in the epigastric region [8;9]

Incisional hernias are another of the many issues related to obesity and are part of the broader category of ventral hernias, defined as an abnormal bulge protruding through the muscular tendinous layer of the abdominal wall. Ventral hernias may be congenital, protruding through naturally occurring weak spots of the abdominal wall, such as the umbilicus and the midline areas where muscles fuse during development. Alternatively, ventral hernias may occur in weakened areas of the abdominal wall that occur as a result of surgery.

Surgical incision sites of the abdomen never regain the full strength of the natural musculotendinous strength-layer of the abdominal wall. During the healing phase and even after the incision is completely healed, significant stress placed upon the abdominal wall can separate the tissue, creating a weak spot or hernia through which the contents of the abdomen can protrude. This is known as an incisional hernia. Such protrusions are much more likely to occur with weight gain and obesity.

The necessity of a traditional open repair involves the disadvantage of a larger scar that comes from open surgery as well as the need for extensive undermining in the plane between the subcutaneous fat and the fascia. This translates into more hospital time and more recovery time in the weeks following surgery. The larger wound also creates a greater opportunity for wound infection, an especially common complication in obese individuals.

1.2 Surgical Techniques of Abdominal Wall Reconstruction

1.2.1 Vertical Incision

An open surgical procedure to repair an incisional hernia often requires an extensive incision as well as extensive undermining in the subcutaneous plane. A vertical incision is made long enough to remove fat and scar tissue from the abdominal wall near the hernia and to adequately expose healthy fascial edges. The undermining that is required is often quite extensive in order to adequately expose healthy fascia in order to do a proper repair. The superficial fascial system is approximated when possible and often a synthetic or biologic mesh is used to reinforce the closure or in very large defects can bridge the fascial defect. A panniculectomy can be performed at the time of hernia repair using the vertical incision, a traditional transverse incision, or with a fleur-de-lis approach as well.

1.2.2 Transverse (Traditional) Incision

A lower abdominal transverse incision for panniculectomy is set at least 6 cm from the anterior vulvar commissure with the tissues on upward stretch, although the exact position of the inferior incision can vary depending on the individual patient's needs. In the mons region, the incision is carried directly down to the deep fascia. In massive weight loss patients, it is not uncommon for the low transverse incision to fall near or even below the inguinal ligament lateral to the mons. The final scar position will still be superior under tension. In such cases, care is taken to keep the dissection superficial until the fascia is approached superior to the inguinal ligament. The abdominal flap is dissected to the level of the umbilicus, which is often preserved on a stalk.

Dissection above the umbilicus is limited to the midline region whenever possible. Lateral abdominal flap dissection is performed as needed to allow for adequate redraping and is often performed in a discontinuous manner with a blunt instrument (e.g., liposuction cannula without negative pressure) to preserve perforating vessels. Fascial plication can be performed if significant laxity is present. After resection of the abdominal skin excess, the superficial fascial system is re-approximated over the mons and the skin is closed. If the tissues of the mons are lax, they are suspended directly to the abdominal wall fascia with permanent braided sutures.[3]

1.2.3 Fleur-de-Lis

The fleur-de-lis procedure may be performed for removal of the pannus alone or in combination with incisional hernia repair. For this procedure, both horizontal and vertical resections are required. After fascial plication is performed (if necessary), the horizontal resection is performed first as with a standard transverse incision. Once tissue is excised in that axis, sharp towel clips

are used to secure the tissue edges, and the limits of vertical resection are then reassessed with a pinch test to avoid over-resection. A vertical supraumbilical incision is extended to a level just caudal to the xiphoid process. Resection of this tissue is performed with minimal undermining outside of the area of resection with an emphasis on direct perforator preservation. The superficial fascial system of the vertical component is approximated and the skin incisions are closed as with the traditional technique. If retained, the umbilicus is inset directly into the vertical incision.

1.3 Post-Open Abdominal Surgery Outcomes

To maximize successful outcomes of open abdominal surgery for incisional hernia repair and/or panniculectomy, preoperative planning is required since considerations such as nutrition, smoking, mobility, wound care, pain management, and intravenous access can affect both surgery and recovery. In addition to the surgeon, dieticians, physical therapists, WOC nurses, pain specialists, aestheticians, and an ergonomist may be involved in the pre and postoperative management of the patient.

One opportunity for improvement may be a focused approach to improving the protection and management of the postoperative incision itself. When skin integrity is compromised for any reason, bacterial invasion can occur. Despite the many advances in the peri-operative care of patients in other areas, simple gauze dressings placed over a clean closed surgical incision remains the standard of care. Gauze dressings however, present a limited physical barrier to the entry of exogenous bacteria. One dramatic in vitro study showed that bacteria were capable of penetrating up to 64 layers of dry gauze.[10] Since postoperative incision management is essentially unchanged and surgical site infections and other surgical site complications continue to be problematic there is a clear need for research that examines postoperative surgical site management.

Surgical site infection (SSI) reduction has specifically been targeted with initiatives such as prophylactic antibiotic use, intra-operative patient warming and exacting handwashing methods, with some success. The very fact that SSIs still occur highlights the need for additional interventions and research.

1.3.1 Surgical Site Complications

In American hospitals alone, the Centers for Disease Control and Prevention (CDC) estimate that healthcare-associated infections (HAIs) account for an estimated 1.7 million infections and 99,000 associated deaths each year.[11] HAIs in hospitals are a significant cause of morbidity

and mortality in the United States. Of these infections, 17% to 22% are surgical site infections (SSIs).[12;13;14]

Certain surgical procedures and conditions can create difficulties in optimal incision healing, which could lead to postoperative incision infection, dehiscence, seromas, hematomas, and/or additional surgeries. Patients with multiple co-morbidities, such as obesity, diabetes, smoking, and poor vascularization, are at higher risk for surgical site complications. These complications include SSI, dehiscence, and seroma or hematoma formation.[15-17] SSI and dehiscence can lead to: 1) delayed healing rates; 2) increased direct medical costs (such as longer hospital stays and additional surgeries); 3) increased indirect costs (such as loss of productivity by the patient and family members); and 4) decreased patient satisfaction and quality of life.[18]

The CDC conducted a survey of operative procedures from 1992 to 2004 and stratified Subjects into groups according to their SSI risk factors. This survey reported SSI rates ranging from 0% to 3.72% for sternotomies, 2.71% to 7.53% for C-sections, 1.36% to 5.17% for abdominal hysterectomies, 0.86% to 2.52% for hip arthroplasty, and 0.88% to 2.26% for knee arthroplasty.[19]

In contrast to these fairly low rates of complications, those patients undergoing abdominal contouring surgeries have been reported in the literature to have a higher range of complication rates. In a retrospective study of 92 consecutive patients, Cooper *et al.,* reported that 43% suffered wound complications, with a reoperation rate of 14%[20], Arthurs *et al.,* in a retrospective cohort study in a tertiary care center, evaluated 126 post-bariatric panniculectomies performed over a 3-year period. Forty percent of patients experienced a complication (complication rates were as follows: seroma 17%, hematoma 13%, surgical site infection (SSI) 17%, transfusion 6%, skin breakdown/necrosis 11%, and re-exploration 11%).[21]

In Greco *et al.,* a retrospective institutional analysis was performed on 222 patients between 2001 and 2006 who underwent either abdominoplasty (N = 89) or panniculectomy (N = 133) procedures. Weight loss surgery (WLS) was performed in 63% of the patients prior to body contouring surgery. Overall, the wound complication rate in these patients was 34%; healing-disturbance 11%, wound infection 12%, hematoma 6%, and seroma 14%. WLS patients had an increase in wound complications overall (41% vs. 22%; $P = 0.01$) and in all categories of wound complications compared with non-WLS-patients by univariate methods of analysis.[7]

The open surgical repair of incisional hernias is associated with complication rates on par with those of panniculectomy surgery. Although the etiology of these surgical procedures differs, the

biological aspects are similar, requiring extensive incisions with undermining of the abdominal wall in the plane between the fascia and the subcutaneous fat.

The question of whether or not repair of incisional hernias are prone to a higher infection rate than other clean surgical procedures was asked by Houck, *et al.,* in a retrospective analysis which included 80 patients with incisional hernia repair. The incidence of wound infection after repair of incisional hernias during a 30 month period was analyzed and compared to the infection rate in all other clean procedures performed during the same period. In the 80 repairs of incisional hernias performed, there were 13 infections proved by culture, yielding an over-all infection rate of 16 percent. The authors conclude that repair of incisional hernias has a significantly higher rate of infection than do other clean general surgical procedures.[22]

Conde-Green *et al.,* conducted a retrospective analysis of 56 patients who underwent primary closure for large incisional hernia repair, of which 23 were treated with NPWT and 33 were treated with conventional dressings. The rates of overall complications in groups I and II were 22% and 63.6% respectively ($p = 0.020$).[23] While this study suggests that NPWT following open abdominal surgery significantly improves complication rates, it also shows that complication rates are comparable to those of abdominal contouring surgeries.

Another retrospective analysis conducted by Gassman, *et al.,* of patients with ventral hernia repair, also focused on treatment with NPWT versus conventional dressings. 63 patients were enrolled in the study, with a subset of 31 patients undergoing primary closure of the incision. Of this particular group of patients, the surgical site infection rate was 18% (primary closure/NPWT), and 55% (primary closure alone) ($p<0.01$).[24]

1.3.2 Additional General Information

The ultimate goal of both the patient and the surgeon is to achieve a successful surgical procedure without complications. To that end, and in order to optimize the outcome of body contouring surgery, it is mandatory to identify predictors both in terms of complications and patient satisfaction[25], as vertical, transverse, and fleur-de-lis incision complication rates in these patients can be quite high.

The past decade has brought about tremendous advances in surgical technique, and instrumentation, as well as other interventions such as prophylactic antibiotic administration, intra-operative patient warming and positive air flow ventilation in operating theaters, to name a few. All of these changes focus on generating a positive outcome for the patients. Despite these advances, a certain percentage of surgical site incisions still develop complications such

as infection, dehiscence, seroma or hematoma, which can put the surgical repair itself at risk and compromise healing. This failure to heal in a normal manner can have far ranging impact, including increases in patient morbidity and mortality. Patient co-morbidities such as obesity, vascular disease, diabetes mellitus, or immunosuppression, can all negatively impact surgical incision healing and are well noted in the surgical literature.

