ATTRACT Revised Site Application
October 25, 2011

Thank you for your interest in the NIH-sponsored ATTRACT Trial. This landmark study, which has been publicly endorsed by the Office of the U.S. Surgeon General, will ultimately represent a tremendous feat of multidisciplinary collaboration of which every participant site will be proud.

That said, this is a challenging study and over the last 2 years we have learned a great deal about the predictors of site success and failure. Among the many potential causes of failure are lack of site PI motivation (meaning a willingness to put in actual work effort on a regular basis to ensure success), lack of strong support from a motivated coordinator, inability to institute high-volume DVT patient identification mechanisms, lack of impetus to learn how to frame the potential benefits of study participation to patients, and lack of clinical equipoise on the study question.

The ATTRACT Clinical Coordinating Center (CCC) staff are very busy with managing 50 study sites and our own study patients, and we assume that you are busy as well. It therefore serves no purpose for us to activate sites that ultimately do not succeed. Accordingly, this application has been designed to prompt you to explore the strength of your commitment to this study, and to enable us both to realistically appraise the likelihood of success at your site. The CCC staff and Dr. Vedantham are happy to speak with you directly to help you make this assessment.

Please answer the questions below and submit the requested attachments. Because we are very busy and have many applications to review, we cannot review incomplete applications.

I. KEY PERSONNEL CONTACT INFORMATION

Name of Site: _____

Address (City, State): _____

Primary Contact Person: _____

E-Mail Address: _____ **Phone:** _____

Site Principal Investigator (PI): _____

E-Mail Address: _____ **Phone:** _____

PI Subspecialty: _____

Important: Attach site PI's medical license, signed/dated CV, and board certificate

II. FINANCIAL CONTACT INFORMATION

Official Site Name (for Contract): _____
(Note – this may be different from the site's common name – please check to be sure)

Federal-Wide Assurance (FWA) Number: _____

Financial Contact <u>for NIH Research Contracts</u>: _____

E-Mail Address: _____ Phone: _____

Financial Contact <u>for Industry Research Contracts</u>: _____

E-Mail Address: _____ Phone: _____

III. HOSPITAL INFORMATION

Please list the Primary Hospital at which you plan to enroll patients into ATTRACT, as well as up to two major affiliate hospital that fall within your IRB's jurisdiction.

Primary Hospital: _____

Number of Registered Beds: _____ Number of DVT Cases: _____

Which of the following categories best describes the nature of your Primary Hospital?

University Hospital ☐

Community Hospital with Strong Academic Affiliation ☐

Private Hospital without Strong Academic Affiliation ☐

Affiliate Hospital #1: _____

Number of Registered Beds: _____ Number of DVT Cases: _____

Which of the following categories best describes the nature of Affiliate Hospital #1?

University Hospital ☐

Community Hospital with Strong Academic Affiliation ☐

Private Hospital without Strong Academic Affiliation ☐

Affiliate Hospital #2: _____

Number of Registered Beds: _____ **Number of DVT Cases:** _____

Which of the following categories best describes the nature of Affiliate Hospital #2?

University Hospital ☐

Community Hospital with Strong Academic Affiliation ☐

Private Hospital without Strong Academic Affiliation ☐

Important: Attach a 1-2 page Resources & Environment Summary describing the resources available at your institution for the conduct of clinical research (see sample).

IV. RESEARCH COORDINATOR INFORMATION

Research Coordinator: _____

E-Mail: _____ **Phone:** _____

Number of Years Research Experience: _____

How Many Studies Is Coordinator Assigned To Currently? _____

How Much Effort (%) Can Coordinator Spend on ATTRACT? _____

Does This Person Perform Research Work on Weekends? _____

Important: Attach research coordinator's signed/dated CV and certifications.

V. OVERSIGHT OF ANTICOAGULANT THERAPY

Designated Medical Co-Investigator: _____

E-Mail: _____ **Phone:** _____

Subspecialty: _____

It is preferred that ATTRACT patients have their outpatient anticoagulant monitored by the designated medical co-investigator. However, it is acceptable for patients to have this done by another physician - but the medical co-investigator is still responsible for providing oversight mainly to ensure that the patient remains on protocol (e.g. anticoagulant regimen is only modified and IVC filters are only utilized as described in the study protocol).

