

**NETWORK FOR CT SURGICAL INVESTIGATIONS**

**GUIDELINES FOR IDENTIFICATION AND ACTIVATION OF  
NETWORK SATELLITE SITES**



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CT Surgery Network Research Group

Data Coordinating Center:  
International Center for Health Outcomes and Innovation Research  
Department of Health Policy  
Mount Sinai School of Medicine  
New York

## **Background**

The primary goal of the Cardiothoracic Surgical Trials Network (CTSN) is to design, conduct, and analyze multiple, collaborative, proof-of-concept, clinical protocols to evaluate surgical and minimally invasive strategies to improve the treatment of cardiovascular disease in adult populations. The CTSN will develop and conduct a number of proof-of-principal clinical studies as an important step in developing a culture of systematic scientific clinical evaluation within the field of cardiac surgery that will inform the use of new interventions in surgical practice and improve the scientific basis of care in cardiovascular disease.

The purpose of this document is to describe the roles, responsibilities, and benefits of being a satellite site in the CTSN. The satellite sites will participate in CTSN trials, specifically the Moderate and Severe Mitral regurgitation trials (see attached protocol synopses MMR/SMR Rev 3.2) to enhance recruitment, provide additional clinical expertise, and participate in the intellectual output of the CTSN.

## **Application and Approval Process**

To obtain approval for participation in a specific CTSN trial, each satellite site will complete a detailed application document. This application requires the satellite site to document:

- Site's clinical trials experience and infrastructure,
- Site's track record in recruiting patients for clinical trials and
- Site's enrollment capabilities for the current CTSN trials (Moderate Mitral Regurgitation and Severe Mitral Regurgitation Trials [see attached protocol synopses MMR/SMR: REV 3.2])

The Satellite Site will submit their application to the CTSN Data Coordinating Center (DCC), International Center for Health Outcomes and Innovation Research (InCHOIR), Mount Sinai School of Medicine, NY, NY, for review of completeness, followed by distribution of the materials to the CTSN Operations Committee for evaluation and to the CTSN Steering Committee for final approval.

Participation in future Network trials will be determined at a later date.

## **Satellite Site Selection Criteria**

The CTSN Operations Committee will be responsible for initial review of satellite site applications. Applications will be reviewed for responsiveness to the requirements specified and ability to perform all study duties within the budget approved by NHLBI.

All sites, regardless of previously expressed interest must apply and undergo review. Additional information may be required from potential satellite sites prior to making a final decision on site selection. Final selection of satellite sites will be made by the Steering Committee by majority vote.

## **Sub-Contract Information**

- Satellite sites are not primary awardees of the CTSN.
- Satellite sites will function as a subcontract to the DCC at the Mount Sinai School of Medicine, NY, NY. Therefore each subcontract will be managed by the DCC.

## **Financial Information**

Satellite sites will receive an infrastructure budget and reimbursement for successful patient enrollment.

### **Infrastructure Payment**

Each selected site will receive fixed funding of up to \$10,000 total costs (including indirect costs), to be paid out after enrollment of the first and second patient (see below). This funding will support training of study personnel and travel to Steering Committee meetings. Expected training expenses include, but are not limited to, sending two coordinators to the Neurocognitive Core Laboratory for one day training. Steering Committee meetings occur three times annually in Bethesda, MD. The principal investigator (PI) and one coordinator are expected attendees. The start-up funds will be administered by the DCC with appropriate receipts and invoicing.

### **Payment for Patient Enrollment**

During enrollment, sites will be paid \$6,936 (including indirect costs) on a per capita basis for each patient successfully enrolled in the MMR trial and \$7,456 (including indirect costs) on a per capita basis for each patient successfully enrolled in the SMR trial. Reimbursement for patient enrollment includes protocol-related costs that are not considered standard of care and for data collection efforts. The payment schedule is as follows: 50% upon enrollment, 30% at year 1 and 20% at year 2. Payment intervals will be quarterly based on patient data entered into the electronic data capture system (EDC). Failure to complete protocol specified data collection may result in a reduced payment.

### **Payment Schedule**

Upon enrollment of the first patient in either the MMR or SMR trial, the per capita patient fee and half of the infrastructure funding fee \$5,000 will be paid to the site. Upon enrollment of the second patient in either the MMR or SMR trial, the per capita patient fee and the second half of the infrastructure funding fee \$5,000 will be paid to the site. For subsequently enrolled patients the satellite site will be reimbursed for the per capita patient fee only.

