Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd., Suite 1800, Los Angeles, CA 90048

IRB APPROVAL NOTICE

May 13, 2026

Dear Devon Callahan:

On 5/13/2026, the IRB reviewed and approved the following submission:

Type of Submission:	Modification / Update
Title of Submission:	MOD00014543: STOP-VTE-EGS EAST Modifications
Protocol Title:	Multicenter Prospective Comparative-Effectiveness Trial: UFH vs LMWH in Emergency General Surgery (EGS)
IRB Protocol ID:	STUDY00004808
Investigator:	Devon Callahan
Funding:	Name: Internal CSMC Funding
IRB Review Level:	Expedited
Approval Effective Date:	5/13/2026
Approval Expiration Date, if applicable:	
Documents Reviewed:	• STOP-VTE EAST MCT IRB 1.12_DSC_7May2026_final.docx, Category: IRB Protocol;

If an expiration date is displayed above, a continuing review must be submitted at least 60 days in advance of this date.

If no expiration date is displayed above, this minimal risk study will not require annual continuing review submissions.

In conducting this research, you are required to follow the IRB approved protocol and all applicable IRB Policies and Procedures.

Please review the following requirements for providing new information to subjects:

Subjects will not be notified

Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd., Suite 1800, Los Angeles, CA 90048

IRB APPROVAL NOTICE

March 13, 2026

Dear Devon Callahan:

On 3/11/2026, the IRB reviewed and approved the following submission:

Type of Submission:	Initial Study
Title of Submission:	STUDY00004808: MCT Prospective Comparative-Effectiveness Trial: UFH vs LMWH in EGS
Protocol Title:	Multicenter Prospective Comparative-Effectiveness Trial: UFH vs LMWH in Emergency General Surgery (EGS)
IRB Protocol ID:	STUDY00004808
Investigator:	Devon Callahan
Funding:	Name: Internal CSMC Funding
IRB Review Level:	Expedited
Approval Effective Date:	3/13/2026
Approval Expiration Date, if applicable:	
Documents Reviewed:	• STOP-VTE EAST MCT IRB 1.1_DSC_4Mar2026_clean_13Mar2026.docx, Category: IRB Protocol;

If an expiration date is displayed above, a continuing review must be submitted at least 60 days in advance of this date.

If no expiration date is displayed above, this minimal risk study will not require annual continuing review submissions.

In conducting this research, you are required to follow the IRB approved protocol and all applicable IRB Policies and Procedures.

1. Early discharge window may dilute event capture. Including patients with LOS 24–48 hours may artificially lower symptomatic VTE rates due to limited time for clinical events and diagnostic testing. Consider excluding LOS that has been used in another study of medical patients.

We will use a LOS>48 hours to ensure that we are not artificially lowering our symptomatic VTE rates, similar to the 48-hour branch point in TQIP and other Trauma databases for early vs. late VTE.

2. Clarify definition of "symptomatic VTE"
- Symptomatic VTE: Ultrasound or CT confirmed DVT or PE obtained because of the following clinical signs, symptoms, or findings: unilateral leg swelling or pain, erythema, tachycardia, hypoxia, pleuritic chest pain, hemoptysis, syncope, or evidence of right ventricular strain on echocardiography or CT
-Asymptomatic VTE: Ultrasound or CT confirmed DVT or PE identified incidentally performed for other indications

Splanchnic thrombosis will be reported as a secondary outcome and will not be considered a primary endpoint with other VTE.

3. Clarify anticoagulation details and outcome definitions
Please clarify how below-knee DVT will be assessed and managed, and whether upper extremity or line-associated thrombosis will be grouped with general DVT outcomes or analyzed separately.
-Symptomatic and asymptomatic below knee DVT will be assessed with ultrasound. Below knee DVT will include any DVT in the following vessels: peroneal, posterior tibial, anterior tibial, gastrocnemius, and soleal veins. These will be grouped with general DVT outcomes.
-Line-associated thrombosis will be excluded from general DVT outcomes and analyzed separately.