Important: Attach medical license, signed/dated CV, and board certificate.

Important: Attach a 1-2 paragraph anticoagulation monitoring plan (see sample).

Important: Attach hospital's unfractionated heparin nomogram for VTE.

VI. ENDOVASCULAR RESOURCES AND CAPABILITIES

Primary Endovascular Co-Investigator: _____

E-Mail: _____ **Phone:** _____

Subspecialty: _____

Note – only credentialed investigators may perform PCDT procedures in study patients.

Important: Attach medical license, signed/dated CV, and board certificate.

Does your facility have an AngioJet Ultra unit? ☐

Do thrombolytic patients stay in an ICU or stepdown unit? ☐

Do you routinely use US-guided venous access for DVT treatment? ☐

Number of US-guided venous accesses performed (any vein): ☐

Number of US-guided popliteal/tibial venous accesses performed: ☐

Number of patients with lower extremity DVT treated: ☐

Number of patients with upper extremity DVT treated: ☐

Number of DVT patients treated with infusion CDT: ☐

Number of DVT patients treated with AngioJet PowerPulse PCDT: ☐

Number of DVT patients treated with Trellis Isolated PCDT: ☐

Number of iliac vein stent placements for obstructive lesions in DVT: ☐

For single-session PCDT, do you prefer to use Trellis or AngioJet? _____

At what hospital will PCDT procedures be performed? _____

What angiographic unit (make, model) will be used? _____

VII. SITE-SPECIFIC ENROLLMENT PLAN

A. High-Volume, Automated, Database-Driven Identification of DVT Patients

Of all DVT patients you identify with an anatomically qualifying DVT that involves the iliac, common femoral, and/or femoral vein, only 1 in 12 will meet all eligibility criteria and perhaps 40-50% of these will agree to participate. Therefore, prior to acceptance of your site, it is an absolute study requirement that you have an iron-clad, IRB-approved, automated method of easily identifying nearly every DVT patient in your hospital.

1. Partial Waiver of HIPAA Authorization

First, to be permitted to pre-screen medical records and ultrasound studies of potential study candidates without their advance informed consent, most IRBs require you to obtain from them a "Partial Waiver of HIPAA Authorization". To avoid delaying study start-up, this simple request (if required) must be submitted along with your initial IRB submission. Note - some sites that incorporate pre-screening consent into their standard HIPAA Notice of Privacy Practices do not require a HIPAA waiver.

I understand that I must ask my IRB what additional permission and documentation are required to allow me to pre-screen patients, and I agree to submit this request (if needed) along with my initial IRB submission.

Investigator Signature: _____ Coordinator Signature: _____

2. Screening Database

Please describe the methods you will use to ensure that you are identifying nearly all DVT patients in your institution. At least one method must involve daily review of an automated log of DVT cases. Common methods used by successful sites include: a) daily review of the ultrasound lab's electronic log of Duplex ultrasound studies for DVT; b) daily review of the hospital's PACS system for Duplex ultrasound studies; c) daily review of a database of hospital admissions sorted by diagnosis code; or d) daily review of another EMR system that incorporates inpatients, outpatients, or both. Please be specific – exactly who will do this routine review and how often?

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3. Ultrasound Laboratories

Please identify all vascular ultrasound labs that are present at your hospital, which departments run them, which ones do DVT studies, and what degree of collaboration you will have from them. Include labs in radiology, vascular surgery, cardiovascular medicine, and/or emergency department – you may need to explore how many exist.

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Please have all US Lab Directors who are willing to collaborate sign this attestation:

As the Director of an Ultrasound Lab that does DVT studies at this site, I certify that I will strongly support the ATTRACT investigators by assisting in developing efficient DVT patient identification mechanisms, facilitating the posting of IRB-approved study advertising materials in the lab, and strongly encouraging lab sonographers to notify the study team of DVT patients in real time to the extent permitted by our IRB.

Director Name and Department: _____
Signature: _____

Director Name and Department: _____
Signature: _____

Director Name and Department: _____
Signature: _____

4. Emergency Departments

Please describe how emergency department physicians and other personnel will assist your efforts to identify DVT patients in real time.

