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| Mount Sinai | Protocol Title: | ***Prophylactic Negative Pressure Wound Therapy to Reduce Surgical Site Infections in Elective Clean-Contaminated Colon Resections*** |
| | Principal Investigator Name/Contact Info: | Joel Bauer, MD<br>x42983, joel.bauer@mountsinai.org |
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| | Date Revised: | 10/10/2018 |
| | Study Number: | |

# HRP-503 Protocol Template

*Instructions:*

1. *Prepare a document with the following sections. Note that, depending on the nature of your research, certain sections below may not be applicable. Indicate N/A as appropriate, explaining where possible.*
2. *For any items described in the sponsor's protocol, grant application or other source documents submitted with the application, you may reference the title and page numbers of these documents rather than cutting and pasting into this document.* ***Do NOT refer to any derived documents, such as the Sample Consent document, or other internal documents required with the submission.***
3. *If you reference page numbers, attach those pages to this protocol.*
4. *When you write a protocol, keep an electronic copy. You will need to modify this copy when making changes.*

## Brief Summary of Research (250-400 words):

The purpose of this study is to see if the Negative Pressure Wound Therapy (NPWT) system is effective and safe for the prevention of superficial and deep incisional surgical site infections (SSI) in high risk patients within 30 days after elective colorectal surgery. It has been shown that patients with an IBD, patients undergoing a reoperation or patients with certain comorbidities are at a higher risk of developing an SSI. The NPWT device is a wound dressing with a vacuum system that can be placed over abdominal wounds. The study will include up to 400 patients at this single site, where these high risk patients will be randomized to receive either one of two arms. The first arm involves the placement of the NPWT device in the immediate postoperative period over abdominal wounds after clean-contaminated and contaminated colorectal surgical procedures. The device would then be left on for 5 days. The second arm would be standard of care and would entail routine postoperative protocols. Subjects will then be seen once at a 30 day (± 7 days) follow-up visit to assess for the development of SSIs.

## 1) Objectives:

Research Question: Does the application of the NPWT device immediately after surgery work and is it safe for the prevention of superficial and deep incisional surgical site infections (SSI) in high risk patients within 30 days after elective colorectal surgery when compared to standard of care of the same population?

## 2) Background

Surgical site infections (SSIs) are a common cause of nosocomial infections, and a major contributor to patient morbidity, mortality and unnecessary healthcare costs

(1,2). The overall SSI rate in elective, clean-contaminated colon resections has been reported as high as 25%, the highest SSI rate among all elective surgical procedures (1). There has been a national trend in instituting pre-operative and post-operative measures to prevent SSIs (colon bundle), which was found to reduce the relative SSI rate by over 50% (3). At the Mount Sinai Hospital, the colon bundle protocol includes bowel decontamination by mechanical preparation and/or oral antibiotics, monitoring and maintenance of a normal perioperative glycemic index, hair clipping outside the OR, a preoperative chlorhexidine wash, a wound protector, intravenous antibiotics, a separate closing tray, and changing of sterile scrubs prior to closing. The colon bundle was first instituted in 2014 at Mount Sinai, and despite these efforts, while the overall SSI rate has declined, for high-risk, clean-contaminated cases in patients with inflammatory bowel diseases (IBD) or who are undergoing re-operative bowel surgery, the SSI rate remains at around 25%.

Negative pressure incision wound therapy represents a possible opportunity to reduce SSIs in colorectal surgery even further. This technology was initially studied in orthopedics and later in trauma surgery. In colorectal surgery, a retrospective study assessed the use of negative pressure incision wound therapy applied in clean-contaminated cases, compared to standard of care, and found a greater than 50% reduction in the SSI rate (4). However, the intraoperative use of NPWT applied immediately following skin closure has not yet been determined in a prospective, randomized fashion to reduce SSI in clean-contaminated colon resection cases (5).

**Citations:**


1: Fry DE. The prevention of surgical site infection in elective colon surgery. Scientifica (Cairo). 2013;2013:896297. Epub 2013 Dec 19. Review.

