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MEDICAL COLLEGE OF WISCONSIN

1. Project Identification

1.0 * **Does this project involve any minor subjects, or use of records or biospecimens related to minors?** Minor status is defined by the legal age of consent for the state or country where the research activity takes place; e.g., under 18 years of age in Wisconsin.

- ○ All minors
- ○ Some adults and some minors
- ● **All adults of legal age**

☐ **If you selected "All minors" or "Some adults and some minors" above, you must consult with the MCW/FH IRB Office (414-955-8422). Check the box to confirm that you have done so and have been advised to submit this project to the MCW/FH IRB.**

1.1 * **Short Title:**
Multi-Center Thoracic Irrigation

1.2 * **Full Title of Project:**
Thoracostomy Tube Irrigation: A Multi-Center Trial Investigating its Efficacy in the Reduction of Secondary Intervention for the Management of Retained Hemothorax

1.3 * **Principal Investigator (PI):**
Thomas Carver

1.3.1 * **Does the Principal Investigator, their immediate family members (spouse and dependent children) or their significant other have a "Significant Financial Interest" with the sponsors of this research or that might affect the result of this research?**
○ Yes ● **No**

1.3.2 * **Does the Principal Investigator need to access Epic for this project?** ● **Yes** ○ No

1.3.3 * **Will the Principal Investigator be involved with any of the following:**
- ☐ Screening subjects for entry into a magnetic environment for MRI
- ☐ Entry into a magnetic environment for MRI
- ☑ **None of the above**

1.4 * **Will there be other project team members in addition to the Principal Investigator?**
● **Yes** ○ No

2. Project Team

2.1 Project Team Members Other Than PI:

	Last Name	First Name	Primary Organization	Department	Position	Is Primary Contact	Can Edit	Receives Emails	Role on Project	Consenting Subjects	MRI Involvement?	Epic?	Human Material?	SFI
View	Boyle	Kelly	Medical College of Wisconsin	Surgery		☐	☑	☑	Key Personnel	☐	☐ *	☑	☐	☐
View	Brandolino	Amber	Medical College of Wisconsin	Surgery	Clinical Research Coordinator III	☑	☑	☑	Project Staff	☐	☐ *	☑	☐	☐
View	De Moya	Marc	Medical College of Wisconsin	Surgery	Chief, Professor	☐	☑	☑	Key Personnel	☐	☐ *	☑	☐ *	☐

	Last Name	First Name	Primary Organization	Department	Position	Is Primary Contact	Can Edit	Receives Emails	Role on Project	Consenting Subjects	MRI Involvement?	Epic?	Human Material?	SFI
View	Emmrich	Amanda	Medical College of Wisconsin	Surgery	Clinical Research Coordinator III	☐	☐	☐	Project Staff	☐	☐ *	☐	☐	☐
View	Gabel	Shelley	Medical College of Wisconsin	Non-MCW	Student | Medical Student	☐	☐	☐	Project Staff	☐	☐ *	☑	☐	☐
View	Kugler	Nathan	Medical College of Wisconsin	Surgery		☐	☑	☑	Key Personnel	☐	☐ *	☑	☐ *	☐
View	Mantz-Wichman	Margo	Medical College of Wisconsin	Surgery	Research Nurse I	☐	☑	☑	Project Staff	☐	☐ *	☑	☐	☐
View	Mccormick	Ali	Medical College of Wisconsin	Surgery	Research Resident	☐	☑	☑	Project Staff	☐	☐ *	☑	☐	☐
View	Packard	Krissa	Medical College of Wisconsin	Surgery	Manager Clinical Research	☐	☐	☐	Project Staff	☐	☐ *	☐	☐	☐
View	Sporleder	Justin	Medical College of Wisconsin	Non-MCW	Student | Medical Student	☐	☐	☐	Project Staff	☐	☐ *	☑	☐	☐
View	Strong	Stephanie	Medical College of Wisconsin	Non-MCW	Student | Medical Student	☐	☐	☐	Project Staff	☐	☐ *	☑	☐	☐

3. Project Category

3.1 * Which category best describes the type of project you are submitting for review?

- ○ **Case Report†** – Involves a description of routine medical care for three patients or less
- ○ **Quality Improvement†** – The entire project is initiated, overseen, and analyzed by an official Froedtert Health Entity Quality Assurance committee
- ● **Research Project† - Including clinical trials, record reviews, specimen reviews, surveys, etc.**
- ○ **Research Project plus distant bank†** - No banking at a local project site
- ○ **Research Project plus creating a new local bank†** - At least one at a local project site *Note: see 3.1.1 below
- ○ **Creating a new local bank†** - No research project being proposed in this submission
- ○ **Treatment Use†** - Use of investigational drugs, medical devices, biologics or Humanitarian Use Devices (HUDs) solely for clinical purposes with no elements of research or research data collection
- ○ **Emergency Use†** - Use of an investigational drug, medical device, biologic or Humanitarian Use Device (HUD) – after-the-fact report to the IRB
- ○ **Deferral to NCI CIRB†** - For Cancer Cooperative Group (RTOG, ECOG, SWOG, etc.) projects in which the NCI CIRB will be the IRB of record
- ○ **Not Human Subjects Research†** – The project will not interact/intervene with living human beings

3.2 * Does the proposed project involve any of the following features?

(check all that apply)

- ☐ Deception projects

(check all that apply)

- [ ] Direct contact with subjects
- [ ] Human Source Material (human blood, tissues, cell lines)
- [x] **None of the above**

3. Project Elements

3.3 * Does this project involve any of the following elements?

