

Outcome Research & Clinical Research Networks

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NHLBI Approaches for Support of Clinical Research

- Researcher-initiated - RO1 (Research Project Grant) – usually single-center, less often multi-center studies. Most Common.
- Institute-Initiated – i.e. SCCOR (Specialized Centers of Clinically Oriented Research). Typically, Bench to Bedside focus, in response to an Institute RFA
- Clinical Research Network – UO1 (Multi-center Cooperative Agreement). More frequent.

NHLBI Clinical Research Networks

- 1st Institute Network Begun in 1993
- In Lung Division :
 - Adult Asthma Research Network,
 - ARDS, Childhood Asthma Research & Education (CARE), COPD, Idiopathic Pulm Fibrosis (new in 2005)
- Blood Division: Blood & Bone Marrow Transplant Clinical Trials Network, Transfusion Medicine/Hemostasis Network, Sickle Cell Disease Clinical Research Network (new in 2006)

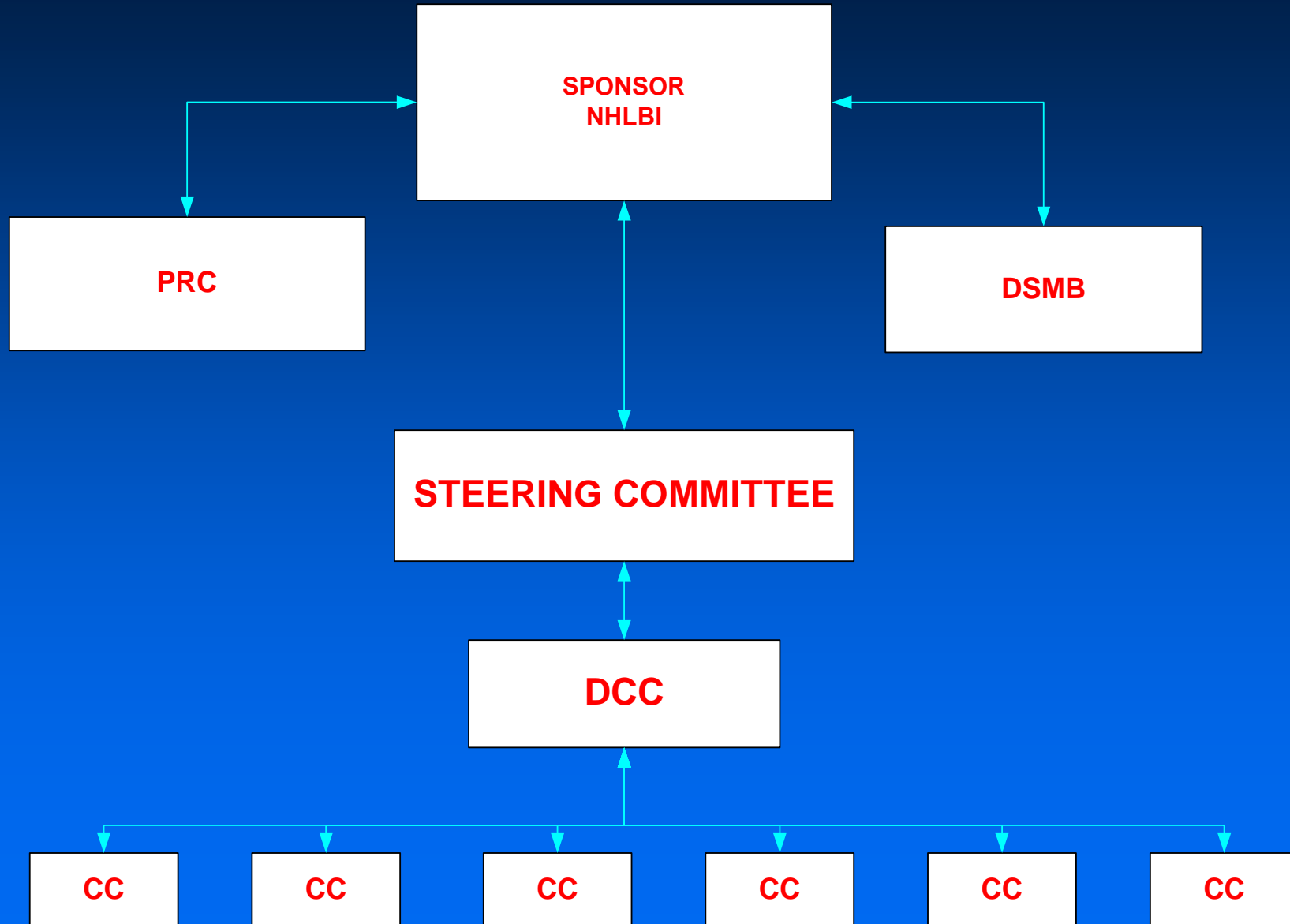
NHLBI Cardiac Clinical Networks

- Pediatric Heart Network, in 2nd 5-year cycle
- Clinical Research Consortium to Improve Resuscitation (ROC)
- Heart Failure Clinical Research Network (new 2006)
- Cell Based Therapy Clinical Research Network (new 2006)
- “Network for Cardiothoracic Surgical Investigations in Cardiovascular Medicine” (in review)

NHLBI's Goals for Clinical Networks

- Address Clinical Topics of Significant Public Health Concern
- Address Clinical Questions that Require Multiple Centers to Secure Sufficient Patients
- Address Multiple Therapeutic Studies and Trials Simultaneously
- Conduct Studies Quickly and Efficiently with Well-trained Clinical Teams that are Prepared to Work Collaboratively with the Other Teams and Closely with NHLBI

Clinical Network Structure



Clinical Research Network Structure

