DIABETIC RETINOPATHY CLINICAL RESEARCH NETWORK

ORGANIZATIONAL STRUCTURE

I. Organizational Structure

A. Introduction

The central units of the project include the Coordinating Center, the Network Chair's Office, and the Fundus Photograph Reading Center.

The committee structure includes an Executive Committee, one or more Steering Committees, a Protocol Concept Review Committee and one or more Data and Safety Monitoring Boards (DSMB). Additional committees will be added as indicated.

B. Central Units

1. Coordinating Center

The Coordinating Center is located at The Jaeb Center for Health Research in Tampa, Florida. Specific responsibilities of the Coordinating Center will include:

- Coordinate the development of study protocols and the protocol development committees
- Develop study documents such as protocols, operating procedures manuals, and data collection forms
- Coordinate the conduct of study protocols
- Develop and implement a data management system capable of supporting multiple projects
- Develop and maintain a multi-functional website for many Coordinating Center, clinical center, Fundus Photograph Reading Center, and committee tasks
- Develop procedures for patient enrollment and randomization
- Develop statistical analysis plans
- Conduct data analyses for Data and Safety Monitoring Board review as well as for manuscripts, abstracts, and ancillary studies
- Coordinate the preparation and publication of study manuscripts
- Develop and implement a system for adverse event reporting
- Develop and implement a quality assurance program that includes training and certification of clinic staff, monitoring of adherence to the protocol, reporting of quality control data, validation of collected data, assessments of the Fundus Photograph Reading Center, and assessment of drug packaging and labeling
- Develop procedures and materials for certification of clinical centers and their staff
- Develop systems to assist the clinical centers in maintaining a high rate of patient retention
- Develop and maintain a system to facilitate communication between the central units, clinical centers, and committees

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- Develop and maintain a system for drug distribution and accountability
- Develop a system, if needed, for integration of a central laboratory into the project
- Develop cooperative arrangements with the Fundus Photograph Reading Center for transmission of data to the Coordinating Center
- Coordinate activities of the Executive Committee, Steering Committee and any other committees
- Coordinate activities of the Data and Safety Monitoring Board
- Coordinate the selection process of clinical centers in conjunction with the Network Chair
- Implement subcontracts with the participating clinical centers
- Develop materials for IRB submissions by the clinical centers
- Track IRB approvals and expirations
- Develop study close-out procedures and materials
- Arrange conference calls
- Arrange study meetings
- Develop summaries of committee conference calls and meetings
- Obtain and maintain INDs and IDEs
- Develop clinical center budgets in conjunction with the Steering Committee
- Develop and maintain directory of project personnel
- Coordinate site visits, prepare site visit agendas, and prepare site visit reports

2. Network Chair's Office

The Network Chair's Office is located at the Joslin Diabetes Center in Boston, Massachusetts. It provides support for the inaugural Network Chair. After completion of the term of the inaugural Network Chair, this office will no longer exist and support services for the subsequent Network Chairs will be provided by the Coordinating Center.

3. Fundus Photograph Reading Center

The Fundus Photograph Reading Center is located at the University of Wisconsin-Madison. Specific responsibilities of the Reading Center include:

- Participate in the development of study protocols
- Develop standardized procedures for fundus photography and other imaging techniques to be used in a protocol
- Develop and implement certification procedures for photographers as well as for technicians of nonphotographic imaging techniques
- Develop and implement quality control procedures for assessing the performance of clinical sites' photographic and nonphotographic imaging techniques

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- Develop and implement grading systems for photographic and nonphotographic imaging techniques
- Develop and implement quality control procedures for all Reading Center grading systems
- Participate in the analysis of study data and in the writing of manuscripts

C. Clinical Centers

The clinical centers will be responsible for carrying out the common study protocols. Clinical center staff will include a principal investigator, at least one co-investigator, a clinic coordinator, and other personnel as needed for the project. Appropriate backup must be available for all positions. Principal investigators will have overall responsibility for all study-related activities and all data collection at the center. Clinical center investigators will have an active role in all aspects of the project including protocol development, data analyses, and publication of results.