One opportunity for improvement may be a focused approach to improving the protection and management of the postoperative incision itself. One dramatic *in-vitro* study showed that bacteria were capable of penetrating up to 64 layers of dry gauze.[26] Since postoperative incision management is essentially unchanged and surgical site infections and other surgical site complications continue to be problematic, there is a clear need for research that examines postoperative surgical site management.

1.3.3 Review of NPWT and Surgical Incisions

NPWT as delivered by V.A.C.® Therapy has become a proven advanced wound therapy system for treating acute and chronic open wounds.[27-32]

Physicians and clinicians recognize the potential utility of this adjunctive therapy in their day-to-day practice and report using it in novel ways to address patient needs. For example, recent publications have documented clinical experience using NPWT over clean closed surgical incisions with successful outcomes.

In a prospective randomized evaluation, Stannard *et al.,* compared the use of NPWT against standard postoperative dressings (control) for draining hematomas and clean closed surgical incisions after high energy fractures.[33] In total, 44 Subjects were randomized into the hematoma study. The control group (n=31) drained for a mean of 3.1 days compared to only 1.6 days for the NPWT group (n=13) (p=0.03). An additional 44 Subjects were randomized into the fracture study. The control group (n=24) drained for 4.8 days compared to only 1.8 days for the NPWT group (n=20) (p=0.02).[34]

The high-energy fracture study was then expanded into a prospective randomized multicenter trial to further confirm the initial results of using NPWT over clean closed surgical incisions. The trial outcomes were presented at the American Academy of Orthopaedic Surgeons Conference in 2008 by Stannard *et al.*[35] The study population consisted of 249 Subjects with 263 calcaneus, pilon and tibial plateau fractures. Of those Subjects, 130 were randomized to NPWT (141 fractures) and 119 were randomized to control, standard postoperative dressings (122 fractures). The analysis revealed 14 total infections in the NPWT group compared to 23 in the

control group (p=0.049).[36] While the NPWT group was discharged on average one-half (0.5) day earlier than the control group, there were 12 cases of dehiscence in the NPWT group after discharge compared to 20 in the control group (p=0.044).[37]

Additional studies using NPWT for treatment of surgical incisions have been reported in the literature. In a retrospective review by Gomoll *et al.,* NPWT was placed over clean closed sutured incisions of 35 Subjects.[38] The procedures included revision hip arthroplasty, proximal femoral and tibial fracture fixation, and foot and ankle trauma. A non-adhesive permeable dressing covered the incision followed by 1-inch strips of reticulated open cell foam. The average length of NPWT per Subject was just over 3 days, and no infections occurred during the 3-month follow up.[39]

In another retrospective review, Atkins *et al,* reported on 57 adult cardiac surgery Subjects whose sternotomy incisions were treated with NPWT for 4 days.[40] These Subjects were deemed high risk for sternal wound infections after sternotomy based on a risk assessment model using pooled data from the Society of Thoracic Surgeons National Cardiac Database.[41] The risk factors included obesity, diabetes, length of cardiopulmonary bypass, and need for intra-aortic balloon pump. Of the 57 NPWT-treated Subjects, 77.2% were obese, 54.4% were diabetic, and 50.9% were both obese and diabetic. Based on the risk assessment model, a minimum of 3 predicted cases of deep sternal wound infection (DSWI) (based on the average estimated risk, 6.1 ± 4%, for postoperative DSWI) were anticipated. No complications were observed in the NPWT group. [42]

Reddix *et al.,* reviewed Subjects treated over a 9-year period and presented the results of 19 morbidly obese (BMI ≥ 40) Subjects who had NPWT applied to clean closed incisions after surgery for acetabular fractures.[43] The mean follow-up period was 21 months. Similar to previous studies, the incision was covered with a non-adherent layer followed by the reticulated open cell foam. There were no incision complications or infections during the peri-operative period and no complications at the final follow-up.[44]

In a more recent analysis by Reddix *et al.,* comparisons of wound infection and dehiscence were made in Subjects over a 5 year period (August 1996–June 2001) before NPWT over closed incisions was used as part of the postoperative protocol for acetabular fracture surgery and over a 4 year period (July 2001–April 2005) after NPWT over closed incisions became standard of care at the author's institution.[45] Sixty-six consecutive Subjects treated with standard institutional postoperative care in the previous 5 years had 4 (6.06%) deep wound infections and 2 (3.03%) dehiscences. After establishment of NPWT on the closed incisions,

235 Subjects had 3 (1.27%) deep wound infections and 1 (0.426%) had a dehiscence. The authors noted that their NPWT infection rate of 1.27% represented a significant decrease in comparison to other groups (infection rates of 4.2%,[46] 4%,[47] and 5%[48]) of similar size (p=0.0282; reference rate = 4%).[49] Collectively, the findings from these studies support using NPWT over clean closed surgical incisions and have led to the development of Prevena™ Incisional Management System (PIMS) to simplify the application of negative pressure over incisions. PIMS incorporates the functional elements of V.A.C.® Therapy that are necessary for use on closed wounds in a portable platform.[50]

In a recent prospective study by Payrits T. *et al.*, (2012), PIMS was applied to the closed surgical groin incisions of 13 Subjects who had just undergone vascular surgery. The duration of therapy ranged from 4-7 days and there were no reported incidences of wound infections during the study. Medical literature estimates that the wound infection rate in this patient population is up to 24%.[51]

A case series by Vargo, *et al.,* compared V.A.C.® Therapy over closed incision to the standard of care of patients with complex abdominal reconstruction. The 30 patients included were identified as having at least two infection risk factors. Historical controls were used for the comparison and those patients had a wound infection rate of 20%. The V.A.C.® Therapy over closed incision had a significantly lower infection rate of 3% ($p<.05$) indicating the benefit of NPWT for incision management.[52] PIMS, while gaining acceptance and clinical adoption, has limitations due to the linear nature and length of the peel and place dressing. Panniculectomy surgical incisions can average 60 cm in length (much longer than the 8 inch PIMS dressing can accommodate) and non-linear incisions such as the fleur-de-lis cannot be covered by the PIMS dressing since alteration of the dressing is not recommended.

Thus to provide for a clinical need, KCI had designed the Prevena™ Customizable™ Dressing, which can be cut-to-size and arranged to cover linear incisions greater than 8 inches in length, as well as uniquely shaped non-linear incisions. Another benefit of this new dressing is its ability to be used with a Prevena™ therapy unit or V.A.C. NPWT devices.

1.4 Description of the Products Under Study

1.4.1. Prevena™ Customizable™ Dressing Kit

Prevena™ Customizable™ Dressing or Prevena Plus™ Customizable™ Dressing kits will be provided by KCI as the study product to be tested in this study and will be labeled as

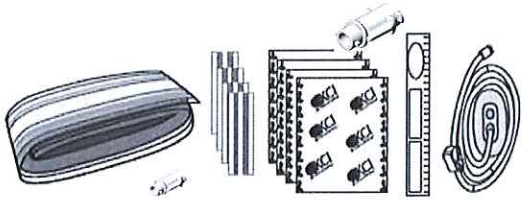
"Investigational Use Only" per FDA requirements. Instructions for use will be provided to each site.

The contents of the kit are listed below (shown in Figure 1):

- Prevena™ Customizable™ Dressing or Prevena Plus ™Customizable™ Dressing sealing strips
- drape
- ruler
- indicator or SensaT.R.A.C.™ pad with tubing
- tubing connector for V.A.C. units (if needed)

Figure 1. Prevena™ Customizable™ Dressing Kit Contents

Prevena Plus™ Customizable™ Dressing Kit



Prevena™ Customizable™ Dressing Kit

1.4.3 Prevena™ Customizable™ Dressing Description

The Prevena™ Customizable™ Dressing is a unique design that gives the clinician the freedom to alter the dressing to cover closed surgical incisions of different sizes and shapes (Figure 2). It is a predicate to and substantially equivalent to the Prevena™ Peel and Place dressing, which should not be altered to fit a closed incision.

The Prevena™ Customizable™ Dressing or Prevena Plus™ Customizable™ Dressing, in conjunction with NPWT, is intended to manage the environment of closed surgical incisions which continue to drain following sutured or stapled closure. The dressing provides a seal

around the incision site, maintains a closed environment, and removes exudate via the application of NPWT.

Figure 2. Prevena™ Customizable™ Dressing or Prevena Plus™ Customizable™ Dressing

While the Prevena™ Customizable™ Dressing was primarily developed for use with the Prevena™ unit and Prevena Plus™ Customizable™ Dressing was primarily developed for use with the Prevena Plus™ unit as the NPWT delivery method, the dressings have been designed to be compatible with V.A.C. Therapy Units as well. The Prevena™ Customizable™ Dressing or the Prevena Plus™ Customizable™ Dressing may be connected to the NPWT device of choice. The NPWT device creates a negative pressure vacuum of 125 mmHg relative to the closed surgical incision and causes exudate to be pumped into a collection canister attached to the NPWT device. The Prevena™ Customizable™ Dressing is constructed of three layers, as described in Table 1.

Table 1. Prevena™ Customizable™ Dressing Description

Layer/Material	Function
Skin Interface layer (Subject skin contacting)	
• Wicking Interface Fabric (polyurethane-coated polyester fabric with 0.019% silver)	Placed directly over the incision. Wicks fluid away from the skin/tissue; contains silver ions to reduce potential for contamination of the fabric with microbes.
• Polyurethane film with acrylic adhesive	Secures dressing to application site on Subject
Hydrocolloid Ring (Subject skin contacting)	
• Hydrophillic polymer ring attached to the outside edge of the foam bolster	Assists with dressing application and helps reduce dressing leaks
Foam Bolster (Subject skin non-contacting)	

• Polyurethane foam with pigment violet 23	Manifolds negative pressure to the surgical incision area through the underlying interface fabric
• Polyurethane film shell	Maintains the negative pressure environment in conjunction with the therapy unit
Pressure Pad with Sterile Tubing (Subject skin non-contacting)	
• Polyurethane film with acrylic adhesive	Connects dressing to the therapy unit, transfers negative pressure and removes exudate
• DEHP-free PVC, medical grade	

1.4.4 ActiV.A.C. Therapy System Description

The ActiV.A.C.® Therapy System is an electric and battery powered device that delivers continuous or intermittent negative pressure to a wound in the selectable range of 25mmHg to 200mmHg. A 300 mL canister is attached to the device to collect wound fluid.

