Cover Page:

Official Title: Topical Negative Pressure Wound Therapy to Prevent Wound Complications Following Cesarean Section in High Risk Obstetric Patients

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UACCESS EDOC NUMBER (FOR PROJECTS REQUIRING AN IRB FEE)

PROJECT TITLE: Topical Negative Pressure Wound Therapy to Prevent Wound Complications Following Cesarean Section in High Risk Obstetric Patients

INVESTIGATOR

Principal Investigator Name, Degree(s):	Meghan Hill, MBBS
Principal Investigator UA netID	meghanhill
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ADVISOR CONTACT INFORMATION (REQUIRED FOR ALL STUDENTS AND RESIDENTS)

Name, Degree(s), UA NetID:	
Contact phone:	
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ALTERNATE/COORDINATOR CONTACT INFORMATION

Name, UA NetID:	Destiny Dicken, dlagrand
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SECTION 1: REQUIRED SIGNATURES

1. PRINCIPAL INVESTIGATOR

I will conduct my research according to the University of Arizona HSPP Investigator Manual.

Signature	Date	Print Name
		Meg Hill

2. ADVISOR (FOR ALL STUDENTS AND RESIDENTS ACTING AS THE PI)

I will oversee the student researcher according to the University of Arizona HSPP Investigator Manual.

Signature	Date	Department

3. SCIENTIFIC/SCHOLARLY REVIEW (CANNOT BE ASSOCIATED WITH THE PROJECT)

I have examined the proposal cited above, and find that the information contained therein is complete and that the scientific or scholarly validity of the project appears appropriate.

Signature	Date	Print Name

Official University Email	Phone number

4. DEPARTMENT/CENTER/SECTION REVIEW

I have reviewed this application and determined that all departmental requirements are met and that the investigator has adequate resources to conduct the Human Research.

Signature	Date	Print Name

Official University Email	Phone number

5. RESPONSIBLE PHYSICIAN (PROJECTS INVOLVING MEDICAL PROCEDURES WHICH THE PI IS NOT AUTHORIZED TO CONDUCT)

I am a physician licensed by the State of Arizona (or US license for the SAVAHCS). I will be responsible for ensuring that all procedures that are part of this project and that require the attendance of a licensed physician will have a suitable physician present during the procedures. If at any time this is not possible, I will inform the IRB before any procedures are conducted.

Signature	Date	Print Name

6. NATIVE AMERICAN OR INTERNATIONAL INDIGENOUS POPULATIONS REVIEW

Signature needed only if research takes place in Indian Country or among international Indigenous populations, actively recruits Native Americans or international Indigenous populations for enrollment, and/or requires stratification of Native Americans or international Indigenous populations as one of the statistical analyses or study aims.

☐ **Social and Behavioral Projects: American Indian Studies,** (520)621-7108
☐ **Biomedical Procedures: Office of Outreach and Multicultural Affairs,** (602)827-2327

I have examined the proposal cited above and advise that further appropriate tribal/Indigenous approval [ ]is [ ]is not necessary.

Signature	Date	Print Name

SECTION 2: GENERAL INFORMATION

1. Not including this project submission, how many:

a. Human Research studies is the PI involved in as key personnel? 14

b. Active subjects are there in the PI's open Human Research study/ies? 0

c. Investigators are involved on the PI's open Human Research studies? 5

d. Research coordinators are involved on the PI's open Human Research studies? 1

2. What is the expected length of this project? Two years

3. Retention of study materials before, during, and after completion of the project:

a. Where will the original signed consent and PHI Authorization documents be stored (building name and room)? University Main Campus, 8319

b. How long will the data/consents be kept after conclusion of the project? ☒ 6 years ☐ Other:_____

4. If the Human Research project is funded, identify all sponsoring entity/ies): N/A

5. If funding support is from a federal agency (such as a training grant, infrastructure grant, salary support, project grant, etc.), list federal agency and grant number Smith & Nephew

