Request for Applications
Data Coordinating Center
of the
Cardiac Neurodevelopmental Outcome Collaborative

I. Introduction: Overview and Background

The purpose of this request for applications (RFA) is to invite applications to develop and implement a Data Coordinating Center (DCC) for the Cardiac Neurodevelopmental Outcome Collaborative (CNOC). CNOC was established as a collaborative multicenter, multinational, and multidisciplinary group of healthcare professionals who are committed to working together and partnering with families to optimize neurodevelopmental outcomes for individuals with pediatric and congenital heart disease through clinical, quality, and research initiatives, intending to maximize quality of life across the lifespan. The overall goals of CNOC include characterization of the pattern and variation of developmental functioning of individuals with pediatric heart disease from infancy through adolescence through the establishment of a central database.

The CNOC DCC will have responsibility for setting up a robust and easily accessible infrastructure to house the data, managethe database, and ensure the quality of the data. The DCC will begin with a focused set of goals, characterizing the development of infants, toddlers, and preschoolers who have undergone neonatal cardiac surgeryusing a limited list of demographic, neurodevelopmental, medical history, and surgical variables. As initial aims are achieved, additional ages of follow-up, neurodevelopmental testing outcomes, quality of life outcomes and medical history data are expected to be added to the database efforts.

II. Roles and Responsibilities

The DCC will fulfill a variety of roles and responsibilities:

- In consultation with CNOC committees, determination of eligibility criteria for patientsto be included in the database as well as demographic, medical history, and surgical variables and neurodevelopmental outcomes for inclusion.
- Development of data forms and a data dictionary.
- Coordination of institutional review board submissions and data transfer/use agreements between the DCC institution and individual sites.
- Development of a secure and robust study database for individual sites that choose to enter their own data, as well as development of standard mechanisms for other sites to transfer data from their internal computerized systems to the DCC. Sites will be expected to follow an agreed upon format and agreed upon time schedule for such data transfer.
- Development of operating procedures for communications between sites and the DCC, including data transfer requirements and timelines, site-specific reports and data sharing, and coordination of individual site personnel working on data submission.
- Development and implementation of mechanisms for assigning subject identification numbers and plans for connecting study subject data longitudinally.

- Development and implementation of data cleaning and data auditing procedures.
- Development and generation of data reports for CNOC committees and individual sites, and for future grant applications involving CNOC and the DCC. Reports would include information about data quality and completeness as well as data outcomes.
- Allowance for the addition of new data-contributing CNOC sites in subsequent years.

The initial scope of the CNOC database is to characterize the pattern of developmental delays in infants, toddlers, and preschoolers with heart disease who undergo neonatal surgery, as well as additional demographic, medical history, and surgical variables for these patients. Specific neurodevelopmental outcomes and study aims and hypotheses for each cohort (infants, toddlers, and preschoolers) are detailed in the appendix (see attached). In addition, a quality improvement (QI) project (to be determined) targeting the school age cohort will be conducted with a limited set of variables. After successful implementation of these efforts is achieved across individual sites, additional ages of follow-up, neurodevelopmental testing outcomes, quality of life outcomes and medical history data are expected to be added to the database efforts. Also, additional data summaries, including benchmarking and descriptive statistics looking at associations between study variables will be added overtime. It is expected that any biostatistical analysis that is required for publications or other research efforts will be funded separately and may be carried out by organizing centers or the DCC depending on the scope and timing of the project.

III. Award Information

Total funds available are $75,000/year for a period of five years, beginning October 2, 2017. Indirect cost should not exceed 10%. Due date for applications is July 31, 2017.

IV. Eligibility Information

Eligibility is limited to CNOC institutional members.

V. Application and Submission Information

The Procedural Plan is the most important component of a DCC application, and should be limited to 10 pages. This plan would includean overall description of aims and plans for data management, data quality assurance, and data summarization, including plans to address the roles and responsibilities of the DCC as mentioned in Section II.

Appendix materials should include the following components:

- Personnel: A management plan describing staffing and roles and responsibilities of staff members should be provided. Prior experience in working in multicenter research studies where the Principal Investigator held significant responsibility for data management and/or statistical analysis should be noted. NIH biosketches of key personnel should be included as additional information.

- Budget: A detailed budget including baseline costs to setup and organize the database as well as ongoing costs to maintain the database should be provided. Salary support for the Principal Investigator and research team members for effort on this project should be included. The total budget may not exceed $75,000 per year including indirect costs.