The ActiV.A.C.® Therapy System is intended to create an environment that promotes wound healing by secondary or delayed primary intention. The application of NPWT prepares the wound bed for closure, reduces edema, promotes granulation tissue formation and perfusion, and removes exudate and infectious material. It is designed to be used in conjunction with all KCI dressing products including the Prevena™ Customizable™ Dressing or the Prevena Plus™ Customizable™ Dressing.

The ActiV.A.C. Therapy System will be the NPWT delivery method for this study. The device will be attached to the Prevena™ Customizable™ Dressing or the Prevena Plus™ Customizable™ Dressing immediately after the dressing is applied to the Subject's closed incision, and programmed to deliver continuous 125 mm/Hg negative pressure for the duration of study treatment.

Figure 3. ActiV.A.C. .® Therapy Unit

1.5 Regulatory Status of the Study Product

The Prevena™ Customizable™ Dressing provides a new dressing configuration that has been designed to allow the clinician to cut the dressing to fit the incision size and geometry. The Prevena™ Customizable™ Dressing and the Prevena Plus™ Customizable™ Dressing have received 510(k) clearance by the Food and Drug Administration (FDA) and are substantially equivalent.

The Prevena™ Customizable™ Dressing or the Prevena Plus™ Customizable™ Dressing Kit is intended to manage the environment of surgical incisions that continue to drain following sutured or stapled closure by maintaining a closed environment and removing exudate via the application of NPWT. The dressing should be applied to the closed incision immediately after surgery, connected to NPWT, and then remain in place for a minimum of 2 days up to a maximum of 7 days.

1.6 Performance Data of the Study Product

Performance testing demonstrates that NPWT is distributed throughout the Prevena™ Customizable™ Dressing when applied to its maximum length. In bench testing, pressure measurements were taken across the entire length of the dressing under wet and dry simulated wound conditions, meeting performance criteria.

Additionally, performance testing established that the Prevena™ Customizable™ Dressing is compatible with marketed V.A.C. Therapy units. When connected to an ActiV.A.C. Therapy Unit, negative pressure was distributed across the entire length of the dressing under wet and dry simulated wound conditions. Performance criteria were met successfully.

1.7 Clinical Data to Date

During the design phase of the Prevena™ Customizable™ Dressing, different dressing prototypes were tested in two healthy human clinical trials with the primary objective of evaluating leak rate of the dressings.

Results of the initial healthy human study exhibited relatively high leak rates of prototype dressings applied to the intact skin of Subjects, which were attributed to a manufacturing defect at the junction of the indication pad and tubing. The study also assessed possible skin reactions to dressing application with mild erythema reported as the most common skin reaction. When the dressing was cut and joined together, there were reports of occasional excoriation to the skin directly underneath the junction. Presumably, this was due to skin pinching between the two foam ends when NPWT was applied. To mitigate this issue, the use of sealing strips at foam ends or joins was proposed for a second healthy human study.

Leak rate and skin response data were collected as part of the second healthy human study, in which three different dressing application configurations were evaluated. All Subjects completed the study with no reports of severe or serious skin reactions; there was one report of skin hyperpigmentation. The addition of a hydrocolloid strip to the foam ends and joins was successful in mitigating the occurrence of skin excoriation. The three dressing configurations tested successfully passed the study's established leak rate parameters.

1.8 Rationale for Study Design and Risk/Benefits

The current literature does not have consistent definitions or measures of surgical site complications (SSC) for large incisions resulting from primary closure of an abdominal surgical procedure. Therefore, it is difficult to assess the true rate of these complications and the impact on health care resources.

Patients undergoing a functional panniculectomy procedure are left with a transverse surgical incision which spans from hip to hip, and depending on other procedures which may be performed at the same time, the patient may have a vertical incision in addition to the transverse incision, which overall looks like an inverted T (fleur-de-lis). Patients undergoing incisional hernia repair are left with a vertical incision which can span from the ribcage to the umbilicus.

These large incisions are not able to be covered by the Prevena™ Peel and Place dressing since the length is too short and the dressing cannot be altered. With Prevena™ Customizable™ Dressing or Prevena Plus™ Customizable™ Dressing, the extensive surgical incisions of abdominal surgery patients may now be covered and NPWT applied. The potential

clinical and economic benefits of prophylactic use of these dressings with NPWT for management of extensive abdominal surgical incisions have been explored, and clinical evidence to support its use in this patient population is warranted. Therefore, this study is proposed to evaluate and compare SSC incidence and collect safety data in Subjects receiving the Prevena™ Customizable™ Dressing or Prevena Plus™ Customizable™ Dressing versus a SOC surgical incision dressing to manage large closed surgical incisions resulting from abdominal surgery for incisional hernia repair and/or functional panniculectomy.

(Prevena™ Customizable™ Dressing or Prevena Plus™ Customizable™ Dressing will be referred to as "Customizable" from this point forward).

2 Study Objectives

The primary objective of the study is to compare surgical incision-related clinical outcomes in Subjects undergoing abdominal surgery for incisional hernia repair and/or functional panniculectomy when managed with Customizable as compared to SOC surgical incision dressing (dry sterile dressing/gauze, steri-strips).

Clinical outcomes of interest are dehiscence and surgical site infection (SSI) within 30 days post-surgical procedure. These short-term clinical outcomes are defined as the collective term SSC for the purposes of this study. SSC will be compared to a control group consisting of Subjects screened for the same inclusion and exclusion criteria but receiving SOC dressing. This study will also collect clinically relevant intervention (CRI) data.

2.1 Summary

The goal of this study is to evaluate the impact of Customizable in the management of extensive closed surgical incisions for Subjects undergoing abdominal surgery for incisional hernia repair and/or functional panniculectomy as compared to SOC dressing, and to significantly reduce the SSC rate experienced by Subjects receiving Customizable vs. SOC surgical incision dressing.

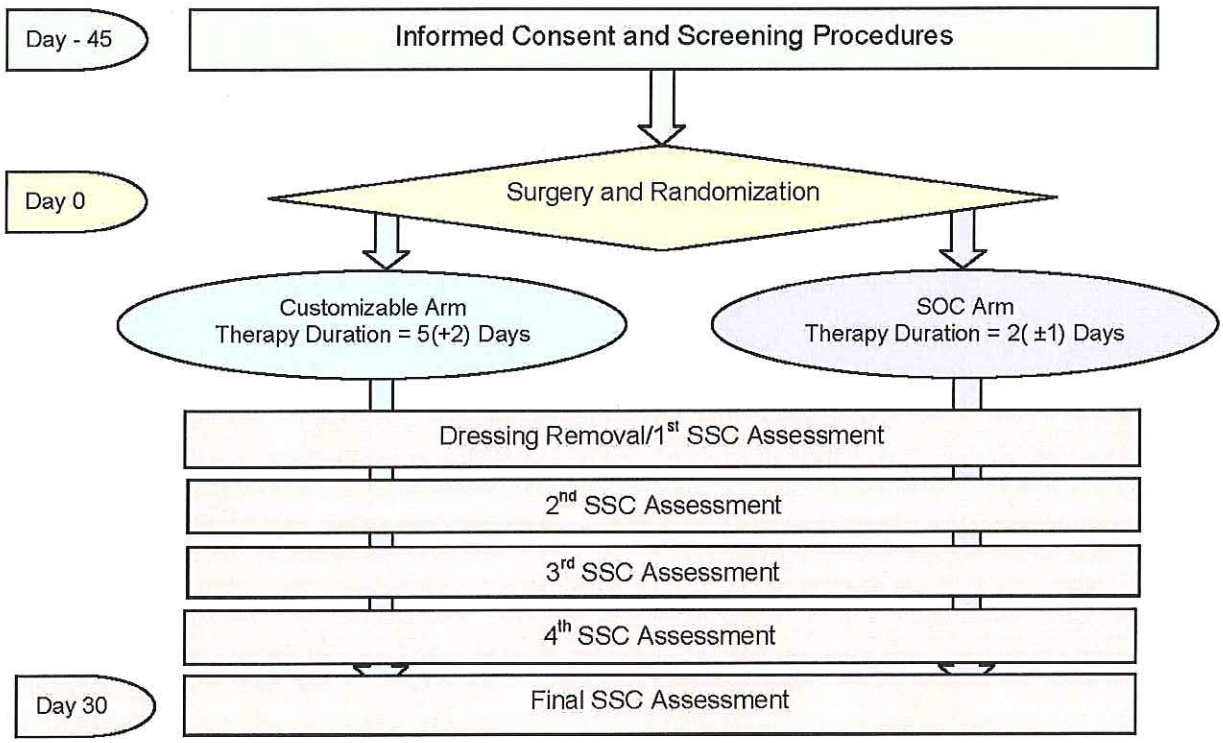
3 Study Design

This is a post-market, prospective, randomized controlled study to evaluate the safety and effectiveness of Customizable when used to manage extensive vertical, transverse, and fleur-de-lis surgical incisions resulting from the primary closure of incisional hernia repair and/or functional panniculectomy procedures. Study data will be analyzed for clinical outcomes through 30 days.

After approximately 60 Subjects have been enrolled and completed the study (ITT population); an interim data review will be performed to verify the study's sample size assumptions. If needed, the sample size may be increased to allow for enrollment of up to 500 Subjects (see Section 10.1, Sample Size Determination).

3.1 Design Summary

3.1.1 Study Design Schematic



3.1.2 Duration of Study Participation

Duration of Study participation per Subject is as follows:

- Screening: 45 days prior to and including Day 0 (day of surgery)

- Treatment Duration:
    - Customizable arm: 5 (+ 2) days
    - SOC arm: 2 (± 1) days
- Active Study Phase (after Randomization): Day 0 through 30 (± 4) days

The maximum participation duration per Subject is 80 days.

3.2 Primary Study Endpoint

Incidence of SSC with Customizable as compared to the control group receiving a SOC surgical incision dressing. For this study, a SSC is defined as one of the following:

- Dehiscence
- Surgical site infection (SSI)

3.3 Secondary Study Endpoint

3.3.1 Clinically Relevant Interventions

Incidence of clinically relevant interventions (CRI) of the surgical incision in Subjects managed with Customizable as compared to the control group managed with a SOC surgical incision dressing. For this study, clinically relevant interventions are defined as the following:

- Antimicrobial treatment of SSI
- Percutaneous and open drainage of the surgical incision (by surgeon)
- Debridement of the surgical incision
- Re-operation related to the surgical incision
- NPWT applied to the open surgical incision

3.4 Other Data Collected

Other data collected will include:

- Height, weight, BMI
- Panniculus weight, and grade using the following scale:

Grade 1	Panniculus barely covers the hairline of the mons pubis but not the genitalia.
Grade 2	Extends to cover the genitalia.