6. Total funding amount **OR** per subject amount: N/A

7. The Principal Investigator hereby affirms that ALL individuals who meet the definition of "investigator" for this project in the current "Policy on Investigator Conflict of Interest in Research" have completed the mandatory Conflict of Interest training (http://orcr.arizona.edu/coi/training) and Disclosure of Significant Financial Interests (https://uavpr.arizona.edu/COI/). ☒ Yes

8. Will this project be registered on ClinicalTrials.gov because …? ☒ Yes ☐ No

a. the local PI is the sponsor of the clinical trial (including NIH-funded clinical trials where the local PI is the funding recipient OR IND holder);

OR

b. The PI has been designated by a sponsor, contractor, grantee, or awardee to register the clinical trial to ClinicalTrials.gov, as the Responsible Party (responsible for conducting the trial, and has sufficient data rights)

If yes, please check the appropriate box:

☐ ClinicalTrials.gov "NCT" number for this trial (define):

☒ Registration pending

☐ Clinical trial does not require registration (click above to see what studies qualify)

SECTION 3. PROJECT NARRATIVE

1) Background

Non-healing wounds required to heal by secondary intention affect the healthcare system and the patients in many ways. For the patient, a non-healing wound considerably increases the pain/discomfort associated with the surgical or medical condition. It affects their quality of life and ability to return to normal activities of daily living. It increases their risk of adverse events related to management of the wound. In addition, a non-healing wound significantly increases the overall cost of medical care- related to the need for more frequent clinic visits and hospitalizations, increased length of stays, the need for repeat operative procedures and wound care supplies (1, 4).

Topical negative pressure (TNP) is a frequently used method to promote the healing of surgical and non-surgical wounds (1). It uses suction to drain excess fluid from the wound thereby reducing the risk of seroma formation and the risk of infection by decreasing the bacterial load. It has also been shown to stimulate localized blood flow and tissue growth, partially by removing excess fluid but also via mechanical stimulation of nearby tissue (1, 3). Understanding these methods of action, TNP is used frequently in the health care setting to assist with wound healing. Management with TNP of chronic wounds and wounds at high risk for separation has been evaluated in many studies. For example, current studies have investigated the use of prophylactic TNP on closed surgical incisions, including investigations in traumatic injuries, hip arthroplasty, acetabular fractures, sternotomy wounds, vulvectomy incisions and post hysterectomy in obese women- all with promising results. However there is a relative lack of adequately powered patient-oriented evidence demonstrating TNP as a statistically significant agent for preventing or treating wound healing complications (1).

Presently, only one study has evaluated TNP in the obstetric population, specifically obese women undergoing a cesarean section. A retrospective cohort study was done at the University of Maryland to evaluate the efficacy of TNP in decreasing postoperative wound complications when placed over a clean, closed incision following cesarean section in obese patients. Their study demonstrated that there were no wound complications in the population receiving TNP versus a 10.4% complication rate in the control group receiving the standard postoperative dressing (2). However, their study was underpowered from its small sample size and did not show statistical significance.

Obesity is widely prevalent in the United States. In 2012, the CDC reported that 35.8% of women were obese, this prevalence increases as income decreases and is highest for non-Hispanic black women (2). Cesarean sections are considered clean-contaminated procedures; this alone increases the risk of a post-operative wound infection. Wound complications occur in 2.5-16% of cesarean deliveries, influenced by many different factors (5). Obesity is a risk factor that nearly doubles the rate of cesarean section; and the risk of post-operative wound infections in obese women after a cesarean

section has been shown to double for every 5 unit increase in BMI above 30 kg/m^2. Given the prevalence and increasing rate of obesity, and the associated complications particularly with operative procedures, it is important that we re-evaluate how to manage the associated complications and utilize the best possible techniques to decrease maternal morbidity.

Additional co-morbidities increase the risk of wound complications in the setting of cesarean section. These morbidities include maternal diabetes mellitus, history of wound infection or breakdown, chorioamnionitis at the time of cesarean, HIV/AIDS, anticoagulant therapies and autoimmune conditions. These patients may also benefit from innovations in wound management.

