NICHD Maternal Fetal Medicine Units Network: RFA HD-04-023 How do I apply?

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NICHD MFMU Origins

- Obstetrical management, especially for high-risk patient, has often adopted practices without objective evaluation
- In an attempt to respond to the need for well-designed clinical trials in maternal fetal medicine, the NICHD established the MFMU Network in 1986

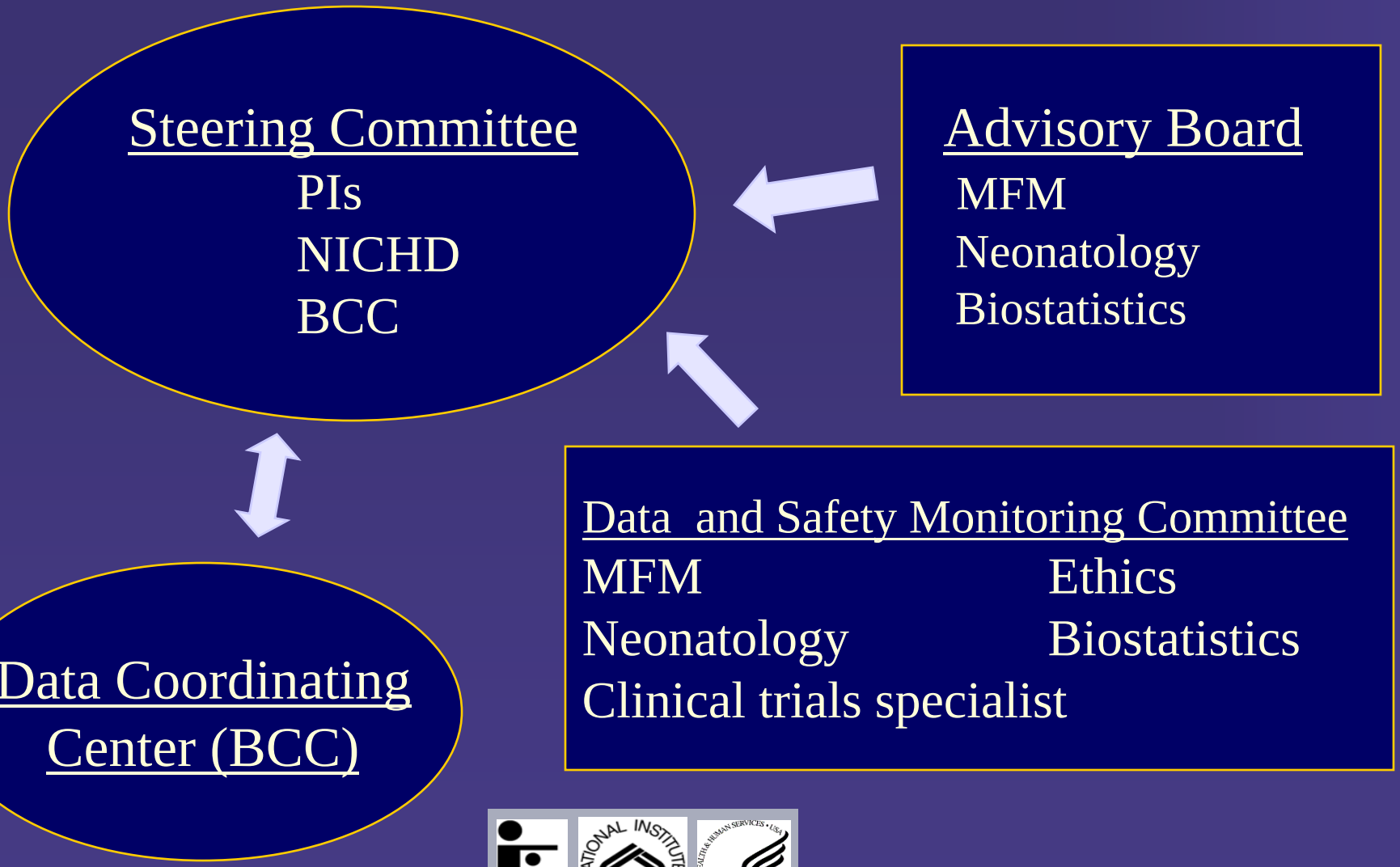
Background MFMU

- 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 MFMU History

- Fourth funding cycle:
  - 1986 - 1991: 7 centers
  - 1991 - 1996: 12 centers
  - 1996 - 2001: 13 centers
  - 2001 – 2006: 14 centers
- Collaborative participation with centers, data center and NICHD on common protocols
- Funding: NICHD; other institutes and offices (ORWH, NHLBI, NINDS)
- Inter-agency collaborations: FDA, CDC