- Steering Committee (SC): Main governing body, with an Institute-appointed Chair and NHLBI Project Officer, and that includes the Principal Investigators of the Clinical Centers and the Data Coordinating Center PI
- SC Subcommittees may include: Publication Subcommittee, Quality Control Subcommittee, Core Lab Selection Subcommittee, Genetics Subcommittee, etc.

Clinical Research Network Structure

- Data Coordinating Center (DCC) Selected through peer review. Organizes and administers central research activities, including data management, recruitment and AE monitoring, statistical analysis, and specific administrative functions, i.e. communication among CCs, budgets, reports. Typically administers “per patient” payments to CCs, as well as expenses of core labs, DSMB and PRC meetings, and site visits to each CC..

Clinical Research Network Structure

- Clinical Centers (CC) Comprised of site PIs, coordinators and data managers. Responsible for protocol implementation, recruitment, QA, etc.
- Some Networks form Regional Clinical Center teams in order to recruit adequate numbers of patients or to access specific specialties.
- Direct Support for each CC is usually \$300k or less. GCRSs should be utilized if available.
- Additional support is provided on a “per patient recruited” basis.

Clinical Research Network Structure

Protocol Development and Implementation

- Clinical trial proposals are selected from protocols submitted by individual CCs.
- Full SC refines and prioritizes protocols. Also, may propose additional protocols
- SC-approved protocols are reviewed by the PRC. Action options are approval, modification & re-review and disapproval.
- Once approved, DCC organizes study operations, including certification that CCs meet all trial requirements.