This study aims to evaluate the use of TNP over a clean, closed incision following cesarean section in high risk women for preventing complications of wound healing. We hypothesize that using TNP over a clean, closed incision following cesarean section in high risk women will significantly decrease and possibly prevent complications to wound healing. This study will be powered appropriately in order to obtain statistically significant results. We anticipate that by using TNP immediately following the operation we can prevent seroma formation, decrease the bacteria load in the wound and stimulate wound healing all to the effect of minimizing or preventing wound separation/breakdown/necrosis.

(1) Ubbink DT, Westerbos SJ, Evans D, Land L, Vermeulen H. *Topical negative pressure for treating chronic wounds.* The Cochrane Database of Systematic Reviews: 2008 July, 16; (3).

(2) Mark KS, Alger L, Terplan M. *Incisional negative pressure therapy to prevent wound complications following cesarean section in morbidly obese women: A Pilot Study*. Surgical Innovation: 2013 Sep 20. Epub ahead of print.

(3) Malsiner CC, Schmitz M, Horch RE, Keller AK, Leffler M. *Vessel transformation in chronic wounds under topical negative pressure therapy: an immunohistochemical analysis*. International Wound Journal: 2013 September 13. Epub ahead of print.

(4) Mees J, Mardin WA, Senninger N, Bruewer M, Palmes D, Mees ST. *Treatment options for postoperatively infected abdominal wall wounds healing by secondary intention*. Langenbeck's Archives of Surgery: 2012 June, 397: 1359-1366.

(5) Tuuli MG, Rampersad RM, Carbone JF, Stamilio D, Macones GA, Odibo AO. *Staples Compared with Subcuticular Suture for Skin Closure after Cesarean Delivery*. Obstetrics and Gynecology: 2011 Mar;117(3):682-90.

2) Lay Summary (approximately 400 words)

We aim to carry out a randomized controlled trial. Patients with a condition that increases their risk of a wound complication will be approached for inclusion in the trial. Each participant agreeing to study inclusion will be randomized to either suture alone or to closure of their skin incision with suture and then with prophylactic placement of a wound vac (PICO). The wound vac will be left in place until the day of discharge. Prior to discharge, the bandage will be removed, the wound inspected and a new bandage will be reapplied to the wound. The patient will remove the bandage and wound vacuum on POD#7 at home. Both items can be discarded in a normal trash receptacle. We will also obtain

permission to call the participants for a patient satisfaction questionnaire at 1 week post-op, and possibly 2 and 6 weeks if they have not presented for their post op/partum appointments or the questionnaire could not be obtained at their visit. The wound will be re-assessed at their 2 week and 6 week post-op follow up visits. The patients will be assessed by either the Principal Investigator, Co-investigator and/or Senior Investigator at their post-operative clinic visits. The investigator will ask the patient if they have had any postoperative complications since their surgery and will be asked to detail any complications if they answer yes to this question. They will also be asked to confirm that their wound has completely closed at this time.

3) Setting of the Human Research

Patients being approached for inclusion in this study are those presenting to labor and delivery for delivery care or to B–UMCT for their regularly scheduled clinic visit (1501 N. Campbell Ave, 8th Floor, Tucson, AZ).

4) Resources available to conduct the Human Research

The Labor and Delivery unit at the Banner –University Medical Center comprises a triage area, up to 14 laboring rooms and 2 fully operational operating rooms.

There are 16 resident physicians, 2 clinical fellows and multiple OBGYN physicians available for the medical care of pregnant and laboring women. There is also around the clock nursing and anesthesia care available 7 days per week.

The postoperative care delivered to patients is on the 7th floor of the hospital, directly below the Labor and Delivery Unit. The same resident physicians and physicians staff this area.

5) Study Population

Pregnant women with high risk obstetric complications who present to Labor and Delivery at B–UMCT for care at time of delivery and/or to the clinic for a regularly scheduled visit will be potential individuals enrolled in our study.

Sample size calculations predict that with a wound breakdown rate of 20% in high risk patients, approximately 80 patients in each group would be needed to show a complication rate decrease to 5%. We will recruit a total of 200 patients, 100 in the control group and 100 in the study group.

