NICHD NEONATAL RESEARCH NETWORK

How do I apply?

Origins of Neonatal Research Network (NRN)

- Neonatal management, especially for high-risk term and preterm infants, has often adopted practices without objective evaluation
- In an attempt to respond to the need for well-designed clinical trials in Neonatal Medicine, NICHD established the Neonatal Research Network in 1986

Background NRN

- Collaborative participation with centers, data center and NICHD on common protocols
- Cooperative agreements
- Competitively peer reviewed
  - Open competition
  - Content of grant, concept proposal, depth of faculty and institution
  - Priority score
  - Diversity in population

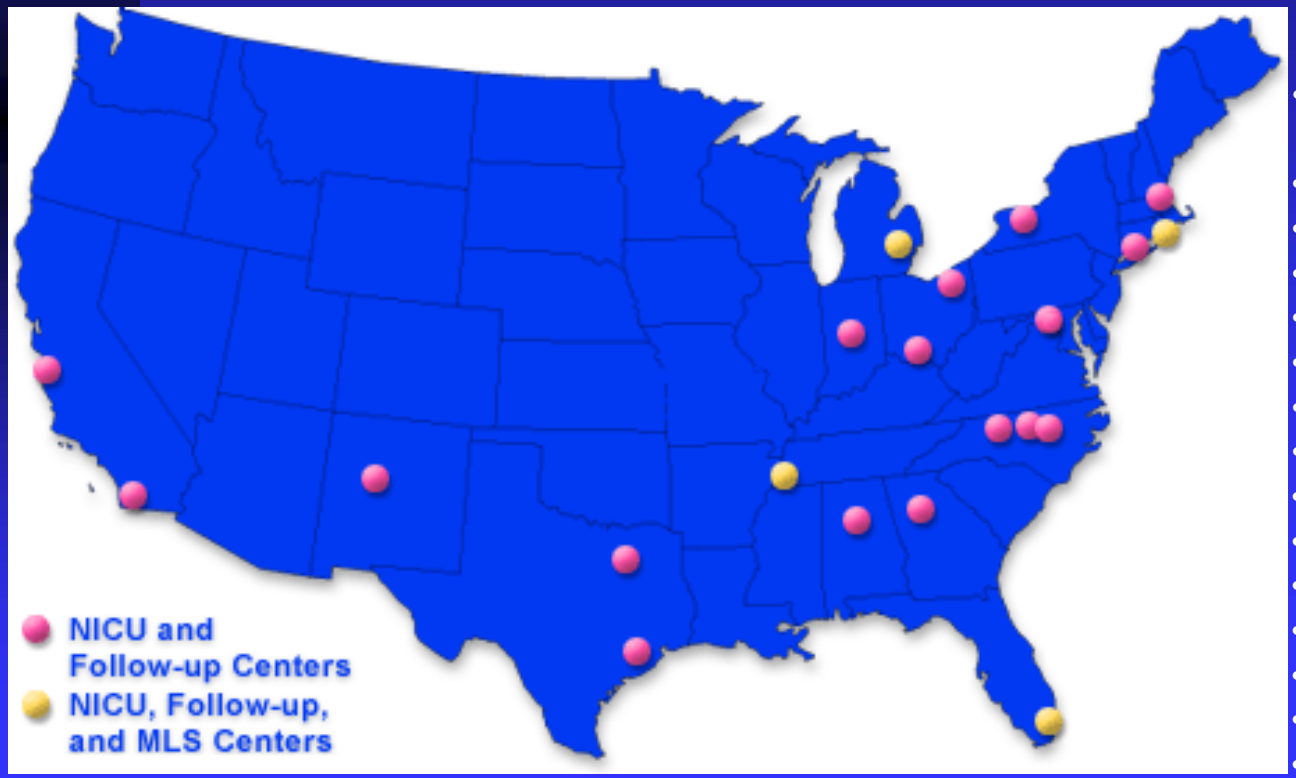
NICHD NRN History

- 16th award year (beginning 4th cycle)
  - 1986 - 1991: 7 centers
  - 1991 - 1996: 12 centers
  - 1996 - 2001: 14 centers
  - 2001- 2006: 16 centers
- 20th year – 13-16 centers
- Data center
- Funding: NICHD; other Institutes and offices (NIDA, NHLBI, NEI): specific studies