### **Role of the DCC**

Satellite sites require the same administrative and regulatory oversight as the core, affiliate and ancillary sites. The satellite site must agree that the DCC will serve in the central oversight role. Once approved by the Steering Committee, the Satellite Site must undergo a study initiation visit by the DCC prior to trial enrollment during which time the satellite PI, co-investigator (co-I), collaborating investigators, and clinical research staff will be trained. In addition to reviewing the relevant protocols and CTSN Operations Manuals, the initiation visit will include evaluation and confirmation that:

- There is a collaborative relationship between the cardiothoracic surgery investigator and cardiology investigators (Interventional Cardiology, Heart Failure and Echocardiography);
- A procedure is in place for ensuring that information in source documents is accurately captured on the case report forms (CRFs) and reported to the DCC in accordance with the CTSN Manual of Operations;
- A procedure is in place for handling data queries and discrepancies identified by the study monitor;

- Compliance with the CTSN requirements in order to ensure that all required regulatory documents (e.g., IRB approvals, financial disclosures, signed and dated curricula vitae (CVs), copies of medical/nursing licenses, documented trainings, etc.) are in place at each satellite site and that these documents (or copies of these documents, as appropriate) are sent to the DCC for their files before enrollment can begin at a satellite;
- A procedure is in place for ensuring that the consent process is being conducted in accordance with the protocol, Good Clinical Practice (GCP) and any applicable Federal, State, and Local regulations, such that study subjects understand the nature of their participation, risks associated with participation, etc.;
- A procedure is in place for satellite site staff to comply with the protocol, adverse event assessment and reporting, and other medical issues that arise during the course of the study;
- A procedure is in place for correcting problems identified by study personnel, outside monitors or auditors, or other parties involved in the conduct of the study;
- Documentation has been provided to the DCC regarding the necessary certification for investigators and coordinators regarding neurocognitive assessment, cardiopulmonary testing and cardiac imaging;
- Conflict of interest (COI) forms have been submitted and either no COI exists or it has been mitigated and/or managed.

Once the approved satellite site is certified by the DCC as having completed the above process, and a sub-contract has been executed, patient enrollment can start. The DCC will monitor regulatory compliance, including quality control review of regulatory documents and data submissions, site monitoring, fielding site's questions, document control, and training and certification oversight as outlined in each protocol.

### **Role and Responsibilities of Satellite Sites**

For participation in the MR trials, all satellite sites must meet the following requirements:

*Principal Investigator and Co-investigator:* PIs will be cardiothoracic surgeons with expertise in surgical repair of the mitral valve. Co-is will be cardiologists with experience in caring for ischemic and valvular heart disease. To qualify as a participating surgeon, the surgical investigator must have performed at least 10 mitral valve repair procedures annually (averaged over a 2-year period). The certified surgeon will either perform the mitral procedure on his/her own patient, or participate in the mitral procedure of an enrolled patient whose surgeon is not certified. Surgical qualifications for all participating surgical investigators will be collected on the Surgical Certification Form and faxed to the DCC prior to accreditation. The site's PI will be responsible for overseeing the ongoing performance of the other participating surgical investigators at that site over the course of the study. In addition, each surgical investigator will participate in at least one of the bi-annual meetings of the Clinical Management Committee. Each Satellite site PI's and co-I's responsibility will also include the following:

- Establish working relationships between Cardiothoracic Surgery and Cardiology, including general cardiology, echocardiography, and interventional cardiology in order to facilitate patient identification and enrollment;
- Obtain IRB approval for the CTSN protocols and informed consent (and their revisions) in a timely manner;

- Recruit patients, collect data and enter it accurately in the EDC;
- Faithfully follow the protocols and adhere to the standards of GCP;
- Provide the DCC with the information necessary for interim, annual, and final reports;
- Provide source documents, data and regulatory documents for study monitors to review;
- Provide prompt responses to DCC inquiries;
- Participate in Steering Committee and subcommittee meetings and conference calls as a non-voting member;
- Participate in analyses and reporting study results, including potential participation on manuscript development subcommittees;
- Submit COI forms to DCC on annual basis.