When the women partake in the study device, they will no longer be pregnant as the device will be applied post operatively (after the cesarean section).

6) Recruitment Methods and Consenting Process

Patients will be identified by the investigators during the course of their clinical work or by designated study personnel during pre-screening (see Appendix F). Patients eligible for inclusion in this study will be approached by the Principal investigator, Co-investigator,Senior Investigator, and/or study personnel if they meet the following cirteria:

Inclusion criteria:

1) Maternal Age 18 or above
2) Cesarean delivery
3) Maternal condition which increases the risk of wound complication. These conditions include: Obesity (BMI >30), diabetes, HIV/AIDS, chorioamnionitis, rheumatologic disease, history of wound complication, anticoagulant therapy.
4) Patient able to read and speak English or Spanish (once the consent form has been approved, a translated Spanish consent will be submitted to the IRB for approval, no Spanish speaking patients will be recruited until approval is received)

Exclusion criteria:

1) Minors (<18 years of age)
2) Non-cesarean wound (ie tubal ligation wound)
3) No high risk maternal condition
4) Patient unable to read and speak English or Spanish.
5) Prisoners

The PI and co-investigators will already be known to the patient per their clinical care and other non-clinical study staff will introduce themselves appropriately when presenting the research material. Please note: A Banner Employee will approach the subject first to ask them if they wish to learn more about the study, before any recruitment may take place. The consent document (see attached to this submission) will be used as an aid in discussing this research with patients. Though there is not script that the study personnel will read out to the patient, the sections of the consent form will be discussed with this patient before study proceedings are undertaken.

Additionally, patients who undergo a C-section when no study personnel are in the hospital may enroll via phone. Eligible patients who have been identified by a physician on Labor and Delivery will be asked if they would like to hear about the study. Those interested will discuss the study via phone with a member of the study staff on the VOTF using the phone disclosure as a guide. Patients will then be consented to the study in person, including access to PHI, by a member of the study staff before they leave the hospital.

We are requesting a partial PHI for recruitment purposes.

7) Procedures involved in the Human Research

The randomization key will be provided by the department of statistics at the University of Arizona. Envelopes with a 1:1 study allocation (wound vac : no wound vac) will be provided and placed in the Pyxis on labor and delivery. The Pyxis is utilized for two reasons: 1) It is a standard place that the allocations can always be kept and 2) Nursing staff are required to access the Pyxis and an electronic log is kept of when the drawer was opened to retrieve an envelope with study allocation. This will provide adequate concealment of the allocations.

Once consent has been obtained from patients, an envelope containing the study allocation will be retrieved from the Pyxis.

- Non-wound vac patients will undergo wound closure with subcutaneous fat closure with Vicryl in all cases that this is practicable (in extremely thin patients, this may not be possible), followed by subcuticular skin closure also using Vicryl. A compression dressing will then be applied. This dressing is usually removed by the clinician the following day.
- Wound vac patients will undergo wound closure with subcutaneous fat closure with Vicryl in all cases that this is practicable (in extremely thin patients, this may not be possible), followed by subcuticular skin closure also using Vicryl. The wound vac system will then be applied over the closed incision. This vac dressing will then be removed on the day of hospital discharge and replaced with a second bandage and the wound vacuum will be re-activated. The patient will remove both and discard on POD#7. This is per the manufacturer's guidelines for length of use.
- If the patient fails the wound vac therapy- ie the wound separates and requires traditional wound care (packing, wet to dry dressing, etc), then the PICO system is no longer used as part of their care.

Essentially, the standard of care is to close the cesarean section incision. Different providers use different kinds or sutures (made of different material, and of different sizes) or staples to close the subcutaneous fat and the skin. Essentially what we are saying is that all patients in this study would have the subcutaneous fat and skin closed in the same manner (with Vicryl suture). To participate in the trial patients would have to agree to these closure materials - some patients would opt out of the study if they particularly wanted to have their skin closed with staples, for example (though I think that this would be rare as patients tend to prefer suture - it dissolves and does not have to be removed). We chose a standard closure with suture as there is evidence suggesting a lower rate of wound complications with suture as compared to staples.