Network organization



NICHD MFMU Vision Statement

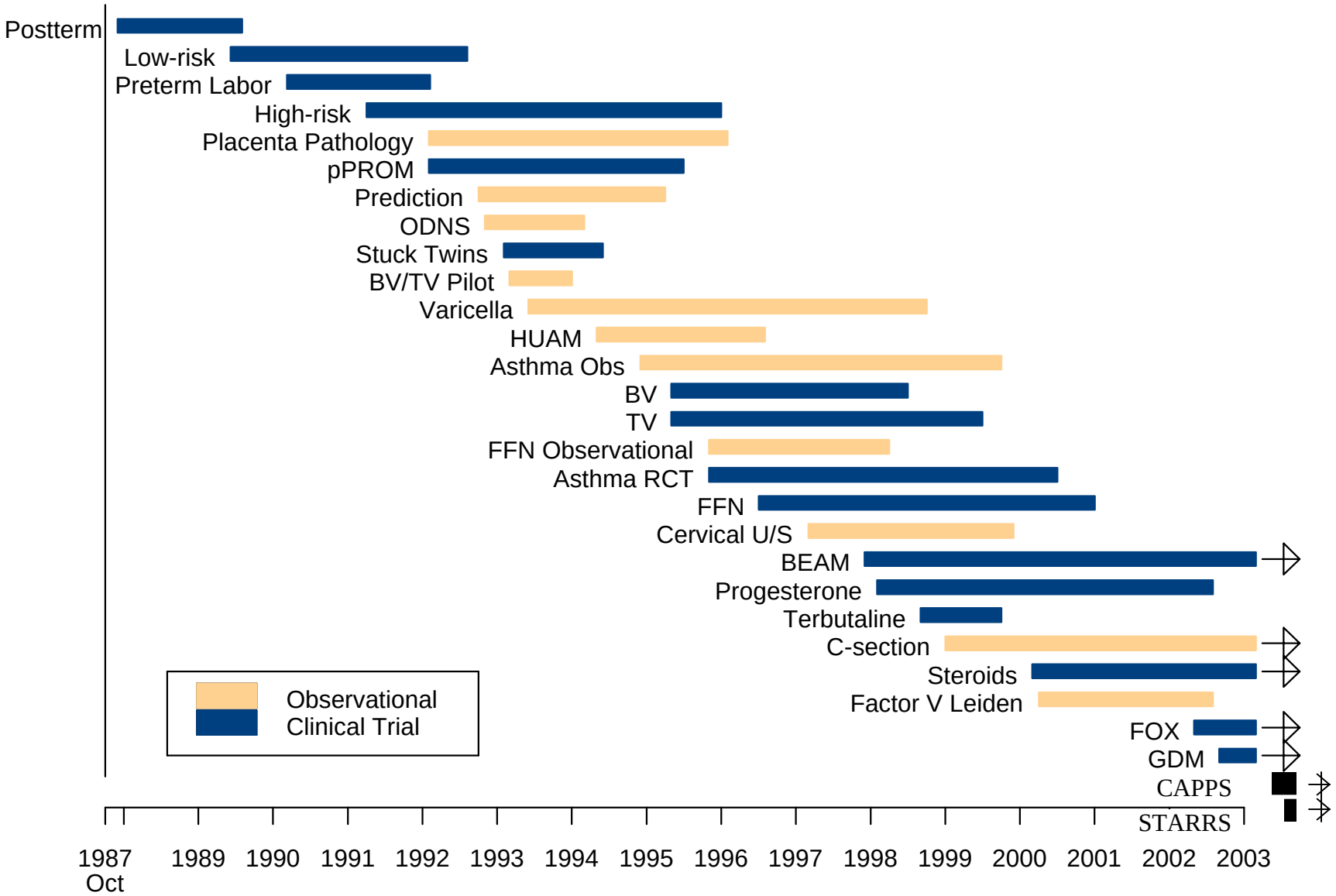
"The MFMU Network is designed to conduct clinical studies to improve maternal, fetal and neonatal health emphasizing randomized-controlled trials"

Specific aims:

- Reduce the rates of
  - Preterm birth
  - Maternal complications of pregnancy
  - Fetal growth abnormalities
  - Neurologic sequelae of the newborn
- Evaluate maternal and fetal interventions including efficacy, safety, and cost-effectiveness.
- Included: translational research, genetics, evaluation of new technologies in the promotion of maternal-child health/prevention of disease

NICHD MFMU 2003

NICHD MFMU Network: Studies & Trials



HD-04-023: MFMU RFA

- The NICHD invites applications from investigators willing to participate with the NICHD under a cooperative agreement in an ongoing multi-center clinical program designed to investigate problems in clinical obstetrics, particularly those related to prevention of low birth weight, prematurity, and medical problems of pregnancy.
- The NICHD intends to commit approximately $10.3 million in total costs in FY 2006 to fund 13 to 16 new and/or competing continuation grants.
- An applicant may request a project period of up to five years and a base budget for direct costs up to $180,000 per year.