2: Shepard J, Ward W, Milstone A, et al. Financial Impact of Surgical Site Infections on Hospitals: The Hospital Management Perspective. JAMA Surg. 2013;148(10):907-914.

3: Tanner J, Padley W, Assadian O, Leaper D, Kiernan M, Edmiston C. Do surgical care bundles reduce the risk of surgical site infections in patients undergoing colorectal surgery? A systematic review and cohort meta-analysis of 8,515 patients. Surgery. 2015 Jul;158(1):66-77.

4: Bonds AM, Novick TK, Dietert JB, Araghizadeh FY, Olson CH. Incisional negative pressure wound therapy significantly reduces surgical site infection in open colorectal surgery. Dis Colon Rectum. 2013 Dec;56(12):1403-8.

5: Chadi SA, Vogt KN, Knowles S, Murphy PB, Van Koughnett JA, Brackstone M, Ott MC. Negative pressure wound therapy use to decrease surgical nosocomial events in colorectal resections (NEPTUNE): study protocol for a randomized controlled trial. Trials. 2015 Jul 30;16:322.

## 3) Setting of the Human Research

Informed consent will be obtained in the offices of one of the investigators while the patient is in for an office visit or at the Mount Sinai Pre-Surgical Testing Center before the patient's screening visit. No study related tests will be performed prior to informed consent. The screening visit and surgery will take place at Mount Sinai Medical Center. The follow-up visits will take place at either the Mount Sinai Medical Center or at Mount Sinai-affiliated off-site practices. Statistical analyses will be performed on de-identified data at Mount Sinai in collaboration with the Department of Biostatistics.

## 4) Resources Available to Conduct the Human Research

There are multiple investigators involved in this study in addition to the Principal Investigator, Joel J Bauer M.D. The Principal Investigator and Co-Investigators all have extensive experience conducting research at the Mount Sinai Medical Center. Additionally, a research coordinator is employed and will be involved in the consent and data collection processes. Prior to participation, each of the investigators will have read the protocol and understand what it involves and what each of their specific responsibilities entail. The recruitment goal for this study is about 400 patients in 24 months. The investigators conduct about 83 clean/contaminated bowel resections each month. In order to meet the recruitment goal, between 15 and 20 patients would need to be consented each month. Because the vast majority of the study data-points are derived from the standard of care perioperative assessments, intraoperative clinical documentation, and the standard of care follow-up visits, meeting this screening and enrollment goal is feasible.

## 5) Study Design

## a) Recruitment Methods

The research coordinator and the investigators will screen the office schedules of the investigators for patients presenting for clean/contaminated colorectal surgeries. A HIPAA waiver was submitted to the IRB to allow the study coordinator to access names, telephone numbers, and medical record numbers (MRN) to inform an investigator of the patient's potential eligibility. Other PHI identifiers have the potential to be seen since the pre-screening does involve opening the electronic medical records of these patients. However, the study team is only specifically looking for elements of PHI that would help them to determine eligibility and be able to identify the patient for consenting (name, MRN, date of birth, date of surgery). After identifying the possible patient, the investigator will approach the patient about the study, to see if the patient is interested. If the patient is interested, the research coordinator will then obtain informed consent during the patient's office visit or prior

to a scheduled screening visit. The patient will not be considered enrolled until it is determined that they have met all inclusion criteria and do not meet any exclusion criteria the day of the procedure.

