**REQUEST FOR OMB CLEARANCE**
**Generic Clearance Request**
**Biospecimen and Physical Measurements Formative Research Methodology Studies for the National Children's Study (NICHD)**

**Part A only**

**CDR Colleen O. Lee, MS, CRNP**
**National Children's Study**
**Eunice Kennedy Shriver National Institute for Child Health and Human Development**
**6100 Executive Boulevard**
**Room 3A01**
**Bethesda, MD 20892-7510**
**Phone 301-451-2135**
**E-mail: leeco@mail.nih.gov**
**General e-mail inquiries: ncs@mail.nih.gov**
**www.nationalchildrensstudy.gov**

## A. Justification

### A.1 Circumstances Making the Collection of Information Necessary

The President's Task Force on Health Risks and Safety Risks to Children recommended in 1999 that a large study to define the actual risks associated with broad environmental exposures is the critical first step in addressing the potential risk factors that may affect the health and development of children in the United States (US). Following the recommendation of the task force, Congress passed the Children's Health Act of 2000 (Public Law 106-310) which authorized the National Institute of Child Health and Human Development (NICHD) to conduct a national longitudinal study of environmental influences on children's health and development. These environmental influences include physical, chemical, biological, and psychosocial aspects.

As stated, by law, the Children's Health Act of 2000 (Sec. 1004) states that the Director of the NICHD shall establish a consortium of representatives from appropriate Federal agencies to plan, develop, and implement a prospective cohort study, from birth to adulthood to fulfill two main purposes justifying the collection of information:

1. "Plan, develop, and implement a prospective cohort study, from birth to adulthood, to evaluate the effects of both chronic and intermittent exposures on child health and human development."
2. "Investigate basic mechanisms of development disorders and environmental factors, both risk and protective, that influence health and development that influence health and developmental processes. "

Required, by law, under the Children's Health Act of 2000 (Sec. 1004), the national longitudinal study, termed the National Children's Study [NCS], outlines three research imperatives justifying the collection of information:

1. "Incorporate behavioral, emotional, education, and contextual consequences to enable a complete assessment of the physical, chemical, biological and psychosocial environmental influences on children's well-being."
2. "Gather data on environmental influences and outcomes on diverse population for children, which may include the consideration of prenatal exposures."
3. "Consider health disparities among children which may include the consideration of prenatal exposures."

The NIH developed a systematic approach to fulfilling the NCS mission. The NCS is an integrated system of activities that include a NCS Vanguard (Pilot) Study for operations and methods development and an NCS Main Study to collect data on exposure and response The NCS

Vanguard (Pilot) Study (OMB #0925-0593), was submitted to OIRA/OMB on and renewed recently by the Office of Information and Regulatory Affairs within the Office of Management and Budget with an expiration date of 7/31/2013. The purpose of the Vanguard Study is to assess the feasibility, acceptability, and cost of the recruitment strategy, study logistics and operations, and study visit assessments that will be used in the second component, the NCS Main Study. 'Feasibility' assessment refers to technical performance and reliability. 'Acceptability' refers to the impact on the study participants and overall study infrastructure. 'Cost' refers to the level of effort, personnel, resources, and money involved in a study development and implementation.

The NCS Main Study, currently in the concept phase, will run in parallel with the NCS Vanguard (Pilot) Study. Additional substudies and formative research projects will inform future NCS design and activities. For more detailed information regarding the NCS Vanguard (Pilot) Study, please see the National Children's Study: An Evolving Concept - Concept of Operations.

With this submission, the NCS seeks approval from OIRA/OMB to develop a topic-based, generic clearance, called the Biospecimen and Physical Measures Generic Clearance. This clearance will provide an approval mechanism solely focusing on formative research related to the collection and storage of biospecimens, physical measurements, and associated information gathered via questionnaires, focus groups, and/or cognitive interviews. This clearance is the first of several topic-based generic clearances intended to streamline submission and review of formative research.

Biospecimen-related formative research can be organized into the areas of specimen collection, processing, transport, storage, and analysis. There are operational opportunities for improvements in best-practices for each of these identified areas to achieve mechanisms that are better, faster, and less costly than conventional approaches. There are similar opportunities for improvements in the collection, analysis, and use of physical measurements especially with regard to development and pilot use of training techniques and procedures for data collectors taking physical measures. This Biospecimen and Physical Measures Generic Clearance will help address a number of outstanding areas within the Vanguard (Pilot) and Main Study.