- Institutional Support/Environment: A description of the environment and available institutional support for the DCC should be provided.

Complete applications should be submitted to Jennifer Butcher, Ph.D. (CNOC Secretary), at jennbutc@med.umich.edu by July 31, 2017.

VI. Application Review Process

Applications will initially be reviewed by the Database Committee with final decisions regarding the choice of the DCC to be made by the CNOC Steering Committee. Selection will be completed by August 31st, 2017, and the new DCC will be announced on September 1, 2017.

Appendix: Specific Aims

Specific Aim 1: **Describe what patient and center level variables are associated with returning for recommended ND follow-up in infancy and the variation in service provided.**

Hypothesis: Socioeconomic status will have a bigger impact on both rate of ND follow-up and services received than individual clinical and center-level variables.

Primary Outcome: Percent of recommended individuals evaluated in cardiac ND follow-up clinics in infancy.

Inclusion: All individuals at a participating CNOC center undergoing cardiac surgery before 30 days of age and eligible for 6-9 month follow-up between October 2017 and September 2018.

Outcome Measures: Data fields from the IWG Neurodevelopment Subsection Worksheet

Co-variates: Diagnosis/intervention specific; complication specific; center specific; ND program specific

Approach: Participating centers performing infant evaluations will submit ND follow-up data from the IWG ND worksheet for all individuals undergoing evaluation at 6-9 months of age. In addition, contributing centers will enter clinical and demographic data for all individuals undergoing cardiac surgery in the first month of life that are eligible for infant ND follow-up, regardless of participation in follow-up clinic. The database will be set up so that centers already contributing to PC4 or STS can submit (or allow review) of that demographic and clinical data. Centers that do not submit to either registry will be required to independently enter a very limited matching dataset. Center-level practice variation will be determined by aggregating clinical/surgical data (age at surgery, LOS, intubation time), and results from the site survey.

Specific Aim 2: **Describe what patient and center level variables are associated with returning for recommended ND follow-up at 18-24 months and their association with ND outcome.**

Hypothesis: Cardiac diagnosis, surgical risk category and hospital LOS will have the biggest impact on ND outcomes independent of the factors associated with rate of ND follow-up.

Primary Outcome: Deficiencies identified from indices of Bayley-III (cognitive, language, motor) and the ABAS-3 (conceptual, practical, social).

Inclusion: All individuals at a participating CNOC center undergoing cardiac surgery before 30 days of age and eligible for 18-24 month ND follow-up between October 2017 and September 2018.

Outcome Measures: Bayley-III; ABAS-3

Co-variates: Diagnosis/intervention specific; complication specific; center specific; ND program specific

Approach: Participating centers performing toddler evaluations will submit ND results for all individuals undergoing recommended testing at 18-24 months of age. In addition, contributing centers will enter clinical and demographic data for all individuals undergoing cardiac surgery in the first month of life that are eligible for toddler ND testing, regardless of follow-up. The database will be set up so that centers already contributing to PC4 or STS can submit (or allow review) of that demographic and clinical data. Centers that do not submit to either registry will be required to independently enter a very limited matching dataset. Center-level practice variation will be determined by aggregating clinical/surgical data (age at surgery, LOS, intubation time), and results from the site survey.

Specific Aim 3:Define the school readiness profile of children who are evaluated at cardiac ND follow-up programs and its association with clinical and regional variables.

Hypothesis: A comprehensive profile from a core battery of tests will identify more children with CHD at risk for difficulty in school than a single school readiness screener.

Primary Outcome: Deficiencies identified in four domains (cognitive skills, functional/adaptive skills, executive function and social/emotional function) from a core battery compared to the deficiency estimated from a single screener (Bracken School Readiness Assessment)

Inclusion: All individuals undergoing ND evaluation at a participating CNOC center between 4-5 years of age from October 2017 and September 2018.

Outcome Measures: WPPSI-IV, BRIEF-2, BASC-3, ABAS-3, CELFPreschool 2, BSRA-3

Co-variates: Cardiac diagnosis, surgical procedure, age at surgery, neonatal length of stay, chromosomal abnormality, major non-cardiac abnormality, race, ethnicity, maternal education, patient zip code, surgical center, ND evaluation center

Approach: Participating centers performing pre-school evaluations will submit all ND testing and survey results from the core battery. The minimal clinical variable dataset for children undergoing ND evaluation will be required.