

# **REQUEST FOR LETTERS OF INTEREST ON FORMATIVE RESEARCH FOR THE NATIONAL CHILDREN'S STUDY JUNE 2010**

## **INTRODUCTION**

The National Children's Study (NCS) has reframed the Vanguard Study scope of activity to focus on feasibility, acceptability, and cost of the elements that will form the NCS Main Study. This is the third in a planned series of announcements for letters of interest to augment Vanguard Study activities with efforts that will accelerate development and deployment of the Main Study. This call for Letters of Interest includes opportunities to develop and enhance real-time assessments that can be shared with participants and communities; to analyze and enhance our study logistics by understanding our efforts to date; to enhance our study infrastructure with new tools and methods, and to augment our toolsets for biospecimen collection and processing, environmental sample collection and processing, physical measures, and questionnaires, to develop enhance study visit assessments; to develop methods to analyze and augment the utility of data collected through the Study; and to test promising methods in pilot studies or formative research with Study participants for possible inclusion in the Main Study. Any new method should demonstrate performance advantages over existing procedures.

Principal Investigators from the Prime Contractor of all Vanguard Centers (VCs) and Study Centers (SCs) currently under contract with the NCS are eligible to respond to this call for Letters of Interest. As part of the submitted Letters of Interest, the Program Office encourages collaboration among SCs, VCs, subcontractors, and other eligible entities. Principal Investigators are encouraged to share this document with department chairs, institutional officials, and for the 20 NCS Study Centers that are co-located with Clinical and Translational Science Award (CTSA) Consortium members, with the CTSA Principal Investigators, to identify potential opportunities in the shortest amount of time and ensure the highest quality and most productive research.

All Letters of Interest must be submitted by e-mail to the [NCS@mail.nih.gov](mailto:NCS@mail.nih.gov) mailbox by each interested Prime Contractor no later than 8:00 p.m. Eastern Standard Time on Friday, July 2, 2010. Letters will be evaluated by the NCS Program Office on the scientific, logistic, and operational quality of the proposal with consideration for factors such as geography and demographics. Study Centers will be contacted by a target date of Monday, July 19, 2010 with an update and/or requests for further information. Using the submitted Letters of Interest as an informational source, the NCS Program Office will work with the NICHD Contracts Management Branch to assign tasks under the current statement of work that will further the goals of the NCS Vanguard Study. Work on assigned tasks can be expected to begin as early as August 2010 and deliverables are expected throughout federal fiscal years 2010 and 2011 (FY2010-FY2011) with a limitation that the work cannot proceed beyond the duration of the existing contract.

Time and resources for preparation of the Letter of Interest are not billable to the National Children's Study as this is a voluntary effort and not a required task issued under any existing contract. Any questions should be addressed in writing to [NCS@mail.nih.gov](mailto:NCS@mail.nih.gov) .

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## **REAL-TIME ANALYSIS OF STUDY SAMPLES, SPECIMENS, AND MEASUREMENTS**

### **RT-01 Open Call for Real-Time Analytics in the National Children's Study**

The National Children's Study Program Office is interested in determining the feasibility, acceptability and costs of real time analysis for research purposes of analytes and other evaluations from specimens and samples collected during the implementation of the National Children's Study. Potential advantages of real time analysis are a regular data flow, ongoing quality assessment of specimen and sample collection, and opportunity to refine and improve processes.

Formative research projects would explore assays and evaluations for technical reliability, for process improvement, and for capacity building to support a scalable infrastructure. Portions of the funds may be used for capital equipment acquisition to support the research projects. Examples of equipment may include Sequential Multiplex Analyzers to be used exclusively for research purposes, chromatographic and spectroscopic equipment for research analytes, robotic specimen handling tools, nucleic acid processing, amplification, sequencing and analysis tools, fluorescent cell sorters, analytic informatics systems, and imaging tools.

Analysis can be of cells, subcellular components, nucleic acid, proteins, organic and inorganic molecules, small molecules such as hormones, pharmaceuticals, neurotransmitters and other molecules of biological or environmental interest. Outcomes can include concentrations, kinetics, sequences, structural analysis, and other dynamic analyses.

Projects should contemplate the potential use of the analysis for biospecimens and environmental samples that may be collected at outpatient clinics, hospital visits, home visits or environmental sampling including images and sounds during the National Children's Study. Biospecimen sources can include existing stored samples in the NCS repository, samples to be collected by the original seven NCS Vanguard Centers and eventually samples collected by the 30 locations involved in the NCS alternate recruitment substudy. Environmental samples can include any of the sources noted for biospecimens plus any additional sources that may be informative. For the use of additional or alternate specimen or sample sources, please inquire.

Establishment of facilities that can be used collaboratively and leveraged is of particular interest. The goal is to establish and test the concept of a dedicated analytic capacity for research as an alternative to outsourcing or using existing institutional clinical care facilities. Resources such as state or commercial laboratories may be engaged as consultants, but the goal is to establish a dedicated research infrastructure.

Project descriptions should include the types of analysis, planned engagement of technical and expert personnel, potential equipment available and possible acquisitions, potential partners and subcontractors and an estimated time frame for preliminary data delivery.

## **RT-02 Quality Assessment of NCS Samples for Genetic Analyses**

**Goals:** The NCS requests proposals for the empirical evaluation of the quality of NCS collected sample materials for genetic and epigenetic analyses. The NCS is seeking to determine the suitability of its current human biological sample materials and associated collection, processing, and storage procedures for the generation of high quality genetic and epigenetic analyses.