### A.2 Purpose and Use of the Information Collection

This information collection involves the collection and storage of biospecimens, physical measurements, and associated information gathered via questionnaires, focus groups, and/or cognitive interviews. Specifically in terms of biospecimens, different sample types may be suitable for different target analytes. The characteristics of the sample type and its role in metabolism dictate what is best measured in that particular matrix. For example, blood or

saliva would be most appropriate for measurement of clinical chemistry analytes or detection of active environmental chemicals; urine would be appropriate for detection of metabolites; hair, nails, or meconium would be appropriate for assessment of cumulative exposures. These aren't mutually exclusive categories but are general rules in toxicology and pharmacology that would direct our approach to a particular research question. These results will inform the NCS Vanguard (Pilot) study and Main Study in a manner that minimizes public information collection burden compared to burden anticipated if these projects were incorporated directly into either the NCS Vanguard (Pilot) or Main Study. Utilizing formative research and pilot studies prior to implementation in the Vanguard (Pilot) or Main Study will ultimately minimize public information collection burden.

This Biospecimen and Physical Measures Generic Clearance will allow the NCS to develop best-practice protocols and answer a number of questions surrounding biospecimen collection, processing, transport, storage, and analysis, and physical measurement gathering to determine the following:

(1) How much of a sample is needed to conduct a specific suite of laboratory analyses?

(2) What is the length of time that samples remain viable under different storage conditions?

(3) Refinement of available laboratory analysis methods

(4) Are there less burdensome or invasive sample collection methods available that can provide similar accuracy and precision in laboratory analyses?

(5) Are there additional types of biospecimen collections that the NCS should consider adding to the Vanguard (Pilot) or Main Study protocol?

(6) Are there newer and perhaps more reliable reference ranges for certain laboratory analyses that can be applied to the available specimens?

(7) Validation of physical measurement techniques and best practices

(8) The development and pilot use of training techniques and procedures for data collectors taking physical measures

Each of these topics is considered separately below:

(1) How much of a sample is needed to conduct a specific suite of laboratory analyses?

Since the required scope of the NCS is necessarily broad, a given biospecimen sample may serve several functions and be analyzed in multiple contexts; however, each test or analysis procedure may require a different minimum amount of sample. This minimum amount of biospecimen collection may be unknown to the NCS for a given suite of analyses. Formative research in this area will help assure that enough sample of each type (samples collected include a variety of body fluids, excreta, secreta, and tissues:  blood, hair, nails, and urine from adults, infants, and children; cervical fluid, and breast milk from women; cord blood, meconium, and placenta from infants and birth processes) is collected in the Vanguard and Main Study to enable a number of varied analyses. This activity would occur in the interest of streamlining biospecimen collections from the public and increasing the acceptability of all types of biospecimen collections.

(2) What is the length of time that samples remain viable under different storage conditions?

Laboratory analyses are continuously improving, and the scientific community is frequently learning additional information regarding how to utilize biospecimens to study the effects of environmental and genetic influences on health. Formative research geared toward storage conditions, length of storage, and viability will allow the NCS to ensure that specimens are usable for a period of time that will allow the NCS conduct analyses on these specimens in the future.

(3) Refinement of available laboratory analysis methods.

Smaller-scale formative research and pilot testing will enable the NCS to remain abreast of cutting-edge technology that may be used to analyze samples. As analysis techniques become better, faster, and less costly to perform, it is necessary to pilot these improvements to determine feasibility prior to implementing them in the Vanguard and Main Study.

(4) Are there less burdensome or invasive sample collection methods available that can provide similar accuracy and precision in laboratory analyses?

The large-scale nature of the NCS requires that a number of collections occur at a consistent rate. Biospecimens formative research and pilot testing will assist in ensuring that the most up-to-date methods of collection and processing are used to increase acceptability of NCS biospecimen collections, and so that public burden will be decreased over time. Ultimately, less burdensome and invasive sample collection methods will result in more efficient and faster Study visits involving biospecimen collections, and therefore a lower participant burden. Engagement with formative research study participants, hospital staff, health care practitioners, and other health care facility staff members via focus groups and cognitive interviews will also assist in establishing the acceptability of biospecimen sample amounts and collection methods.

(5) Are there additional types of biospecimen collections that the NCS should consider adding to the Vanguard or Main Study protocol?

The list of biospecimens currently collected under the Vanguard Study protocol (OMB #0925-0593; specific information collection describing biospecimens was approved by OIRA on 4/13/11) is not exhaustive and could be expanded. However, it will be necessary to evaluate the feasibility, acceptability, and cost of any new biospecimen collection prior to implementation in either the Vanguard or the Main Study.

(6) Are there newer and perhaps more reliable reference ranges for certain laboratory analyses that can be applied to the available specimens?

Reference ranges for specific substances to be analyzed associated with certain conditions, diseases or known or unknown risk factors have been determined in some cases. In other cases, however, there is a lack of information, or a consistent change in information related to these reference ranges. Formative research and pilot studies will enable the NCS to collect biospecimens that are used to determine optimum reference ranges for selected substances to be analyzed; these ranges will provide data that will further inform the Vanguard (Pilot) and Main Study.

