Interagency Registry of Mechanical Circulatory Support for End-Stage Heart Failure
RFP: NHLBI-HV-05-08

PROJECT DESCRIPTION/RATIONALE FOR PROJECT

The goal of the proposed program is to establish a data and clinical coordinating center (DCC) to manage a registry of patients receiving a mechanical circulatory support device (MCSD) to treat heart failure. The purpose of the registry is to collect and analyze clinical and laboratory data and tissue samples from patients who are receiving MCSDs as destination therapy for end-stage heart failure at 60 to 70 participating hospitals. It is anticipated that the registry will collect data, blood and tissue samples from approximately 2,000 new patients per year for a period of 5 years. Specifically, the DCC will perform the following tasks:

- select, with approval of the National Heart, Lung, and Blood Institute (NHLBI), steering committee (SC) members
- develop, in collaboration with the SC and the NHLBI, the study protocols to collect data, blood and tissue samples
- develop, in collaboration with the SC and the NHLBI, study policies, a manual of operations, study forms and informed consent documents
- set criteria that participating hospitals must meet to become members of the MCSD registry
- train staff of participating hospitals in registry methods of data, blood and tissue collection
- collect, format and store data
- provide customized reports to the NHLBI, The Centers for Medicare and Medicaid Services (CMS) and the Food and Drug Administration (FDA)
- provide statistical analysis of the data and develop necessary software for this analysis
- establish methods and procedures for tissue collection and storage
- prepare reports for the NHLBI-appointed Data and Safety Monitoring Board
- develop methods, including site visits, to assure accuracy and quality of data and monitoring of participating hospitals
- facilitate interaction among the participating hospitals
- provide administrative and logistical support for publication and dissemination of findings

General Description of the Required Objectives and Desired Results

The broad purpose of the registry is to enable research to determine best medical practices for advancement of public health with respect to the use of MCSDs for the treatment of heart failure. The registry will: 1) develop standard methods to collect data and specimens which will be used for research to characterize heart failure patients receiving MCSDs, demographics of MCSD use and patient outcomes, 2) collect, process and store patients' clinical data (including related costs) and tissue/blood samples, 3) analyze data collected, 4) provide these resources to researchers outside the registry who are interested in advancing application of MCSDs for patients with heart failure, and 5) publish and disseminate results.

The MCSD registry through its DCC will collect information pertaining to patients, care providers, hospitals, and devices and provide customized data sets on a regular basis to the NHLBI, the CMS and the FDA. The registry will also collect and store blood and tissue specimens in the NHLBI supported tissue repository. Through its Steering Committee (SC), the registry will develop protocols to collect data to answer research questions. A Data and Safety

Monitoring Board (DSMB) will perform independent monitoring and analysis of clinical outcomes and adverse events. Additionally the registry will develop policies and procedures for sharing data and biological materials that will permit parties outside the investigative group to request data or specimens for research purposes.

Background Information

Over the last two decades, MCSDs have been developed to augment or supplant failing myocardial performance. This therapy has been used successfully as a bridge to heart transplantation, occasionally, a bridge to recovery, and most recently as permanent implantation or "destination therapy" for intractable heart failure. Although cardiac transplantation offers life saving therapy for selected patients, its use is limited by a supply of donor organs which currently meets less than one-tenth the need. As a consequence, the number of MCSD implantations has increased in recent years and this trend is expected to continue especially in view of the October 1, 2003 decision of the CMS to provide reimbursement for MCSD implantation surgery.

Despite favorable survival and quality of life outcomes, MCSDs do have severe and sometimes life-threatening complications associated with infection, thrombosis, and device failure. The development of new procedures and devices to reduce these complications will be expedited by the work of this proposed registry involving the systematic, independent analysis of MCSD implantation procedures and outcomes. NHLBI will collaborate with the CMS and the FDA in monitoring the work of the proposed registry to permit the development of standard reporting of patient characteristics, indications, implantation procedures, and adverse events. These results are expected to facilitate clinical evaluation and patient management while aiding better device development. The work should also enhance future research and facilitate appropriate regulation and reimbursement of MCSD implantations.