4. ***Clarify whether the enoxaparin group will include all dosing strategies (e.g., 40 mg daily, 40 mg twice daily, 30 mg daily) or whether these regimens will be subdivided. Please also describe anti–factor Xa monitoring protocols, dosing strategies, and whether specific LMWH agents (e.g., enoxaparin, dalteparin, tinzaparin) will be grouped together or analyzed separately. Clarify whether patients requiring therapeutic anticoagulation will be excluded****.*

All dosing strategies for enoxaparin will be included and analyzed as one group. All LMWH agents will be analyzed together. Patients requiring therapeutic anticoagulation will be excluded. Given the inconsistency of Anti-Xa monitoring protocols at centers, we had not intended to include this in the study.

5. Feasibility of enrollment
The proposed sample size (n = 3,700) will require sustained accrual across multiple centers. Please confirm sites willing to participate and provide projected enrollment per site and anticipated study timeline to demonstrate feasibility.

Our target for site participation is between 20-30 sites. If each site is able to contribute 150 patients, we will have ~3,000-4,500 patients. We have verbal confirmation from UCLA and Harbor-UCLA Medical Center as one site, but have deferred contacting other sites until further discussion with EAST.

We are completing a single site retrospective review examining this topic, and over a 5-year period of time we were able to identify ~3,200 unique patients that met the inclusion/exclusion criteria for this study. Given these numbers, we anticipate that the contribution of 150 patients per site to this study should be feasible.

A sample timeline is included below:

0-3 months: Start-up and Site Activation: Site recruitment, Local IRB approval, DUA execution

3-12 months: Patient enrollment

12-15 months: Follow up and Data completion

16-18 months: Analysis and Manuscript

4. ***Clarification of primary analytic framework***
   The observational design introduces potential treatment-selection bias (e.g., UFH vs LMWH chosen based on renal function, bleeding risk, or institutional practice). Propensity weighting and hierarchical modeling are appropriate, but the analytic population is not fully specified. Please clarify how UFH versus LMWH exposure will be defined in the primary analysis, particularly for patients who switch agents or receive both during hospitalization (e.g., initial exposure, as-treated, or time-varying approach). Please also specify how crossovers will be handled and whether sensitivity analyses using alternative exposure definitions are planned.

The primary exposure will be an as-treated, time-varying approach, where each day will be reported as either LMWH exposed, UFH-exposed, both, or neither.

Patients who receive both agents during the hospitalization will remain in the analysis. Crossovers will be modeled according to their actual prophylaxis exposure over time, with exposure status noted daily and incorporated into multivariable models that adjust for patient-level covariates and center-level clustering.

We will also perform prespecified sensitivity analyses using alternative exposure definitions, including: initial prophylaxis agent**,** predominant hospitalization exposure**,** and per-protocol exposure excluding patients with early crossover or substantial mixed exposure. These analyses will test whether the primary findings are robust to different clinically plausible definitions of UFH versus LMWH exposure and will help distinguish treatment-selection effects from true differences in prophylaxis effectiveness.

Aspirin exposure will be measured. If there are a significant number of patients receiving ASA in place of LMWH or UFH, we will analyze these patients as a subgroup.

5. ***Diagnosis heterogeneity and event rate assumptions***
   The broad EGS inclusion increases generalizability but may dilute effect size due to variable baseline VTE risk across diagnoses. Please clarify expected overall versus high-risk event rates and specify how diagnosis category will be incorporated into the primary modeling.

We anticipate an overall event rate of 2-3% with a high-risk event rate of 5-8%. The primary analysis will therefor adjust for diagnosis category(e.g. normal risk, high risk) to ensure adequate treatment effects across this clinically varied cohort. These categories will be included as a prespecified covariate in the primary hierarchical model. We will perform a prespecified subgroup and interaction analyses comparing all EGS patients to those in the high risk subgroups.

6. ***Multiple secondary and subgroup analyses***
Multiple secondary and subgroup analyses are planned. Please explicitly define the hierarchy of primary, key secondary, and exploratory analyses to preserve interpretability.

The primary analysis will compare LMWH versus UFH for the primary effectiveness outcome of symptomatic VTE during the index hospitalization or within 30 days, using the prespecified adjusted hierarchical model.

Secondary analyses will evaluate major bleeding, transfusion requirements, PE, proximal DVT, distal DVT, mortality, and prophylaxis adherence/interruption.