(7) Validation of physical measurement techniques and best practices.

Similarly, formative research and pilot studies undertaken by the NCS under this generic clearance may be used to answer questions regarding the collection, analysis, and use of physical measurements. This generic clearance will allow the NCS to validate physical measurement techniques and establish best practices in obtaining physical measures. Formative research will allow for small-scale evaluation of physical measurement techniques prior to large-scale incorporation of physical measures (for example, infant length; child height; infant and child weight, head circumference, middle upper arm circumference, ulnar length) within the Vanguard (Pilot) and Main Study. Formative research and pilot studies focused on physical measurement techniques may center on the reproducibility of a specific type of measurement (as compared to the conventional standard); use of specific measurements as a means to calculate other characteristics (for example, ulnar length, arm span, and lower leg length as a means to calculate the length and height of infants and young children); or to evaluate the feasibility, acceptability, and cost of utilizing a specific tool for taking physical measures.

(8) The development and pilot use of training techniques and procedures for data collectors taking physical measures.

Additionally, formative research involving physical measures will assist in the development and pilot use of training techniques and procedures. Prior to physical measurement collection, NCS

staff is trained in a consistent manner so that measures remain reliable regardless of the data collector. Formative research to test the reliability of measurements taken following a new training technique or course will further help the NCS establish best practices to be used in physical measurements across all Study Centers. Small, focused surveys, focus groups, and cognitive interviews may also be employed to focus on physical measures training techniques and procedures for measurement collection. Such activities can assist in determining the feasibility, acceptability, and cost of training techniques and procedure-development for physical measurement collections. This may include:

(a) Administering limited questions about adult learning and cultural sensitivity in specified populations that might provide insight into how best to teach NCS staff and validate their understanding and performance accuracy and reproducibility in taking physical measures;

(b) Gathering information about the burden on hospitals, clinics, and other healthcare professionals, practitioners, staff, facilities, and organizations with regard to training techniques and procedure-development in physical measures (3)

(c) Gaining cooperation of and insight from key stakeholder groups in training techniques and procedure-development for physical measurement collections in targeted populations with a particular focus on cultural sensitivity. In some specific US populations (for example, rural areas, American Indian/Alaska Native groups, etc.), scientific research funded by government entities is regarded cautiously and with skepticism. Conversations with key stakeholder groups such as community leaders, community organizations, cultural and faith-based centers, and other community stakeholders may be necessary to fully evaluate how the participants can be placed at ease with the obtaining the physical measure collections. These conversations may take the form of small, focused surveys, focus groups, and/or cognitive interviews and would be aimed at evaluating how to approach individuals when recruiting for biospecimen and physical measure formative research, as well as how best to leverage community ties to achieve the goals of the NCS on a national level.

The exemplar study in this clearance is *LOI2-BIO-18*, *Placenta Studies: Cell Collection*, *Banking*, *and Morphology Assessment*. In this information collection, study centers will pilot test a collection protocol in order to establish best practices for sample collection and preservation of tissue for storage and future analyses. The following list of projects represents a set of examples of the types of information that will be gathered under the scope of this generic clearance. These projects will be forwarded for review under this clearance mechanism once it is established. Overall, these projects examine less invasive, cost-effective methods for the collection, processing, storage and evaluation of specimens such as blood, placentas, and umbilical cord samples. They are:

1. Analysis of Chemicals in Dried Blood Spots (LOI3-BIO-0)
2. Placenta Studies: Cell Collection, Banking, and Morphology Assessment (LOI2-BIO-20)
3. Collection of Circulating Fetal DNA from Maternal Blood and from Cervical Fluid (LOI2-BIO-24)

The purpose, study design, and intended study outcome(s) are listed below in Table A1.

**Table A1. Formative Research Exemplar Study and Potential Future Projects**

| | **Background/Purpose** | **Study Design** | **Intended Study Outcome(s)** |
|---|---|---|---|
| **Placenta Studies: Cell Collection, Banking, and Morphology Assessment**<br><br>**LOI2-BIO-18** | To determine the impact of the quality of tissue collection on the assessment of placental morphology and detection of possible contaminants. | Study Centers will pilot collection protocols by collecting placentas, umbilical cord samples, and cord blood samples from mothers not geographically eligible for the NCS Vanguard Study. Samples will be shipped to a central processing site and assessed for morphology. | To establish best practice for sample collection and preservation of tissue for stem cell banking, genetics, environmental analyses, and morphology/pathology. This project will help identify the optimum storage conditions for samples and best practices for collecting and processing samples prior to storage |
| **Analysis of Chemicals in Dried Blood Spots**<br><br>**LOI3-BIO-0** | To determine a less invasive and more cost-efficient method of assessing the presence of toxins in children's blood compared to the current practice of venous blood draws | Study participants will have approximately five drops of blood and one 10 cc tube of blood drawn. A 2-question survey asking age and sex will be administered. | To establish a best practice for blood sample collection to assess toxins. This project will help the NCS evaluate potentially less burdensome and more cost-effective methods of sample collection, and will also help the NCS refine available laboratory methods. |
| **Metagenomic Assessment of the Microbiome** | To characterize changes that may occur to the human-associated microbiome throughout early development. | Study Centers will collect a vaginal swab specimens, placental tissue and infant meconium at birth and one | To determine the feasibility of banking microbial specimens with the intent |