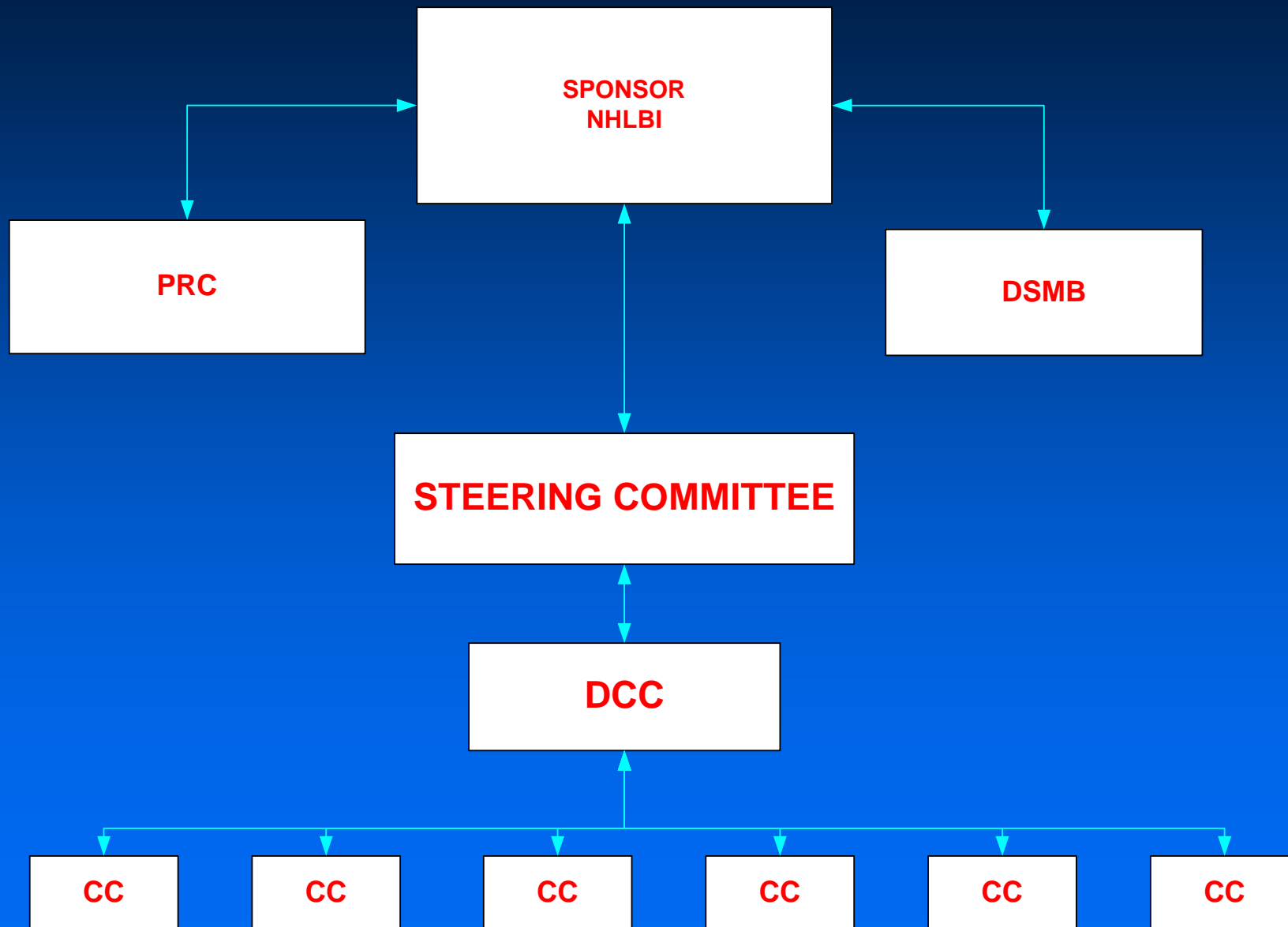
Clinical Research Network Structure

- Protocol Review Committee (PRC) Assesses scientific merit and design of each proposed protocol. Protocols are developed by the SC, often based on protocols proposed by the CC applicants. PRC Chair and members are appointed by NHLBI, to include expertise in basic & clinical research, clinical trial design, biostatistics, outcomes measures and ethics.

Clinical Research Network Structure

- Data Safety & Monitoring Board (DSMB) Is independent of the PRC and advises the Institute on conduct and progress of studies, the quality of the data and safety or ethics issues. Reviews serious adverse events, monitors data, protocol adherence. There is an independent chair and broad-based committee.

Clinical Network Structure



Structure of Clinical Research Networks

- Comprised of multiple Clinical Centers (CC). Clinical Centers can employ Regional Clinical Center concept.
- Managed by a Data Coordinating Center (DCC)
- Clinical Centers must agree to collaborate on the development and conduct of multiple intervention/therapy studies
- Clinical Centers do not have the option of selecting which studies or trials for participation

Why So Many New Networks at NHLBI?

- Networks fill a perceived gap in clinically-based research that addresses relevant and even compelling patient management questions
- Networks are set up to rapidly address multiple related questions
- Networks are efficient in sharing data and clinical expertise
- Networks form a critical mass of clinical skills and increase recruitment potential
- Networks result in rapid discoveries that contribute to future projects

Why NHLBI Likes Clinical Networks

- Networks Create “Communities of Practice” with a Common Purpose
- Networks “Seize” the Collaborative Advantage
- Networks Turn the Competitive Focus “Inside Out”
- Networks Harness the Skill and Knowledge of Many rather than a Few

Another Network Opportunity - The Skills Development Core

- Additional funding opportunity for Clinical Research Networks, SSCORs and Multicenter Clinical Studies
- Institute recognizes that Networks are an outstanding environment for training in clinical research
- CC applicants may request SDC award
- Goal is to assist new clinical investigators (fellows and junior faculty) in enhancing research skills
- Provides up to \$100k per year (direct costs) for support of experienced investigator who will devote 5% effort in mentoring

Outcomes Research & CT Surgery

Required Elements

- Rationale for the study – specific hypothesis
- Clearly defined primary end point and proposed secondary end points
- Power Calculations – estimated number of patients based on the expected effect and the resulting statistical power
- Recruitment projections
- Expected project length, end points, required staff and collaborations
- Participation of clinical trialist, biostatistician, etc.