Grade 3	Extends to cover the upper thigh.
Grade 4	Extends to cover the mid thigh.
Grade 5	Extends to cover the knees or beyond.

Source: American Society of Plastic Surgeons [ASPS], 2007d

- Material used to reinforce hernia repair incision
- Incision type, location, and incision measurement in cm (measure vertical and transverse aspects of fleur-de-lis separately)
- SOC dressing materials
- Digital photographs of the closed surgical incision
- Customizable replacement (if required to maintain a seal)

3.5 Safety Endpoint(s)

All AEs will be tabulated and reported overall and by treatment arm.

3.6 Randomization Plan

This is a randomized controlled clinical trial. Randomization will occur intra-operatively after surgical incision closure and confirmation that all of the intra-operative inclusion criteria and none of the intra-operative exclusion criteria are met. Enrolled Subjects will be assigned to either Customizable or SOC surgical incision dressing in a 1:1 ratio stratified by incision type of either transverse/vertical or fleur-de-lis. Sealed randomization envelopes will be provided to the Investigator and will be used to obtain an intra-operative randomization assignment for each Subject. (Technical description of randomization is provided in Section 10.3). The assignment will be:

- Customizable arm; **or**
- SOC surgical incision dressing arm

4 Subject Selection

Subjects undergoing an abdominal surgery for incisional hernia repair and/or functional panniculectomy resulting in a vertical, transverse or fleur-de-lis incision, and who meet all inclusion and none of the exclusion criteria, will be enrolled in the study. No deviations or waivers of inclusion/exclusion criteria will be granted by KCI.

4.1 Inclusion Criteria

4.1.1 Pre-Operative Inclusion Criteria

The Subject:

1. Is an adult ≥ 18 years old of either gender;
2. Is able to provide their own informed consent;
3. Will undergo:
   a. A functional panniculectomy with a transverse or a fleur-de-lis incision;

   – AND/OR –

   b. An incisional hernia repair with a vertical incision at least 20 cm in length and at least 10 cm of undermining on each side of the incision;
4. Has a BMI ≥ 30;
5. Has maintained a stable weight for at least 3 months as determined by the Investigator (applies to post weight loss patients only);
6. Is pre-operatively assessed to undergo a procedure with a CDC Wound Classification of:

   a. Class I (Clean): An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tract is not entered;

   – OR –

   b. Class II (Clean Contaminated): An operative wound in which the respiratory, alimentary, genital or uninfected urinary tract are entered under controlled conditions and without unusual contamination;
7. Is willing and able to return for all scheduled study visits;
8. If a female of child-bearing potential, must test negative on a urine pregnancy test; and
9. If a female of child-bearing potential, must be willing to utilize an acceptable method of birth control (i.e. oral contraceptives, condom with spermicide, diaphragm with

spermicide, implants, IUD, injections, vaginal rings, hormonal skin patch) for the duration of the study

4.1.2 Intra-Operative Inclusion Criteria

Subjects must meet the following intra-operative inclusion criteria to be eligible for randomization.

The Subject:

1. Continues to meet all pre-operative inclusion criteria
2. Has undergone a Class I or II CDC Wound Classification procedure resulting in a closed surgical incision able to be covered completely by Customizable dressing

4.2 Exclusion Criteria

4.2.1 Pre-Operative Exclusion Criteria

The Subject:

1. Has a systemic bacterial or fungal infection at the time of surgery for incisional hernia repair and/or functional panniculectomy;
2. Has a remote-site skin infection at the time of surgery for incisional hernia repair or functional panniculectomy;
3. Is preoperatively assessed to undergo a procedure with a CDC Wound Classification of:

    a. Class III (Contaminated): Open, fresh, accidental wounds, and/or major breaks in sterile technique or gross spillage from the gastrointestinal tract;

    – OR –

    b. Class IV (Dirty-Infected): Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera;

4. Will have a transverse or fleur-de-lis incision that extends beyond the flank area and requires moving the Subject from the supine position during surgery;
5. Has a known allergy or hypersensitivity to silver, or drape materials that contain acrylic adhesives;
6. Has participated in a clinical study within the past 30 days; and

7. Who, in the investigator's opinion, would have any clinically significant condition that would impair the Subject's ability to comply with the study procedures

4.2.2 Intra-Operative Exclusion Criteria

Subjects who meet any of the following intra-operative exclusion criteria are considered screen failures and are not eligible for randomization.

The Subject:

1. Is found to meet any of the pre-operative exclusion criteria;
2. Is determined to have a CDC Wound Classification of:

   a. Class III (Contaminated): Open, fresh, accidental wounds, and/or major breaks in sterile technique or gross spillage from the gastrointestinal tract;

   – OR –

   b. Class IV (Dirty-Infected): Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera.

5 Study Procedures

5.1 Informed Consent

The Investigator will discuss the purpose of this study with potential Subjects. Each potential Subject will review the IRB-approved Informed Consent Form (ICF). The Subject and the Investigator (or designated medically licensed sub-investigator), must sign and date the ICF before the Subject can undergo any study-related procedures. The Subject's informed consent will be obtained under these conditions:

- Subjects must be made aware of the purpose of the study and the potential risks and benefits known or that can be reasonably predicted or expected;
- Subjects must be given the opportunity to ask the Investigator questions and must be provided time to consider participation in the study;
- ICFs will be written in a manner that is non-technical and understandable to the Subject;
- Subjects will not be led to believe that they are waiving their legal rights to release the Investigator, KCI, the Institution, or any of their agents from liability from negligence;

- Subjects will be asked to sign and date the ICF indicating their informed consent to be enrolled in the study;
- The Investigator's responsibilities during the ICF process include;
    - Screening out potential Subjects who may not be able or willing to comply with the clinical investigation protocol,
    - Ensuring that Subjects have signed and dated the ICF prior to undergoing any clinical investigation related procedures, and
    - Ensuring that each Subject receives a copy of their signed ICF.

5.2 Numbering of Study Subjects

After signing the ICF, the site will assign a unique, consecutive screening number to each Subject for screening log tracking purposes. At randomization, a Subject number will be assigned. The number will be a combination of the study site number (provided by KCI), followed by 1001 for transverse/vertical incisions and 2001 for fleur-de-lis incisions, and increasing sequentially in the stratum.

Once a Subject number is assigned, it is not to be re-assigned to another Subject. For example, if a Subject is randomized but does not receive study treatment and is withdrawn, limited Case Report Forms (CRFs) will be completed with the assigned Subject number, noting the reason(s) for withdrawal.

If a screened Subject does not meet the intra-operative inclusion criteria or meets any intra-operative exclusion criteria, the Subject will be considered a screen failure and the reason for the failure should be included in the screening log. If a Subject is rescreened, a new Screening number must be assigned.

5.3 Laboratory Tests

A urine hCG test will be performed during the Screening Visit and at Day 0 prior to surgery (unless Screening and Day 0 occur on the same day), to determine pregnancy status in all female Subjects of child-bearing potential. If the Subject's urine pregnancy test is positive, the Subject cannot continue in the study and will be considered a screen failure.

Positive and clinically significant wound cultures (superficial or deep) obtained at any time during the study will be documented.

5.4 Concomitant Medications

Concomitant medications will be documented in accordance with the following:

- All medications the Subject is taking at baseline (Screening);
- All medications the Subject is given to treat an AE during the study;
- All antimicrobial medications the Subject is given from time of informed consent and throughout the duration of the study;
- Opioid medications (i.e. morphine) given to the Subject for at least 14 consecutive days after randomization.

For all concomitant medications recorded, only the INITIAL dose is required. Changes in dosage, for the same indication, do not need to be recorded (i.e. the medication does not need to be recorded again with a different dose). If the medication is stopped, record the stop date.

5.4.1 Antimicrobial Use

Antimicrobial use for the treatment of an SSI or other infection not associated with the surgical incision will be prescribed at the discretion of the Investigator. For the surgical procedure, Subjects will receive intravenous antibiotics within 24 hours of the surgical procedure, followed by a course of oral antibiotics.

5.5 Surgical Procedure

Subjects will undergo a functional panniculectomy and/or incisional hernia repair with a vertical, transverse, or fleur-de-lis incision as deemed clinically appropriate by the Investigator. The vertical incision must be at least 20 cm in length and require at least 10 cm of undermining on each side of the incision. The resultant surgical incision (whether vertical, transverse or fleur-de-lis) will be closed with absorbable sutures only, Staples may not be used. Incisional glue may not be used for those subjects randomized to the Customizable treatment arm but may be used for those subjects randomized to the SOC treatment arm. After closure of the incision, length will be measured in centimeters. If a fleur-de-lis incision, the vertical and transverse aspects will be measured separately. All surgical incision measurements must be documented.

5.6 Placement of Customizable and N.P.W.T.

5.6.1 Customizable with ActiV.A.C. Therapy Unit

Subjects randomized to the Customizable arm will receive therapy for 5 (+ 2) days.

Prior to dressing application, a topical skin adhesive (ie Mastisol, benzoin, Cavilon™) will be applied to the area around the closed incision, unless the Subject has a known allergy. The skin adhesive must not come in contact with the closed incision and will be applied after the Customizable foam is in place.

Customizable will be altered to cover the entirety of the incision and the tubing will be attached in close proximity to the center of the dressing. JP drains must not be covered by the dressing. An ActiV.A.C. Therapy Unit will then be connected to Customizable in the operating room and activated immediately.

After powering on the ActiV.A.C. Therapy Unit to deliver 125 mm/Hg of continuous negative pressure to the closed incision, the Investigator will ensure that Customizable is maintaining a seal.
The time of Customizable placement and the ActiV.A.C. Therapy Unit settings must be documented.

Customizable is intended to remain in place for the duration of therapy (at least 5 days) without requiring replacement. However, if Customizable develops a leak and all attempts to mitigate are unsuccessful, the dressing may be replaced to ensure continuity of negative pressure therapy. There is a two dressing replacement limit after the first Customizable is applied. If two replacements are attempted and negative pressure cannot be maintained, therapy will be discontinued and the subject will be treated as clinically appropriate. Customizable replacement will be documented.