| | | | |
|---|---|---|---|
| **LOI2-BIO-20** | | infant stool sample between one month and six months of age. | to continue analysis of the microbiome. This project will help the NCS assess the feasibility, acceptability, and cost of incorporating a specific type of sample collection and associated analyses into the NCS. |
| **Collection of Circulating Fetal DNA from Maternal Blood and from Cervical Fluid**<br><br>**LOI2-BIO-24** | To demonstrate the feasibility, acceptability, and cost associated with the storage and analysis of human cellular and fluid samples to enable efficient nucleic acid sequencing. | Study Centers will collect blood samples at pre-pregnancy, first trimester, third trimester, and post-delivery. Cervical fluid will be collected during the first or third trimester. Infant saliva will be collected by Study Center staff at the postnatal follow-up exam. | To develop methods for the detection, evaluation, and storage of fetal DNA in maternal blood and cervical fluid. This project will help the NCS establish optimum storage conditions and length of viability for these samples. Additionally, this project will enable the NCS to evaluate specific laboratory analyses. |

Forthcoming NCS Vanguard (Pilot) Study generic clearance requests will feature environmental, neuropsychosocial, and study logistic information collections.

### A.3 Use of Information Technology and Burden Reduction

The specific focus of these formative research data collections is the improvement of biospecimen collection procedures and physical measurements for the NCS, and may include computer-assisted interviewing, automated data collection, and other procedures designed to decrease participant burden, study costs, and improve data accuracy. Other appropriate information technology solutions will be embraced to reduce respondent burden and improve data quality. The NCS will use methods that minimize burden and make use of available information technology.

### A.4 Efforts to Identify Duplication and Use of Similar Information

Formative research projects will be utilized as a way to demonstrate proof-of-concept in a manner that minimizes participant burden and study costs, prior to testing in the NCS Vanguard Study protocol if results warrant. For example, formative research projects submitted through this clearance mechanism may evaluate the methods used to measure levels of cortisol activity using hair samples. In this example, if results suggest that cortisol measurement from hair is a more reliable, less burdensome, and more cost-effective measure of stress than buccal cell collection, the NCS may implement the piloted approach in the context of the NCS Vanguard

Study to further test logistics of implementation among a larger, and perhaps more diverse, study population. In this way, formative research projects will not duplicate, but rather, guide NCS Vanguard Study and Main Study information collection.

### A.5 Impact on Small Business and Other Small Entities

The potential impact of these formative research projects on small businesses will include largely health care providers such as physicians, nurses, and others. Local NCS staff may work with physicians and other medical care providers or facilities to provide information about the study to their patients. With the consent of the participant, key medical diagnostic and treatment information on study participants may also be requested of medical providers. Where requested, the study will reimburse providers for any expenses incurred as part of filling requests for information.

### A.6 Consequences of Collecting the Information Less Frequently

These formative research data collections will be conducted as needed on an on-going and concurrent basis, and are designed to decrease participant burden and improve data collection for the both the NCS Vanguard Study (currently on-going) and the NCS Main Study, a crucial requirement given the mandated scope of the Study. Without these small studies, data collection for the NCS is likely to be less efficient than it could be.

### A.7 Special Circumstances Relating to the Guidelines of 5 CRF 1320.5

There are no special circumstances that would cause this information collection to be conducted in a manner inconsistent with 5 CFR 1320.5.

### A.8 Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency

The 60 day Federal Register Notice regarding the NCS is published on pages 23609-23611 of the Federal Register on April 27, 2011.

Two written comments and two verbal comments were received. The verbal comments expressed support for the broad scope of the study. One of the individuals requested additional information about the study, particularly if the study was active in his local geographic area, and additional information was provided. The second verbal commenter requested a more detailed explanation of the formative research program, and expressed satisfaction that the NCS was proposing to do formative research and pilot testing before committing scarce federal taxpayer dollars to the full-scale study.