### Surgical Requirements

- Satellite sites must have a large volume of cardiothoracic surgery with a minimum of 500 cases annually
- Surgeons must be willing to perform:
  - *For Severe MR Trial*
- Mitral valve repair with annuloplasty and a sub-valvular procedure for severe tethering or
- Mitral valve replacement and complete preservation of the sub-valvular apparatus
  - *For Moderate MR Trial*
- Coronary Artery Bypass Grafting (CABG) + Mitral Valve Repair
- CABG Alone

Previous Experience: Satellite sites must demonstrate prior and ongoing experience with patient-oriented research, preferably in surgically treated patients, including prospective studies requiring patient recruitment into clinical trials. Satellite sites must also have dedicated clinical coordinators (e.g., research nurses) to assist with screening and enrolling patients and act as liaison between surgeons and cardiologists, including the echocardiography and catheterization laboratory personnel.

Volume of Recrutable Patients: Sites must demonstrate a large patient population eligible to participate in the MR trials based on integrative echocardiography assessment method (see attached Echo Acquisition Protocol). Sites must be able to demonstrate through prospective screening logs that they have a patient volume sufficient to recruit at least xxx patients who are MR surgical candidates into the trials, or approximately xxx patients per month.

Ability to Recruit Patients from surgical services: Participating sites must have concurrence from Surgical leadership that equipoise exists and patients will be enrolled and randomized. If equipoise does not exist on the part of specific surgeons, then measures will be taken to allow those patients to be enrolled by surgeons collaborating on these trials.

Ability to Recruit Patients from cardiology services: Participating sites must have access to echocardiography and catheterization laboratory facilities and the ability to recruit patients within those facilities.

**Clinic Practice Model:** Sites must be able to facilitate consented patients' study-related evaluation according to the protocol defined time points (within 30 days prior to randomization, post-operative Day 1 and then again at 6, 12, and 24 months). These evaluations will consist of medication history, physical examination, echocardiogram (echo), cardiopulmonary exercise test, neurocognitive tests, and quality-of-life surveys. The randomization procedure is performed intra-operatively, following sternotomy and before cannulation of aorta.

**Clinical Equipoise:** The pre-randomization transthoracic echo will be read by the site's echocardiography investigator using the intragative echo indices to assess the degree of MR to determine eligibility for participation in the trial regardless of the degree of MR as assessed by the intra-operative trans-esophageal echo. After randomization, the study echos will be sent to the Echocardiography Core Laboratory for centralized reading by a blinded investigator.

**Absence of Competing Studies:** The satellite sites should not have competing studies and must agree in writing to prioritize patient recruitment into the CTSN trials.

**Institutional Support:** Each satellite site must have the full support of their overseeing institution clinical and research enterprise and provide a letter of support.

**Participate in Mandatory Training by Core Laboratories:**

- ***Electronic Data Capture System:*** A university-based DCC (InCHOIR) located at Mount Sinai School of Medicine, NY, NY will provide EDC training.
- ***Echocardiography Core Laboratory:*** All echos will be performed according to a standardized protocol (see attached Echo Acquisition Protocol) and will be centrally analyzed by the Network Echocardiography Core Laboratory directed by Judy W. Hung, MD, located at the Massachusetts General Hospital, Boston, MA. Each site will send 2 sample echos to the core laboratory for review and certification prior to enrollment of the first patient.
- ***Cardiopulmonary Exercise (CPX) Core Laboratory:*** All exercise testing will be performed according to a standardized protocol and will be centrally analyzed by the Network CPX Core Laboratory directed by Steven J. Keteyian, PhD, located at Henry Ford Hospital, Detroit MI. The CPX core laboratory will provide onsite training and standardization of the CPX protocol.
- ***Neurocognitive Core Laboratory:*** The Neurocognitive Core Laboratory is comprised of two academic centers, Duke University and Columbia University. The core laboratory will be responsible for training the clinical site personnel in administration of the specific tests. All neurocognitive tests will be scored centrally by the core laboratory.

**All satellite sites must adhere to the following timelines in conducting the clinical trial:**

- Commitment of dedicated personnel for at minimum 24 months, especially since the majority of personnel effort will be required during the 1<sup>st</sup> month of patient screening and randomization;
- Completion of patient follow-up (up to 24 months)
- Completion of data collection and closing out queries as per DCC standard operating procedures.

**Application Content**

- The information required in response to this solicitation has been determined to be essential in the evaluation, review and sub-award contract process. The survey application should demonstrate your organization's capability and approach to carrying out the tasks described in the protocols and manual of operations.
- Provide standard NIH Biosketches or CVs, license and human subject training certification for the PI, Co-I, collaborating investigators and all other key personnel assigned to work on this project.

**Due Date**

All materials must be received at the DCC by March 15, 2010.