Rigorous operational quality assessment of nucleic acids and proteins in NCS samples is needed to ensure the integrity and viability of these desired products for genetic and epigenetic study purposes by the research community. The timeframe for research utilization of the nucleic acids and proteins is expected to range from near-term (months) to far future (years). The products will be used across the entire range of current and anticipated protocols, from single candidate gene and protein approaches to comprehensive high-throughput genomic/epigenomic/proteomic array platforms.

NCS genetic quality assessment needs include qualitative and quantitative determination of DNA, RNA, and protein extraction through spectrophotometry and electrophoretic techniques. Use of efficient nucleic acid and protein bioanalyzer instrumentation is desirable. Extraction of nucleic acids and protein from a variety of sample types stored under diverse conditions, including frozen or formalin-fixed and paraffin-embedded, is needed. Current sample types include, but are not limited to, whole blood, PBMCs, plasma, serum, saliva, breast milk, placental tissue, umbilical cord tissue, urine, meconium, and hair. Quality assessment may extend to analysis of storage condition effects on nucleic acid and protein stability including temperature, stabilizing reagents, and storage time.

Feasibility testing for the functional quality of the isolated nucleic acids and proteins is additionally sought. Analysis utilizing array technology is of interest, including expression, microRNA, single-nucleotide polymorphism, copy number variation, DNA methylation and chromatin immunoprecipitation 2X. Investigation for epigenetic modifications can also be based on bisulfite sequencing and candidate protein-DNA CHIP methods.

**Requirements:** Proposals should consider feasibility and cost in their proposal. Critical to NCS genetic quality assessment is demonstrated expertise in genetics, epigenetics, microarrays, molecular biology and/or biochemistry. Evaluations should compare the information obtained with that expected under optimal conditions and determine the acceptability of sample material for potential future use. Proposals should meet applicable human subjects research protection and laboratory regulatory requirements. A combination proposal addressing the real time analysis noted in the prior proposal RT-01 and the current technical proposal can be considered.

### **RT-03 Emerging Contaminants in Food and Drinking Water**

**Background:** Due to the incomplete elimination of some chemicals used in livestock production or consumer products some of these chemicals including antibiotics, hormones and pharmaceuticals can be found in processed foods or in surface water or groundwater used as raw water for drinking water production. The treatment efficiency to completely eliminate these chemicals or to partially remove them will determine the quality of the final treated product. Because the use and disposition of these compounds are not consistently regulated they are not measured routinely for regulatory compliance. Consequently their distribution and persistence in drinking water and food supplies has knowledge gaps.

**Goal:** The aim of this research is to compile a list of unregulated emerging contaminants that may be found in food and drinking water and to develop and implement a plan to monitor these compounds in food and drinking water at Study Locations to determine the likelihood of exposure to Study participants.

**Requirements:** Specific features of this research should: identify important emerging unregulated contaminants that may exist in food and drinking water, select sample collection procedures and analytical methods to detect these chemicals, pilot test collection and analysis of samples to demonstrate the need to incorporate these analyses into the NCS and describe how sampling and analysis should be incorporated into the NCS efficiently. A combination proposal addressing the real time analysis noted in the prior proposal RT-01 and the current technical proposal can be considered.

### **RT-04 Real Time Analysis for Environmental Samples**

**Background:** The current NCS protocol calls for the collection of a variety of environmental samples at specific intervals that are stored for possible analysis at a later date. This approach is time consuming and expensive for both sample collection and storage. Moreover, this approach does not generate immediate information that could be used to alter subsequent environmental sample collection in a more efficient and economical manner. Recent technological advances have been made to permit real time or near real time analysis of environmental samples. The NCS Program Office is interested in the ability to identify suitable technologies that can be tested and evaluated for deployment in the NCS.

**Goal:** The aim of this research is to evaluate the feasibility, acceptability and cost of devices, methods or procedures that can generate real time or near real time data in a manner that can expand the flexibility and utility of sample collection and analysis for a wide array of environmental contaminants in the NCS.

**Requirements:** Study Centers interested in this research should submit proposals that aim to: identify and test promising devices, methods, or procedures that are more efficient and economical than current environmental sample collection and analysis procedures, consider sample collection duration, frequency, and location and participant self collection to expand the potential use of these technologies in the NCS. A combination proposal addressing the real time analysis noted in the prior proposal RT-01 and the current technical proposal can be considered.

## **RT-05 Feasibility Studies of Molecular Markers to Identify Pharmacogenomic Profiles and Ancestry**

**Goals:** Real-time molecular analysis of pharmacogenomic and ancestral markers in consenting adults

**Requirements:** High-throughput capability to perform these molecular analyses and IRB approval

### **Specific evaluation factors include:**

- Immediate (within the first 4 weeks of IRB/OMB approval) access to and use of DNA from consenting adults from a wide distribution of possible ancestral groups
- High-throughput capabilities to perform arrays in real-time (within 2 weeks of receipt of biospecimen) and DNA storage either on site or at other locations including the NCS repository
- Description of completeness of ancestral information derived from pharmacogenomic assays vs. ancestral markers alone
- Training in protection of these data as Personally Identifiable Information (PII)
- Description of security plan and facilities to store PII
- Description of array-based markers to be used and breadth of coverage of ancestry
- Exporting functionality

**Discussion:** Information on NCS enrollees' pharmacogenomic profile and ancestry will be useful in interpreting data from many NCS study assessments. Pharmacogenomic array data will contribute to understanding an enrollee's observed response to various medications, environmental exposures, etc. Pharmacogenomic and ancestral marker studies will reduce spurious conclusions caused by population sub-structure. They will identify 'at risk' and 'protective' alleles and allow accurate risk assessment across all groups whose alleles may vary with ancestry.