5.6.2 Standard of Care Dressing

Subjects randomized to the SOC surgical incision dressing arm will receive SOC dressing for 2 (±1) days immediately following surgery. The closed incision will be covered with materials which may include: a cyanoacrylate adhesive (applied to the incision), skin adhesive (ie Mastisol, benzoin, Cavilon™) to the area around the incision unless the Subject has a known allergy, dry sterile dressing/gauze, medical tape, and/or steri-strips. At a minimum, a dry sterile dressing must be applied. Advanced wound care dressings and NPWT are disallowed from use in this treatment arm. Any materials used for the SOC dressing will be documented.

5.7 Post-Operative Assessments

5.7.1 Surgical Site Complications (SSC) Assessment

SSC is a collective term used to describe adverse surgical incision events that may occur in the short term following primary closure of a surgical incision. Each event after placement of study treatment through Visit 9 is considered an SSC and will be assessed and documented by the Investigator as indicated in this section.

5.7.1.1 Dehiscence: Disruption of a surgical incision. Each instance of dehiscence will be documented as a separate SSC if multiple dehiscences occur along the same incision line. Dehiscence not related to seroma, hematoma or infection will be classified as a primary dehiscence. Dehiscence related to seroma, hematoma or infection will be classified as a secondary dehiscence and the primary cause will be documented. The linear dimensions of the dehiscence must be recorded and categorized as follows:

5.7.1.1.1 Superficial: Separation of the skin and subcutaneous tissue but not the muscular fascia

5.7.1.1.2 Deep: Separation of the muscular fascia

5.7.1.2 Surgical Site Infection (SSI) (derived from the CDC definition, Superficial and Deep Only):

5.7.2.1.1 Superficial SSI: Involves only skin and subcutaneous tissue of the incision and has at least one of the following:

1) Purulent drainage from the superficial incision

-OR-

2) Fluid accumulation with purulent fluid that is drained

-OR-

3) A positive culture with one of the following: i) clinical signs/symptoms (may include pain, tenderness, heat, and/or swelling) or ii) is deliberately opened by a surgeon

-OR-

4) Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision

-OR-

5) Diagnosis of Superficial SSI by the Investigator or designee

Reporting Instructions for Superficial SSI:

- Do not report a stitch abscess (minimal inflammation and discharge confined to the points of suture penetrations) as an infection.
- Do not report a localized stab wound infection as a SSI, instead report as skin or soft tissue infection, depending on its depth.
- "Cellulitis", by itself, does not meet the criteria for Superficial SSI.
- If the surgical incision infection involves or extends into the fascial and muscle layers, report as a deep incisional SSI.

5.7.2.1.2 Deep SSI: Involves deep soft tissue (e.g., fascial and muscle layers) of the surgical incision and has at least one of the following:

1) Purulent drainage from the deep surgical incision but not from the organ/space component of the surgical site.

-OR-

2) An abscess or other evidence of infection involving the deep surgical incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination

-OR-

3) A positive culture with one of the following: i) clinical signs/symptoms (may include pain, tenderness, heat, and/or swelling), ii) spontaneously dehisces, or iii) is deliberately opened by the Investigator or designee

-OR-

4) Diagnosis of deep SSI by the Investigator or designee

Reporting Instructions for Deep SSI:

- Classify infection that involves both superficial and deep surgical incisions as deep incisional SSI.

- Report culture specimen from superficial incisions as ID (incisional drainage)

5.7.2 Clinically Relevant Interventions (CRI)

If a SSC requires intervention, the procedure must be documented. Any subsequent CRI for a SSC that resolves and then recurs will be documented as a separate CRI.

5.7.2.1 Antimicrobial treatment of SSI: administration of antibiotics, antifungals, or other antimicrobials for the treatment of an infection related to the surgical incision.

5.7.2.2 Percutaneous or Open Drainage (by surgeon): decompression of the fluid accumulation using either:

1) Percutaneous drainage of incisional fluid;

- OR –

2) Open technique (at bedside) drainage of incisional fluid;

- OR –

3) Open surgical intervention (in a procedure room or operating room) drainage of incisional fluid.

If infection is suspected, Customizable should be discontinued, cultures should be obtained, and clinically significant results documented as an adverse event.

5.7.2.3 Debridement: Removal of necrotic, damaged, or infected wound tissue either at the bedside or in the operating room. Debridement involving muscular fascia or deeper tissues should be documented as reoperations.

5.7.2.4 Reoperation: Procedure requiring dissection deeper than the skin and subcutaneous tissue, repair of the muscular fascia, entry into the retro-peritoneum, renal transplant revision or graft removal, flaps, and skin graft procedures.

5.7.2.5 NPWT: Application of NPWT for management of the opened surgical incision (wound).

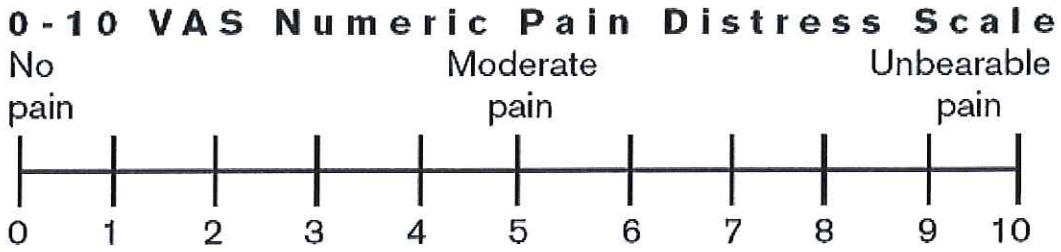
5.7.2.6 Digital Photographs of the Closed Surgical Incision

Digital photographs of the closed surgical incision will be taken at Visits 2, 4, 5, 6, 7, 8 and 9; and at any time there is a SSC. Digital photograph instructions specific to this study will be provided by KCI with the study documents.

5.7.2.7 Incisional Pain Assessment - Visual Analog Scale (VAS)

The VAS is a psychometric, numeric response scale which is used to measure a patient's subjective characteristics or attitudes which cannot be directly measured. The Subject will rate perceived pain of the surgical incision using the VAS. See Figure 4.

Figure 4. Visual Analog Scale



5.8 Adverse Events Reporting

Subjects will be monitored regularly during visits for development of AEs, and data on all AEs will be documented as described in Section 9 of this protocol. KCI, the IRB, and regulatory authorities will be informed in a timely manner about all serious adverse events (SAEs), according to applicable regulatory guidelines. Assessment and reporting of AEs is detailed in Section 9 of this protocol.

6 Study Visits

6.1 Study Visit Calendar

	Visit 1	Visit 2	Visit 3[4]	Visit 4[5]	Visit 5	Visit 6	Visit 7	Visit 8		
	Screening	Day of Surgery	Post-Op	Post-Op	Post-Op	Post-Op	Post-Op	Follow-Up	Unplanned Visit	Early Withdrawal Visit
	Day -45 to 0	Day 0	Day 2 (±1)	Day 5 (+2)	Day 10 (± 1)	Day 14 (± 2)	Day 21 (± 3)	Day 30 (± 4)		
Informed Consent	X[1]									
Pre-Operative Inclusion & Exclusion Criteria	X[1]									
Subject Demographics	X[1]									
Physical Exam	X[1]	X[2]								
BMI	X[1]									

Medical & Surgical History	X[1]									
Urine Pregnancy Test	X[1]	X[2]								
Concomitant Medications	X[1]	X	X	X	X	X	X	X	X	X
Functional Panniculectomy Surgery		X								
Intra-operative Inclusion & Exclusion Criteria[3]		X								
Randomization		X								
Incision Site Description		X								
Panniculus Grade/Weight[6]		X								
Surgical Incision Measurement (length)		X								
Customizable or SOC Application		X								
Digital Photographs of Closed Surgical Incision		X	X	X	X	X	X	X	X[7]	X[7]
VAS Pain Assessment			X	X	X	X	X	X	X	X
SSC Assessment			X	X	X	X	X	X	X	X
CRI Reporting			X	X	X	X	X	X	X	X
SOC End of Therapy and Dressing Removal			X						X[7]	X[7]
Customizable End of Therapy, Dressing Removal, and Collection of ActiV.A.C. unit				X					X[7]	X[7]
Adverse Event Reporting		X	X	X	X	X	X	X	X	X

[1]Screening procedures may be performed on Day 0.
[2]Perform only if Visit 1/Screening occurs prior to Day 0.
[3]If intra-operative inclusion/exclusion criteria are not met, Subject is a screen failure.
[4]Visit occurs for SOC arm only.
[5]Visit occurs for Customizable arm only.
[6]Perform for panniculectomy Subjects only.
[7]Perform if indicated based upon timing of Visit. See Sections 6.10 and 6.11.

6.2 ***Visit 1: Screening / Day - 45 up to and including Day 0***

The following procedures will be performed and documented:

- ICF
- Subject demographics
- Medical and surgical history
- Pre-operative inclusion and exclusion criteria
- Physical exam (including dermatological exam and surgical site inspection)
- Height, weight, BMI
- Concomitant medications
- Urine for hCG screening (all female Subjects of child-bearing potential)

6.3 *Visit 2: Day of Surgery / Day 0*

The following procedures will be performed and documented:

- Repeat physical exam (including dermatological exam and surgical site inspection), if Visit 1 occurs prior to Day 0
- Repeat urine for hCG screening (all female Subjects of child-bearing potential), if Visit 1 occurs prior to Day 0
- Baseline pre-operative VAS pain assessment of surgical incision site
- Surgical procedure
- Panniculus grade/weight
- Intra-operative inclusion/exclusion criteria
- Randomization
- Incision type, location and measurement (length in cm) (measure the vertical and transverse aspects of fleur-de-lis separately)
- Digital photographs of the closed surgical incision (AP & LAT)
- Customizable or SOC dressing placement by random assignment
- Concomitant medications
- AE reporting

6.4 *Visit 4: Post Operative / End of SOC Therapy / Day 2 (±1) – SOC Arm Only*

The following procedures will be performed and documented:

- SOC surgical incision dressing removal
- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.5 *Visit 5: Post Operative /End of Customizable Therapy / Day 5 (+2) – Customizable Arm Only*

The following procedures will be performed at least 2 hours after dressing removal, and documented:

- Customizable removal and collection of ActiV.A.C. unit
- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.6 ***Visit 6: Post Operative Assessment / Day 10 (± 1)***

The following procedures will be performed and documented:

- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.7 ***Visit 7: Post Operative Assessment / Day 14 (± 2)***

The following procedures will be performed and documented:

- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.8 ***Visit 8 Post Operative Assessment / Day 21 (± 3)***

The following procedures will be performed and documented:

- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.9 *Visit 9: Post Operative Assessment / Day 30 (± 4)*

The following procedures will be performed and documented:

- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.10 *Early Withdrawal Visit*

The following procedures will be performed and documented, as applicable:

- Customizable or SOC surgical incision dressing removal
- Collection of ActiV.A.C. unit
- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

6.11 *Unplanned Visit*

The following procedures will be performed and documented, as applicable:

- Customizable or SOC surgical incision dressing removal
- Collection of ActiV.A.C. unit
- VAS pain assessment of surgical incision
- Digital photographs of the closed surgical incision (AP & LAT)
- SSC assessment
- CRI reporting
- Concomitant medications
- AE reporting

7 Study Discontinuation and Withdrawal of Study Subjects

7.1 Premature Discontinuation of the Study

If the study is terminated prematurely or suspended, the IRB will be informed promptly and provided with the reason(s) for the termination or suspension by KCI or by the Investigator. If applicable, regulatory authorities and the personal physicians of the Subjects will also be informed.