(check all that apply)

- [ ] 100% of subjects are known to be deceased, e.g., work with cadavers or biospecimens of deceased persons; record reviews where all subjects are demonstrably deceased
- [ ] In-vitro or laboratory diagnostic tests in the absence of FDA approval and/or CLIA certification: chemistry, drug monitoring, immunological/hematologic, tumor marker, genetic disorder, infectious disease, microorganism, bio-threat tests
- [ ] Dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus from any source, commercial or otherwise
- [x] **More than one site. Project activity will take place at other institutions or locations that are not under the supervision of the PI listed on this IRB application.**
- [ ] Any part of the project takes place in another country. Check here if the PI is the lead PI for a multi-site project where one or more sites are in another country or if any project related work or oversight work is being done in another country.
- [ ] Application to waive informed consent requirements for certain types of planned emergency medicine research [(21 CFR 50.24 or 45 CFR 46 Waiver of Informed Consent Requirements in Certain Emergency Research) or (FR doc. 96.24968)]
- [ ] Research using the internet as a source of information or a survey tool
- [ ] None of the above

3.4 * Does this project involve ONLY one or more of the following minimal risk activities?

(check all that apply)

- [ ] Biospecimens collected for non-research purposes
- [ ] Blood draws with collection limited to finger, heel or ear stick, or venipuncture
- [ ] Educational
- [ ] Non-invasive collection of biospecimens
- [ ] Non-invasive Procedures
- [ ] Psychosocial Interventions
- [x] **Records collected for non-research purposes**
- [ ] Surveys, questionnaires, interviews, focus groups, or observation of behavior
- [ ] Voice, Image or digital recording for research purposes
- [ ] No, my project involves activities which are not minimal risk, or the identified activity no longer qualifies as minimal risk

3.5 * Use of Identifiers - indicate the level of "subject identification" you require to BEGIN this work.

- If any element of your records, data files, or administrative records contains an identifier, you should select Identified Data.
- If you plan to de-identify data at any time other than the first day you access the information, you should select Identified Data.
- If different levels apply, choose the "most identified" one, e.g., if level A and level B apply, choose level A.

- ● **A - IDENTIFIED DATA: Utilizes one or more identifiers, including those defined by HIPAA Privacy Rule but not using a "limited data set." See help text for complete listing.**
- ○ **B - CODED DATA, KEY held by project team**: Data is coded; **and** key code held by any person at MCW, Froedtert Hospital, Children's Hospital of Wisconsin, or Versiti, Inc. whether or not they are part of the project team.
- ○ **C - CODED DATA, KEY not held by project team**: Data is coded; key code not held by any MCW/Froedtert faculty member, employee, fellow, resident, or student; key code not held by any member of the project team; **and** the key code will never be accessible to any member of the project team.
- ○ **D - LIMITED DATA SET**: The only HIPAA identifiers utilized are dates or certain allowable geographic subdivisions; an IRB "limited data set" data use agreement has been executed by the PI; and is uploaded into this IRB application.
- ○ **E - DE-IDENTIFICATION PROCESS**: The IRB application describes how the project team will de-identify data in one of two approvable methods: 1) reliance on an MCW/FH IRB-sanctioned "honest broker" or 2) receiving coded data/specimens without identifiers and without a key code. For details see *"Two ways to de-identify data or biospecimens for IRB purposes."* To use these options, no code keys may be created or saved and the resulting dataset can never be re-identified. In addition, a complete list of project variables must be uploaded in Section 52.
- ○ **F - ANONYMIZED**: The investigator receives data in anonymized form and no other party has the potential to re-identify data (i.e. no code key exists anywhere in the world). In this case, the IRB application must include a detailed description of how the data was collected, e.g., anonymous surveys, or who provided the anonymized data or biospecimens, so the IRB can verify the source and the irreversibility of anonymization. In addition, a complete list of variables, e.g., data recording sheet, Case Report Form, anything that summarizes all the information that will be recorded, must be included in Section52 Attached Documents.

3F. Records Research - Part I

You received this section because in Section 3. Project Elements, Question 3.4, you checked "Records collected for non-research purposes"

3F.1 * **For what purpose were the records originally created?**

(check all that apply)

- ☑ Clinical Care
  - * **Identify the Sources:**
    - ☐ Medical College of Wisconsin
    - ☑ **Froedtert Hospital Campus (including all speciality clinics, the Cancer Center and the Eye Institute)**
    - ☐ Versiti, Inc. and Blood Research Institute
    - ☐ Other
- ☐ Quality assurance
- ☐ School or teaching records
- ☑ **Billing or insurance**
- ☐ Program administration
- ☑ **Hospital or community surveillance**
- ☐ Different research project
- ☐ Other

3F. Records Research - Part II

3F.2 * **Do you plan to use/analyze records created before the date of IRB approval (retrospective records)?** (i.e., NO additional cases created after that date, and NO opportunity to include follow-up

information created after that date)
○ Yes ● **No**

3F.3 * **Do you plan to access records created after the date of IRB approval (prospective records)?**
● **Yes** ○ No

If Yes,
* **3F.3.1 How will you get permission to access these records?**
(check all that apply)

- ☐ Using informed consent
- ☐ From an IRB approved bank
- ☑ **Other**

* **3F.3.1.1 Specify other:**
Waiver of Consent

3F.4 * **Estimate the total number of subject records that you intend to:**
(The IRB expects the investigator to provide meaningful estimates and to adhere reasonably to these estimates. It is often better to make a slight over-estimate of numbers.)

Screen, whether you use the record for this project or not.
10,000

Use for this project.
1,000

3F.5 * **Explain how you determined the number of records to include in the project at this site.**
We plan to analyze the records of patients who undergo thoracostomy tube placement with and without prophylactic thoracic irrigation. This prospective observational study will include participants from multiple trauma centers around the country. Historically, between 10-30% of patients who undergo standard thoracostomy tube placement for the management of traumatic hemothorax require secondary intervention. A recently completed study demonstrated a 5% secondary intervention rate among individuals who underwent thoracic irrigation at the time of thoracostomy tube placement for the management of traumatic hemothorax. A power analysis utilizing 10% and 20% secondary intervention rates for the irrigation and standard cohorts, respectively, demonstrates that 108 patients are needed for analysis within the irrigation cohort. In order to appropriately perform a propensity score matched analysis, enrollment of patients into the standard thoracostomy tube cohort in a 3:1 fashion requires approximately 324 patients within this cohort. The rate of thoracostomy tube needs at our institution is approximately 10%. Based on this, it is anticipated that nearly 10,000 records overall will be briefly scanned for potential inclusion.