The two written comments were identical. They opposed the NCS in general, stating that it was too costly, and expressed concerns about the effects of federal programs. The comments are provided below:

I OPPOSE THIS LONGITUDINAL STUDY. I BELIEVE IT IS INEFFECTIVE AND IT IS ALSO TOO COSTLY. AND I DONT BELIEVE THE RESULTS WOULD BE TRUTHFUL BECAUSE THIUS AGENCY HIDES FROM THE PUBLIC. IT HAS SECRET, DECEPTIVE MEETINGS THAT NEVER INCLUDE

MEMBERS OF THE PUBLIC TO SIT IN. IT HAS ALWAYS HAD SECRET MEETINGS WHERE THEY DO WHAT THEY WANT TO DO INSTEAD OF RESPONDING TO WHAT THE PUBOLIC WANTS AS PUBLIC SERVANTS. THIS AGENCY IS IN FACT OUT OF CONTROL. THIS IS MY COMMENT FOR THE PUBLIC RECORD. THIS AGENCY IN FACT HURTS CHILIDREN. 70 DOSES OF VACCINES WITH TOXICES LIKE MERCURY, ALUMINUM FORMALDEHYDE, GELATIN WHICH COULD BE FROM MAD COWS AND OTHER TOXICS ALL INJECTED INTO KIDS. WITH NO REAL CUMULATIVE TESTING AT ALL DONE. I DO NOT WANT ONLY FAT CAT FEDERAL BURAEUCRATS SITTING IN SECRET TO MAKE HEALTH DECISIONS ANY MORE. ALL OF THEIR COMMITTEES SHOULD INCLUDE MEMBERS OF THE AMERICAN PUBLIC, CHOSEN AT RANDOM TO SIT IN TO BRING SOME COMMON SENSE TO WHAT THIS AGENCY IS GETTING AWAY WITH. MEMBERS OF THE AMERICAN PBULIC WITH NO FINANCIAL INTEREST IN DRUGS OR VACCINES SHOUDL SIT IN AS 51% OF ALL MEMBERS OF ANY DECISION MAKING COMMITTEE AND YOU HAVE TO EXPLAIN TO THEM WHAT YOU PLAN. BECAUSE YOUR PLANS ARE GOING COMPLETELY OUT OF CONTROL. WE ARE NOT "HERDS" .WE ARE PEOPLE WITH DIFFERNT SYSTEMS, DIFFERENT DNA, ETC. YOU CANNOT CONSIDER US A "HERD". YOU ALSO SEEM TO BE WANTING TO VIOLATE THE NUREMBERG DECISIONS, WHICH SAID PEOPLE HAVE THE RIGHT TO CONTROL THEIR OWN BODY. WHERE DO YOU GET OFF THINKING YOU CAN INJECT ANYTHING you WANT INTO SOMEBODY'S BODY. THAT IS OUTRAGEOUS. THEY PUT PEOPLE TO DEATH AND IN JAIL IN GERMANY FOR THAT CRAP AND YOU ARE APPROACHING THE SAME STUFF HERE IN AMERICA. THE SAME APPROACH. THE SAME WANTING TO DO TO SOMEBODY'S BODY WHAT YOU WANT. GET OFF IT PLEASE. YOU HAVE CAUSED THE AUTISM EPIDEMIC IN AMEICA AND THEN YOU HIDE FROM INVESTIGATING IT BECAUSE YOU KNOW YOU CAUSED IT.

Response to the comment(s): The National Children's Study was mandated by Congress through the Children's Health Act of 2000 (Public Law 106-310), which states:

*PURPOSE.—It is the purpose of this section to authorize the National Institute of Child Health and Human Development* to conduct a national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children's health and development.*
*(b) IN GENERAL.—The Director of the National Institute of Child Health and Human Development* shall establish a consortium of representatives from appropriate Federal agencies (including the Centers for Disease Control and Prevention, the Environmental Protection Agency) to—*
*(1) plan, develop, and implement a prospective cohort study, from birth to adulthood, to evaluate the effects of both chronic and intermittent exposures on child health and human development; and*
*(2) investigate basic mechanisms of developmental disorders and environmental factors, both risk and protective, that influence health and developmental processes.*
*(c) REQUIREMENT.—The study under subsection (b) shall—*
*(1) incorporate behavioral, emotional, educational, and contextual consequences to enable a complete assessment of the physical, chemical, biological, and psychosocial environmental influences on children's well-being;*
*(2) gather data on environmental influences and outcomes on diverse populations of children, which may include the consideration of prenatal exposures; and*
*(3) consider health disparities among children, which may include the consideration of prenatal exposures.*

The NCS is designed to fulfill the Congressional mandate provided above. The generic clearance requested for formative research will enable the NCS to fulfill these requirements and produce research that benefits the American public, with the lowest possible burden and cost to taxpayers.