D. Network Chair

The inaugural Network Chair will be appointed by the National Eye Institute to serve an initial three-year term.

Subsequent Network Chairs will be selected following an application and formal review process. The final selection will be made by the Executive Committee, subject to approval by the National Eye Institute.

Responsibilities of the Network Chair will include:

- Chair the Executive Committee
- Ad hoc member of all standing committees
- Communications with industry
- Communications with FDA
- Communications with non-NIH funding sources (such as JDRF)
- Lead monthly investigator conference calls
- Principal media contact
- Primary public communicator regarding the network

E. Protocol Chairs and Protocol Development Committees

Each protocol, including primary protocols and ancillary studies, will have a designated Protocol Chair. Multi-phase protocols may have a separate protocol chair for each phase. For a given protocol, the Protocol Chair may be the Network Chair, a member of the Executive Committee or another investigator. Generally, the Protocol Chair will be the lead investigator on the writing committee for the related manuscript.

A protocol development committee will be formed for each protocol. This will include the Protocol Chair, representatives of the Coordinating Center and Reading Center, and other

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selected investigators and coordinators. The activities of the Protocol Development Committees will be coordinated by the Coordinating Center.

An investigator can only serve as protocol chair for one major project at a time.

F. Committees

1. Executive Committee

The standing members of the Executive Committee will include the Network Chair, the Director and Associate Director of the Coordinating Center, the Emeritus Director and Director of the Fundus Photograph Reading Center, and the NEI Project Officer. The inaugural Network Chair will remain on the Executive Committee as a permanent voting member. Subsequent Network Chairs will serve on the Executive Committee for one year prior to beginning their term, during their 2-year term, and one year following their term as Network Chair. Two site investigators will serve on the Executive Committee for staggered one-year terms.

For issues requiring a vote, the Director and Associate Director of the Coordinating Center will share a single vote. The Emeritus Director and Director of the Fundus Photograph Reading Center will also share a single vote.

The Executive Committee has overall responsibility for directing all of the activities of the project. This committee formulates all policy decisions related to the maintenance and conduct of the project.

Responsibilities of the Executive Committee include:

- Develop and enforce network policies
- Develop requirements for the participation of clinical sites and investigators
- Select protocols to be developed following recommendation of Protocol Concept Review Committee
- Select Protocol Chairs
- Select a Protocol Development Committee, if indicated, for each protocol to be developed
- Review and approve clinical center budgets
- Develop and maintain a program of quality assurance in the study
- Review 'competing studies' proposals, with regard to impact on existing or planned DRCR.net protocols
- Monitor the performance of participating sites and central units
- Identify potential funding sources
- Select network Chairs subject to approval by the National Eye Institute following a formal review process

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The Executive Committee will convene by conference call once per month. Additional calls will be held as needed. Additional individuals (e.g., Protocol Chairs) may be asked to participate as indicated.

2. Steering Committees

The members of the Steering Committees include the members of the Executive Committee, the Protocol Chairs, and other investigators on a rotational basis (generally for a one-year term). The committees will be chaired by the Director of the Coordinating Center. The committees will have conference calls once or twice a month.

Specific functions of the Steering Committee include:

- Review and approve final protocol, informed consent form, data forms, study procedures, and other study material
- Approve specific requirements for investigators to be certified for the protocol
- Pilot test study forms and procedures prior to start of patient recruitment
- Consider changes or modifications in the protocol as may be necessary or desirable
- Advise and assist the Coordinating Center on operational matters
- Review performance of all participating clinical centers
- Approve protocol dissemination plans including manuscripts and presentations
- Review and approve a writing committee for each manuscript and the authorship listing
- Approve manuscripts and abstracts
- Provide input on protocol close-out procedures
- Review and approve ancillary studies
- Provide input on clinical center budgets
- Review clinical site monitoring reports
- Review site visit reports
- Review site performance issues identified by the Coordinating Center

3. Protocol Concept Review Committee

The members of the Protocol Concept Review Committee include investigators on a rotational basis (generally for a one-year term). The committee will be chaired by a member of the Executive Committee. The committee will convene via teleconference as needed.