4. Safety and Research Review Committees

4.1 * **Does this project include any of the following regulated items or resources?**
Selections will determine if there are additional review requirements prior to IRB review process beginning, per MCW policy:
(check all that apply)

- ☐ Biological Toxins
- ☐ Project with a cancer focus (including healthy subjects)
- ☐ CTSI Adult Translational Research Unit (facility or resources)
- ☐ Human Gene Transfer
- ☐ Human stem cells
- ☐ Human/Non Human Primate (NHP) Cell Lines, Tissues, or Blood Products
- ☐ Microorganisms
- ☐ Magnetic Resonance Imaging (MRI) (that is not Standard of Care)
- ☐ Radiation therapy, radioactive materials/brachytherapy, CT, X-ray, fluroscopy

(check all that apply)

- [ ] Recombinant DNA (non-Viral vectors)
- [ ] Viral Vectors
- [x] **None of the above**

6. Project Locations

6.1 * **Under the direction/supervision of this Principal Investigator, project activities will take place at the following locations:**

(check all that apply)

- [x] Froedtert & the Medical College of Wisconsin Hospitals and Health Partners
  - [ ] Cardiothoracic Surgery Clinic
  - [ ] Drexel Town Square Health Center
  - [ ] Endocrinology Clinic (Oconomowoc)
  - [ ] Endocrinology Clinic (Waukesha)
  - [ ] Fitness Center (Sports Medicine)
  - [x] **Froedtert Hospital (including all specialty clinics, the Cancer Center and the Eye Institute)**
  - [ ] Froedtert Menomonee Falls Hospital
  - [ ] Froedtert West Bend Hospital
  - [ ] Germantown Health Center
  - [ ] Greendale Medical Clinic
  - [ ] Greenfield Highlands Health Center
  - [ ] Hartford Health Center
  - [ ] Jackson Health Center
  - [ ] Jackson Rehabilitation and Sports Medicine Center
  - [ ] Kewaskum Health Center
  - [ ] Lincoln Avenue Health Center
  - [ ] Menomonee Falls Behavior Health Center
  - [ ] Moorland Reserve Health Center
  - [ ] North Hills Health Center (previously Community Memorial Medical Commons – CMMC)
  - [ ] Orthopaedic, Sports and Spine Center
  - [ ] Sargeant Health Center
  - [ ] SpineCare Clinic (Oconomowoc)
  - [ ] Springdale Health Center

- [ ] St. Joseph's Health Center (attached to SJH)
- [ ] Sunnyslope Health Center
- [ ] Sussex Health Center
- [ ] Tosa Health Center
- [ ] Town Hall Health Center
- [ ] West Bend Health Center
- [ ] Westbrook Health Center

- [x] **Medical College of Wisconsin - Milwaukee Campus**
- [ ] Medical College of Wisconsin - Green Bay Campus
- [ ] Medical College of Wisconsin - Central Wisconsin Campus
- [ ] Center for AIDS Intervention Research (CAIR)
- [ ] Adult Translational Research Unit (TRU)
- [ ] Versiti, Inc.

- [ ] Children's Hospital of Wisconsin†
- [ ] Clement J. Zablocki Veteran's Affairs Medical Center†
- [ ] UW-Milwaukee†
- [ ] Marquette University†
- [ ] Milwaukee School of Engineering†
- [ ] Other

6.1.1 For all locations other than MCW, Froedtert Hospital, or Versiti, Inc. list the lead collaborator at each institution, their role at each institution, and the name of the institution.
Exact participating sites are being determined on an on-going basis. This study is being hosted by the Multi-Center Trial Committee of the Western Trauma Association (WTA) which provides improved ability to seek participating centers throughout the country. Once exact sites are determined, we will create a listing of all sites where data will be collected, including the name and CV for the lead investigator at each site. This listing will be provided to both the MCW IRB and all participating sites. This was discussed at a meeting with Kathryn Gaudreau on 9/18/17.

6.2 * **Will any subject recruitment activities or research procedures under the responsibility of this Principal Investigator take place outside of Wisconsin but within the US?**

● **Yes** ○ No

If Yes,
6.2.1 Identify those states (within the US) where project activities will take place; and describe the activities that will take place in those jurisdictions.
As stated in 6.1.1, exact participating sites are being determined. As we hear of participating sites, lead investigators, and specific states, this information will be provided to MCW IRB.

It will be expected that each participating site will submit this study to their own IRB for review. All IRB approval letters will be collected by the lead site. We will not be submitting a reliance agreement.

The same study protocol will be disseminated to all participating sites. We anticipate some variability in the standard of care of thoracic irrigation at participating sites. At MCW, thoracic irrigation is standard of care, so we will be requesting a waiver of consent. Participating centers where this is not the case may need to obtain consent.

There will be no minimum or maximum number of patients enrolled at each site. The methods, power analysis, and sample size are discussed in more detail in the separate study protocol. There will be an interim analysis, and once an adequate number of patients has been collected based on our current power analysis, no further patients will be enrolled at each site.