7.1.1 By Sponsor

KCI reserves the right to discontinue any study for business or ethical reasons at any time, such as, but not limited to:

- The study is not conducted in accordance with the approved protocol
- Information on the study product causes doubt as to the benefit/risk ratio
- Changes in medical practice limit utility of the data obtained from the study.

KCI reserves the right to terminate a study at an investigative site at any time based on the terms and conditions set forth in the Clinical Research Agreement (Section "Termination"), or for other good cause, including, but not limited to, any of the following reasons:

- Investigator(s) lack of compliance to protocol and/or with applicable regulatory or IRB guidelines in conducting the study
- Incidence or severity of AEs indicates a potential health hazard or poses an unreasonable risk to the study participants
- Subject enrollment is unsatisfactory.

7.1.2 By IRB

The IRB may choose to discontinue the study at the site for which they granted approval if the:

- Study is not conducted in accordance with the IRB 's requirements
- Study is associated with unexpected serious harm to Subjects.

7.2 Premature Discontinuation of Subject

Subjects will be discontinued from the study if their randomly assigned treatment is ended prematurely, or if Customizable cannot maintain a seal even after replacing the dressing twice (see Section 5.6.1).

Subjects may withdraw from participation in the study at any time at their own request, or they may be withdrawn at any time at the discretion of the Investigator for safety, behavioral, or administrative reasons. If a Subject does not return for a scheduled visit, every effort should be made to contact the Subject, per the site's local protocol.

In any circumstance, every effort should be made to document Subject outcome. The Investigator should inquire about the reason for withdrawal, request that the Subject return for a final visit, if applicable, and follow-up with the Subject regarding any unresolved AEs. Any related SAEs occurring within 14 days following Subject discontinuation must be reported to KCI, and any applicable regulatory agencies and must be followed until stabilization or resolution.

If the Subject withdraws from the study, and also withdraws consent for disclosure of future information, no further study evaluations will be performed, and no additional data will be collected. The Investigator may retain and continue to use any data collected before such withdrawal of informed consent.

7.2.1 By Investigator

The Investigator may choose to discontinue the Subject from study with or without his/her consent for any of the following:

- AEs;
- Noncompliance; or
- Any reason that may, in the opinion of the Investigator, affect negatively the safety or well-being of the Subject.

If for any reason the Subject is withdrawn from the study, the Investigator will inform the Subject and KCI accordingly.

8 Risks Associated with Participation in the Study

Participation in this study presents low risks to Subjects. Risks associated with Customizable and the ActiV.A.C. Therapy Unit are generalized and are listed in Table 5 (Section 8.1).

8.1 Potential Risks Associated with Customizable and ActiV.A.C.

All risks known (based on prior relevant experience) or anticipated on reasonable grounds are listed. This table, and if needed this document, will be updated in the presence of new information of relevance to the safety of the Subject or the conduct of the study.

Table 5. Risks Associated with Customizable and ActiV.A.C.

Risks	Disorders/Conditions
Skin and Subcutaneous Tissue	• Local cutaneous reaction (i.e. redness, rash, significant pruritis, urticaria) • Allergic reaction • Maceration • Minor soft tissue damage • Epidermal (skin) stripping • Minor bleeding • Pain • Contusion (bruising)
Other	• Bleeding complications (associated with the surgical procedure, concomitant therapies and co-morbidities) • First degree burn (if device gets warm) • Exposure related infection • Localized infection • Physical discomfort • Minor desiccation (due to dressing leak) • Moderate soft tissue damage (i.e. due to trip hazard, tubing entanglement) • Deterioration of the wound (due to lack of visibility of incision site through dressing)

9 Safety and Adverse Events

9.1 Definition

9.1.1 Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including clinically significant abnormal laboratory findings) in Subjects, whether or not related to the study product.

This definition includes events:

- Related to the study product or the comparator,
- Related to the study procedures involved,
- Resulting from user error or from intentional misuse of the study product.

9.1.2 Serious Adverse Event (SAE)

An adverse event is considered serious if it results in any of the following outcomes:

- Death;
- Life-threatening adverse experience;

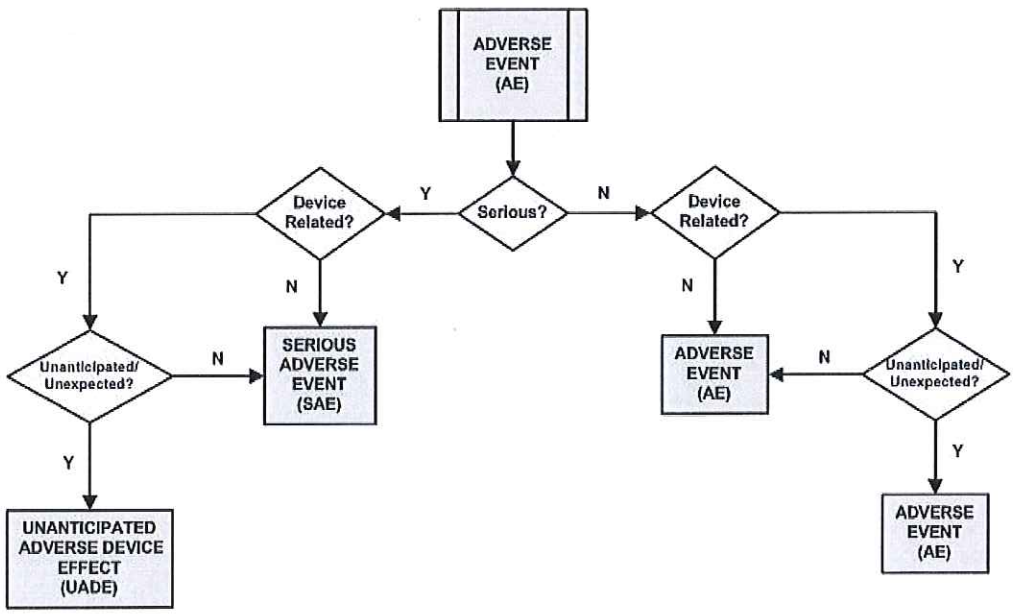
- Inpatient hospitalization or prolongation of existing hospitalization;
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or
- Congenital anomaly/birth defect.

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse experience when, based upon 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 (FDA, 21 CFR 312.32; ICH E2A and ICH E6).

9.1.2.1 Unanticipated Adverse Device Effect (UADE)

An UADE is any **serious adverse event** on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. (21 CFR 812.3)

9.2 Classification



9.3 Causality

The Investigator will assess the causality of the AE as:

- Related to the study product: any adverse event for which there is a reasonable possibility that the study product caused the adverse event.
- Not Related to the study product: when is determined that there is no relationship between the adverse event and the use of the study product.

9.4 Severity

All AEs will be assessed for severity by Grade based upon the following definitions:

- **Grade 1: Mild**; Awareness of signs or symptoms, but easily tolerated and are of minor irritant type to the Subject, causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- **Grade 2: Moderate**; Events introduce a low level of inconvenience or concern to the Subject and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning; minimal, local or noninvasive intervention indicated.
- **Grade 3: Severe**; Events interrupt the Subject's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating.

9.5 Expectedness

All SAEs will be assessed for expectedness based on the following definitions:

- **Expected, Anticipated:** the effect, problem, or death had been previously identified in nature, severity, or degree of incidence in the study or product documentation.
- **Unexpected, Unanticipated:** if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the study or product documentation.

9.6 AE Reporting Procedures

The Investigator is responsible for monitoring the safety of all Subjects enrolled in the study, and reporting adverse events as described in this protocol.

9.6.1 AE Collection/Reporting Period

The AE collection/reporting period will begin after the Subject has completed any study related procedures after informed consent. Exceptions to this are clinically significant laboratory findings or diagnostic tests performed as part of screening. These will be recorded on the Medical History CRF and not as adverse events.

Study Subjects should be instructed to report any AE that they experience to the Investigator. Investigators should assess for AEs at each visit. All AEs, regardless of perceived relationship to study product, will be reported and recorded on the appropriate CRFs in a timely manner. In addition, **clinically significant** changes in physical examination findings, worsening of a medical condition in the medical history and abnormal test findings should also be recorded as AEs.

The AE description will include the nature of the event (AE term), the start date, the end date, the severity of each sign or symptom, the seriousness of the event or experience, causality, the course of action taken, and the outcome of the event.

9.6.2 SAE Reporting to KCI

Serious Adverse Events (SAE) will be reported via the KCI SAE Report Form within 24 hours of learning of the event. This form should be completed by the Investigator, or designee, and faxed or emailed to KCI Initial notification of the event may occur via telephone call to a KCI study contact, but must always be followed by written notification using the SAE Report Form by the close of the next business day. The KCI SAE fax line is available for SAE reporting 24 hours per day and is monitored during normal business hours. The SAE fax number and email address can be found in the Study Reference Binder.

9.6.2.1 UADE Reporting to KCI

UADEs must be reported by the Investigator to the Sponsor and the reviewing Institutional Review Board (IRB) per their reporting requirements (see SAE Reporting, Section 9.6.2). The Sponsor (KCI) will then immediately conduct an evaluation of a UADE and report the results of the evaluation to the FDA and participating Investigators within 10 working days after the Sponsor first receives notice of the event. (21 CFR 812.46(b), 812.150(b) (1)).

If KCI determines that the event presents an unreasonable risk to the study Subjects, it will terminate all clinical studies or parts of studies presenting risk as soon as possible. In this case,

termination will occur ≤ 5 working days after KCI makes the determination and ≤ 15 working days after KCI first received notice of the event.