Responsibilities of the committee will include:

- Solicit ideas for new studies from investigators
- Review concepts for new studies received from investigators, research the topic when needed, and decide on degree of merit and priority
- Submit recommendations to Executive Committee

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4. Data and Safety Monitoring Boards (DSMB)

The responsibility for reviewing the ethical conduct of the study and for monitoring the data for evidence of adverse or beneficial treatment effects is assigned to the Data and Safety Monitoring Board (DSMB).

The members of the DSMB will be selected by the National Eye Institute, which will select one of the members to serve as the Chair. The members will include individuals with expertise in clinical trials, biostatistics, diabetic retinopathy, and diabetes as well as a layperson. The NEI Project Officer will be considered an ex-officio nonvoting member.

Prior to the initiation of recruitment for a protocol, the DSMB must approve the study protocol, including the informed consent procedure and form. Subsequent protocol changes that are substantive must be approved by the DSMB prior to implementation. Minor changes that do not impact patient safety or the assessment of efficacy do not require prior DSMB approval and will be reported to the DSMB at its semi-annual meetings. At its discretion, the DSMB may recommend to the Steering Committee that a protocol change be considered.

The DSMB will periodically review the progress of each protocol (at least twice each year either at a meeting or a conference call). In conjunction with the Coordinating Center, the committee will determine specific plans for evaluating adverse effects and efficacy, including deciding whether a formal interim analysis should be performed.

Recommendations made by this committee relating to protection of patient rights and/or resulting from data analyses are forwarded to the National Eye Institute. For randomized clinical trials, results are not available to the participating investigators involved in patient care until the DSMB recommends that this information be released.

Further details of the role of the DSMB appear in the DSMB Standard Operating Procedures.

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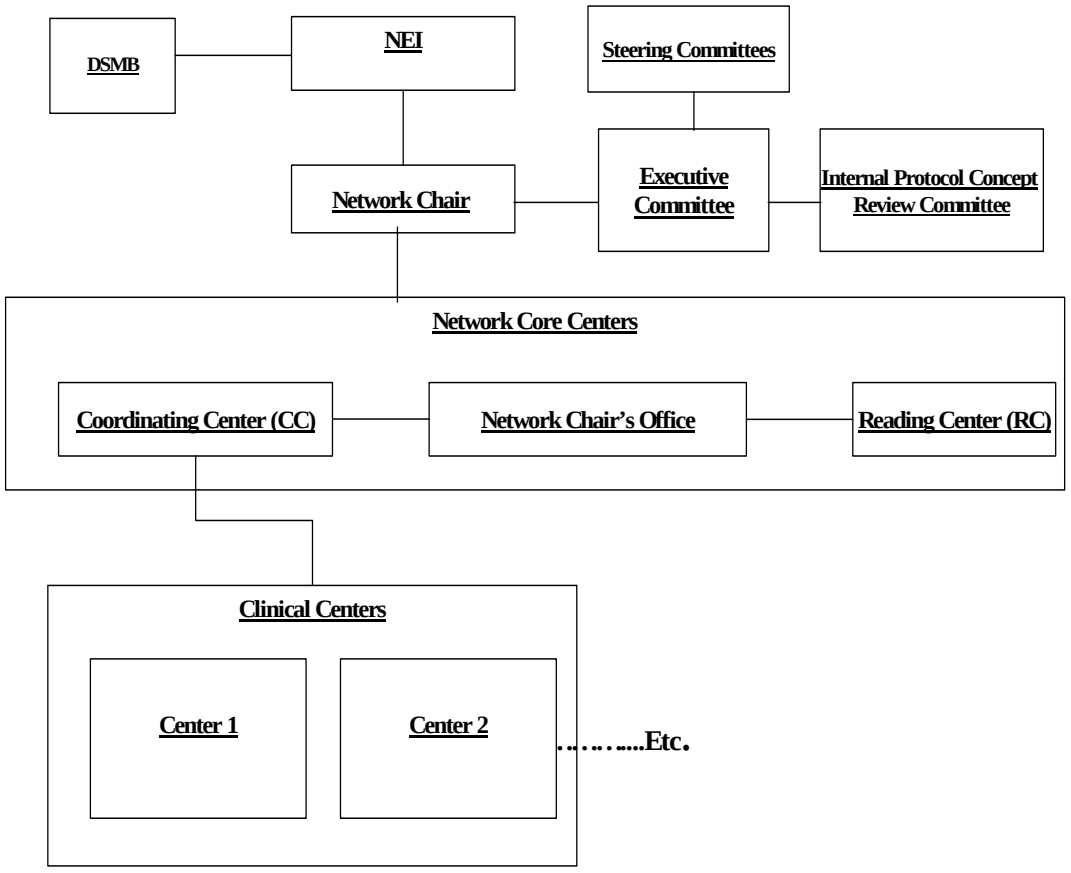