Detailed Description of the Technical Requirements

Statement of Work

This program is proposed to establish a DCC to manage a registry of patients receiving an MCSD for the treatment of heart failure. The purpose of the registry is to collect and analyze clinical and laboratory data from eligible, participating hospitals in the United States, on patients receiving MCSDs as destination therapy for end-stage heart failure. In order to understand demographics of MCSD use, patients receiving a MCSD for bridge to transplantation will also be collected. The registry will provide data on the hospital, device implantation and support team, and device and patient characteristics and outcomes in hospital and during outpatient follow-up. It is estimated that 1,000 patients will receive MCSDs in 2004. The suggested capacity for annual collection of new patient data is 2,000. Actual expansion of utilization of MCSDs, availability of new devices, device design, and consideration of patient safety and requirements for valid statistical evaluation will influence the decision about needed capacity and the sample size requirements of categories of patients in the registry. Patient categories include:

1) patients receiving MCSDs for destination therapy and
2) patients receiving a MCSD while awaiting a donor organ.

The DCC shall:

1. Work with the SC and the NHLBI to prepare the final protocol, establish standard procedures and forms, and provide and distribute the forms. SC membership includes at least one representative each from FDA and CMS, the study chairman, the DCC principal investigator and members from representative participating hospitals.

2. Develop, in consultation with the NHLBI, criteria for certification and approval of participating hospitals as members of the registry and methods to expeditiously implement certification and to monitor hospital performance. The DCC, with the SC, will establish policies and procedures to insure satisfactory performance from participating hospitals. The DCC is responsible to train staff of participating hospitals in registry methods of data, blood and tissue collection such that eligible hospitals can be certified to participate in the registry. The DCC shall identify and eliminate hospitals that fail to meet or maintain performance standards.

3. Prepare, in consultation with the SC and with approval of NHLBI, a manual of operations based on the registry protocol for the participating hospitals. The manual of operations shall contain plans for collecting patient data in compliance with patient privacy regulations, and for proper cross referencing to the source documents. A special concern is to protect proprietary (device specific) information such that analysis of safety and outcomes of device prototype(s) is enabled while maintaining confidential product information that would be part of a restricted data set available only to the manufacturer and/or appropriate federal agency. The manual of operations will contain registry policies and procedures, including standard definitions of adverse events, and other key definitions of endpoints of interest. Operating policies such as publications, conflict of interest, and data sharing would be included.

4. Develop, in consultation with the SC, an informed consent document that would contain required elements for use by each participating hospital in its preparation of protocol and informed consent materials for their IRB approval. The DCC will establish methods to ensure that each IRB-approved informed consent contains required elements and that IRB approvals are current.

5. Serve as the repository for the clinical data collected during the study and provide oversight for collection and transfer of tissue or blood specimens to an NHLBI-supported storage facility. This will require the following:

    I. inform the appropriate personnel at each participating center of the requirements for data collection, as outlined in the registry protocol and manual of operations;
    ii. monitor hospitals to ensure the data are forwarded to the DCC in a timely manner;
    iii. review all clinical data transmitted by the participating hospitals to ensure completeness and quality control prior to processing;
    iv. develop a procedure for analysis of a large number of clinical measures needed to characterize patients enrolled and their outcomes including functional status, adverse events, subsequent hospitalizations, quality of life and survival.
    v. maintain liaison with each participating hospital to assist in the solution of operational problems involved in collecting and reporting data;
    vi. process and store all clinical data electronically; the coordinating center will be

responsible for development of computer software necessary for these functions;

vii. develop procedures to process and transfer tissue/blood samples to the designated storage facility.

Note: The offeror will not be responsible for storing samples and should propose costs only for preparation of samples for shipping.

6. Provide statistical analysis of the data and develop the necessary software for this analysis.

7. Prepare monthly reports for NHLBI to include patient recruitment in various categories and the hospitals providing the data, status of follow-up data collection, data analysis and problems, if any, with the quality of data received.

8. Prepare routine standard reports for FDA and CMS.
   I. In accordance with FDA requirements adverse events must be submitted within one week of the event
   ii. In accordance with FDA requirements serious adverse events must be submitted within 48 hours of the event.

9. Every three months provide to the NHLBI a summary of data collected and received during that period on patients receiving MCSDs. This will be included as part of the quarterly progress reports.