Subgroup analyses will be explicitly labeled as exploratory unless otherwise prespecified as key secondary, and will include renal dysfunction, obesity, ICU admission, emergency laparotomy, malignancy, high-risk EGS diagnosis category, and center-level prophylaxis practice. We will interpret these analyses as hypothesis-generating and will report effect estimates with confidence intervals.

Eastern Association for the Surgery of Trauma

Advancing Science, Fostering Relationships, and Building Careers

EAST MULTICENTER STUDY
DATA DICTIONARY

UFH vs. LMWH in EGS – Data Dictionary

Data Entry Points and appropriate definitions / clarifications:

Entry space	Definition / Instructions
Standard Study Questions	
Admit Date	Admission date of the patient enrolled
Admitting Service	Drop down (ACS, IM [or IM subspecialty], Non-ACS Gen Surg Service, OB/Gyn, Neurosurgery, Urology, ICU, other
Discharge Date	Discharge date of the patient enrolled
Discharge Disposition	Drop down (Home independent, Home with services, Subacute Rehab, Acute Rehab, SNF, Hospice, Expired, Other
Age	Age of patient enrolled
Case Information	
Gender	Gender of Patient enrolled
Race	Race of the patient enrolled
Ethnicity	Hispanic/Non-hispanic/Unknown
BMI	BMI of the patient enrolled
Comorbidities/PMH	Check if applies; MI, CHF, Peripheral Arterial Disease, CVA/TIA, Dementia, COPD, Liver Disease, PUD, DM, CKD/ESRD, Hx of Cancer, Recent central venous catheter placement (within 2 weeks), History of VTE
Chronic Antiplatelet Use	Drop down, select Antiplatelet agent
EGS Diagnosis	The diagnosis that the patient was either admitted for, or for which ACS was consulted
Operative Intervention	Name of operation
Duration of operation	(HH:MM)

SOFA Score on Admit	Free text
Laboratory Values	
Hb	First hemoglobin level obtained for the admission (includes ED labs)
HCT	First hematocrit level obtained for the admission (includes ED labs)
Platelets	First platelet count obtained for the admission (includes ED labs)
INR	First INR level obtained for the admission (includes ED labs)
aPTT	First aPTT level obtained for the admission (includes ED labs)
Fibrinogen	First fibrinogen level obtained for the admission (includes ED labs)
BUN	First BUN level obtained for the admission (includes ED labs)
Creatinine	First Cr level obtained for the admission (includes ED labs)
Calcium	First Ca level obtained for the admission (includes ED labs)
Bicarbonate	First HCO3 level obtained for the admission (includes ED labs)
TEG	TEG results obtained for the admission (includes ED labs)
ROTEM	ROTEM results obtained for the admission (includes ED labs)
Quantra	Quantra results obtained for the admission (includes ED labs)
Inpatient Medications	
Type of ppx anticoagulation	Drop down, select first prophylactic anticoagulant agent started after admit and dose
Ppx anticoagulant changed during hospitalization	Yes/No
Number of days receiving initial anticoagulant	Free text number of days
Name and dose of second Prophylactic anticoagulant	Drop down, select second prophylactic anticoagulant agent (if applicable) and dose
Number of days receiving second anticoagulant	Free text number of days
Ppx anticoagulation held during Admission	Yes/no
Duration of hold	Enter in the form (DD:HH:MM)
Indication for hold	Drop down; Bleeding/concern for bleeding, Operative intervention, Procedural neuraxial intervention (i.e. epidurals et al.), Radiological procedural intervention, Other procedural intervention, Not indicated, other

Antiplatelet agent given during admission	Yes/no
What type of antiplatelet agent	Drop down; Aspirin 81mg, Aspirin 325mg, Plavix 75mg, Prasugrel 60mg, Ticagrelor, Cangrelor
Duration of antiplatelet agent while admitted	Free text (days)