We thought it would be unrealistic to try to standardize the entire operative approach (closure of the uterus, closure of the fascia) as the different providers working at the hospital may choose not to participate if the approach specified deviated too much from their usual technique.

8) Risks to subjects

The risks to subjects are minimal. All wounds will be closed in a way considered evidence-based. The only difference is the wound dressing applied over the closed wound and the time of removal. Though it is possible that the vac remaining over the wound may delay diagnosis of a wound complication this is very unlikely as the dressing is small, and a wound complication without significant surrounding erytheema is uncommon.

There is a small risk of loss of protected health information. The PI will mitigate this risk by keeping all consents in a locked cabinet and not keeping any patient identifiers with the data analysis documents.

9) Potential benefits to subjects and/or society

Patients will receive no monetary benefit from being in this study.

If the hypothesis of this study is correct, those in the treatment arm (ie the wound vac arm) may experience a lower rate of wound complications.

Wound management is a common clinical problem encountered in obstetrics. Implications of a lower complication rate with the utilization of wound vacs would include offering this treatment in high risk groups in the future.

10) Provisions to protect the privacy of subjects and the confidentiality of data

Privacy of subjects will be respected at all times during the study. Patients will only be consented in a private area (pre-operative area, clinic room or laboring room). Patients are asked during all encounters with a physician whether or not they would like their family or friends present. Patients will not be required to have support people leave the room for inclusion in the study.

Patient confidentiality will be respected at all times. The records review required for the study will only be performed by those personnel appearing on the VOTF. All documents with traceable patient data (ie consent forms/data collection forms) will be stored in a locked cabinet in the fellow's office (Room 8327 G). These records will be stored for a period of 6 years.

A data sheet will be created to include all data pertaining to the study without any patient identifiers. This document will be kept separate from the consent forms and data collection forms.

Additionally, a REDCap database will be used to facilitate tracking patient follow-up and statistical analysis when study procedures are completed. The REDCap database will store identifiable information. The REDCap data base will be maintained for 6 years after completion of the study.

11) Access to Private Information

a. Authorization for Access to Protected Health Information

Patients agreeing to participate in this study will be made aware that record review of their protected health information will occur as a part of the study. The consent form includes a HIPPA consent.

b. Authorization for Access to Educational Information

N/A

12) Cost to subjects

Patients will not be charged for use of the wound vac. They will otherwise be billed for their hospital care.

13) Subject compensation

Subjects will not be compensated for participation in this study.

14) Medical care and compensation for injury

This study includes no more than minimal risk to subjects. If a patient has a complication during their hospitalization, their insurance will be billed for their care.

15) Monitoring the data for subject safety

N/A as this research poses no more than minimal risk to subjects.

16) Withdrawal of subjects

Patients may withdraw from this research at any time. If withdrawal occurs before vac placement, no additional interaction with an investigator will be needed. If withdrawal occurs after the vac has been placed, the physician caring for the patient will remove the vac as soon as practicably possible.

17) Sharing of results with subjects

Patients will not be contacted regarding the outcome of this research. If the outcomes are published at a later date, subjects will have access to overall results through this medium.

18) Information management

Information management will be the sole responsibility of the investigators. This will be carried out at the University of Arizona. The sponsoring company makes no stipulations regarding publication.

19) Drugs, Devices, and Gases

The wound vac (PICO system) is an FDA approved device for wound care. This is not an FDA trial.