10. Prepare and distribute brief semi-annual, summaries of the progress of the registry to the participating hospitals

11. Arrange meetings of the DSMB to be held at least twice a year, provide summaries of the data analysis and specific patient data sets as requested and prepare and distribute minutes.

12. Assist the NHLBI in coordination and managing meetings of the SC; prepare and distribute minutes.

13. Assist the NHLBI in planning and conducting an annual conference of registry investigators (at least one representative for each participating hospital) in order to present and review MCSD Registry data.

14. Provide a final consolidated copy of patient data in hard copy and computerized tape formats, along with the supporting documents, to NHLBI program office.

15. Assist in the preparation of publications resulting from the registry.

16. Transcribe into registry forms and enter into the registry data base, information on patients that received MCSDs as destination therapy for heart failure prior to the initiation of the MCSD Registry. It is estimated that approximately 200 patients have already received therapy.

17. Perform site visits with record audits to determine the accuracy of web-based data submitted and information contained in source documents.

NOTE: The following is for solicitation purposes only.

18. Based on the offeror's draft protocol, proposals must provide plans to:

    I. develop a manual of operations based on the registry protocol, to be used by participating hospitals,
    ii. standardize, print and distribute patient reporting forms,
    iii. review and monitor data to insure quality control of data,
    iv. collect, process, and store data from the participating hospitals,
    v. collect and transfer patient tissue or blood samples to the designated repository,
    vi. determine access to stored tissue and data for investigators and for outside requests,
    vii. assess adverse events, quality of life, and hospital costs,
    viii. perform data analysis that demonstrate the offeror's understanding of the objectives of the registry; in this regard detailed statistical design should be submitted to analyze the registry data to a) evaluate the quality of life, b) costs of therapy, c) adverse events, and d) predictors of outcome,
    ix. prepare and distribute technical, statistical and data analyses reports,
    x. conduct meetings of the SC, DSMB and an annual conference of the participating hospitals to present and review data, and
    xi. organize and manage the registry including how the SC and its subcommittees will be selected, governance of the registry and communication with NHLBI.

d. Reference Material

Offerors should reference literature cited in discussing the background and rationale for the registry and forecasting availability of new or improved devices for implantation.

e. Level of Effort

The Government considers that the personnel and estimated levels of effort identified below will be necessary for successful completion of the DCC's objectives. Effort is shown as a percentage of FTE (full-time equivalent) labor. The personnel and levels of effort listed below except as noted are for information only and are not considered restrictive for proposal purposes. The levels were formulated by NHLBI staff experienced in the conduct of patient registries.

Labor Category	Phase I (0-6 mos)	Phase II (7-60 mos)
Principal Investigator	40%	30%
Co-Investigator	40%	40%
Bioengineer	10%	10%
Biostatistician	100%	100%
Programmer	50%	50%
Project Manager	100%	100%
Data Manager	100%	50%
Data Coordinator	100%	50%
Clinic Auditor (Nurse)	0%	20%
Program Assistant	75%	25%
Secretary	100%	50%
TOTAL	715%	525%

NOTE: A physician's time commitment of at least 16 hours per week (40% FTE) shall be required for this program. In addition, the full-time effort of a Biostatistician is required in Phase I and Phase II.

Offerors shall ensure that the Principal Investigator and all other personnel proposed will not be committed on federal grants and contracts for more than a total of 100% of their time. If the situation arises where it is determined that a proposed individual is committed for more than 100% of his or her time, then the Government will require action on the part of the offeror to adjust the time commitment.

f. Phasing

The program will have two phases: Phase I and Phase II.

Phase I (03/31/05 - 09/30/05)
During this phase the DCC in consultation with SC will finalize protocol, submit protocol for DSMB review and approval, establish criteria to certify participating hospitals, and develop training for registry personnel. The SC will meet monthly to finalize study protocol and procedures. The DCC will develop a manual of operations, study forms and formats for web-based collection, and methods to insure accuracy of data submitted to the registry. Policies for publication, conflict of interest and for use of stored data will be established and included in the manual of operations.