7. Multi-Site Project

7.1 * **Is the project being implemented as identical protocols at multiple sites (US or international) under the direction of multiple Principal Investigators (not counting coordinating sites, data coordinating sites, or statistical coordination centers)?**

- (●) **Yes**
- ( ) No
- ( ) N/A

7.2 * **Are different activities being performed from one site to the next under the direction/supervision of different Principal Investigators?**

- ( ) Yes
- (●) **No**
- ( ) N/A

7.3 * **Approximately how many total sites are participating in this project?**
10

7.4 * **Is this Principal Investigator managing the Coordinating Center of this multi-site project?**
(●) **Yes** ( ) No

If Yes,
7.4.1 Describe the Coordinating Center leadership structure:
MCW principal investigator is responsible for the guiding and overseeing of all phases of this multi-center research study. Other approved MCW study staff will assist with organization and communication, including research fellows, surgery residents, and surgery department research coordinators. MCW will provide the administrative, clinical, technical expertise, and leadership in the design and coordination of this multi-center research project. MCW PI will be responsible for data monitoring for accuracy and integrity, subject screening & enrollment, data and safety monitoring, data collection and analysis, adherence to the protocol-directed procedures and guidelines, and the prompt review, reporting, and resolution of adverse events. Lead investigators at the participating sites will submit this study for review by their local IRB. MCW as lead site will maintain records of IRB reviews and approval for all participating sites throughout the duration of the study.

7.4.2 Describe the Coordinating Center's responsibilities:
All participating sites will be provided with the most current version of the study protocol. If any changes are made, the updated protocol will promptly be disseminated to all sites via email. We will obtain IRB approval documentation from all participating sites. Any IRB approved modification to the study protocol will be communicated in writing to all participating sites.

In the startup phase, there will be communications as needed with participating sites to assist with IRB submission and study initiation. These communications will be email, with conference call options pending availability and interest of participants. Once all IRBs have been approved and study enrollment has begun, monthly communications via email or phone will be conducted with the study staff at all participating sites to ensure continued compliance with the protocol. All sites will conduct the study according to established IRB protocol. All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy and reported to MCW. All participating sites will safeguard data as required by local information security policies.

MCW PI bears the ultimate responsibility for safeguarding the rights and welfare of humans participating in the study.

7.4.3 If the project is supported by any federal grants, contracts or subcontracts, list here the FWA # for each institutional site:
N/A

Instruction: When this Principal Investigator is managing the Coordinating Center, upload the following documents in Section 52:

a. Local IRB approval with approved consent form or documentation of consent waiver for each performance site
b. Protocol or procedure manuals to be used by any of the performance sites
c. Central data collection and management plan
d. Comprehensive multi-site safety monitoring plan

e. If federally funded, all grants, contracts and subcontracts to non-MCW/FH performance sites related to this project

8. National Cancer Institute (NCI) Cooperative Groups

8.1 * **Is this project part of a NCI cooperative group?**

○ Yes ● **No**

10. Intervention Evaluation

10.1 * **Is this research project designed to evaluate the safety or effectiveness of a research treatment/intervention?**

○ Yes

● **No**

10.2 * **Does the research involve:**

(check all that apply)

☐ Drug: FDA-approved, investigational, or other

☐ Device: FDA-approved, 510(k), investigational, HUD, or other

☐ Biologic: FDA-approved, investigational, or other

☐ Botanical, medical food, or dietary supplement

☑ **None of the above**

11. Funding Source

11.1 * **Do you have funding to support any of the activities for this project:**

○ Yes ● **No**

12. Project Subject Types

12.1 * **Enter the disease/affliction that is the focus of this project (e.g. pancreatic cancer):**

Blunt or penetrating injury resulting in traumatic hemothorax or hemopneumothorax

12.2 * **Identify all categories of subject populations that will be included in this project:**

(check all that apply)

☐ Cancer patients

☑ **Inpatients**

☐ Outpatients

☐ Healthy Subjects (i.e. subjects NOT selected because they have a particular medical condition or history)

☐ Elderly - age 70 and over

☐ Employees including faculty, staff, residents or fellows

(check all that apply)

- [ ] Fetuses
- [ ] Issues of cognitive or decisional impairment
- [ ] Limited or non-reader
- [ ] MCW students
- [ ] Neonates
- [ ] Non-English speaking
- [ ] Nursing home residents
- [ ] Persons with alcohol or drug use disorders
- [ ] Persons with developmental disabilities - neurologic or psychiatric
- [ ] Persons with mental illness
- [ ] Poor and/or uninsured
- [ ] Pregnant women
- [ ] Prisoners - see help text
- [ ] Terminally ill patients
- [x] **Traumatized, sedated, or comatose patients**
- [ ] Visually / hearing impaired
- [ ] Other (SPECIFY)

12.3 * **Are the exclusion criteria for this project likely to exclude groups or categories of subjects based on race, socioeconomic status, or insurance coverage?**

○ Yes ● **No**

15. Inclusion/Exclusion Criteria

15.1 * **List inclusion criteria (e.g., age, gender, ethnicity):**

1) Trauma patients admitted with initial indication for thoracostomy tube placement of hemothorax or hemopneumothorax.

(Once all participating sites have been established, a complete listing of hospitals will be provided in section 6.)

2) Patients must present to Froedtert Memorial Lutheran Hospital (or participating site hospitals) within 24 hours of the traumatic event, either blunt or penetrating injury.

3) Follow up data available including radiologic studies performed within 24 hours of tube placement and hospital records to determine if any additional intervention(s) was performed.

4) 18 years of age or older.

15.2 * **List exclusion criteria (e.g., age, gender, ethnicity):**

1) Less than 18 years of age.

2) Patients who had the thoracostomy tube removed (intentionally or unintentionally dislodged) prior to 24 hours TT duration.

3) Patients requiring operative exploration of the thoracic cavity within 6 hours following thoracostomy tube placement.

4) Patients with Thoracotomy or Video Assisted Thorascopic surgery as initial treatment for hemothorax and / or hemopneumothorax.

5) Patients with TT placed for isolated pneumothorax.

6) Patients who have a TT placed for hemothorax or hemopneumothorax more than 24 hours after presentation, or more than 24 hours after their traumatic event.