20) Multi-site Human Research'

N/A

SECTION 4: LIST OF ATTACHMENTS FOR THIS SUBMISSION	
Document Name	**Version Date**
1. Consent form	**1.** 8/22/16
2. Data Collection Form	**2.**
3. Research Protocol	**3.**
4. Appendix F	**4.** 8/22/16
5. Patient Satisfaction Questionnaire (for telephone interview)	**5.**
6. PICO patient information (Smith and Nephew brochure)- PDF	**6.**

Submission List for F200: Application for Human Research

Required items for all F200 submissions:

- F107: Verification of Training Form
- Current PI/Co-PI CVs or biosketch, if not included with copy of grant application

Other Items as applicable:

- **Biosafety Review letter** (for UA - Institutional Biosafety Committee)
- **Certificate of Confidentiality**
- **Compressed Gases Review letter** (for UA – Research Instrumentation)
- **Contract** – complete or draft copy of contract including budget
- **Data Collection Tools** – surveys, questionnaires, diaries not included in the protocol, data abstraction form for records review
- **Data Monitoring Charter and Plan**
- **Drug/Device information** – Investigator's Brochure, drug product sheet, device manual, user's manual, instructions for use, package insert, IND/IDE documentation, FDA 1572 form, 510k indication, FDA exemption, sponsor determination of device risk, etc.
- **Export Control Review**
- **Grant Application(s)** – complete copy of grant, regardless of home institution or funding agency, and a copy of the Notice of Grant Award

- **Informed Consent/Permission/Assent Form(s)** – including study specific release of information documents, DHHS approved sample consent forms. If consent will not be documented in writing, a script of information to be provided orally to subjects
- Other Approval letters (e.g., school districts, Tribal, other IRB approvals)
- **Participant Materials** – All written materials to be provided to or meant to be seen or heard by subjects (e.g. study newsletter, physician to participant letter, wallet cards, incentive items, holiday/birthday cards, certificates, instructional videos/written guides, calendars, certification of achievement, etc.)
- **PHI Authorization Form(s)**
- **Protocol** – including all amendments/revisions, sub- or extension-studies
- **Radiation Safety Review** letter
- **Recruitment Materials** – telephone scripts, flyers, brochures, websites, email texts, radio/television spots, newspaper advertisements, press releases, etc.
- **Scientific Review Committee** letter (for cancer related projects – AZCC SRC; other units as applicable if the unit has a scientific review committee)
- **Site Authorizations** for research purposes and/or access to administrative records/samples
  - External sites (such as schools, other hospitals or campuses, etc.)
  - UAHN University Campus, South Campus and clinics Site Review Authority (SRA) approval
- **Supplemental site information** (for sites engaged in research where the UA is the IRB of record)
  - Copy of any approvals granted from that site (including determinations if this site has an IRB of its own)
  - Site-specific F107
  - Copy of the site's human subjects training policy
  - CV and medical license (if applicable) of site PI
- **Travel Authorization documentation** (for UA – Office of Global Initiatives)
- **Use of retrospective research samples and/or data** – IRB approval letter, original consent under which samples/data were collected, letter allowing access to samples

Submitting documents to the IRB

All materials must be typed and submitted electronically. Maintain electronic copies of all information submitted to the HSPP office in case revisions are required. It is recommended that version dates be used while naming documents.

1. Documents must be submitted to the VPR-IRB@email.arizona.edu account and not to individual staff email accounts. After contact by a staff member future correspondence may be communicated directly to the staff member concerning the submission.

2. **If acknowledgement of receipt is needed, please request a "Read Receipt" through your email server.** If you use Microsoft Outlook 2007, this is accomplished by clicking "Options" and choosing the "Request a Read Receipt" checkbox in a new email.

3. One submission request per email (e.g. one new project submission, one continuing review plus attachments, or one modification request).

4. All submissions must have signatures. An email acknowledgement in place of a signature will not be acceptable. If electronic signatures are not available for use, the signature pages may be signed and scanned as a separate Adobe PDF document and attached to the submission email.

5. **Microsoft Word documents are REQUIRED** for (applications, consents, recruitment materials, and data collection instruments (if available). PDFs may be submitted for documents that typically are not revised by the IRB (e.g. Investigator Brochures, sponsor protocols).

6. The email subject line must include: IRB # (if assigned one), PI Last Name, and type of submission (Modification, New Project, Continuing Review, Reportable Item, etc.).

7. The email must provide a list of the documents submitted for review. While the documents attached do not have to adhere to a specific naming scheme, it is requested that each document be named to clearly reflect what is inside.

Submissions not following these guidelines will be returned without review