Phase II (10/01/05 - 03/30/10)
For the remainder of the study the DCC will provide overall coordination of the program. Participating hospitals will be trained, certified and maintain required performance standards. Eligible patients will be consented, enrolled and their data collected. The DCC will monitor study progress including site visits to assure data accuracy and study performance. The SC will meet twice yearly to review, analyze and publish data. The DCC will prepare reports for the DSMB at intervals of 6 months and submit routine reports to the NHLBI, FDA and CMS. The DCC will conduct a site visit of each participating hospital during this phase. Visits "for cause" will also be conducted as needed. The DCC, in consultation with the SC, will consider revision of protocol and methods as appropriate in response to new devices or changes in knowledge and treatment of heart failure patients.

g. Clinical Research/Human Subjects

Research involving the collection of clinical data and biological specimens will be proposed in response to this solicitation. The following guidelines and policies, which may be applicable to this solicitation, can be viewed at http://www.nhlbi.nih.gov/funding/ethics.htm.

- Inclusion of Women and Minorities As Subjects in Clinical Research - NIH Guidelines
- Inclusion of Children as Participants in Research Involving Human Subjects - NIH Guidelines
- Terms and Conditions for Accrual of Research Subjects
- Establishing Data and Safety Monitoring Boards and Observational Study Monitoring Boards
- Responsibilities of DSMBs Appointed by NHLBI
- Responsibilities of OSMBs Appointed by the NHLBI
- Data Quality Assurance in Clinical Trials and Observational Studies - Guidelines
- Avoiding Conflicts of Interest in Multi-Center Clinical Trials—Guidelines
- Serious Adverse Event Reporting to the NHLBI - Policy
- Medicare Coverage of Clinical Trials
- Human Tissue Repositories—Guidelines
- Tissue Sharing in Informed Consent—Guidance

h. Special Requirements

- Once the study protocol and forms have been approved, a request for clinical exemption for the requirement of OMB clearance for study forms will be coordinated by the NHLBI Project Officer for submission to the NIH OMB Clearance Officer. It is expected that the forms will be exempt from OMB forms clearance requirements.

- The DCC and all participating clinical sites will be required to obtain Institutional Review Board approval prior to initiation of Phase II patient activities.

- This program is subject to the DHHS Automated Information System Security Program. The security level designations are included in Section L of the RFP. The overall security level designation for this requirement is Level 3 for sensitive information.

i. MCSD Registry Committees

The SC, consisting of the Principal Investigator of the DCC, the study chairperson, and representatives from the FDA, CMS and selected participating hospitals, will work together during Phase I to 1) define enrollment, 2) establish eligibility for detailed follow-up, 3) determine a target number of patients for each device, 4) finalize the MCSD protocol, and 5) provide scientific direction to the MCSD registry at an operational level. During Phase I, the SC will meet approximately monthly including four meetings and teleconferences as needed. During Phase II the SC will meet every six months. Each representative to the SC has one vote on issues pertaining to the MCSD Registry.

The Operations Committee is an executive committee of the SC with oversight and authority for the day to day operations of the study. The Operations committee will include the principal investigator of the DCC, the study chairman, and representatives from the FDA and CMS. The Operations Committee will hold weekly meetings by teleconference.

An NHLBI-appointed DSMB will be established to monitor overall progress, data outcomes and patient safety. The DSMB will periodically evaluate procedures, findings, and adverse events and advise the NHLBI when changes should be made. The DSMB will meet at least once per year and conduct teleconferences as needed. Responsibilities of DSMB's appointed by the NHLBI can be found at http://www.nhlbi.nih.gov/funding/ethics.htm.

j. Travel

Travel costs should be based on DSMB and SC meetings held in Bethesda, Maryland and conducting site visits of participating hospitals during Phase II.

During Phase I (03/31/05 - 09/30/05) the SC will meet four times for a 2-day meeting in Bethesda, Maryland. For planning purposes the SC will include up to 20 representatives from participating hospitals and the Study Chair. The DSMB will meet once during this phase and it is anticipated there will be 10 members.