## b) Inclusion and Exclusion Criteria

All patients from aged 18 or older who will undergo an open or laparoscopic-assisted clean-contaminated or contaminated colorectal surgical procedure will be included if they meet the following criteria. Patients must either have an inflammatory bowel disease, undergoing a stoma reversal, undergoing reoperation within 30 days, or have two or more of the following risk factors: presence of an ostomy, creation of an ostomy, type II diabetes, BMI greater than 30, immunosuppression, malnutrition, current smoker, chronic kidney disease (creatinine > 1.2), and disseminated cancer. Exclusions include patients currently enrolled in another interventional clinical trial, patients with a current infection (including a known urinary tract infection), patients allergic to or hypersensitive to silver, patients planning to undergo a second colorectal surgical procedure (e.g., colostomy or ileostomy takedown) or any other general surgery in less than 30 days of index-surgery, any patient in which the planned surgery would include: i) placement of a stoma in the principal incision; ii) placement of a drain into the supra-peritoneal fascia space that emerges through the principal incision; iv) placement of a drain into the intraperitoneal space that emerges through the principal incision; and v) supplementation of any of the irrigation fluid with antibiotic or antiseptic drugs, patients with healing disorders, pregnant women, prisoners, or any patient that is deemed unsuitable for the study by the Principal Investigator or the operating surgeon/Co-Investigator.

## c) Number of Subjects

Up to 400 subjects are expected to be consented at this site. A series of 330 high risk patients undergoing elective, open or laparoscopic-assisted, clean contaminated cases involving colon resection will be enrolled in this study, of which 110 patients will receive an intraoperative application of NPWT and 220 control patients will receive the standard of care. This number was chosen based on a power analysis. Assuming the NPWT group will have a 50% reduction from the current clean-contaminated colon resection SSI rate of approximately 25%, a two-sided, chi-square power analysis indicated that with a 2:1, control to experimental ratio, 330 total subjects will be needed to detect this difference with 80% power. This number was rounded up to a

total of 400 patients expected to be consented in order to account for screen failures, changes in operative and post-operative treatments, and subjects lost to follow-up. These patients will be allocated to each study arm using a simple randomization scheme. Mount Sinai performed almost 1,000 clean-contaminated colon resections in 2015, and we believe the proposed study can be completed in less than 2 years from the first enrollment.

## d) Study Timelines

Subjects will be contacted and consented prior to surgery, and will then be followed for up to 37 days after the surgery. It is anticipated that subjects will be enrolled through June 2020. The study should be closed out between September 2020 and September 2021. An interim analysis will be conducted when approximately 50% of the subjects have completed 30 day follow-up (55 treatment; 110 control). This will allow the assumptions used to plan the study to be verified or it will allow the planned study enrollment to be adjusted.

## e) Study Endpoints

**Primary Outcome:** Development of SSI within study follow-up period.
**Secondary Outcomes:** Length of hospital stay and serious adverse events.

## f) Procedures Involved in the Human Research

Subjects will be consented prior to each eligible surgery. Prior to surgery, each prospective subject will be interviewed by a member of the study team and a medical history will be obtained. Randomization will occur prior to the start of surgery. The subject will then undergo their scheduled surgery and if they are placed in the experimental arm, they will receive the negative pressure wound therapy. If the subject is in the control arm, they will receive the standard of care wound dressings. Post-operatively, each patient will be followed for up to 37 days and monitored for the development of an SSI and secondary outcomes. If there is no evidence of a wound infection by post-operative day 5, the NPWT device will be removed. A follow-up, outpatient assessment at 30 days (± 7 days) post-operatively will be included for all patients who did not develop a SSI.

It is anticipated that approximately 2% or less of subjects enrolled into this study will require re-operation of the principal incision for within 5-7 days after the original surgery due to various life-threatening complications which may include bleeding, anastomotic dehiscence or other septic complications. For subjects requiring re-

intervention, who did not develop an SSI prior to the reoperation, the NPWT device will be re-applied and the study period re-defined based on the latter procedure.

| *Study Activity* | Screening ≤ 30 days preop | Baseline | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Final Visit 23 to 37 days post op |
|---|---|---|---|---|---|---|---|---|
| Informed Consent | X | | | | | | | |
| Enrollment Criteria | X | | | | | | | |
| Demographic/ Clincal Information | | X | | | | | | |
| Medical History | X | | | | | | | |
| Inclusion/Exclusion Criteria | X | | | | | | | |
| Randomization | | X | | | | | | |
| Surgery | | X | | | | | | |
| Application of NPWT Device | | X | | | | | | |
| Bloodwork | X | | | X* | | | X* | |
| SSI Assessment | | X | X | X | X | X | X | X |
| AE Monitoring | X | X | X | X | X | X | X | X |
| Concomitant Medications | X | X | X | X | X | X | X | X |

Study schedule of events. * indicates that study event may occur with 24 hours of study visit.