### A.9 Explanation of Any Payment or Gift to Respondents

To maximize response rate, many research studies, particularly those involving medical procedures, offer compensation for participants. For example, the National Health and Nutrition Examination Survey (NHANES) has offered their participants compensation since the 1970s. Incentives are effective in increasing response rates for in-person surveys and can help increase response rates especially for minorities and low-income households.

Participants in NCS formative research projects and pilot studies will receive monetary and non-monetary incentives for their time, effort, and any expenses incurred (for example, transportation costs). The incentive amount will be determined by the amount of time required of the participant, as well as the type of activities that will be required. Incentive amounts will be consistent with the approved incentive schedule for the NCS Vanguard and Recruitment Substudy. Participants agreeing to provide biospecimen samples will be offered a monetary incentive or equivalent not exceeding $25. Should a particular formative research project proposed through this generic clearance request testing of a slight modification of the incentive structure described in Table A.1, we will provide appropriate justification in that request. Compensation amounts will be addressed specifically in IRB submissions for each pilot. Small gifts of appreciation for participation may be provided to participants in lieu of cash incentives. These may include items such as t-shirts, tote bags, etc., and are intended as tokens of appreciation.

| **Table A.1. Maximum NCS Incentives, by Study Activity and Impact on Participants** | | | | |
|---|---|---|---|---|
| **Data Collection Activity Characteristics** | **Initial NCS Vanguard Study** | **NCS Recruitment Substudy and Formative Research** | | |
| | | Phase 1 | Phase 2 | Formative Research |
| Time for encounter | 3 hours | 0.5 to 1 hour | 0.5 to 1 hour | 0.5 to 1 hour |
| Sensitivity of questions | Sensitive, including sexual activity | Few sensitive questions | Few sensitive questions | Few sensitive questions |
| Physical measures | Yes | No | No | Yes* |
| Environmental specimens | Yes | No | Yes | Yes* |
| Biospecimens | Yes | No | Yes | Yes* |
| Participant observation | Yes | No | No | No |
| Monetary incentive, per visit | $100 | $25 | $25 for the group of study questionnaires, plus $25, in total, for any bio-specimens collected during a contact and, where appropriate for environmental specimens | $25, in total, for any bio-specimens collected during a contact. For questionnaires, or any environmental specimens – up to $25 when deemed necessary |
| Non-monetary incentives (tote bags, post its, key chains, etc.) | In addition to the monetary incentive, non-monetary incentives valued at $25 or less may be offered to participants | As an alternative to the monetary incentive, NCS logo gifts valued at $25 or less may be offered to the participants in lieu of cash or local incentives not exceeding $25 in value and deemed non-coercive by local | In addition to the monetary incentive, NCS logo gifts valued at $25 or less may be offered to the participants if these are deemed acceptable by local IRBs | Instead of monetary incentives, NCS logo gifts valued at $25 or less may be offered to the participants if these are deemed acceptable by local IRBs |

| | | | | |
|---|---|---|---|---|
| | | IRBs | | |

*Specific information proposed for formative research purposes will align with requested generic clearance mechanisms (that is, the 2008 Generic Clearance, request for Recruitment and Retention projects; 2011 Generic Clearance Request for Biospecimen and Physical Measurements projects, the 2011 Generic Clearance Request for Environmental Science projects, and the 2011 Generic Clearance Request for Study Logistics Projects.)

**A.10 Assurance of Confidentiality Provided to Respondents**

NCS formative research projects will follow the same procedures and standards of confidentiality applicable to the NCS Initial Vanguard Study and Recruitment Substudy. Participants will be informed about the Certificate of Confidentiality granted to NCS to protect data from involuntary disclosure.

The study centers, under contract to conduct the NCS, will have policies and procedures regarding confidentiality and protection of study data which will be reviewed and monitored by the NCS Program Office.

In addition to their own confidentiality procedures and policies, study centers will implement all federally required study-related confidentiality and data security procedures. All NCS Project Office staff, NCS study center staff, and other NCS contracting staff with access to NCS data must receive data confidentiality and security training provided by the NCS Program Office or its agent. These include completion of the NIH Computer Security Awareness Training, completion of a Human Subjects Protection Training, and signing an Assurance of Confidentiality or similar pledge that NCS data will only be used for the intended scientific purpose. All NCS Staff are required to complete security background checks consistent with Office of Personnel Management requirements. Only those cleared for Security Level D or higher will be eligible to request NCS data access.