17. Recruitment Strategies

17.1 * **Will potential subjects be identified or screened by searching records of any source outside MCW/FH/CHW/Versiti, Inc.?** (e.g., motor vehicle records, military service records, state registries, Medicare files, other hospitals including International hospitals)

○ Yes ● **No**

17.2 * **To recruit potential subjects, will you use any of the following:**

- ☐ **Print advertisements (e.g. newspapers, magazines, flyers, posters, brochures)**
- ☐ **Letters/emails**
- ☐ **Radio or television advertisements**
- ☐ **Web solicitations**
- ☐ **Telephone**
- ☐ **Recruiting company**
- ☐ **Physician referrals (includes in-house and/or outside referrals)**
- ☐ **Approach subjects in-person** (Example: a public place or knocking door-to-door)
- ☐ **Other strategies (not already covered) to identify, screen, or recruit subjects**
- ☑ **No recruitment activities**

Instruction: Upload all recruitment materials in Section 52.

18. Subject Compensation/Reimbursement

18.1 * **Will you offer subjects stipends, gifts or compensation for their participation, or reimbursement for project-related expenses, e.g., transportation, baby-sitting, parking?**

○ Yes

● **No**

26. Connecting with a Bank

26.1 * **Will this project contribute data, records, or biospecimens to a local bank?**

○ Yes ● **No**

26.2 * **Will this project access data, records, or biospecimens from a local bank?**

○ Yes ● **No**

28. Purpose

28.1 * **Why is it significant or important to conduct this project?**

Tube thoracostomy (TT) is the most common procedure performed to treat traumatic pneumothorax (PTx), hemothorax (HTx), and hemopneumothorax (HPTx).[1] While the majority of hemothoraces are successfully managed with TT placement, retained HTx may occur in up to 20% of patients, resulting in significant morbidity and mortality.[2-8] There is abundant research on the optimal management of retained collections,[9-17] however, few studies have focused on prevention of retained hemothorax. A pilot study using thoracic irrigation performed at the time of TT placement resulted in fewer secondary interventions for retained hemothorax.[22] This was expanded to a single institution prospective comparative study that yielded similar findings. Based on these promising results, it is necessary to validate the efficacy of thoracic cavity irrigation to prevent retained HTx requiring secondary intervention in a larger, multi-institutional patient population.

28.2 * **Briefly summarize findings from previously published data or pilot projects that substantiate the soundness of protocol being proposed; or describe formulation of research questions:**

Most thoracic trauma resulting in the formation of pneumothorax (PTx), hemothorax (HTx), or hemopneumothorax (HPTx) is successfully managed with thoracostomy tube (TT) placement to evacuate blood and / or air from the pleural space.[1] Thoracostomy tubes have been a staple of hemothorax management for years, with successful management remaining stable at 80% for decades.[2-5] When TT fails, however, the resulting retained collection can lead to complications such as empyema and fibrothorax.[3,6-8]

A majority of thoracic trauma research has focused on the timing and treatment of these retained collections. Compared to traditional thoracotomy, Video Assisted Thorascopic Surgery (VATS) was revolutionary in decreasing morbidity associated with such complications.[8-17] However, early VATS does nothing to prevent the formation of retained collections. There is little published data on thoracic irrigation at the time of TT placement. A study published in 1991 looked at penetrating gastric injuries and demonstrated an increased rate of empyema amongst these patients, especially with associated diaphragm injury.[18] The study suggested that pleural lavage could possibly help decrease complications rates in combined gastric and diaphragm patients. Additionally, a pilot study published in 2012 examined 10 patients in whom suction catheter was utilized for hemothorax evacuation prior to thoracostomy tube placement.[19] This study found a 45% decrease in their secondary intervention rate (18.2% vs. 10%), increased percentage of total TT output in first 24 hours (72.7% vs. 46.2%, $p < 0.0059$), and shorter overall TT duration (4.2 days vs. 5.8 days, $p = 0.04$). However, when Savage and colleagues then evaluated 99 consecutive patients treated with suction evacuation prior to TT placement, they demonstrated a significant reduction in recurrent PTx, but no significant reduction in retained HTx or rate of secondary intervention.[20] These studies suggest that improving pleural fluid evacuation may be beneficial in preventing the complications of retained hemothorax and empyema. The first study lays the basis for pleural irrigation as a means of improving outcomes, while the second study has conflicting results in the literature.

Some of the faculty members in the Medical College of Wisconsin (MCW) Division of Trauma and Acute Care Surgery routinely perform TT irrigation, while others practice selective irrigation. There have been two trials conducted at this institution investigating TT irrigation. The pilot study, published in 2016, was a prospective observational trial of 20 patients who underwent thoracic irrigation at the time of TT placement.[21] This study demonstrated a 75% reduction in our secondary intervention rate (from 20% to 5%). This was then expanded to a single institution prospective comparative study, which consisted of a non-irrigation control arm and a thoracic irrigation experimental arm. Again, secondary intervention rates were significantly lower within the irrigation group, 5.6% vs 21.8%. Given these promising results, it is essential to expand this study to multiple institutions to validate the data our institution has established.

29. Hypotheses and Objectives

Some projects are designed around explicit scientific hypotheses. Others (chart reviews, pilot projects) may be better described in terms of Aims or Objectives. Answer the question (29.1 or 29.2) that suits your project best.

29.1 **State the hypotheses. If this project involves community-based research, indicate so and explain the project goals:**

Thoracic cavity irrigation at the time of initial thoracostomy tube placement will decrease the secondary intervention rate for retained hemothorax.

29.2 Describe the Aims and Objectives of this project in such a way that the reader can determine the appropriateness of the project design:
Determine the efficacy of thoracic cavity irrigation to prevent secondary interventions for retained hemothorax.