During Phase II (10/01/05 - 3/30/10) the SC will meet twice every year for a 2-day meetings in Bethesda, MD. For planning purposes the SC will include up to 20 members including the Study Chair. Site visits in order to ensure quality performance and accuracy of data submitted will begin. Each participating hospital will have a site visit review at least once during the course of the contract. Site visits to resolve problems will occur as needed. For planning purposes, the site visit team will include four members and there will be 100 site visits. The DSMB will meet every six months during this phase and include 10 members.

Travel funds for members of the SC and the DSMB and for the representatives of the participating hospitals attending the annual conference should not be included in the proposal.

k. Past Performance

Offerors shall submit the following information as part of their business proposal (for both the offeror and proposed major subcontractors): A list of contracts completed during the past two (2) years and all contracts currently in progress for products or services similar to the solicitation work scope. Contracts listed may include those entered into with the Federal Government, agencies of state and local governments and commercial customers. Offerors that are newly formed entities without prior contract experience should list contracts and subcontracts as required above for all personnel. Include the following information for each contract or subcontract:

- Name of contracting organization
- Contract number (for subcontracts, provide the prime contract number and subcontract number)
- Contract type
- Total contract value
- Description of requirement
- Contracting Officer's name, telephone and Email address
- Project Officer's name, telephone number and Email address

Each offeror will be evaluated on its performance under existing and prior contracts for similar products or services. Performance information will be used for responsibility determinations.

The Government will focus on information that demonstrates quality of performance relative to the size and complexity of the acquisition under consideration. The Government is not required to contact all references provided by the offeror. References other than those identified by the offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of an offeror's past performance.

I. Specific Issues Offerors Must Address

Offerors should submit one proposal that addresses all technical objectives 1-5 listed below. The proposal should be submitted in one volume. The proposal will be reviewed as a whole.

1. To design and implement a Registry of MCSDs for Treatment of Heart Failure

This program will establish the MCSD Registry, a research registry of patients receiving MCSDs for treatment of heart failure through a DCC. Collaborations of the contractor with existing registries, medical centers or hospitals, professional societies or industry experienced in the use of mechanical devices for treatment of heart failure such as local research institutions or organizations or individual research projects are encouraged.

The DCC shall have overall responsibility for organization, management and operation of the registry. The DCC, with NHLBI approval, will establish a SC that will provide scientific direction for the program. So that the program can expeditiously complete Phase I, it is expected that the DCC proposal will include investigators from experienced hospitals that are capable of contributing to the development and testing of methods proposed for the MCSD Registry. Hospitals selected by the offeror to participate in Phase I will be called vanguard hospitals. Vanguard hospitals would be expected to apply for certification which will be required for each hospital participating in Phase II. An investigator from a vanguard center who participates during Phase I, may be invited to continue as a SC member during Phase II. The plan for the SC membership should include rotation of members such that all participating hospitals will have representation on the SC over the course of Phase II in the program.

The DCC proposal should include plans for establishing set standards for performance and provide training so that eligible hospitals will be certified as members of the registry. Plans for monitoring quality should include performance standards and procedures to eliminate hospitals that don't maintain performance standards. The DCC must provide training and assistance so that it is reasonable to expect eligible hospitals to become certified for participation in the MCSD Registry.

Hospitals that wish to participate must be capable of implanting MCSDs and have a team of well-trained and experienced professionals who meet performance standards to adhere to registry procedures, and have appropriate facilities to record clinical data, including web-based entry, and to prepare and transfer biological specimens. All clinical data will be stored at the DCC. Biological specimens collected by the participating hospitals will be stored in a designated tissue repository.

2. To establish a set of standardized procedures for recording clinical data and cost data, and for preparing and transferring biologic specimens.

The contractor shall develop patient data forms, data collections methods, and policies that govern the activities of the registry including but not limited to publications, data sharing, conflict

of interest, classification of adverse events, and performance standards required for hospitals to participate in the registry. A manual of operations must be developed to detail the registry protocol, policies and data forms. The protocol and manual of operations should be submitted for approval by the NHLBI-appointed DSMB before the end of Phase I. Following approval by the NHLBI, the protocol will be submitted for local IRB review and approval in order to participate in Phase II. This shall occur in the first six months of the contract.