Outcomes

Symptomatic VTE	Yes/No; During admission of within 30 days of discharge
Specific VTE symptom prompting imaging	Drop down: Unilateral leg swelling or pain, Erythema, Tachycardia, Hypoxia, Pleuritic chest pain, Hemoptysis, Syncope, Evidence of RH strain on echo or CT
Asymptomatic VTE	Yes/No; During admission of within 30 days of discharge
VTE definition	DVT = Deep Vein Thrombosis or PE = Pulmonary embolism. Diagnosis must be confirmed radiographically (Ultrasound, Computed tomography, venography, etc.)
Post-operative complications	Drop down; Intra-abdominal Bleeding, Hematoma, Surgical Site Infection, DVT, PE, MI, AKI/Renal Failure, Acute Respiratory Failure, PNA, Upper GI Bleed, Lower GI Bleed, Splanchnic(i.e. portal vein, splenic vein, SMV) thrombosis, Other, none
Other complications not listed	Free text
Unplanned return to the OR	Yes/No: For the purposes of this study this is defined as any unexpected operative intervention requiring return to the operating room after the index procedure or admission, not planned at the time of the initial operation or routine care pathway.
ISTH major bleeding event	Yes/No: Major bleeding was defined using modified ISTH criteria, requiring clinically apparent or radiographically evident bleeding plus ≥2 g/dL hemoglobin decline, ≥2-unit transfusion attributable to bleeding, reoperation/intervention for hemorrhage, bleeding in a critical organ/space(see below for definition), or death from hemorrhage.
Type of ISTH bleeding event	Drop down: Fatal bleeding, Bleeding requiring >2 units PRBCs/WB, Bleeding causing >2 g/dl decrease in serial Hb, Symptomatic bleeding in critical organ/area (defined below)
Hospital LOS (H-LOS)	Free text; Days
ICU LOS	Free text; Days – If none leave blank
Intubated during admission	Yes/No: Excluding intraoperative/procedural mechanical ventilation
Length of mechanical ventilation	Free text; Days – If none leave blank
Discharge disposition	Drop down: Home independent, Home with services, Subacute rehab, Acute rehab, SNF, Hospice, Expired, Other

Outcomes (continued)

Code status change during admit	Yes/No
Code status at discharge	Full code, DNR/DNI, DNR may intubate, May resuscitate but DNI, Palliative supportive care/Hospice, Expired in hospital
If patient died during admission	Free text; indicate cause, location (ward, ICU, OR, other) and whether death occurred as a result of discontinuation of life saving measures

Definitions of complications included in this section:

Pneumonia	Check if applies. Definition below.

Pneumonia: Confirmed by the presence of the following after 48 hours of hospitalization:

1. purulent sputum
2. associated systemic evidence of infection:
   a. WBC > 11,000 or < 4,000
   b. Fever > 100.4 degrees F / 38 degrees Celsius
3. Two or more serial chest radiographs with new or progressive and persistent infiltrate, consolidation or cavitation.
4. BAL, mini-BAL or sterile endotracheal specimen with:
   a. Limited number of epithelial cells
   b. WBC (2-3+)
   c. Dominant organism(s) identified on gram stain or culture with quantitative culture > 100,000 cfu/mL

DVT / PE	Check if applies. DVT = Deep Vein Thrombosis PE = Pulmonary embolism. Diagnosis must be confirmed radiographically (Ultrasound, Computed tomography, venography, etc.)
Acute Kidney Injury/Renal Failure	Check if applies. Defined for the purpose of this study as rise in serum creatinine ≥0.3 mg/dL from baseline OR ≥1.5× baseline during hospitalization.
Acute respiratory failure	Check if applies. Defined for the purpose of this study as any of the following during hospitalization: • Endotracheal intubation and mechanical ventilation for respiratory deterioration, **OR** • Need for noninvasive positive pressure ventilation (BiPAP/CPAP) for acute hypoxemia or hypercapnia, **OR** • Documented hypoxemic or hypercapnic respiratory failure, defined as: ○ PaO_2 <60 mmHg on room air, or ○ $PaCO_2$ >50 mmHg with acidemia (pH <7.35)
Hospital LOS (days)	Free text entry for number of consecutive days patient hospitalized at initial admission (Day of admission = hospital day #1) LOS = Length of Stay

ICU LOS (days)	Free text entry of number of consecutive days patient required ICU admission (ICU = Intensive Care Unit, LOS = Length of Stay) - Day of admission = hospital day #1
Critical areas/organ spaces	Intracranial, Intraspinal, Intraocular (typically excluding conjunctival bleeding) Retroperitoneal, Intra-articular, Intrapericardial, Intramuscular bleeding with compartment syndrome