_____
_____
_____
_____

Please have all Emergency Room Directors willing to collaborate sign this attestation:

As the Director of the Emergency Department at this site, I certify that I will strongly support the ATTRACT investigators by assisting in developing efficient DVT patient identification mechanisms, facilitating the posting of IRB-approved study advertising materials in the department, and strongly encouraging ED personnel to notify the study team of DVT patients in real time to the extent permitted by ED workflow.

Director Name and Hospital: _____
Signature: _____

Director Name and Hospital: _____
Signature: _____

Director Name and Hospital: _____
Signature: _____

B. Proper Determination of Eligibility

In the ATTRACT Trial so far, many eligible patients are missed solely because the site personnel misunderstood one or more eligibility criteria. Investigators should have an "inclusive" posture toward enrolling all patients that do not clearly exclude, with rare exceptions. Given the challenge of getting even one person to properly understand the eligibility criteria, eligibility determination should be limited to a very small number of people (e.g. just the site PI and coordinator). There must be routine communication among the site PI, site research coordinator, Dr. Vedantham, and CCC staff to double-check that all exclusions are appropriate and to continuously improve site personnel understanding of the criteria – **this interactive process is part and parcel of agreeing to participate in the study**. Accordingly, please provide the requested attestation below:

As the site PI, I attest that I will take a **hands-on approach** towards ensuring that all eligible patients at my site are properly identified. Specifically, I will: a) meet with my research coordinator at least twice per month to review patient exclusions, ensure that they are appropriate, and ensure that the eligibility criteria are properly understood; b) routinely communicate with Dr. Vedantham and the CCC staff about patient eligibility questions; and c) participate in CCC-initiated teleconferences (with fair advance notice) to discuss my site's progress and to improve my understanding of patient eligibility.

Site Principal Investigator Signature: _____

C. Clinical Equipoise

The ethical premise that justifies randomizing patients in ATTRACT is that we just don't know if PCDT will improve long-term patient outcome with acceptable safety. Therefore, decisions on the part of a site PI to not offer study participation to eligible patients violate the ethics of the study and are detrimental in three ways: a) they violate DVT patients' rights to participation in a study from which they might possibly benefit; b) they reduce enrollment to the study, which breaches our enrolled patients' rights to expect that their sacrifices will be matched by our best efforts to ensure a successful, adequately-powered study; and c) they bias the included study cohort in a way that can result in an inaccurate answer to the primary study question. For example, off-study lysis of severely affected iliofemoral DVT patients leaves only those with less-severe DVT in the study – if these patients benefit less from PCDT, the study could inappropriately fail to show a benefit.

In determining if you wish to participate, please review the Protocol eligibility criteria carefully and also consider the following situations: a) A 21 year-old woman presents with massive left lower extremity swelling and is found to have a large left iliofemoral DVT suggestive of May-Thurner Syndrome; and b) A 75 year-old ambulatory man with stable congestive heart failure and a history of GI bleeding 4 months ago is found to have a DVT in the left femoral and popliteal veins. Both of these patients are study-eligible.

Please provide the following attestation:

I attest that I accept the premise that it is ethically reasonable to offer study participation and randomization to all patients who meet the study eligibility criteria. That includes young patients with major iliofemoral DVT and older patients with co-morbidities. I understand that with rare exceptions, keeping study-eligible patients out of the study of my own initiative is a violation of study ethics and will ensure that this does not occur.

Site Principal Investigator Signature: _____

D. Consenting Eligible Patients

The longer the time after DVT diagnosis, the less likely a patient is to enroll – they are more likely to be discharged home, more likely to have formed an opinion of standard DVT therapy (good or bad), and less likely to agree to be randomized.

Please describe your plan for ensuring that your screening process will enable you to approach eligible patients as soon as possible after their DVT diagnosis is made. Indicate how this process will differ, if at all, for patients presenting on weekends.

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E. Competitive Enrollment

Please name any ongoing studies at your site that enroll patients with proximal DVT.

_____
_____

Are you willing to certify that during the enrollment period of the ATTRACT Trial, you will not initiate any study at your site that is enrolling patients with proximal DVT who might qualify for the ATTRACT Trial? _____