30. Procedures and Analysis

30.1 * Narrate project procedures listing in sequential order the steps that will be followed to conduct the protocol:
Study Design

All trauma patients ages 18 years or older presenting within 24 hours of blunt or penetrating injury resulting in traumatic hemothorax or hemopneumothorax will be eligible for enrollment. Inclusion and exclusion criteria are listed separately (section 15). This prospective comparative study will consist of a non-irrigation control arm and a thoracic irrigation experimental arm. Thoracic irrigation is performed at the time of the initial TT placement, and is done at the discretion of the attending Trauma surgeon. All patients enrolled will be entered in a prospectively maintained thoracic trauma database. The primary outcome is need for secondary intervention, defined as additional TT placement, VATS, tPA, or thoracotomy for the management of retained hemothorax. Secondary interventions will be screened according to indication. Only secondary interventions directed at management of retained collection will be considered in the analysis for our primary outcome. Secondary intervention aimed at persistent air leaks or post-pull pneumothorax will be considered separately in any analysis.

This is an observational prospective data collection study. We will not alter our standard of care practice at MCW in any way during the study duration. Data abstraction will occur from FMLH medical records program (EPIC). We will also request data from our Froedtert Trauma Registry Program. Each participating site will also practice according to their standard of care. If a site chooses to implement a TT irrigation protocol, approval should be obtained from their local divisional & IRB committees. If a participating site already performs thoracic irrigation, efforts should be made to follow the TT irrigation protocol provided with this study.

The Froedtert Hospital Trauma Program Trauma Registry will be accessed for the purpose of data collection. The following variables will be pulled: All possible variables from “DCF – Multi-Center TT Irrigation Data Sheet_AME21315 tracked changes”.

At MCW, education will be provided monthly to the residents, APPs, and faculty on the Trauma service to notify study staff when eligible patients are admitted. We will also review the Trauma division inpatient list for eligible patients. Each participating site will develop a method to screen for patients based on the resources available at their institution; this method should be included in the proposal submitted to their IRB. The attached data sheet includes all the variables that will be collected.

The data at each participating site will be collected by a member of the study team and entered into the secure REDCap database specifically created for this project. Data will be transferred from participating sites to MCW via REDCap. REDCap (Research Electronic Data Capture) is a secure web application for building and managing online databases. All data entered into REDCap and transferred between sites will be deidentified. Only approved study staff at each site will be granted password protected access to the REDCap database. Ultimately, the MCW PI will have control over who can access the database and what type of access is granted.

Sample Size

This prospective comparative study will include participants from multiple Trauma Centers around the country. Nationally, approximately 10-30% of patients who undergo standard TT placement for the management of traumatic hemothorax require secondary intervention.[6] Both our pilot study & single institution prospective study demonstrated a 5% intervention rate for retained hemothorax among patients who underwent thoracic irrigation at the time of TT placement.[21] Collaboration with the biostatistics department at MCW suggests that a propensity matched analysis to a separate group of patients who did not undergo irrigation is the best study design.

To power the experimental cohort, a sample size calculation was performed utilizing a two-sample z-test with an alpha of 0.05 and 80% power. A power analysis utilizing 10% and 20% secondary intervention rates for the irrigation and standard cohorts, respectively, demonstrates that 108 patients are needed for analysis within the irrigation cohort. To appropriately perform a propensity score matched analysis, enrollment of patients into the standard thoracostomy tube cohort in a 3:1 fashion requires approximately 324 patients within the control cohort. A power analysis using 5% and 20% secondary intervention rates for the irrigation and standard cohorts, respectively, requires 52 patients within the irrigation cohort and 156 in the control cohort. A power analysis using 5% and 10% secondary intervention rates for the irrigation and standard cohorts, respectively, requires 239 patients in the irrigation cohort and 717 in the control cohort. A complete power analysis with variation in treatment proportions is attached.

We will start this study using 20% as the approximate national intervention rate, based on current literature, with the goal of detecting a 50% reduction in the experimental arm (i.e. 10% secondary intervention rate after thoracic irrigation). Therefore, we will plan to enroll 108 patients in the irrigation cohort and 324 patients in the control cohort. An interim analysis will be conducted once 54 patients have been enrolled in the irrigation cohort. The

secondary intervention rate in the irrigation cohort and the standard cohort will be determined, and any adjustments to sample size will be made at that time.

Thoracostomy Tube Protocol

Indications for TT insertion have been well established.[22] At MCW, thoracostomy tube insertion will be performed according to Division of Trauma Policy (TPP.0027), using 28-36 French TT. Irrigation will be performed according to the attached protocol, at the discretion of the attending Trauma surgeon. The tube will then be managed in accordance with Division of Trauma Policy (TPP.0028), with secondary interventions performed as deemed necessary according to the Trauma faculty.

Each participating site will insert thoracostomy tubes according their divisional policies. Thoracic irrigation will be performed at the discretion of the attending Trauma surgeon, according to standard of care at each institution. Each site will follow the attached protocol for TT irrigation.

Note: If desired, upload an activity table into Section 52 listing tests that will be conducted (e.g., lab draws, EKG, chest x-ray, genetics, proteomics, H&P, survey) as well as the frequency of these tests.

30.2 * **Explain how you intend to analyze the data:**
The data at each site will be collected by a member of the study team and entered into the secure REDCap database specifically created for this project. At MCW, our institution's data will also be entered into a secure password protected electronic excel spreadsheet, with all electronic data stored on the secure MCW Box platform.

Once REDCap data entry from each site has been completed, all data analysis will take place at MCW in conjunction with MCW biostatisticians. There will be an interim analysis once 50% of patients have been enrolled in the experimental arm, and any changes to sample size will be made at that time. Any changes to protocol or sample size will be communicated to all participating sites. Final data analysis will be conducted at MCW once all patients have been recruited in the propensity score matched design. All patients who underwent thoracic irrigation will be analyzed with an intent-to-treat model. Data will be analyzed using a logistic regression model for the categorical outcome (secondary intervention) and a linear regression model for the log-transformed numeric outcomes (TT duration, ventilator days, ICU LOS, hospital LOS, etc.). Propensity score methods will be used to isolate the effect of thoracic irrigation on a patient's outcomes, and adjust for potential selection bias in this comparative study. Propensity scores will be estimated using a logistic regression model with age, sex, mechanism of injury, abbreviated injury score - chest, and TT size as predictors. The predicted probabilities will then used to obtain the weights as the inverse probability of treatment. Corresponding estimates (odds ratio & mean differences) and p-values will be reported. Continuous variables will be reported as mean (standard error of the mean) if normally distributed and median (interquartile range) if not normally distributed. Categorical variables will be reported as counts and percentages.