HD-04-023: MFMU RFA

- This funding opportunity will use the NIH Cooperative Clinical Research (U10) award mechanism.
- And investigator may submit an application if his/her institution has any of the following characteristics: For-profit or non-profit organizations, public or private institutions, such as universities, colleges, hospitals, and laboratories, Units of State and local governments, eligible agencies of the Federal government.

HD-04-023: MFMU RFA

- Eligible principal investigators include any individual with the skills, knowledge, and resources necessary to carry out the proposed research. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.
- Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 9/2004).
- http://grants.nih.gov/grants/guide/rfa-files/index.html

Research Objectives

- Cooperative agreement: Ongoing multicenter clinical program designed to investigate problems in clinical obstetrics, particularly those related to prevention of LBW, prematurity, and medical problems of pregnancy
- Objective: to facilitate resolution by establishing a network of academic centers that, by rigorous patient evaluation using common protocols, can study the required numbers of patients and can provide answers more rapidly than individual centers acting alone.

Eligible Institutions

- For-profit organizations
- Non-profit organizations
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State government
- Units of local government
- Eligible agencies of the Federal government
- Domestic Institutions only

Eligible Institutions

- Academically-oriented divisions of MFM
- $\geq$ 2700 births / year
- $\geq$ 30% documented high risk pregnancies
- Majority receiving PNC at the institution

MFMU: Personnel at each center

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

Special Eligibility Criteria

- Academic productivity
- Maternal fetal staffing
- Population available for clinical trials
- NICU
- Perinatal data system
- Research Staff
- Intent to participate
- Department and institutional commitment
- Acceptance of the budgetary mechanism

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

Maternal-Fetal Staffing

- At least 3 full time, Ob-Gyn and MFM board certified, practicing MFM and academic physicians
- Complete description of staff qualifications including clinical research, administrative, academic commitments
- Alternate PI
- If multiple sites – collaboration + publications

Population For Clinical Trials

- ≥ 2700 births/year
- ≥30% high risk
- Majority receive prenatal care at institution
- Population specifics (births, Cesareans, obstetrical admissions, outpatient visits, PNC by trimester, obstetric complications, neonatal outcomes)
  - If more than one center, separate into columns
- Demographics, OB parameters, payment status

Neonatal Intensive Care Unit

- NICU
- Neonatal collaborator
- Describe NICU population/demographics
- Letter of collaboration
- Neonatal follow-up program
- NRN application (HD-04-010)– describe interaction

Perinatal Data System

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

Research Staff

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

Intent to Participate

- Clearly expressed intent to participate
- MFMU 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

Other Submission Requirements

- Clinical Capabilities
- Concept Proposal
- Special Strengths of PI / Institution
- Budget

Clinical capabilities

- Description of clinical attributes including ambulatory facilities, pharmacy, policies and procedures for conducting clinical research
- Capabilities for patient recruitment on nights and weekends

Concept Proposal

- Indicates ability to participate in development, design of protocols in MFMU
- Multicenter design
- Use of perinatal data system
- 2-3 pages maximum
- Hypothesis, specific aim(s), background, methods, data analysis

Strengths of PI or Institution

- Special or Unique strengths
- State-of-the-art capabilities, modern imaging techniques, proteomics, genomics, microanalysis, etc
- 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
- Research Coordinator - 100% effort
- Research Nurse – 100% effort
- Data Entry Clerk – 50% effort
- Supplies/equipment – up to $5,000
- Travel – 10 trips per year to DC metro area
- Other costs – up to $3,000
- Base budget direct costs – limited to $180,000

Capitation

- Paid on per patient basis based on projected enrollment
- Study dependent
- Capitation budgets rectified yearly

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

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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 MFMU sites