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DRCR.net Committee Structure
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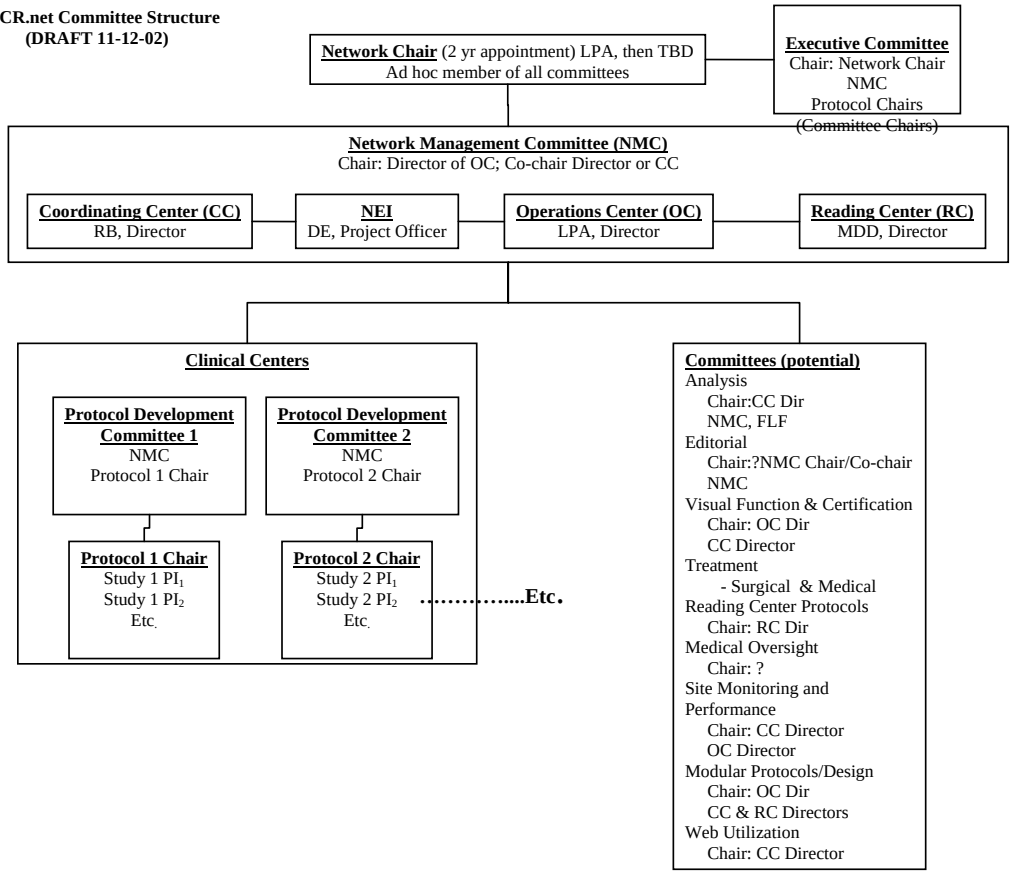

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