31. Procedures and Expenses for Subjects

31.1 * **Explain which procedures are research-related:**
The collection of data is the research related procedure for this project.

31.2 * **Explain what expenses are NOT covered in the project, i.e., the expenses the subject is expected to pay:**
There are no expenses the subjects are expected to pay.

31.3 * **Explain what expenses ARE covered in the project, i.e., the expenses the subject is not expected to pay:**
There are no expenses for this project.

32. Risks and Safeguarding Against Risks

32.1 * **List all reasonably foreseeable risks or discomforts. Consider physical, psychosocial, confidentiality, and privacy risks. List in order of frequency (likelihood), but be sure to include uncommon risks that might influence a person's decision to participate.**
Potential loss of patient privacy / confidentiality is the risk of this study.

32.2 * **Identify features of the project, e.g., recruitment practices, project design, procedural plans, intended to minimize safety risks to subjects**:
Only approved study staff will have access to the data in question and to patient PHI, which will be used to determine eligibility. All collected PHI will be kept in a locked filing cabinet in the locked office of study staff when not in use. MCW institution data will be entered into a secure password protected electronic excel spreadsheet, will all electronic data stored on the secure MCW Box platform. Each participating site will store their data according to their institutional security protocols. Deidentified data from all participating sites will eventually be entered into a REDCap database created for this project.

The MCW Box platform is a secure data storage system provided through the Medical College of Wisconsin. The MCW Box platform provides data encryption utilizing 256-bit SSL, SSAE 16 Type II, and maintains a safe-harbor certification for security. Box sync's encrypted authorization token technology keeps user data secure and work seamlessly with existing MCW desktop encryption systems.

MCW Box is licensed for storage of PHI data as it provides maximum security and allows users to assign different levels of security based on individuals' roles within a project. All files stored on MCW Box are stored within a secure server on the MCW campus and can be synced to MCW owned computers kept in locked offices within Froedtert Hospital.

Content from Box is available remotely through their encrypted website which requires two step verification and login each time the site is accessed. Users have access only to files in which they have been granted access, increasing the security of data storage.

In the startup phase, there will be weekly communications with participating sites to assist with IRB submission and study initiation. These communications will be email, with conference call options pending availability and interest of participants. Once all IRBs have been approved and study enrollment has begun, monthly communications via email or phone will be conducted with the study staff at all participating sites to ensure continued compliance with the protocol and discuss any adverse events. All participating sites will safeguard data as required by their local information security policies. The lead investigator at each participating site will be responsible for data storage according to institutional policy. All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy and reported to the PI at MCW. Data will be collected from all participating sites using a deidentified REDCap database created for this project.

35. Benefits

35.1 * **Identify any potential benefits to subjects:**
There is no direct benefit to participants of the study. We do hope to benefit science and / or society with the results, as it relates to irrigation of a thoracostomy tube placed for hemothorax or hemopneumothorax decreasing the secondary intervention rate.

35.2 * **Identify any potential benefits to science and society:**
This study will describe current statistics, and may give some insight to optimal care, resulting in fewer complications, and improved morbidity / mortality in thoracic trauma patients.

38. Informed Consent

38.1 * **Indicate your approach to the informed consent process requirement for this project:**

(check all that apply)

- ☐ Subjects or parents of minor subjects participate in an informed consent process and sign an informed consent document
- ☐ Waiver or Alteration of the Informed Consent Process is granted by the IRB. This option is not permitted for most FDA regulated research.
- ☐ Subjects participate in an informed consent process, but a Waiver of Documentation of Informed Consent is granted by the IRB
- ☑ **None of the above**

38.1.1 Please identify which pathways are applicable to this project.

(check all that apply)

- ☑ **Project will not have direct contact with subjects, and a consent form or process is not required per MCW institutional policy**
- ☐ Project will have direct contact with subjects, and an informational letter will be provided
- ☐ Project qualifies for Approval without the Requirements of Informed Consent under the 2006 FDA guidance regarding In-vitro diagnostic evaluation using de-identified, discard clinical specimens
- ☐ Informed consent has already been obtained (i.e. previously IRB approved bank, incoming data form another institution, etc.)

42. HIPAA: Protected Health Information

42.1 * **Will potential subjects be identified or screened by searching any kind of pre-existing MEDICAL records before consent is obtained?** (e.g., medical records, hospital census or procedure

logs, emergency room visit rosters)

○ Yes ● **No**

42.2 * **Indicate the HIPAA authorization pathway applicable to this project.** Generally, the Health Insurance Portability and Accountability Act (HIPAA) prohibits collecting, accessing, using or disclosing a person's protected health information (PHI) for research without valid authorization. Under some circumstances, a waiver of authorization may be granted by the IRB:

(check all that apply)

- ☐ **No Protected Health Information (PHI) will be Accessed or Used For This Project**
- ☐ **An IRB-Approved Consent Process and Document will be Used** that incorporates the required HIPAA authorization
- ☑ **Waiver of HIPAA Authorization Is Requested. Generally, this request should accompany the "Waiver of the Informed Consent Process" at 38.1.**
- ☐ **Research using only information on deceased persons**
- ☐ **Limited Data Set**, as defined by HIPAA regulations (download "Data Use Agreement" form located on InfoScope HIPAA website, complete it or an equivalent, and upload in Section 52)
- ☐ **De-identification of data** subject to the IRB's definition and verification of de-identification
- ☐ **None of the above**

48. Waiver of HIPAA Authorization: Justification

Note: Here "practicable" refers to the size of the burden and/or cost of obtaining authorization from subjects, on a scale from "difficult" to "impossible". Explain how difficult it would be. It is not acceptable to argue that obtaining authorization would be "inconvenient".