These data are as private as any PII and must be secured in the same manner as non-molecular PII. The ancestral marker set to be used must be shown to capture the widest range of ethnicities known globally. Utility of pharmacogenomic vs. ancestral markers in capturing exposure risk is requested as part of this Project. A combination proposal addressing the real time analysis noted in the prior proposals RT-01 and RT-02 with the current technical proposal can be considered.

## STUDY LOGISTICS ANALYSIS AND IMPROVEMENTS

### SL-01 Evaluation of Commercial Resources for Tracing/Locating NCS Participants

**Goals:** Determine the feasibility, quality and cost of using a commercial database to trace NCS participants and monitor changes in residential status of specific dwelling units. The NCS is interested in maintaining up-to-date data on both individual participants (mother, fathers, and babies) as well as dwelling units. Examples assessments might include the rate of successful person-level tracking using these services and the rate of identifying turnover in dwelling-unit composition. Examples of commercial vendors include Lexis-Nexis, Intelius, Anchor Inc, and Merlin. (Note that this list is not exhaustive and interested SCs should plan on researching the full scope of available vendors).

**Requirements:** SCs interested in this task should plan to partner up with a research organization experienced in using these products and with available sampling statisticians who can evaluate coverage issues and make appropriate recommendations.

#### Specific evaluation factors include:

- Pros and cons of having the NCS conduct tracing in a centralized manner, versus having each Study Center purchase separate accounts. What are limitations of access on both types of contractual agreements?
- Package options (Do some options provide greater levels of information, what are the user requirements for the various options? Do government clients have greater access than commercial ones, but less than law enforcement?)
- Quality of data
- Timeliness of updates
- Sample coverage (How is this measured? What percent of a geographic area/population/other unit of measurement is covered? With what frequency?)
- De-duplication processes (How “clean” are the results and how much manual or programmatic editing is required of the user?)
- Security issues
- Ease of use
- Batching of cases
- Exporting functionality
- Cost/benefit analysis addressing above criteria

The above vendors and factors are only a preliminary list and should not be considered exhaustive. Interested SCs should propose additional metrics and provide a detailed work plan. Analyses should not rely on advertised services described in public materials. SCs should plan on doing a “hands-on” evaluation of vendors, using existing contracts, trial packages, or structured demonstrations that fully address each evaluation area. SCs may consider using test sample frames from previous studies to which they have access. No direct contact with NCS (or other study) participants will be made. The work plan should include the following categories: development; implementation; evaluation; proposed deliverables; and timeline. SCs should plan to begin this effort as soon possible once all necessary contract modifications are in place. Work should be completed within approximately 9 months.

## **SL-02 Study Center Training Centers**

**Goals:** The NCS requests proposals for the development of NCS Study Center Training Centers for the initial and ongoing training of NCS managerial, supervisory, technician, field collector, and informatics staff. Cognitive labs and focus groups may also be featured. Field documentation training (that is, development of biweekly, standard and brief communications to the NCS Project Office of Study Center operations and field progress) is a priority.

Interested centers may propose to develop facilities for all or a subset of these features. Centers may also propose additional features for consideration by the NCS Program Office. All proposals should include building, facilities, staff, training, equipment, materials office, software, security, and regulatory requirement level of effort, as appropriate, needed to establish a research data center with the data and materials capabilities proposed by the centers.

**Requirements:** All proposed training plans must consider feasibility (that is, the scientific robustness of the method); acceptability (that is, the impact on study participants and study infrastructure); and cost (including training time, equipment and processing). NCS priority training areas include managerial, supervisory, technician, field collector and informatics staff, particularly in relation to the Recruitment SubStudy data collection events. All proposed training must include a training plan with proposed materials prior to implementation, a schedule for completion, a certification process, and refresher training as appropriate. Proposals which feature an empirical evaluation of training methods with a view to informing the feasibility, acceptability, and cost of the Study will be given priority.

Interoperability of training materials across Study visits, Training Centers, and with other Study platforms is preferred. All training and certifications must be documented, including instructor, course, content description, staff, role and date of completion. All training programs should be evaluated by the attendees and the instructor with a view to improved future training.

### **SL-03 Study Visit Measurement Evaluation Support**

**Background:** Each visit of the Vanguard Study has a schedule that may contain some variation of questionnaires, physical and laboratory measurements, biological samples, environmental sample collections, or other assessments. For each outcome assessment for each visit an *a priori* analysis is desired to determine the estimated count of informative events to provide 95% confidence limits around the reproducibility of the assessment that will allow an evaluation to determine whether to: scale up with an acceptable standard deviation, modify the outcome assessment and retest empirically, or eliminate the outcome assessment from consideration for the Main Study. Under the direction of the NCS Program Office Data Analysis Team (DAT) support is needed to conduct analyses of these study visit measurements for questionnaires, physical measures, environmental analyses, and biological analyses.

**Goal:** Develop appropriate data handling infrastructure and staff support to assist the DAT with analysis and evaluation of NCS study visit measurements.