NICHD NETWORK CENTERS 2001-2006

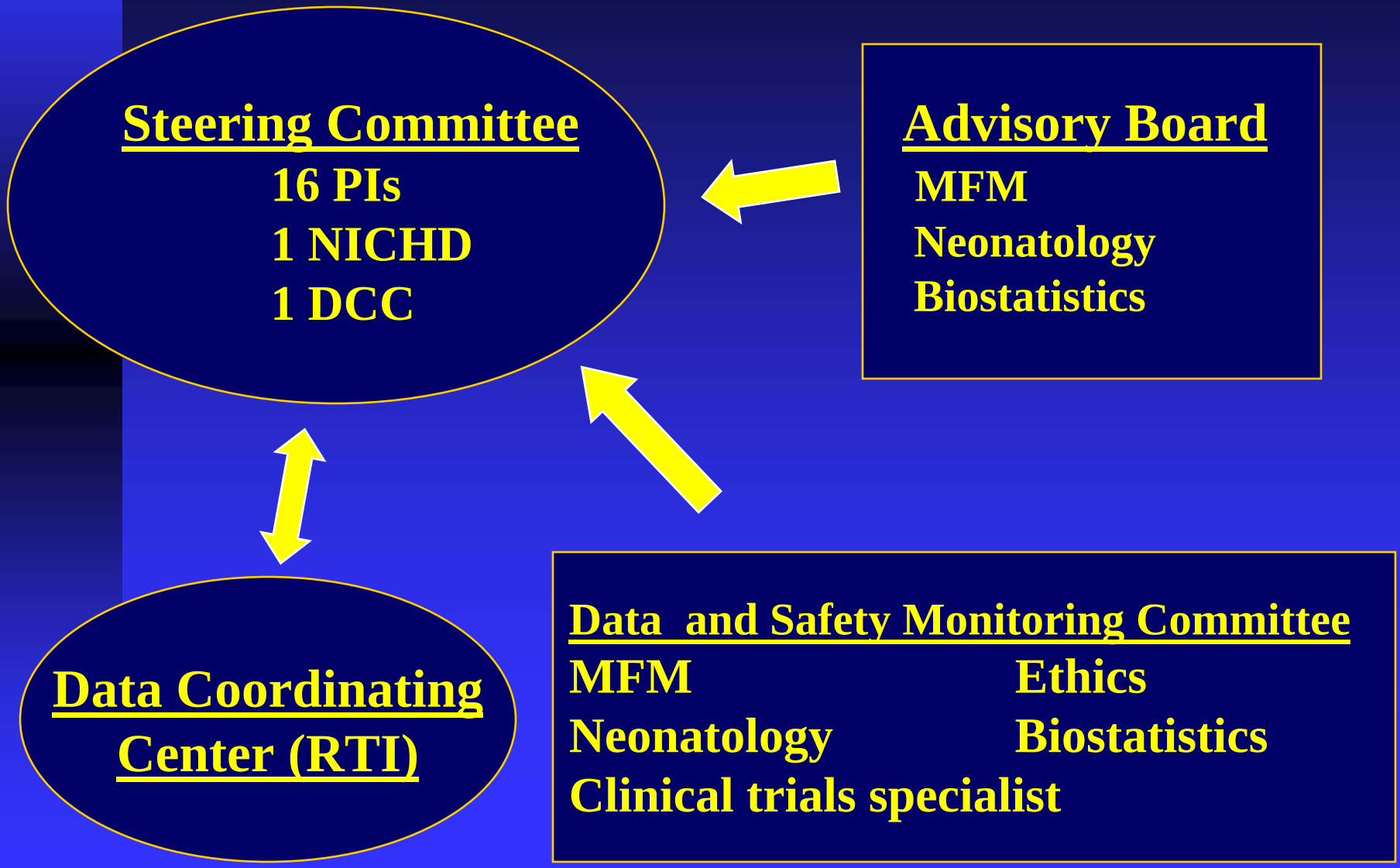
- Data center
- 16 Clinical Sites
- NICHD

- > 60,000 admissions/yr
- Recompetition every 5 years



- Case Western Reserve University
- Univ. Texas – Southwestern
- Univ. Texas – Houston
- Wayne State
- Univ. Miami
- Emory
- Univ. Cincinnati
- Indiana Univ.
- Yale
- Brown
- Stanford
- Univ. Alabama
- Univ. Rochester
- Wake Forest
- Duke
- Univ. Cal. San Diego

NRN Organization



NICHD NRN Mission

The Neonatal Research Network is designed to conduct studies to investigate the safety and efficacy of treatment and management strategies to care for newborn infants.