3. To provide training and technical support to participating hospitals regarding MCSD procedures and policies.

The contractor shall provide training and technical support so that eligible hospitals can fully understand the goals of the registry, successfully adhere to protocols and become proficient in MCSD Registry methods for data acquisition and submission, and specimen collection.

The contractor shall develop methods to monitor site performance including data audits and site visits to assure data accuracy and timely submission.

4. To collect, process, store, ship, and analyze clinical information and biological specimens from patients enrolled.

The contractor shall:

a. collect patients' clinical data including patient characteristics (including but not limited to age, sex, race, birth date and place, education, occupation, address, height, weight), medical history, genetic background of the patient, current cardiac status, etiology of heart failure, medications, and results of standardized sets of laboratory tests;

b. collect surgical data associated with MCSD implantation including but not limited to such as type of device, indication, operative procedure data, and peri-operative complications, device characteristics, in hospital care and related costs;

c. monitor enrollment of all categories of patients and collect detailed information on all patients receiving an MCSD;

d. register and collect adverse events on all patients receiving any MCSDs following reporting requirements established during Phase I;

e. establish methods for statistical analyses of data and adverse events and prepare periodic reports for review by the NHLBI-appointed DSMB;

f. prepare and submit standard reports to NHLBI, CMS and FDA including number of patients enrolled, data transmission and quality, and adverse events; (These reports will be refined in the first year of the contract);

g. store and maintain patients' information in a data base at the DCC using appropriate commercially available hardware and software which provide the capability to search the database with various parameters. (Access to this information must be securely controlled in order to protect the privacy of the patient information);

h. provide oversight for collection, storage and maintenance of the specimens collected

from patients to ensure the proper conditions to preserve the quality of the specimens for future histopathologic and genomic investigations. (These specimens shall be processed according to procedures specified in the protocol and access to specimens should be strictly controlled in order to protect the privacy of the patient information);

l. provide plans to register and process the data of the specimens, analyze results, and store this information in the database.

5. To disseminate to researchers clinical information and biological specimens from patients receiving MCSD for heart failure.

The contractor, in conjunction with the SC, shall develop dissemination procedures for the purpose of providing clinical data and biological specimens to investigators for basic and clinical research. A Dissemination Plan will be approved by the SC and become part of the protocol prior to any dissemination of clinical information or biological specimens to researchers. The SC of the MCSD Registry shall develop qualification requirements as well as a review mechanism for providing clinical data and specimens stored in the MCSD Registry to investigators interested in using such materials. Beginning in the third year of the contract, the MCSD Registry will begin disseminating clinical information and biological specimens to researchers. The application form requesting information and /or materials stored in the MCSD Registry should include:

a. the purpose/use of the MCSD Registry information and specimens

b. the assurance that the use of the data and specimens will comply with privacy regulations;

c. the capabilities of the proposed researcher(s) to conduct high quality research in application of MCSD for treatment of or elucidation of pathophysiology of heart failure;

d. a description of the research projects, which should elucidate prevention, treatment or pathophysiology of heart failure or improve the application or design of MCSDs;

e. an agreement that all results derived from studies using the clinical data and/or biological specimens shall be reported to the MCSD Registry three weeks prior to publication or dissemination; and

f. An acknowledgment to the MCSD registry shall be included in all publications which contain any results from registry-derived data or specimens. The following materials are considered to be publications: a) articles in journals, b) abstracts and presentations in meetings, conferences, and symposia, and c) book chapters.

ADDITIONAL TECHNICAL PROPOSAL INSTRUCTIONS

Each proposal shall include:

1. How the proposed MCSD Registry would improve: a) application of MCSD in the management of heart failure and how this resource may lead to a resolution or better understanding of the etiology, pathogenesis, and potential treatments of heart failure;
b) facilitate improvement of existing MCSDs and on development of new devices; and
c) stimulate research on additional strategies to halt disease progression or organ replacement.

2. A background section briefly reviewing the following: a) the current diagnostic criteria used to establish end-stage disease and predictors of favorable outcomes with an MCSD implant (e.g., a discussion on the strength and weakness of each baseline characteristic useful for management, and what modifications should be made); b) the current research status of etiology, pathogenesis, and treatment of end-stage heart failure relevant to application of MCSDs; c) MCSDs and discussion of device-related complications; and
d) future studies that will become feasible because of the availability of the proposed research registry.