Facilities and Management

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

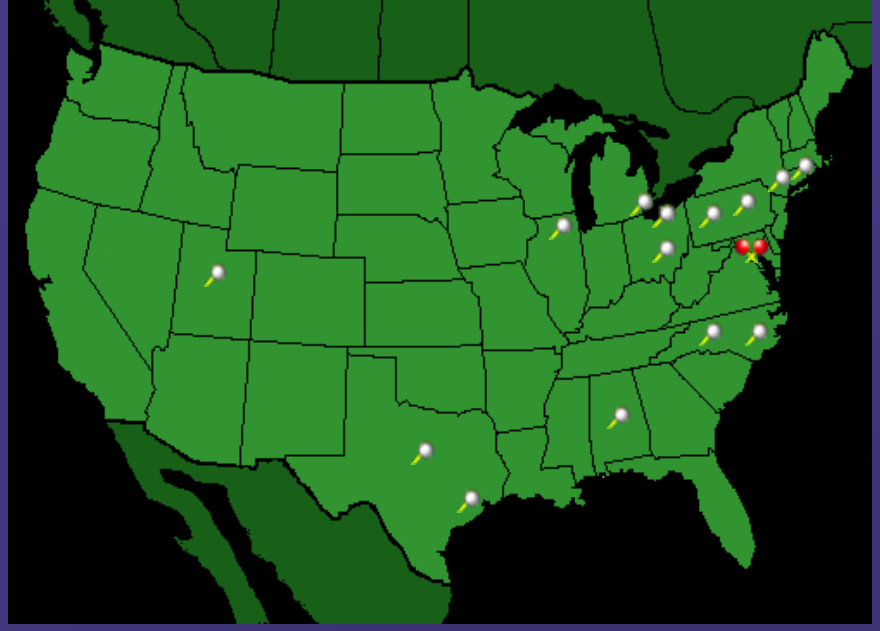
Review Criteria: Concept proposal

- 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

NICHD MFMU NETWORK



NICHD's Maternal-Fetal Medicine Units Network

Ongoing MFMU Trials

FOX

Fetal Pulse **Ox**imetry trial

- **Aim:** To determine if fetal pulse oximetry affects overall cesarean delivery rate; CS for FD
- **Design:** RCT
- **Eligibility criteria:** Singleton, >36 wks
- **Intervention:** 2 arm trial
- **Primary outcome:** Cesarean delivery
- **Sample size**: 10,000
- **Status**: 5087 patients enrolled (/5/05)

CAPPS:

Combined **A**ntioxidant, **P**reeclampsia **P**rediction **S**tudy for the prediction and prevention of preeclampsia

- **Aim:** To determine if antioxidants (Vits C and E) can prevent preeclampsia in low risk women and identify markers to predict preeclampsia
- **Design:** RCT
- **Eligibility criteria:** Singleton, 9-13 wks
- **Intervention:** Vit C and E vs placebo
- **Tests:** plt volume, cytokines, dopplers, clinical findings genetic, oxidative stress, renal markers
- **Primary outcome:** composite
- **Sample size**: 10,000
- **Status**: 2080 patients enrolled (1/5/05)

*co-funded by NHLBI

Mild gestational diabetes trial

- **Aim:** To test whether identification and dietary treatment of mild GDM reduces composite outcome
- **Design:** RCT with additional observational cohorts
- **Eligibility criteria:** 24-29 wks gestation, normal FBS, abnormal 3h-GTT
- **Intervention:** treatment (counseling, dietary management) vs standard non-GDM care
- **Primary outcome:** Fetal composite
- **Sample size**: 700 (trial), 1050 (cohorts)
- **Status**: 649 patients enrolled (1/5/05)

STTARS (Seventeen alpha-hydroxyprogesterone caproate in Twins and Triplets: A Randomized Study)

- Double-masked placebo-controlled trial to determine whether 17 alpha hydroxyprogesterone prevents preterm birth in multifetal pregnancies.
- Intervention: 17-OHP (1 ml IM with 250mg) or placebo weekly
- Primary outcome: Preterm delivery < 35 wks
- Sample size: 600 twin and 120 triplet
- Status: 195 twins and 37 triplets enrolled (1/5/05)

A Randomized Clinical Trial of Omega-3 Supplementation to Prevent Preterm Birth

- **Design**: Double-masked placebo-controlled trial to determine whether Omega-3 in conjunction with 17-P reduces the risk of PTD in women at high risk for sPTD
- **Intervention:** weekly17-OHP (1 ml IM with 250mg) with daily 2000 mg Omega-3 or placebo (po)
- **Primary outcome**: Preterm delivery < 37 wks
- **Sample size**: 800
- **Status**: 1 recruited (1/5/05)

BEAM

Beneficial **E**ffects of **A**ntenatal **M**agnesium

- **Aim:** To determine if antenatal $MgSo_4$ can reduce the risk of cerebral palsy in offspring
- **Design:** double-masked, placebo-controlled trial
- **Eligibility criteria:** 24 - 31 wks gestation with PROM, PTL or planned delivery
- **Intervention:** $MgSo_4$ or placebo
- **Primary outcome:** composite outcome of death <1 yr or cerebral palsy at 24 months
- **Sample size:** 2220, 2241 enrolled!

**co-funded by NINDS*

Progesterone Follow-up study

- **Aim**: To determine whether there is a difference in achievement of developmental milestones and physical health between children exposed to progesterone and those exposed
- **Intervention:** Observational cohort study
- **Primary outcome**: Ages and Stages Questionnaire score; Differences in developmental milestones
- **Sample size**: 348 children
- **Status**: 17 patients seen (1/5/05)

Questions?

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