**Requirements:** This research will address approaches to identify data sources and data elements for analysis, development of metrics for specific measurement evaluations, analysis of Vanguard Study data according to these criteria:

- Feasibility - technical performance of the study visit measure
- Acceptability – study implementation and participation completion rates
- Cost – field staff time, administration, equipment and supply costs
- Scalability – ability to apply the measurement throughout the Study
- Informative Value – results provide intended information for the desired parameter
- Lack of redundancy with other measurements.

Study Centers must develop and maintain secure computing facilities with appropriately trained staff to handle confidential data and develop a communication mechanism to coordinate their data analysis activities with the DAT to ensure efficient data evaluation.

### **SL-04 Enhance Intra-NCS Communications**

**Goals:** The NCS requests proposals for the development of mechanisms, standard operating tools, technologies, and workflows to enhance communications among persons at all NCS Study Centers and NCS partner organizations. Across all study organizations, communications could be enhanced among investigators, field staff, laboratory technicians, community outreach staff members, and all other groups employed in the carrying out the study. Projects could target one or more of these target groups. Interested parties may wish to work within the structures, technologies, and mechanisms implemented by IMS and IT contractors, and/or work collaboratively with other Study Centers. Work products could include finalized documents or systems, or instead plans for implementation by the IMS or IT contractor or by the Program Office.

**Requirements:** All proposed enhancement plans must consider feasibility, acceptability, and cost. All proposed projects for enhanced communications must include a schedule for completion and plans for empirical evaluation of the implemented product.

## **SL-05 Terminology**

**Background:** Data sharing and integrated analyses are facilitated and sometimes only possible if the terminology to describe critical concepts and specific terms and data fields is harmonized and even standardized. Child health research is in need of consistent terminology to bridge concepts among multiple disciplines and across developmental stages.

**Goal:** The proposed formative research project would be the selection of consensus concepts and terms for events along the developmental timeline using the methodology of use or value cases.

**Requirements:** Multidisciplinary teams would meet and follow the logical and semantic framework introduced at <http://nichd.nih.gov/health/clinicalresearch/terminology/> and supplemented by orientation materials and discussions by Dr. Steven Hirschfeld and collaborators to develop terminology that would be incorporated into repositories such as the National Cancer Institute Data Standards Registry and Repository (caDSR see <https://wiki.nci.nih.gov/display/caDSR/caDSR+Wiki+Home+Page> ), the Clinical Data Interchange Standards Consortium (CDISC) SHARE Project (see <http://www.cdisc.org/cdisc-share>) and potentially other resources where the terminology would be accessible to researchers internationally. Conferences, tutorials, and collaborative activities would be encouraged as well as consideration of mechanisms for curation and maintenance of child health terminology. The major goal will be construction of a system for normal child development linked by a temporal dimension that can relate similar concepts and terms across different stages. Episodic exploration of specific conditions may be of supplemental value provided the primary focus supports the framework of normal child development.

## **BIOSPECIMEN COLLECTION AND PROCESSING**

### **BIO-01 Analysis of Environmental Chemicals in Dried Blood Spots**

The NCS requests proposals for the empirical evaluation of filter paper adsorbed dried whole blood spot samples for analysis of infant exposure to environmental chemicals.

Filter paper adsorbed dried blood spots (with and without anticoagulant) are collected and/or produced as part of the current NCS Vanguard study protocol. Filter paper blood collection is widely used for newborn metabolic screening, and because of its advantage as a sample type in terms of handling and storage has been investigated for a wide variety of additional uses. However, as a sample matrix it presents some additional challenges not associated with liquid samples. Current information about suitability of filter paper adsorbed dried whole blood for measurement of environmental chemicals in blood is limited.

The NCS is seeking to determine the suitability of filter paper adsorbed dried whole blood spot samples for analysis of environmental chemicals, to address the issue of avoiding environmental contamination of filter paper samples, and to establish reference data for environmental chemicals and clinical chemistry analytes in filter paper adsorbed dried whole blood spot samples.

**Requirements:** Proposals should consider feasibility (that is, scientific merit, including reliability), acceptability (that is, burden on respondents and impact on study centers), and cost in their proposal. Evaluations should compare the information obtained from filter paper adsorbed dried whole blood spot samples with that provided by analysis of conventional liquid blood or blood derivative samples. Both persistent and non-persistent chemicals should be evaluated. Additional evaluation of other clinical chemistry analytes in filter paper adsorbed dried whole blood spot samples may be proposed. Proposals should demonstrate the ability to collect, process, store, and analyze the requisite sample types. Proposals should meet applicable human subjects research protection and laboratory regulatory requirements. This proposal may be combined with proposal RT-01.

## **BIO-02 Analysis of Environmental Chemicals in Breast Milk**

The NCS requests proposals for the empirical evaluation of breast milk sampling schedules for analysis of maternal and infant exposure to environmental chemicals.

Breast milk is an important indicator of both historical (for persistent chemicals) and current maternal exposure to several contaminants, and of current dietary exposure for breast-fed infants. Current information about time-trends in breast milk contaminant concentrations is insufficient to define the number and timing of collection points needed to determine decay curves (for fat-stored and persistent pollutants) and temporal variability (for non-persistent chemicals and transient exposures).

The NCS is seeking to determine optimal schedules for breast milk sampling to minimize collection burden while retaining information on exposure time trends for environmental chemicals and normal constituents in breast milk, and to establish reference data for environmental chemicals and clinical chemistry analytes in breast milk.