9.7 Follow-Up Period for Ongoing AEs

Treatment-related AEs and SAEs which are ongoing at the final study visit, or treatment-related AEs that occur within 30 days of the final study visit, will be followed until resolution or stabilization. All other AEs will be closed at the time the Subject completes participation in the study.

10 Statistical Plan

The primary objective of the study is to compare surgical incision-related clinical outcomes in Subjects undergoing abdominal surgery for incisional hernia repair and/or functional panniculectomy when managed with Customizable as compared to SOC surgical incision dressing.

10.1 Sample Size Determination

The primary endpoint of this study is the incidence of SSC as defined in Section 5.7.1. The incidence rates of SSC will be compared between the treatment groups using Fisher's exact test.

A review of relevant literature shows that both Neaman and Greco reported surgical site complication rates for obese patients of 53.4% and 43.0%, which included rates of dehiscence and SSI of 12.3-15.4% and 16.9-26.0%, respectively.[53;54] Vargo and Condé-Green reported large treatment effects of NPWT over closed incision versus the standard of care in complex abdominal wall reconstruction of 85% and 65%, respectively.[55;56] Considering these references and the design of the current trial, a 35% rate of SSC is projected for the SOC arm, which is consistent with the clinical experience of the Investigators. Based on the primary endpoint of incidence rate of SSC, Fisher's exact test with a two-sided significance level $\alpha = 0.05$ will have approximately 80% power to detect the difference between an incidence rate of 35% in the SOC arm and an incidence rate of 8.75% in the Customizable arm (a 75% reduction) when the sample size in each arm is 44. To account for possible Subject replacement, the sample will be increased by up to 15% for a maximum total of 102 Subjects (51 in each treatment arm).
Due to the wide ranges of SSC incidence rate for the SOC group found in published literature, and no data from use of Customizable dressing for this study population, one planned interim data review will be performed to allow for an adjustment of the sample size. The total number of

treatment emergent AEs and SAEs (Section 10.6) and the SSC incidence rates (Section 10.5.1) will be calculated for each treatment group using the ITT population (Section 10.2.2). Since the purpose of the interim data review is not for any statistical comparison of effectiveness, no adjustment for multiplicity will be made in the final analysis.

Estimates in Table 8 were prepared to examine the SSC rates in the interim data review for sample size justification purposes only. The observed SSC incidence rates may be used to justify increasing the sample size up to 500 Subjects if the original sample size assumptions are incorrect.

Table 8 contains the estimated total sample size based on possible SSC incidence rates using Fisher's exact test with a two-sided significance level $\alpha = 0.05$ and $\beta = .20$. If the observed rates fall between the values displayed in Table 8, the SOC rate will round to the lower rate (e.g., 33.8% will round to 32.5%) and the Customizable rate will round to the higher rate (e.g., 13.4% will round to 15.0%).

Following the interim data review, the sample size will not be adjusted if the observed rates of SSC within the ITT population do not belong to the pre-specified estimates in Table 8, and the sample size will remain at 102 Subjects. The sample size and power calculations were performed using SAS version 9.3.

Table 8: Total sample size estimate for the observed SSC incidence rates of the first 60 subjects in the ITT population.

	SSC Incidence Rate	Standard of Care								
		40.0%	37.5%	35.0%	32.5%	30.0%	27.5%	25.0%	22.5%	20.0%
Customizable	20.0%	196	248	324	452					
	17.5%	152	184	234	418	424				
	15.0%	118	142	174	220	286	394			
	12.5%		112	134	162	202	264	360		
	10.0%			102	122	148	184	236	322	468
	7.5%					112	134	164	210	280
	5.0%							116	142	180

To account for possible Subject replacement, sample estimates were modified using the following calculation:

Total Sample = (Estimated Sample - 60)*1.10 + 60

Sample estimated as described in Section 10.1

10.2 Subject Populations for Analysis

There are two principle analysis populations for this clinical study:

10.2.1 **Full Analysis Set (FAS) Population** – The FAS subject population will consist of all Subjects who i) met all of the pre-operative and intra-operative inclusion criteria and none of the pre-operative and intra-operative exclusion criteria, ii) have been randomized, and iii) received treatment with either Customizable or SOC dressing. Subjects without SSC will need to receive at least 5 days of Customizable or at least 1 day of SOC dressing to be included in this set and completed Visit 9/Day 30 (± 4 days). Subjects with SSC prior to Visit 9/ Day 30 (± 4 days) will be included in this set regardless of length of Customizable or SOC dressing treatment and treatment follow up. Subject data will be analyzed in the arm to which they were randomized and treated. The primary and secondary effectiveness analyses for this study will be based on the FAS population.

10.2.2 **Safety Population (SP) / Intent-to-Treat (ITT)** – The safety population / ITT will consist of all Subjects who are randomized and do not withdraw before the attempt to apply the assigned treatment with Customizable or SOC surgical incision dressing regardless of its duration. Subject data will be analyzed in the arm to which they were randomized. All safety results and supportive analyses for this study will be presented based on the safety population.

10.3 Randomization

Subjects who meet all inclusion criteria and no exclusion criteria and who consent to participate in the study will be randomized in a 1:1 ratio to be treated with either Customizable or SOC surgical incision dressing. Due to the variances in complication rates between incision types, a stratified randomization will be used to ensure balance between the groups. The randomization will be stratified for each site and incision type of vertical/transverse and fleur-de-lis. Within each stratum, permuted blocks will be used to achieve equal numbers of Subjects assigned to Customizable or SOC surgical incision dressing. For each stratum, a randomization schedule will be generated to include Subject numbers and treatment assignments with the stratum of transverse/vertical incision starting with 1001 and the stratum of fleur-de-lis incision starting with 2001. Corresponding randomization envelopes will be prepared in sequential order by Subject number to provide randomization to each Investigator.

Randomization envelopes will be prepared corresponding to each row in the randomization schedule. Subject numbers will be printed and labeled clearly on the top of each envelope. Additionally, the envelopes will be color coded for incision type stratum, sealed, and organized by stratum and in ascending by Subject number

Once the Subject has been screened, deemed eligible, and provided informed consent, the next available sequentially numbered randomization envelope within the corresponding stratum according to incision type; a sealed Customizable box and ActiV.A.C. unit will be taken into the operating room with the Subject. Randomization will be conducted in the operating room after closure of the surgical incision and confirmation of intra-operative eligibility. The envelope will be opened prior to surgical incision dressing placement and the assigned treatment arm will be used. If Customizable is not selected, the sealed box and ActiV.A.C. unit will be returned to appropriate storage area.

10.4 General Considerations and Baseline Parameters

Unless otherwise stated, all statistical tests will be performed using 2-sided tests at the 5% significance level. Baseline is defined as the last observation before surgery. Continuous parameters, such as the Subject's age at the time of surgery, will be summarized using descriptive statistics (N, mean, standard deviation, median, minimum and maximum value, and 95% confidence interval) and compared between treatment arms using a 2-sample t-test or a nonparametric test, as appropriate. Categorical parameters, such as gender, will be summarized as a proportion and compared using a either a Chi-square test or Fisher's exact test, as appropriate.

10.5 Effectiveness Analyses

10.5.1 Primary Effectiveness Analysis

The primary endpoint for this study is the incidence of SSC up to Visit 9, which will be computed and compared between the two treatment arm (Customizable versus SOC) based on the FAS population. The incidence rate of SSC will be calculated for each treatment arm as follows:

$$SSC\ rate = [Number\ of\ Subjects\ who\ experienced\ SSC] / [FAS\ Population]$$

Subjects included in the numerator for the incidence computation must have experienced SSC post surgery up to Visit 9 If a Subject has the same SSC event on multiple occasions or experience several events of SSC, the Subject will be counted only once in the numerator for the primary event and the highest intensity.

The incidence of SSC results will be presented by treatment arm and overall. The Fisher's Exact test with a two-sided significance level $\alpha = 0.05$ will be used to compare the SSC

proportions between the two treatment arms. The null and alternative hypotheses are listed below. A 95% confidence interval for the rate difference between the two treatment arms will be provided.

H_0: The Customizable and SOC treatment arms have equal incidence rates of SSC
$SSC_{CUSTOMIZABLE} = SSC_{SOC}$

H_1: The Customizable and SOC treatment arms have different incidence rates of SSC
$SSC_{CUSTOMIZABLE} \neq SSC_{SOC}$

If the incidence rate of SSC of Customizable is smaller than the incidence rate of SSC of SOC dressing (i.e. $SSC_{CUSTOMIZABLE} < SSC_{SOC}$) and the P-value from the above Fisher's Exact test is below 0.05 (i.e. P-value < 0.05), then we conclude that the incidence rate of SSCs decreased statistically significantly in Customizable compared with SOC dressing in this clinical study. As supportive analysis, the incidence of SSC will be compared using the ITT population.

As additional supportive analysis, logistic regression analysis may be performed with the ITT and FAS populations. Covariates to be included in the logistic regression will be incision type (i.e., transverse, fleur- de-lis, and vertical incisions), total incision length, BMI, and any other baseline covariates identified following the methods proposed by Hosmer and Lemeshow. Once covariates have been determined, logistic regression will be used to evaluate the treatment with adjustment for the statistically significant covariates. Hospital and hospital by treatment effects will be included as random effects in the logistic regression model to evaluate heterogeneity of treatment effect. If more than three covariates are identified, the treatment will also be evaluated by separate models controlling for each covariate with random effects of hospital and hospital by treatment.

10.5.2 Secondary Effectiveness Analyses

10.5.2.1 Number of Clinically Relevant Interventions (CRI)

The secondary endpoint for this study is the number of CRI of the surgical incision. The number of CRI will be computed and compared between the two treatment arms (Customizable versus SOC) based on the FAS population. The number of CRIs will be calculated for each treatment arm as follows:

The Number of CRI = Number of CRI experienced per Subject in FAS Population

If a Subject has the same CRI for a complication on multiple occasions, or experiences multiple CRIs post surgery up to Visit 9, each CRI will be counted separately until the complication resolves or the study ends. The number of CRI results will be presented by treatment arm and overall. Depending on the estimate of the dispersion of the data, a zero-inflated Poisson (ZIP) or zero-inflated negative Binomial (ZINB) model will be used to model the number of CRI to account for excess zeros. Treatment factor, number of days in study from time of therapy initiation, and significant covariates (e.g. BMI, incision type), will be included as independent variables in the analysis of the number of CRIs.