Eastern Association for the Surgery of Trauma
Advancing Science, Fostering Relationships, and Building Careers

EAST MULTICENTER STUDY
DATA COLLECTION TOOL

Multicenter Study: _____

Enrolling Center: _____
Enrolling Co-investigator: _____

Demographics / Patient Specific Variables:

Age: _____ Gender:_____ BMI:_____

Race ___American Indian or Alaska Native, ___ Asian ___ Black or African American |___ Native Hawaiian or Pacific Islander ___ White ___ Unknown

Ethnicity: Hispanic / Non-Hispanic / Uknown

Date of Admission:_____ Date of Discharge:_____

Discharge Disposition:___Home independent, ___Home with services, ___Subacute rehab, ___Acute rehab, ___SNF, ___Hospice, ____Expired, ___Other

Comorbidities/PMH: __MI __CHF __PAD __CVA/TIA __Dementia __COPD __Liver Disease __PUD __DM __CKD/ESRD __Hx of Cancer __Recent CVC placement (within 2 weeks) __Hx of VTE

Chronic antiplatelet use: YES / NO

Which antiplatelet agent: __ASA 81mg __ASA 325 mg __Plavix __Prasugrel __Ticagrelor __Cilostazol __ASA + dipyridamole

EGS Diagnosis: _____

Operative intervention: YES / NO

Name(s) of operation(s) and duration(HH:MM): _____

SOFA Score on Admit: ___

Laboratory Values

Hb___, HCT___, Plts___, INR___, aPTT____, Fibrinogen___, BUN____, Creatinine___, Calcium___,

Bicarbonate___, TEG/ROTEM/Quantra_____

Inpatient Medications

Type of ppx anticoagulation(AC): ___Subcutaneous heparin 5000 Units TID ___Subcutaneous heparin 5000 Units BID ___Lovenox, 40 mg, daily ___Lovenox, 40 mg, BID ___Lovenox, 30 mg, BID ___Lovenox, 30mg, daily ___Therapeutic AC ___none ___other

Ppx AC changed during admission: YES / NO

Number of days receiving initial AC: ___

Name and dose of second ppx AC: ___Subcutaneous heparin 5000 Units TID ___Subcutaneous heparin 5000 Units BID ___Lovenox, 40 mg, daily ___Lovenox, 40 mg, BID ___Lovenox, 30 mg, BID ___Lovenox, 30mg, daily ___Therapeutic AC ___other

Number of days receiving second AC: ___

Ppx AC held during admission: YES / NO

Duration of hold (DD:HH:MM): ____

Indication for hold: __Bleeding/concern for bleeding ___Operative intervention ___Procedural intervention (___neuraxial ___radiologic ___other) ___Not indicated ___Other

Antiplatelet agent given during admission: YES / NO

Which antiplatelet agent: __ASA 81mg __ASA 325 mg __Plavix 75mg __Prasugrel 60mg __Ticagrelor __Cangrelor

Duration of antiplatelet agent (Days): ___

<u>Outcomes</u>

Symptomatic VTE: YES / NO

Specific VTE sx prompting imaging: ___Unilateral leg swelling or pain ___Erythema ___Tachycardia ___Hypoxia ___Pleuritic chest pain ___Hemoptysis ___Syncope ___Evidence of RH strain on echo or CT

Asymptomatic VTE: YES / NO

Post-operative complications: ___Intra-abdominal Bleeding, ___Hematoma, ___Surgical Site Infection, ___DVT___PE, ___MI, ___AKI/Renal Failure, ___Acute Respiratory Failure, ___PNA, ___Upper GI Bleed, ___Lower GI Bleed, ___Splanchnic(i.e. portal vein, splenic vein, SMV) thrombosis, ___Other, ___none

Other complications not listed:_____

Unplanned return to the OR: YES / NO

ISTH Major Bleeding event: YES / NO

Type of ISTH Major Bleeding event: Fatal Bleeding / Bleeding requiring >2 unites PRBCs/WB / Bleeding causing or suspected as the cause of >2 g/dL decrease in serial Hbs / Symptomatic bleeding in critical organ space/area

Hospital LOS: ___ ICU LOS:___

Mechanical Ventilation(MV) during admission(excluding MV during surgery/procedural intervention): YES / NO

Length of MV:____