**Requirements:** Proposals should consider feasibility (that is, scientific merit, including reliability), acceptability (that is, burden on respondents and impact on study centers), and cost in their proposal. Evaluations should compare the information provided by the current NCS Vanguard protocol collection schedule (one and six months) with sampling at three or more points, to determine the optimal minimum number and timing of collections. Both persistent and non-persistent chemicals should be evaluated. Additional evaluation of time trends in normal constituents in breast milk may be proposed. Proposals should demonstrate the ability to collect, process, store, and analyze human milk. Proposals should meet applicable human subjects research protection and laboratory regulatory requirements. This proposal may be combined with proposal RT-01.

### **BIO-03 Isolation and storage of *intact* cells from NCS enrollees for long term storage**

**Goals:** The goal of this project is aimed at improvements in Isolation and storage of *intact* cells from NCS enrollees for long term storage including but not limited to maternal and infant urine and buccal mucosa. To increase scientific flexibility of the NCS via storage of intact cells derived from tissues not currently a part of the NCS biospecimen protocol. (Note: BIO-03 and BIO-04 are complementary topic areas, and any resulting projects may benefit from harmonized submissions among collaborators.)

**Requirements:** High-throughput capability and multiple storage conditions

#### **Specific evaluation factors include:**

- Variety of tissues proposed
- Feasibility of protocol designs
- High-throughput isolation and storage is critical
- Utility of storage conditions proposed
- Quality assessment and control of selected specimens

**Discussion:** Isolation of cells from a variety of tissues and their storage in two or more conditions will provide the NCS with increased scientific flexibility. These cells are intended for long-term storage in anticipation of new technologies capable of multiple ‘-omic’ assays using minute numbers of cells. Future study of these cells for environmental exposures for which we currently have no assay could be one outcome. Use of these cells for study of heritable or transmissible phenomena is another. The goal is to plan for future scientific research that we can only imagine now.

NOTE: Some cells isolated in Project BIO-03 may be used in Project BIO-04 for mitochondrial extractions.

### **BIO-04 Extraction and storage of mitochondria and mitochondrial (mt) DNA from cells**

**Goals:** Extraction and storage of intact mitochondria and mt DNA from multiple different tissues not currently a part of the NCS biospecimen protocol (Note: BIO-03 and BIO-04 are complementary topic areas, and any resulting projects may benefit from harmonized submissions among collaborators.)

**Requirements:** High-throughput capability and storage

#### **Specific evaluation factors include:**

- Variety of tissues proposed
- Feasibility of protocol designs
- High-throughput isolation and storage is critical
- Quality assessment and control of selected specimens

**Discussion:** Mitochondria, their number, and DNA sequence varies from tissue to tissue. Changes in mitochondria may be maternally inherited. They may also be induced by toxicant exposure or a disease process. Isolation and storage of intact mitochondria and extraction of mt DNA are requested for this Project. No study of these species is requested at this time. Rather, they are intended to be a resource as important research questions arise.

## **ENVIRONMENTAL SAMPLE COLLECTION AND PROCESSING**

### **ENV-01 House Dust Sampling and Analysis**

**Background:** House dust is frequently collected in environmental exposure studies and analyzed for a wide array of contaminants to assess exposure. Dust samples have been collected in several ways: vacuum samplers, wipes, deposition plates, or as bulk dust from household vacuum cleaners. In the NCS Vanguard Study dust samples and wipe samples are collected at various times for inorganic compounds, semi-volatile organic compounds (SVOCs), pesticide residues, allergens, endotoxin, and mold.

**Goal:** evaluate the feasibility, acceptability and cost of procedures to sample and analyze dust samples in a manner that will expand the utility of this sample for analysis of contaminants and optimize the informative value of this sample for the NCS.

**Requirements:** Study Centers interested in this research should submit proposals should aim to: critically review the NCS Protocol for dust sample collection and analysis, investigate sample collection methods and procedures to optimize the efficiency and economy of dust collection with consideration for sampling collection frequency, duration and location; participant self collection of samples; sieving and storage procedures for collected dust samples; and analytical procedures to expand the range of contaminants that can be measured. Consideration of different technologies such as wipes, aspirated samples or other collection methods, use of various filters, and sample recovery and analyte assays are all relevant topics to explore.

### **ENV-02 Dermal exposure to consumer products**

**Background:** Dermal exposure is currently not being addressed in the National Children's Study (NCS) but may be an important route of exposure for chemicals found in consumer products for infants and young children. Research is needed to determine the extent, if any, important exposures might occur, their frequency and duration, and how sampling and analysis for this route of exposure could be incorporated into the NCS in an efficient manner.

**Goal:** Assess the need for development of efficient, economical, acceptable procedures to estimate dermal exposure of chemical contaminants in infants and young children for the NCS.

**Requirements:** This research should address the need for dermal exposure measurement in the NCS based on the kinds of chemicals likely to be present in consumer products that can be absorbed through the skin of infants and children, procedures to sample and analyze these chemical compounds, and the frequency and time intervals samples should be collected in the NCS.

### **ENV-03 Dwelling Unit Observation Form Evaluation**

**Background:** Dwelling unit observation (DUO) is employed as an instrument in the current NCS study visits to evaluate housing characteristics and pollutants sources at or near residences. Given the expense incurred with study visits there is a desire to evaluate this instrument and expand its information collection potential.

**Goal:** Evaluate and optimize the existing DUO instrument for implementation in the NCS to maximize its informative value about housing characteristics and pollutant sources in residences.