To further assure confidentiality of participant data, the study will employ rigorous methods to provide security for personal identifying information. Each study center and the NCS Program Office Data Warehouse will be required to submit an NCS Security Plan and Assessment that complies with the Federal Information Security Management Act (FISMA). This Security Plan will include: a) certification and accreditation of proposed data capture and case management software; b) configuration of those systems on study equipment; c) full disk encryption and two-factor authentication of study computers housing NCS data; and d) security assessment of the physical computing environment. After study centers complete the self-assessment of their security plans, the NICHD Chief Information Officer will review all study center security plans to determine study center's authority to operate. Frequent and regular monitoring visits will assist in compliance with these terms.

Privacy Impact Assessments will be conducted prospectively and recurrently as needed.

Specific NCS data and materials to be collected, disclosure review, and data access are described in detail in the Data Access and Confidentiality Committee Manual. Principles and policies are available at http://www.nationalchildrensstudy.gov/about/organization/dacc/Pages/

PolicyManualandDataUseAgreements.aspx; the manual is available to the public upon request. Specifically, all NCS data files will undergo disclosure review for personally identifiable information, using procedures consistent with or exceeding those named in Working Paper 22 of the Federal Committee on Statistical Methodology, and steps will be taken to appropriately manage disclosure risk. For example, genome-wide scans conducted on NCS specimens will be considered personally identifiable information and treated as such. Some biologic analyses (for example, HIV status, exposure to specific toxicants), results of some mental health screening tests, and reports of abuse are also considered sensitive.

### A.11 Justification for Sensitive Questions

There are a number of questions that may be contained in NCS formative research questionnaires that could be considered sensitive such as pregnancy status, reproductive and medical histories, and income. As part of the informed consent process, women will be informed that their participation in NCS is voluntary and that they may refuse to answer any question. Fathers and other family members may also be asked to participate through the informed consent process. All study questionnaires that would be proposed for formative research under this clearance mechanism have been or will be reviewed by Human Subjects Review Boards at NICHD and participating institutions.

Each of these sensitive questions is necessary to allow comparisons between the formative research sample and persons potentially eligible for the Main Study, thereby informing whether proposed questionnaire items and biospecimen collections would warrant further testing in the NCS Vanguard Study.

### A.12 - 1 Estimates of Hour Burden

**Table A.2 Estimated Hour Burden for Biological and Physical Measures**

| Data Collection Activity | | Type of Respondent | Estimated Number of Respondents | Estimated Number of Responses per Respondent | Average Burden Hours Per Response | Estimated Total Annual Burden Hours |
|---|---|---|---|---|---|---|
| Blood | Adult | NCS participants | 4,000 | 1 | 0.5 | 2,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.5 | 2,000 |
| | Infant/ Child | NCS participants | 2,000 | 1 | 0.5 | 1,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.5 | 1,000 |
| Urine | Adult | NCS participants | 4,000 | 1 | 0.25 | 1,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.25 | 1,000 |
| | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS | 2,000 | 1 | 0.25 | 500 |

| Data Collection Activity | | Type of Respondent | Estimated Number of Respondents | Estimated Number of Responses per Respondent | Average Burden Hours Per Response | Estimated Total Annual Burden Hours |
|---|---|---|---|---|---|---|
| | | target population (not NCS participants) | | | | |
| Hair | Adult | NCS participants | 4,000 | 1 | 0.25 | 1,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.25 | 1,000 |
| Nails | Adult | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Cervi-cal Fluid | Women | NCS participants | 4,000 | 1 | 0.5 | 2,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.5 | 2,000 |
| Breast Milk | Women | NCS participants | 4,000 | 1 | 0.5 | 2,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.5 | 2,000 |
| Cord Blood | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Meco-nium | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Placenta | Infant | NCS participants | 4,000 | 1 | 0.25 | 1000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.25 | 1000 |
| Length | Infant | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Height | Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Weight | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population | 2,000 | 1 | 0.25 | 500 |

| Data Collection Activity | | Type of Respondent | Estimated Number of Respondents | Estimated Number of Responses per Respondent | Average Burden Hours Per Response | Estimated Total Annual Burden Hours |
|---|---|---|---|---|---|---|
| | | (not NCS participants) | | | | |
| Head Circum-ference | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Middle Upper Arm Circum-ference | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Ulnar Length | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | 500 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | 500 |
| Small, focused survey and instrument design and administration | | NCS participants | 4,000 | 2 | 1 | 8,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 2 | 1 | 8,000 |
| | | Health and Social Service Providers | 2,000 | 1 | 1 | 2,000 |
| | | Community Stakeholders | 2,000 | 1 | 1 | 2,000 |
| Focus groups | | NCS participants | 2,000 | 1 | 1 | 2,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 1 | 2,000 |
| | | Health and Social Service Providers | 2,000 | 1 | 1 | 2,000 |
| | | Community Stakeholders | 2,000 | 1 | 1 | 2,000 |
| Cognitive interviews | | NCS participants | 500 | 1 | 2 | 1,000 |
| | | Members of NCS target population (not NCS participants) | 500 | 1 | 2 | 1,000 |
| **Total** | | | **113,000** | | | **60,000** |