The hypothesis for testing the treatment effect is as follows:

H_0: *The parameter estimate for the treatment effect equal to 0*
$\beta_{treatment} = 0$

H_1: *The parameter estimate for the treatment effect not equal to 0*
$\beta_{treatment} \neq 0$

If the number of CRI for one treatment group is inadequate for the proposed analysis, the incidence of CRI will be calculated for each treatment arm as follows:

CRI rate = [Number of Subjects who experienced CRI] / [FAS Population]

If a Subject has the same CRI event on multiple occasions or experience several events of CRI, the Subject will be counted only once in the numerator.

The incidence of CRI results will be presented by treatment arm and overall. The Fisher's Exact test with a two-sided significance level $\alpha = 0.05$ will be used to compare the CRI proportions between the two treatment arms. The null and alternative hypotheses are listed below. A 95% confidence interval for the rate difference between the two treatment arms will be provided.

H_0: *The Customizable and SOC treatment arms have equal incidence rates of CRI*
$CRI_{CUSTOMIZABLE} = CRI_{SOC}$

H_1: *The Customizable and SOC treatment arms have different incidence rates of CRI*
$CRI_{CUSTOMIZABLE} \neq CRI_{SOC}$

As supportive analysis, the incidence of CRI will be compared using the ITT and FAS populations.

Covariates to be included in the logistic regression will be incision type (i.e., transverse, fleur-de-lis, and vertical incisions), total incision length, BMI, and any other baseline covariates following the methods proposed by Hosmer and Lemeshow. Once covariates have been

determined, logistic regression will be used to evaluate the treatment with adjustment for the statistically significant covariates. Hospital and hospital by treatment effects will be included as random effects in the logistic regression model to evaluate heterogeneity of treatment effect. If more than three covariates are identified, the treatment will also be evaluated by separate models controlling for each covariate with random effects of hospital and hospital by treatment.

10.5.3 Supportive / Supplementary Effectiveness Analysis

Supportive, supplementary, and descriptive analyses will also be performed using specified and subset populations on data collected including other data specified in Section 3.1, which includes incision type, location, length, material used for hernia repair, length of therapy, interventions, pain assessments using the visual analog scale, etc.

The specifics of any additional analyses will be determined at the time of analysis. In general, summary statistics will include N, mean, standard deviation, median, range (minimum, maximum) and 95% confidence interval for continuous variables, and frequencies and percentages for categorical variables. If appropriate, continuous variables will be compared using a 2-sample t-test or Wilcoxon Rank-Sum test and categorical variables will be compared using Fisher's Exact test or Chi-Square test. When possible, OLS, logistic regression, and time-to-event analysis, will be performed to control for covariates, such as BMI, incision length, etc., to confirm effect of Customizable versus SOC.

Given the exploratory nature of the supportive or supplementary analyses, no adjustment for multiplicity will be made in these analyses.

10.6 Safety Analyses

Safety analyses will be carried out using the Safety Population to allow a benefit/risk assessment within the same study population.

All AEs recorded during the course of the study will be coded according to the MedDRA (version 13.0) classification system. An event will be considered as *treatment emergent* if the time of onset is after placement of study treatment.

Number and percentage of treated subjects who experienced at least one adverse event in each system organ class by preferred term will be used to summarize all serious and non-serious adverse events. Summary tables by treatment arm and overall will be provided of incidences for all treatment emergent adverse events, treatment – related adverse events, adverse events by maximum severity, serious adverse events, and adverse events that led to study discontinuation. In any given category (e.g., system organ class or preferred term) a Subject

will be counted only once. If a Subject has the same adverse event on multiple occasions, only the one with maximum severity will be presented. The denominator for the calculation of percentages will be the number of Subjects in the sub-arm of Subjects being tabulated and not the number of events.

10.7 Deviations to the Study Protocol

All protocol deviations will be identified, recorded and presented in a protocol deviation log. Additionally, any major protocol deviations which increase Subject risk or impact clinical study endpoints will be identified and subsequently tabulated in summary tables. These may include but are not limited to improper consent of Subject, failure of Subject to meet all inclusion criteria and none of the exclusion criteria prior to randomization, and Subject noncompliance.

Any departure or deviation from the originally planned statistical methodologies will be documented and discussed in the SAP, which will include the statistical rationale for diverting from the originally planned statistical summaries and/or analyses.

10.8 Interim Data Review

There is no formal planned interim analysis for this clinical study. However, there is one planned interim data review with one planned final data analysis. Planned interim data review will be conducted when approximately 60 subjects have completed Visit 9 or completed the study. Data from this interim data review will be used to verify the assumptions for sample size calculation or to re-estimate the sample size (Section 10.1). The interim analysis will be based off of the ITT subject population of available data.

10.9 Handling of Missing or Spurious Data

There will not be a specific algorithm for imputing missing data for this clinical study. All recorded data will be used in the analysis of pertinent endpoints and will be presented in the subject data listings as well.

11 Receiving, Storage, Dispensing and Return of Study Products

11.1 Shipment and Receipt

KCI will ensure that no study product will be released to a site until KCI receives written confirmation that the IRB has approved the study at that site.

Prior to the release of study product to the sites, KCI will complete the appropriate accountability forms, which will accompany the shipment of the study product and serve as a shipping record from KCI.

Upon receipt of product, the Investigator, or designee, will inventory the shipment and verify the lot numbers (Customizable kits) and serial numbers (ActiV.A.C. units) against the information provided on the accountability forms. The Investigator, or designee, will sign the form(s) and return it to the KCI monitor, or designee, with notations regarding any missing study product or other discrepancies.

11.2 Study Product Storage

The Customizable kit (Customizable dressing and other materials) and ActiV.A.C. units, are to be stored in a dry location at controlled room temperature away from direct sun exposure in a secure, limited access area under the control of the Investigator.

If storage issues are identified, the site will insure that conditions be brought into compliance. The deviation should be relayed to KCI and the governing IRB as applicable to local or central IRB policies. Situational guidance and corrective means will be assessed and provided by KCI as appropriate.

At the time of the initial site training for the clinical investigation, the KCI monitor will verify that the study products are stored in a secure, limited-access location.

11.3 Study Product Accountability

Each site will inventory and account for study product used throughout the course of the study utilizing accountability forms provided by KCI.

All study products and study-related supplies must be accounted for whether used or unused. The KCI monitor will verify that study product documentation is maintained in the appropriate Subject or study files during monitoring visits. If there is an urgent need to replace any missing or otherwise discrepant shipment contents, the Investigator, or designee, will contact the KCI monitor, or designee, immediately.

ActiV.A.C. units will be returned to KCI after use by a Subject. Each site has authorization from KCI to destroy dispensed Customizable dressings on site per their local biohazard policy.

In the event a malfunction or an adverse device-related event occurs with a dispensed ActiV.A.C. unit, the device will be returned to KCI USA, Inc. as expeditiously as possible.

At the completion of the study, there will be a final reconciliation of study product shipped, used, and returned. Undispensed ActiV.A.C. units and Customizable kits will be returned to KCI.

12 Data Handling and Record Keeping

12.1 Investigator/Site Staff Training

The Investigator and site staff will be trained on the study as a whole, use of the study products, and any specialized procedures prior to and/or during the site initiation visit. KCI will provide clinical support to site staff for any questions or concerns related to study products and treatments; however, KCI will not have influence on Subject care.

12.2 Electronic Case Report Form and Source Documents

Source documents include all information in original records, certified copies of original records, of clinical findings, observations, or other activities necessary for the reconstruction and evaluation of the study. All source documents should be completed in their entirety in a neat, legible manner to ensure accurate interpretation of the data.

Data from source documents of each Subject will be entered into the Subject's electronic Case Report Form (eCRF). Guidance for eCRF completion will be provided and reviewed with the site staff before the start of the study.

12.3 KCI USA, Inc. Monitoring of Study Data

The Investigator will allow access to his/her clinical study records for periodic on-site monitoring visits by a KCI representative, with the understanding that the representative is bound by professional secrecy and will not disclose a Subject's personal identity or personal medical information. The KCI representative will review eCRFs for completeness during on-site monitoring visits and after the eCRFs are submitted to KCI; any discrepancies will be resolved with the Investigator or designee, as appropriate. The data will be entered into the clinical study database and verified for accuracy.

12.4 Data Handling

KCI is responsible for compilation and verification of the clinical study data, retention of the clinical study database, performance of statistical analysis, and preparation of the data reports.

12.5 Records Retention

The Investigator will maintain all study documentation in his/her possession and/or control and institute measures to prevent accidental or premature destruction of any data and/or documents related to the study.

After formal discontinuation or completion of the study, the Investigator will retain all clinical study documentation produced by the Investigator and/or designee(s) for a minimum of three (3) years or in accordance with the regulations in effect for the jurisdiction where the site is located.

13 Administrative Requirements

13.1 Good Clinical Practice

This study is to be conducted according to US and international standards of good clinical practice (FDA Title 21 part 312 and International Conference on Harmonisation guidelines), applicable government regulations and institutional research policies and procedures.

13.2 Ethical Considerations

This protocol and any amendments will be submitted to a properly constituted IRB in agreement with local laws, for formal approval of the study. The decision of the IRB concerning the conduct of the study will be made in writing to the Investigator and a copy of the decision will be provided to KCI before initiation of the study at the site. The Investigator will provide a list of IRB members and their affiliates to KCI.

13.3 Subject informed Consent

Written informed consent will be obtained from a potential Subject after the study has been fully explained and prior to the conduct of any study-related procedures. Obtaining informed consent is a process that must be documented in compliance with GCP, IRB and other applicable regulatory requirements. The Investigator is responsible for continuing an open conversation with the Subject in regard to their continued participation in the study.

13.4 Confidentiality

Information collected about Subjects during the study will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). This law requires signed Subject authorization informing the Subject of the following:

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

In the event that a Subject revokes authorization to collect or use PHI, the Investigator retains the ability to use all information collected prior to the revocation of Subject authorization. For Subjects who have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period. *Clinicaltrials.gov Registration*

A description of this study will be available on http://www.ClinicalTrials.gov as required by U.S. law. This website will not include information that identifies Subjects. At most, the website will include a summary of the results of the study and will be available for public review at any time.

13.5 Auditing and Inspecting

Participation as an Investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable compliance and quality assurance offices.

The investigator will permit study-related monitoring, audits, and inspections by the IRB, KCI, and government regulatory bodies of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.).

14 Publication Plan

Use of the study data for publications and/or presentations is prohibited without prior approval from KCI.

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