**Requirements:** This research should address the following factors: the informative value of the current DUO instrument, modifications or enhancements that can expand its information collection ability, procedures to document and verify its informative value to the NCS, and procedures to efficiently deploy it with consideration for other study visit activities to improve the efficiency of its use in the NCS.

### **ENV-04 Ambient Air Quality Analyses**

**Background:** Elevated levels of ambient air pollution can affect health and may be important in several NCS segments. Routine measurement of ambient air pollutants is generally limited to compounds of regulatory interest at fixed sites and times. Consequently temporal and spatial variation exists that may make it difficult to utilize these data in the NCS.

**Goal:** The aim of this research is to develop a feasible, acceptable and economical approach to measure ambient air pollutants in NCS segments.

**Requirements:** Study Centers interested in this research should submit proposals that aim to consider the specific needs of the NCS for ambient air pollution measurements, the heterogeneity of NCS locations, and the organizational structure of NCS Study Centers such that the proposed approach or approaches can be deployed throughout the Study in an acceptable and efficient manner.

## **PHYSICAL MEASURES**

### **PHYS-01 Tools for Screening Pulmonary Function in the NCS**

The NCS seeks to ascertain a valid and reliable screening tool for pulmonary function that can be accomplished within a reasonable amount of time in the context of an NCS clinic visit or field visit to the home. An important aspect of the NCS is studying the trajectory for asthma and other respiratory disease. To do so, we must institute objective tests of pulmonary function throughout the course of the Study. Methodological studies are needed to explore ways to assess pulmonary function at various ages, to include accuracy and reliability, time commitment, cost of equipment, burden on participant and on Study infrastructure, discomfort, and other factors. Questions include: ‘What is the youngest age at which a reliable test of respiratory function could reasonably be accomplished in the NCS setting?’ and “What pulmonary function measure or battery of measures can be used serially from early childhood through adolescence.” It is important that proposed methods are appropriate for an observational, multi-site, population-based study such as the NCS.

Testing with NCS participants or within sampled segments is not required, but proposed methods must be applicable to both. Any proposed data collection occurring with target populations outside off NCS segments may be subject to IRB and OMB review and clearance. Letters should detail proposed sampling strategies.

### **PHYS-02 Evaluation of Ulnar Length Measurement for Use in the NCS**

**Background:** Assessment of growth and body size is generally a challenging and relatively imprecise endeavor. For non-ambulatory children, particularly neonates and infants, recumbent length from crown to rump or crown to heel is often used, but is difficult to assess consistently. For ambulatory children, variations in strength, posture, movement and anatomy introduce further imprecision. A useful surrogate would have the properties of rapid and easy measurement, excellent correlation with other parameters of growth and size, be reproducible, relatively precise and simple to learn. Candidates for a useful surrogate include segmental lengths. The ulnar bone is of particular interest because of its ease of accessibility and the presence of simple to identify landmarks.

**Goal:** The formative research project would examine correlations of ulnar length in children of multiple ages, races, ethnicity, gender and conditions with other parameters of size such as total height or other measures. In addition, correlation between ulnar length and Body Mass Index z-scores would be of interest.

**Requirements:** An analysis of ulnar length data combined with field testing of simple and cost effective techniques to assess and record ulnar length should be proposed.

### **PHYS-03 Evaluation of Dental Health for Use in the NCS**

**Background:** Oral health and oral flora have been both surrogates and linked to multiple states of health and disease. Rapid and cost effective assessment of oral and dental health through a combination of questionnaire, physical assessment, imaging, saliva collection or other means is an important goal of the NCS.

**Goal:** Rapid and cost effective assessment of oral and dental health for NCS participants

**Requirements:** Analysis of current options and development and field testing of proposed solutions with sensitivity and specificity to identify selected markers or conditions considered relevant.

## **QUESTIONNAIRE DEVELOPMENT AND VALIDATION**

### **QUEX-01 Self-Reported Stress and Cortisol Measurement**

**Goals:** The NCS requests proposals for the empirical evaluation of maternal stress measurement for use in the NCS Program. The NCS Vanguard Protocol currently contains several self-reported assessments of maternal stress, each administered through in-person data collection. The NCS Vanguard Protocol also collects saliva through a self-administered and mail-in procedure. The planned analyses for these samples include a measurement of cortisol concentration as an indicator of stress, but this analysis is not done at this time. The NCS is now seeking an evaluation of the most efficient and robust measures of maternal stress.

**Requirements:** Interested Study Centers should consider the feasibility (that is, scientific merit, including reliability), acceptability (that is, burden on respondents and impact on study centers), and cost in their evaluation of measures. More than one indicator may be proposed to gauge concurrent validity, and repeated measures may be appropriate for exposure-outcome analysis in the Main Study implementation. However, parsimony is valued.

### **QUEX-02 Measurement of Adult Mental Health**

**Goals:** The NCS requests proposals for the development, empirical testing and evaluation of a self-reported measure of adult mental health that gauges the severity, incidence, and duration of illness episodes. This measure would complement established self-reported measures of adult depression, such as the CESD. The proposed measure should be appropriate for administration by respondents and/or lay field collectors.