## A.12 - 2 Annualized Cost to Respondents

**Table A.3 Estimated Cost for Biological and Physical Measures**

| Data Collection Activity | | Type of Respondent | Estimated Number of Respondents | Estimated Number of Responses per Respondent | Average Burden Hours Per Response | Hourly Wage Rate | Estimated Total Annual Respondent Cost |
|---|---|---|---|---|---|---|---|
| Blood | Adult | NCS participants | 4,000 | 1 | 0.5 | $10.00 | $20,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.5 | $10.00 | $20,000 |
| | Infant/ Child | NCS participants | 2,000 | 1 | 0.5 | $10.00 | $10,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.5 | $10.00 | $10,000 |
| Urine | Adult | NCS participants | 4,000 | 1 | 0.25 | $10.00 | $10,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.25 | $10.00 | $10,000 |
| | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Hair | Adult | NCS participants | 4,000 | 1 | 0.25 | $10.00 | $10,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.25 | $10.00 | $10,000 |
| Nails | Adult | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Cervi-cal Fluid | Women | NCS participants | 4,000 | 1 | 0.5 | $10.00 | $20,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.5 | $10.00 | $20,000 |
| Breast Milk | Women | NCS participants | 4,000 | 1 | 0.5 | $10.00 | $20,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.5 | $10.00 | $20,000 |
| Cord Blood | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Meco- | Infant/ | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |

| Data Collection Activity | | Type of Respondent | Estimated Number of Respondents | Estimated Number of Responses per Respondent | Average Burden Hours Per Response | Hourly Wage Rate | Estimated Total Annual Respondent Cost |
|---|---|---|---|---|---|---|---|
| nium | Child | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Placenta | Infant | NCS participants | 4,000 | 1 | 0.25 | $10.00 | $10,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 1 | 0.25 | $10.00 | $10,000 |
| Length | Infant | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Height | Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Weight | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Head Circum-ference | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Middle Upper Arm Circum-ference | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Ulnar Length | Infant/ Child | NCS participants | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| | | Members of NCS target population (not NCS participants) | 2,000 | 1 | 0.25 | $10.00 | $5,000 |
| Small, focused survey and instrument design and administration | | NCS participants | 4,000 | 2 | 1 | $10.00 | $80,000 |
| | | Members of NCS target population (not NCS participants) | 4,000 | 2 | 1 | $10.00 | $80,000 |
| | | Health and Social Service Providers | 2,000 | 1 | 1 | $10.00 | $20,000 |
| | | Community Stakeholders | 2,000 | 1 | 1 | $10.00 | $20,000 |
| Focus groups | | NCS participants | 2,000 | 1 | 1 | $10.00 | $20,000 |
| | | Members of NCS | 2,000 | 1 | 1 | $10.00 | $20,000 |

| Data Collection Activity | Type of Respondent | Estimated Number of Respondents | Estimated Number of Responses per Respondent | Average Burden Hours Per Response | Hourly Wage Rate | Estimated Total Annual Respondent Cost |
|---|---|---|---|---|---|---|
| | target population (not NCS participants) | | | | | |
| | Health and Social Service Providers | 2,000 | 1 | 1 | $10.00 | $20,000 |
| | Community Stakeholders | 2,000 | 1 | 1 | $10.00 | $20,000 |
| Cognitive interviews | NCS participants | 500 | 1 | 2 | $10.00 | $10,000 |
| | Members of NCS target population (not NCS participants) | 500 | 1 | 2 | $10.00 | $10,000 |
| **Total** | | **113,000** | | | | **$600,000** |

### A.13 Estimate of Other Total Annual Cost Burden to Respondents or Recordkeepers

Participants will be reimbursed for any expenses resulting from their participation in formative research. This may include transportation costs to and from activities, and babysitting or elder care expenses. There are no other known costs to participants.

### A.14 Annualized Cost to the Federal Government

The estimated cost to the federal government for these pilot and formative studies is $600,000 per year over the three year period.

### A.15 Explanation of Program Changes or Adjustments

This request proposes a new data collection.

### A.16 Plans for Tabulation and Publication and Project Time Schedule

The proposed data collections include biospecimen collection, physical measurements, focused survey and instrument design and administration, focus groups, and cognitive interviews intended to increase data and biospecimen collection efficiency for the NCS. Each formative research project will adhere to a customized information collection evaluation and publication schedule, among other study deliverables. The studies will take place over the three year period specified in this submission.

### A.17 Display of Expiration Date of OMB Approval

The NCS is not seeking an exemption from displaying the expiration date of OMB approval.

### A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

The NCS is not requesting any exceptions.