NICHD NRN Mission Aims

- Identify priority issues for research
- Evaluate interventions including efficacy, safety, and cost-effectiveness.
- Included: translational research, genetics, evaluation of new technologies in the promotion of infant health/prevention of disease

NRN Committees

- Protocol specific committees
  - Each ongoing study/trial has a subcommittee
- Standing committees
  - Publications
  - Protocol Review
  - Concurrent Research
  - Generic Data Base
  - Data Access
  - Liaison
  - Genomics

STEERING COMMITTEE

- Four SC meetings per year in DC metro area
- Meetings via teleconference as needed
- Composed of site PI's (Currently 16), DCC PI, and NICHD Program Scientist
- Works collaboratively

NRN ONGOING TRIALS

- Observational Studies
  - Generic Data base
  - Follow up
  - aEEG
  - PCV-7
  - Candida
- Interventional studies
  - SUPPORT
  - Phototherapy
  - Inositol

NRN: Personnel at each center

- Principal Investigator (PI)
- Alternate PI
- Follow Up PI
- Other investigators
- Research nurse coordinator
- Research nurses
- Data entry clerk

SPECIAL REQUIREMENTS: ACADEMIC PRODUCTIVITY

- Prior or ongoing clinical trials (multi-center)
- Key contribution areas
  - Research development/design
  - Patient recruitment
  - Patient retention and study completion
  - Data collection and analysis
  - Publication track record

SPECIAL REQUIREMENTS: Neonatology Staffing

- At least FOUR full time, neonatal-perinatal medicine board certified, academic physicians
- Complete description of staff qualifications (biosketch)
- Clinical, research, administrative, academic commitments
- Alternate PI
- If multiple sites – collaboration + publications

SPECIAL REQUIREMENTS: POPULATION FOR CLINICAL TRIALS

- At least 500 admissions per year
- No more than 30% outborn
- Population specifics (births, NICU admission, transports, average daily census, length of stay, ventilation, ECMO, surgical cases)
- If more than one center, separate into columns
- Demographics, OB parameters, payment status

SPECIAL REQUIREMENTS: MATERNAL FETAL MEDICINE UNIT

- MFM service – high risk pregnancy and delivery
- MFMU collaborator
- Maternal population (deliveries, C-sections, multiples, diabetes, hypertension)
- Consults performed by neonatal service
- MFMU application – describe interaction

SPECIAL REQUIREMENTS: CLINICAL CAPABILITIES

- Pediatric subspecialists
- Support staff- research coordinator, coverage for patient recruitment
- Pharmacy
- Respiratory therapy
- Current involvement in clinical trials

SPECIAL REQUIREMENTS: FOLLOW UP PROGRAM

- Established neonatal follow up program
- Follow up rate – at least 80%
- 18-22 month FU
- Number of FU visits
- Designated facility

SPECIAL REQUIREMENTS: FOLLOW UP PROGRAM

- Mechanisms for compliance
  - Maintaining family contact
  - Scheduling appointments
  - Actions for missed appointments
  - Home visits

SPECIAL REQUIREMENTS: FOLLOW UP PROGRAM

- Designated FU PI (biosketch)
- Components of FU visit
  - Bayley Scales of Development II
  - Neurologic exam
  - Hearing assessments
  - Vision assessments

Concept Proposal

- Hypothesis
- Specific Aims
- Background
- Methods
- Data Analysis

PERINATAL DATA SYSTEM

- Description of electronic data system
- Recent application using data system

RESEARCH STAFF

- Full time research coordinator
- Additional research staff
- Describe training, experience, qualifications and prior clinical trials experience

Intent to Participate

- Clearly expressed intent to participate
- NRN projects given priority
- Expected to participate in all trials unless describe conflicts in application

Departmental & Institutional Commitment

- Letters of support
- Evidence of past support
- Support: personnel management, space allocation, procurement, equipment, etc

SPECIAL REQUIREMENTS: STRENGTHS OF PI OR INSTITUTION

- Special or Unique strengths
- State-of-the-art capabilities
- GCRC – document support
- Administrative strengths or experience
  - IRB
  - DSMC
  - Advisory Board for clinical research
  - Clinical research committees
  - Other strengths

BASE BUDGET – COOPERATIVE AGREEMENT

- Principal Investigator – 10% effort
- Alternate PI, PI, or FU PI – up to additional 10% effort
- Research Coordinator 100% effort
- Data Entry Clerk – 50% effort
- Supplies/equipment – up to $5,000
- Travel – 10 trips per year to DC metro area (4 for PI, at least 2 for coordinator, 4 – other)
- Other costs – up to $3,000
- Base budget direct costs – limited to $180,000

CAPITATION

- Paid on per patient basis
- Study dependent
- Paid for enrollment (NOT screening)

Receipt, review and start dates

- Letters of Intent Receipt Date(s): June 22, 2005
- Application Receipt Date(s): July 22, 2005
- Peer Review Date(s): Oct/Nov 2005
- Council Review Date(s): January 2006
- Earliest Anticipated Start Date: April 1, 2006

Letter of Intent

- Descriptive title of proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

Not required, not binding

Sending application to NIH

- PHS 398 research grant application
- RFA label
- Signed, typewritten original + 3 signed copies

  Center for Scientific Review
  National Institutes of Health
  6701 Rockledge Drive, Room 1040, MSC 7710
  Bethesda, MD 20892-7710