## g) Specimen Banking

N/A

## h) Data Management and Confidentiality

All research data for this study will be kept in individual patient research folders, which are locked in either a storage office on the [redacted] of 19 East 98th Street or in the locked office of the research manager. In addition, data will be entered into the secure study database which will only be accessible by the research personnel. All patients will only be identified by a unique ID on all study related materials in patient research folders and on the database. The log linking ID numbers to patient identities will be kept in a password protected file on a Mount Sinai networked computer. The research manager, research coordinator, and investigators will have access to the file containing identifiers.

The data and related publication will be stored according to MSSM's institutional guidelines. The principal investigator will keep the data on a mass storage device (example: Mount Sinai's server) for a minimum period of six years after publication. The study investigators will have access to the study data, which will be stored on a Mount Sinai secured, shared network drive. The de-identified data will be analyzed using statistical software that is installed on a secure Mount Sinai computer. Descriptive analysis and univariate tests will be performed. Logistic and linear multivariate analyses will also be run.

## i) Provisions to Monitor the Data to Ensure the Safety of subjects

**Part I: Elements of a Data and Safety Monitoring Plan**

1. List the name(s) of the individual(s) at MSSM who will be responsible for data and safety monitoring of this study. For each individual, indicate their role, name, title, and department information. The Principal Investigator may be the only monitor of a study.
If the qualifications of an individual to serve as a monitor are not contained in the PPHS application, they must be added to the DSMP either as a narrative description or as a CV.

**MSSM Principal Monitor:**
Principle Investigator:

First Name: Joel
Last Name: Bauer
Academic Title: Clinical Professor
Department: Surgery
Mailing Address: 1010 5th Ave.
New York, NY 10028
Phone: 646-859-1400
Fax: 212-650-9981
E-mail: joel.bauer@mssm.edu

2. Justify your choice of principal monitor in terms of the assessed risk to the research subject's health and wellbeing. In high risk studies when the principal monitor is independent of the study staff, indicate the individual's credentials, relationship to the PI, and the rationale for selection. Dr. Joel Bauer is the PI of the study and

designated principal monitor. He is a certified, accomplished colorectal surgeon with extensive clinical and research experience on colorectal operations and wound management.
3. List the specific items that will be monitored for safety: Adverse events
4. Indicate the frequency at which **ACCUMULATED** safety and data information: At least annually—more often depending on volume of enrollment.
6. Where applicable, indicate dose selection procedures that will be used to minimize toxicity: This is a phase 3 trial, so dosing ranges to minimize toxicity have already been established.
7. List any specialized grading system that will be used to evaluate adverse events: N/A
8. Describe procedures that will be used to assure data accuracy and completeness: Periodic monitoring visits where the monitor will go through collected data, confirming with source documents the accuracy and completeness of the data.
9. Should a temporary or permanent suspension of your study occur, in addition to the PPHS, indicate to whom (NIH, FDA, sponsor, IRB) will you report the occurrence: IRB.

All serious adverse events (SAEs) will be reported to KCI Inc. within 24 hours of learning of the event. SAEs will be reported for the entire duration of the study protocol, up to 37 days post operation.

## j) Withdrawal of Subjects

Subjects may voluntarily withdraw from the study at any time without risk that their clinical care will be jeopardized in any way. Subjects wishing to withdraw must do so in writing to the principal investigator whose contact information will be provided on a copy of the informed consent document that has been signed by the participant and given to them to take home.

## 6) Risks to Subjects

1. There is the risk of loss of private health information; this risk always exists, but there are procedures in place to minimize the risk.