**Requirements:** Study Centers should provide a development and analysis plan for their proposed measure. This plan should include, at a minimum: 1) constructs to be captured; 2) population of interest; 3) mode and length of administration; 4) plans to gauge reliability and validity of the proposed measure; 5) cognitive lab and/or focus group pre- testing; 6) plans to implement the measure in such a way as to determine the psychometric characteristics of the proposed assessment in a general population; 7) criteria by which recommendations would be made to the NCS Program. In calculation of

recommendations, Study Centers should consider the feasibility (that is, scientific merit, including reliability), acceptability (that is, burden on respondents and impact on study centers), and cost in their evaluation of measures. All elements of the analysis plan should then be implemented, documented and delivered to the NCS Program. Training materials should be provided by the Study Center.

## **STUDY INFRASTRUCTURE DEVELOPMENT**

### **INF-01 Evaluating the Use of Text Messaging as a Data Collection Mode in the NCS**

**Goals:** Determine the feasibility, quality and cost of using Short Messaging Service (SMS) – otherwise known as “text messaging” to communicate with NCS participants. Text messaging may be a method of contact that is acceptable to women in our targeted age-range, allowing the NCS to maintain contact over time and increase response rates. In this LOI, the NCS is interested in understanding whether this method is technically feasible and acceptable to participants for questionnaire administration, and what are the specific system requirements to implement this methodology. Ideally, if the method is determined to be a useful option, one deliverable may be the software infrastructure for NCS-wide use.

**Background information:** Westat has done some preliminary work in this area (unrelated to the NCS, see: Hicks et al. 2010. “Exploring SMS as a Data Collection Method.” Presented at the Federal Fed CASIC 2010 Workshops, Washington DC). Please plan on communicating with them as to their findings. SCs may decide to partner with Westat or another research organization with experience in this area if so desired.

**Questions for Evaluation:** this list is not exhaustive. Interested SCs should propose additional evaluation criteria as appropriate.

- Systems Development
  - Ability to link response data to questions due to disconnect between outbound and inbound messages
    - Develop unique response code frames
  - Preventing acceptance of unsolicited text or special characters
  - Character limits
  - Legibility of messages on device screen
  - Cost
- Systems Implementation – includes both outbound and inbound messages/responses
  - Ease of use
  - Timeliness
  - Reliability
  - System requirements to prevent known errors (data loss, timeouts, slow process due to volume of queue, etc.)
  - Costs (including participants)
- Data Management and Post-Processing
  - Response rates
  - Data quality
  - Security concerns

- Data management issues (exporting, linkages, deduplication of responses)

Interested SCs should provide a detailed work plan and propose evaluation metrics. The work plan should include the following categories: development; implementation; evaluation; proposed deliverables; and timeline.

### **INF-02 Development of Web Data Collection Systems for Use in the NCS**

**Goals:** Determine the feasibility, quality and cost of using web-based data capture and collection systems, such as secure forms. A common feature of many websites and marketing campaigns is to allow complete interaction through the use of web and email. Use of these technologies in research federally funded through contracts poses particular data collection restraints and security precautions. This call for Letters of Interest, the NCS is interested in the development (or further development) of web data capture systems that can be shared with all NCS Study Centers or more broadly. The Program Office is interested in receiving LOI on a variety of projects, particularly those that capitalize on existing open-source or freely available tools and systems.

**Suggested points to consider in this development activity** (not all inclusive and not all are required, but all are encouraged):

- Systems Development
  - Open source or freely available
  - Built on open-source or freely available platforms
  - Security
  - Interoperability with case management systems, data storage systems, or data analysis systems, ideally through the offering of standard APIs for all major functions
  - Flexibility for complex and nested skip patterns, grid entry, and looped questions
  - The ability to be implemented in a variety of environments, not just at the developing institution
  - Section 508 compliant, and highly accessible to a variety of interaction models.
  - Cost
- Evaluation of use by participants
  - Ease of use
  - Timeliness
  - Reliability
  - System requirements to prevent known errors (data loss, timeouts, slow process due to volume of queue, etc.)
  - Costs (including participants' time)
- Evaluation of Data Management and Post-Processing
  - Response rates
  - Data quality
  - Security concerns
  - Data management issues (exporting, linkages, de-duplication of responses)

Interested SCs should provide a detailed work plan and propose evaluation metrics. The work plan should include the following categories: development; implementation; evaluation; proposed deliverables; and timeline.

### **INF-03 Alternative Mechanisms for Documenting Informed Consent from Participants in the NCS**

**Goals:** The NCS is interested in exploring the potential for alternative mechanisms of documenting participants' informed consent for Study participation. Because the NCS is pursuing numerous approaches to electronic mechanisms for data capture in the field, we would like to determine the feasibility and cost of approaches, such as e-pens, for obtaining electronic documentation of informed consent. Additionally, as the Study explores the potential for telephone and web based data collection, we will need to develop approaches to capturing consent using these modalities as well.

**Requirements:** SCs interested in this task should plan to identify and pilot tools for capturing consent electronically in the field, over the telephone, and over the internet. Whatever tools are used, they should:

- Include a mechanism for authentication of the consent (that is a method to verify that a particular individual provided consent) - the authentication mechanism should be described in writing
- Lend themselves to generating a copy of a "signed, dated" consent that can be left with participants in the field or generating a receipt that consent was given.
- Allow for timely transmission of documentation of consent to a data center or other repository.

No direct contact with NCS participants will be made. The work plan should include the following categories: development; implementation; evaluation; proposed deliverables; and timeline. SCs should plan to begin this effort as soon possible once all necessary contract modifications are in place. Work should be completed within approximately 9 months. At this time no formal budget is requested, but interested SCs should provide an estimated level of effort and proposed staffing plans.