48.1 * **Is it practicable for the investigator to conduct this project without a waiver of HIPAA authorization?**

○ Yes ● **No**

If No,
48.1.1 Explain:
Without this data, we will be unable to analyze inclusion / exclusion criteria for admission to the study. This is a prospective observational study. There will be no changes to current standard of care, and there will be no consent form. The act of obtaining consent could create significant bias and eliminate those high-risk patients who present as an emergency. As there will be no consent and thus no interaction with the patients, it will be impossible to obtain HIPAA authorization.

48.2 * **Is it practicable for the investigator to conduct this project without access to and use of the identified health information?**

○ Yes ● **No**

If No,
48.2.1 Specify:
Identified health information is needed to verify the correct subject along with the mechanism of injury. It is also needed for data collection.

49. Waiver of HIPAA Authorization: Safeguards

49.1 * **How will subjects' rights and welfare be protected to assure that use or disclosure poses no more than minimal risk?**
To ensure that no identifying data is released, we will not disclose the PHI to anyone, and the study team members will only record the least information necessary. Only approved study staff will have access to the data in question and to patient PHI, which will be used to determine eligibility. All collected PHI will be kept in a locked filing cabinet in the locked office of study staff when not in use, or in the MCW Box platform if electronic. MCW institution data will be entered into a secure password protected electronic excel spreadsheet, with all electronic data stored on the secure MCW Box platform. Each participating site will store their data according to their institutional security protocols. Deidentified data from all participating sites will eventually be entered into a REDCap database created for this project.

49.2 * **What is the plan to ensure that the identified health information will NOT ever be removed from the institution?**
All collected health information will be maintained in the secure MCW Box platform. No data will be removed from the institution. All data collected from participating sites will be de-identified and collected via the secure REDCap database.

50. Waiver of HIPAA Authorization: Procedures

50.1 * **Who will have access to the identifiers?** (List by name, class or organization)
All approved study staff.

50.2 * **How will the identifiers be protected from improper use and disclosure?**
Any identifiers from this institution will be kept in the secure MCW Box platform. Only approved study staff will have access to the Box folder. All data collected from participating sites will be deidentified and collected via the secure REDCap database.

52. Supporting Documents

52.1 * **Select all items that will be included for IRB review:**

(select all that apply and upload documents in Section 52.1.2, using the prefix in the title of the document. For example, ICF-PRO1234 (document name), IB-PRO1234(document name))

- [x] **PRO - Sponsor's protocol, protocol summary or narrative**
- [ ] IB - Investigator Brochure
- [ ] ADV - Advertisement
- [ ] ICF - Informed Consent form
- [ ] SMP - Safety Monitoring Plan
- [ ] DM - Device Manual
- [ ] SUR - Surveys / Questionnaires
- [x] **DCF - Data Collection forms/tools**
- [ ] INF - Informational material for subjects
- [ ] TBL – Activity table, schedule of assessments
- [ ] BNK – Bank documents and forms
- [ ] SAF – Ancillary Safety Committee or Human Stem Cell Committee approvals, Adult Treatment Research Unit (TRU) approvals
- [ ] LET - IND/IDE/HDE or 510(k) documentation, communication from/with the sponsor, IRB approvals or administrative letters from other institutions
- [ ] DA - Data agreements or contracts
- [x] **Other(s) (SPECIFY)**

52.1.1 Give a brief description of "Other" items:
Other - MCW Thoracic Irrigation Protocol
Other - MCW_FMLH TPP 0027 Chest Tube Insertion
Other - MCW_FMLH TPP 0028 Chest Tube Removal
Other - PRO29527 TT Irrigation Power Analysis
Other-PRO29527-AME21315 List of changes to the SmartForm

52.1.2 Upload each item specified from 52.1 and 52.1.1 in the section below:

	Name	Last Modified Date	Version
	Other-PRO29527-AME21315 List of changes to the SmartForm	2/25/2020 8:48 AM	0.01
	PRO 29527 - Multi Center Thoracic Irrigation IRB Proposal_AME21315 tracked changes	1/7/2020 8:39 AM	0.03

	Name	Last Modified Date	Version
	Other - MCW Thoracic Irrigation Protocol_AME21315 tracked changes	11/27/2019 12:35 PM	0.02
	DCF - Multi-Center TT Irrigation Data Dictionary_AME21315 tracked changes	11/27/2019 12:35 PM	0.02
	DCF - Multi-Center TT Irrigation Data Sheet_AME21315 tracked changes	11/27/2019 12:35 PM	0.02
	PRO 29527 - Multi Center Thoracic Irrigation Coordinating Site Protocol_AME21315 tracked changes	11/27/2019 12:35 PM	0.02
	Other - MCW_FMLH TPP 0027 Chest Tube Insertion	10/12/2017 8:17 AM	0.01
	Other - MCW_FMLH TPP 0028 Chest Tube Removal	10/12/2017 8:17 AM	0.01
	Other - PRO29527 TT Irrigation Power Analysis	10/12/2017 8:17 AM	0.01

Final Check

(a) Submission Instructions:

- **The Principal Investigator must click the "Submit Application" activity in the workspace to submit this Project for Departmental, Ancillary and/or Safety Committee(s) review. Once these reviews have been completed, the submission will automatically get routed to the IRB for review.**
  - **Clicking "Go to Workspace" does NOT submit this Project for review.**
  - **Clicking "Go to Workspace" saves your work and exits the SmartForm, taking you back to the Workspace.**

(b) **Spelling and Grammar:**
IRB will not accept any application that has not been checked by the submitter for spelling and grammatical errors. Spell checking capability is not available within the eBridge system at this time.

(c) **Attached Documents:**
Make sure all documents have been uploaded before submission.

(d) **Copy and Pasting from Word or PDF:**
If the format of your text is altered when it is pasted into eBridge, please refer to the "*How to Cut & Paste from a Word Document*" directions.