3. A detailed description of the research plan, which shall clearly state the following:

a. the organizational structure, and operation of the DCC for the MCSD Registry; (NHLBI will provide a suitable tissue repository facility.)

b. a full justification of the criteria by which hospitals are eligible to participate, such as the availability of a fully or partially characterized patient population; and experience in implanting MCSDs.

c. a list and justification of the personnel proposed for the DCC for the MCSD Registry.

4. The DCC shall identify up to 15 vanguard hospitals that will provide clinical investigator representatives with appropriate cardiology, critical care, surgical, and engineering, scientific and practical experience who are willing to collaborate with the DCC during
Phase I as the temporary SC for the MCSD Registry. A biosketch including publication list for each key person with an advanced degree and qualifications of the vanguard hospital and its representative(s) to the SC shall also be included.

5. The contractor shall provide a detailed description of:

a. office space, research facilities, and equipment which are available for the use by the registry.

b. the organization and collaboration mechanisms including how the entire MCSD Registry will be supervised, how communications between the Principal Investigator at the DCC and the Principal Investigators at the participating hospitals will occur and how exchange of information among participating hospitals will be facilitated.

c. plan for collecting, processing, shipping of biological specimens, and storing clinical data. The plan shall include:

I. a detailed description of the methods and procedures which will be used in collecting, processing, shipping and storing biological specimens;

ii. information about the training, expertise, and experience of the personnel participating in registering, collecting, processing, and shipping biological specimens

iii. a detailed quality control plan to collect, process, and transfer biological specimens;

iv. a detailed discussion of anticipated pitfalls and problems in methodology and procedures, and potential resolutions; and

v. a description of the database which will be used to register and store the data associated with biological specimens.

d. Plan for patient recruitment. Such a plan should include the following:

I. the number of patients to be recruited and a justification to support this number;

ii. what clinical data will be collected and how the information selected will accomplish the goal(s)of the registry;

iii. a detailed quality control plan to collect, process, and interpret clinical data;

iv. a discussion of anticipated problems and resolutions;

v. a description of the computer programs which will be used to store clinical data; and

vii. statistical analysis plan (and software) to meet the goals of the MCSD Registry

6. A proposed plan for providing clinical data and biological specimens to researchers.

A plan for disseminating clinical data and biological specimens from the MCSD Registry to researchers. Rationale for the plan such as a description of future research projects that would become feasible because of the availability of the proposed research registry should be discussed. The plan will be incorporated into the Manual of Operations as a policy for access and sharing of data. This information should be included as part of the proposal.

The contractor shall provide:

a. a plan to receive, register, and process requests for clinical data and specimens. A description of the procedures and equipment used for this purpose should be included;

b. the staff who will be responsible for this process;

c. a qualification standard for the investigators interested in using the clinical data and specimens stored in the repository;

d. a review and approval procedure for providing clinical data and specimens stored in the repository. The procedure should include a description of the review committee and the review and approval procedures; and

e. a follow-up plan for monitoring the use of the clinical data and biological specimens.

7. A description of the plan to establish the following two committees: Operations Committee (OC) and a SC.

a. MCSD OC: The OC is an executive committee of the SC, meets frequently and has responsibility for oversight for day to day operations of the MCSD Registry. The OC shall include at least the NHLBI project officer, the principal investigator of the DCC, the study chairperson and representatives from the FDA and CMS. The operations committee will meet

by teleconference weekly to review and direct the activities and resolve issues related to the daily operation of the registry. The operations committee will seek ratification of changes in procedures by the SC.

b. MCSD SC: The SC includes members of the OC and representative(s) from the participating hospitals. The SC is the governing body for the registry. Decisions to alter procedures will require ratification by the SC. The SC shall communicate at least monthly and as often as is necessary to plan the study, develop and finalize the protocol in Phase I. The SC will meet twice yearly in Phase II to assess periodic evaluation and progress of the project. The SC may establish subcommittees to performs tasks such as morbidity and mortality, publications and access to data reviews.

8. A description of a plan to transition the MCSD registry to become at least partially self supporting should be submitted to NHLBI during year three of funding.