2. There is the risk of an adverse allergic reaction in patients who are allergic or hypersensitive to acrylic adhesives or silver.

3. There is a slight possibility that NPWT device could cause local wound erythema and irritation.

The following AEs are theoretically possible following the application of NPWT device. If reported these events should be considered as unexpected:

(1) Hypersensitivity or inflammatory reaction to surfaces of the device.
(2) The risks to unborn or nursing (breast-feeding) infants are unknown. The NPWT device, although unlikely, may be hazardous to unborn or nursing infants.

## 7) Provisions for Research Related Injury

In the event of any personal injury or adverse event resulting from the administration of the device, medical expenses for the treatment will be billed to the patient's insurance as per standard of care. There is no compensation available for injury resulting from the subject's personal conduct or participation in activities outside the scope of the study protocol. Financial compensation for such things as lost wages, disability or discomfort due to injury is not routinely available.

## 8) Potential Benefits to Subjects

It is possible that subjects who receive the NPWT device will be less likely to experience a wound infection postoperatively.

## 9) Provisions to Protect the Privacy Interests of Subjects

Subjects' privacy will be respected and steps will be taken to put the subject as ease in regards to study procedures. The consent processes will take place in a private office or exam room. All study procedures will be explained to the subject, and any and all questions about the procedures will be answered. When subjects are contacted for follow up, the research team will not leave voicemails identifying the subject's participation in this study. Subjects will only be approached if they are planning on receiving an open bowel surgery, which is one of the main inclusion criteria for this study. PHI will not be released, as described in 5h on this form.

## 10) Economic Impact on Subjects

The cost of the NPWT device will be paid for by KCI Inc. The expense of any tests, or treatments related to standard medical care will be billed to the subject or the subject's insurer in the regular way.

## 11) Payment to Subjects

Subjects will not receive any payment from the Mount Sinai or KCI Inc. for participating in this study.

## 12) Consent Process

Patient consent will be obtained after a full and complete explanation of the study. The consent process will take place in the offices of the investigators or at the Mount Sinai Pre Surgical Testing Center. Participants will be provided with a consent form written in a language they can understand. If English is not the primary language of a potential participant, a translated informed consent will be provided. Should a translated consent or short form be needed, the translated consent document, IRB approved English version of the consent document, and a letter attesting to the accuracy of the translation will be submitted to the IRB for approval before use of the translated document. Patients will be approached with care and will be allowed as much time as necessary to review the study. The investigators, clinical team(s), and research coordinator(s) will make themselves available for questions or concerns in person in the clinic or by phone. Patients will be asked to repeat their understanding of the purpose of the research; requirements of participation; potential risks, benefits, costs, and alternatives to participation; the voluntary nature of participation; and termination of participation. SOP HRP-090 Informed Consent Process for Research will be followed through the consent process.

The ICF and any other written information provided to patients will be revised whenever important new information becomes available that may be relevant to the patient's consent, or there is an amendment to the protocol that necessitates a change to the content of the patient information and/or the written ICF. The investigator will inform the patient of changes in a timely manner and will ask the patient to confirm his/her participation in the study by signing the revised ICF. Any revised written ICF and written information by receive IRB approval in advance of use.

## 13) Process to Document Consent in Writing

The informed consent of all subjects will be documented in writing. The standard PPHS consent template will be used to obtain informed consent (HRP-502a).

## 14) Vulnerable Populations

The following vulnerable populations will be excluded: Adults unable to consent, individuals who are not yet adults (e.g. infants, children, teenagers), wards of the state (e.g. foster children), pregnant women, prisoners.

## 15) Multi-Site Human Research (Coordinating Center)

N/A

## 16) Community-Based Participatory Research

N/A

## 17) Sharing of Results with Subjects

Results will not be shared with subjects.

## 18) IRB Review History

N/A

## 19) Control of Drugs, Biologics, or Devices

The devices will be stored in a locked office room of the principal investigator at the Mount Sinai Hospital, Guggenheim Pavillion 8th floor room 187.