  Bethesda, MD 20817 (express/courier service)
- Two copies

  Robert Stretch, Ph.D.
  Director, Division of Scientific Review
  National Institute of Child Health and Human Development
  6100 Executive Boulevard, Room 5B01, MSC 7510
  Bethesda, MD 20892-7510
  Rockville, MD 20852 (express/courier service)

Review and Selection Process

- Reviewed for completeness and responsiveness
- Evaluated for scientific and technical merit by peer review group
- Top half of applications discussed and given a priority score
- All receive written critique
- Second level of review by NACHHD Council

Review Criteria: Qualifications and commitment of key personnel

- Scientific administrative, clinical and academic qualifications of PI and research team; qualifications of applicant institution
- Knowledge and experience in areas relevant to collaborative clinical research
- Commitment of staff time
- Experience and qualifications for data quality and management activities

Review Criteria:
Protocols and Procedures

- Quality of unit's participation in RCTs
- Willingness to work and cooperate with other NRN sites

Facilities and Management

- Adequacy of administrative, clinical, data management facilities
- Institutional assurance
- Optional administrative strengths

Review Criteria: Concept proposal

- Quality of proposed hypotheses, specific aim(s), background, methods, data analysis

Review Criteria: Other

- Inclusion of minorities
- Plans for recruitment and retention
- Reasonableness of proposed budget
- Adequacy of protection for humans

NRN ONGOING TRIALS

- Observational Studies
  - Generic Data Base
  - Follow Up
  - aEEG
  - PCV-7
  - Candida
- Interventional studies
  - SUPPORT
  - Phototherapy
  - Inositol

GENERIC DATA BASE

- To provide baseline and outcome data for infants 401-1500 grams BW
- Prospective cohort study
- Admitted to NICU by day 14
- Baseline evaluation
- Outcome evaluation – pulmonary, cardiac, neurological, infection, GI, Hearing, ophthalmology, syndromes, growth, LOS, cause of death
- 36 week physiologic definition of BPD

NRN Follow Up

- Follow up at 18-22 months corrected age of infants with birth weights 401-1000 grams
- Follow up rate > 80%
- Development assessed by Bayley exams
- Neurological exam
- FU PI's meet at PAS and at one steering committee meeting per year

aEEG STUDY

- To determine if aEEG is a better predictor of clinical outcome following HIE than clinical exam at < 6 hours of age
- Currently recruiting

PCV-7 Observational study

- S. Pneumoniae is a significant pathogen for which the pneumococcal vaccines is now available
- Little information in < 1500 gram infants
- To determine serologic titer against S. pneumoniae in VLBW infants undergoing vaccination

PCV-7 Observational study

- Recruitment at the time of first vaccination
- 8 sites
- N = 200 with appropriate vaccine receipt and titer; aiming for 400, stratification by 100 gram birth weight increments from 401-1500 grams
- Began July 2004; 90 enrolled; 28 have completed the protocol

Candida Observation Study

- Objective – to determine if new diagnostic tools (Beta glucan assay, PCR, D/L arabinotol ratios) are useful for early detection of candida and to develop a risk stratification model for predicting candida
- Began March 2004
- Enrollment criteria < 1000 grams birth weight with presentation for a sepsis workup
- N = 1750 infants with 100 positive for candida
- Currently, 418 enrolled with 23 positive for candida

PHOTOTHERAPY STUDY

- To determine if aggressive versus conservative phototherapy results in difference in death or neurodevelopmental impairment
- Randomized, stratified, multicenter study
- 501-1000 grams
- Phototherapy intervention (bilirubin of 5 versus 8)

PHOTOTHERAPY STUDY

- N = 1976, enrolled 1977 as of April 4, 2005
- Enrollment completed
- Null hypothesis – no difference in treatment
- Follow up in progress
- Anticipate results in mid-2007

SUPPORT Trial

- To determine the effect of delivery room trial of positive end expiratory pressure versus intubation and surfactant and randomized pulse oximetry levels
- Randomized trial – 16 sites
- Gestational age 24 - 27 6/7 weeks
- Enrollment began 2/28/05
- NHLBI Co-Funding

INOSITOL TRIAL

- To determine if supplemental 6-myo-inositol will decrease the incidence of severe ROP and death
- Secondary outcomes – BPD, long term FU
- Ross Abbot to provide drug
- NEI Co-funding

INOSITOL TRIAL

- Several phases
  - Pilot to test random levels in infants
    - Being initiated at 7 sites
  - Single dose pK study
  - Multiple dose pK study
  - Large scale clinical trial

Questions?

- Program: Rose Higgins MD
  - 301 4357909
  - higginsr@mail.nih.gov
- Grants Management Branch: Chris Robey
  - 301 435 6996
  - robeyj@mail.nih.gov
- Review: Bob Stretch PhD
  - 301 496 1485
  - Stretchr@mail.nih.gov

http://grants.nih.gov/grants/guide/rfa-files/index.html