### **INF-04 Development of an Assent Process for Children Enrolled in the NCS Vanguard Study**

**Goals:** The NCS is interested in exploring the potential for an interactive, video based assent tool and in determining the feasibility, quality and cost of developing a robust assent process for children enrolled in the NCS. As the cohort of children in the NCS ages, we will have to develop an ongoing assent process that is age appropriate for children starting at age 7 and continuing into adolescence. Our focus now is on developing the initial assent process, for children about 7 years of age.

**Requirements:** SCs interested in this task should plan to develop a video based assent tool and test the comprehension of the information conveyed in the tool among a group of healthy children between 7-8 years of age. The tool could be compared to other approaches to assent – for instance, a conversation with a study staff member, etc.

**Specific evaluation factors include:**

- Length of assent administration.

- Measures of children’s comprehension of basic elements of participation in the NCS. For instance, that the benefit of participating in the Study is helping other children, that the risks include spending time answering questions and taking tests, having a blood draw, giving hair samples, etc.
- Children’s attention to, and interest in, the assent tool.
- Parental acceptance of assent process.

No direct contact with NCS participants will be made. The work plan should include the following categories: development; implementation; evaluation; proposed deliverables; and timeline. SCs should plan to begin this effort as soon possible once all necessary contract modifications are in place. Work should be completed within approximately 9 months. At this time no formal budget is requested, but interested SCs should provide an estimated level of effort and proposed staffing plans.

## SUBMISSION INSTRUCTIONS

To be considered for selection, each interested NCS Study Center should prepare a Letter of Interest that describes their interest in participating in a development activity or study.

Please submit a separate letter for each proposed activity in a separate email to [ncs@mail.nih.gov](mailto:ncs@mail.nih.gov). For example, a Center proposing to conduct two activities would submit two Letters of Interest in two separate emails. Each submission will be acknowledged by a response email.

To aid the routing of these Letters of Interest, each letter should be submitted as a separate electronic document in a common format (.PDF, .RTF, .DOC, .DOCX) with a filename that includes information regarding topic area, the submitting Study Center, and a title for the proposed activity. For instance, the XYZ Study Center submitting an analysis of tracing resources focused on the USPS DSF and Intelius would use the filename **SL-01-XYZ-Tracing using DSF and Intelius.pdf**.

Each letter is limited to a maximum of three letter-sized pages in length. No additional cover letters or materials should be submitted for consideration at this time. Submissions should be formatted for readability, including typefaces of 11 or 12 points and margins of 0.75 inches or greater.

Collaboration is encouraged among all NCS Study Centers and Study Locations, as these are complex issues requiring detailed investigations to evaluate performance and document efficiency and acceptability. In addition, collaboration with resources within NCS Study Centers such as Centers of Excellence, CTSA investigators and core facilities, and other programs are encouraged. Further collaboration with non-NCS institutions that have relevant resources and expertise is also encouraged. Note that, in particular for RT-01, infrastructure and capital equipment will only be provided to NCS Study Centers.

Any testing must be applicable to NCS participants. Any proposed data collection could be subject to Institutional Review Board (IRB) review and Office of Management and Budget (OMB) clearance as appropriate and applicable. Letters should detail proposed sampling strategies. All communications developed for NCS participants or the general public must adhere to the tenets of Plain Language ([www.plainlanguage.gov](http://www.plainlanguage.gov)). Similarly, all training programs and associated materials should incorporate best practices for adult learning. Any resulting publications or communications of results and activities must be consistent with the NCS Publication Policy. Note that all data linking must be done in accordance with the NCS Data Access and Confidentiality Committee (DACC) policies. For further details see

<http://www.nationalchildrensstudy.gov/about/organization/dacc/Pages/PolicyManualandDataUseAgreements.aspx>

Describe your proposed scientific approach to the task(s), highlighting key socio-demographic considerations and the geographic locations of interest. The utility and relevance of each proposed method or activity to the larger NCS should be described, along with the significance of any specified subgroups.

Candidates should provide information on relevant evaluation criteria, data collection methodology, analytic plans, and organizational experience. At this time, please just respond to the stated scope of work. No formal budget, schedule or deliverables should be submitted; however, descriptions of cost effective implementation plans that include estimates of the general number and types of personnel, estimated levels of effort, and timelines to start and complete the proposed projects are encouraged.

All Letters of Interest must be submitted by e-mail to the [NCS@mail.nih.gov](mailto:NCS@mail.nih.gov) mailbox by each interested Prime Contractor no later than 8:00 p.m. Eastern Standard Time on Friday, July 2, 2010. Letters will be evaluated by the NCS Program Office on the scientific, logistic, and operational quality of the proposal with consideration for factors such as geography and demographics. Study Centers will be contacted by a target date of Monday, July 19, 2010 with an update and/or requests for further information. Using the submitted Letters of Interest as an informational source, the NCS Program Office will work with the NICHD Contracts Management Branch to assign tasks under the current statement of work that will further the goals of the NCS Vanguard Study. Work on assigned tasks can be expected to begin as early as August 2010 and deliverables are expected throughout federal fiscal years 2010 and 2011 (FY2010-FY2011).

Time and resources for preparation of the Letter of Interest are not billable to the National Children's Study as this is a voluntary effort and not a required task issued under any existing contract. Any questions should be addressed in writing to [NCS@mail.nih.gov](mailto:NCS@mail.nih.gov).