REQUEST FOR OMB CLEARANCE
Provider-Based Sampling Feasibility Study for the Vanguard (Pilot) Study and Data Collection Updates for the National Children's Study (NICHD)

Part A only

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A. Justification

A.1 Circumstances Making the Collection of Information Necessary

Legislative Mandate

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 *Eunice Kennedy Shriver* 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.

1. 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 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. "

This national longitudinal study, termed the National Children's Study [NCS], is required by law to include 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."

Purpose of Vanguard (Pilot) Study

The NCS Vanguard (Pilot) Study (OMB #0925-0593) was approved 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 (Pilot) 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. Currently, the design of the Main Study is being informed by the experience obtained in the Initial Vanguard Study, combined with data from the Alternate Recruitment Substudy.

Purpose of this Submission

The National Children's Study is an integrated system of activities that includes a Vanguard (Pilot) Study for operations and methods development, and an NCS Main Study to collect data on exposure and response. The Vanguard (Pilot) Study, which includes the Initial Vanguard Study, the Alternate Recruitment Substudy (Phases 1 and 2), and the Provider-Based Sampling Feasibility Study (proposed in this information collection request), is currently underway. The Main Study is expected to follow within the next year. This request for revision includes (1) the addition of a Provider-Based Sampling Feasibility Study, and (2) supplemental measures for the Alternate Recruitment Substudy involving revised study visit assessments, physical measurements, and additional biospecimen collections. These information collections, revisions of instruments, physical measure implementation, and biospecimen collections will evaluate the feasibility, acceptability, and cost of study design elements to inform the Main Study.

History of the NCS Vanguard (Pilot) Study Data Collection Activities

NCS Initial Vanguard Study

In 2009, the NCS began data collection in the Initial Vanguard Study at 7 locations, within Primary Sampling Units (PSUs, or counties). The Initial Vanguard Study protocol was designed to enroll approximately 1,750 pregnant women residing within selected geographic segments of the Primary Sampling Units termed Secondary Sampling Units at the seven study locations after 12 months of data collection using a household enumeration and screening strategy to identify eligible women for recruitment. As of May 2010, however, approximately 900 pregnant women had been enrolled, signaling that the initial approach of conducting a household survey would take much longer than intended, resulting in increased costs and delays in implementing the critical data collection for the NCS. In total, approximately 1,100 participant families were enrolled during the Initial Vanguard Study phase of the Vanguard (Pilot) Study.

Alternate Recruitment Substudy Phases 1 and 2

Based on data analysis from the Initial Vanguard Study, the NCS designed an approach termed the Alternate Recruitment Substudy (ARS) to systematically explore three recruitment strategies based on how members of the public were informed of the Study: 1) Provider-Based Recruitment; 2) Enhanced Household-Based Recruitment; and, 3) Two-Tiered "High-Intensity/Low-Intensity" Recruitment. The guiding research goal for the ARS was to characterize recruitment strategies that could be used to identify, recruit, and enroll eligible participants into a population-based cohort study. A secondary goal of the ARS was to systematically determine the effect of how initial contact between the public and the Study influenced recruitment. The comparison was between initial contact with a trusted individual (health care provider – Provider-Based Recruitment), with a stranger (NCS field worker – Enhanced Household-Based Recruitment), and with direct outreach through media and staged events (Two-Tiered "High-Intensity/Low-Intensity" Recruitment). Each of these three recruitment strategies was

implemented in 10 locations for a total of 30 locations. Coupled with the seven study locations collecting data in the Initial Vanguard Study, information collection occurred at a total of 37 locations in the Vanguard (Pilot) Study.

Phase 1 of the ARS involved the administration of questionnaires at each study visit and began in July 2010 when the NCS obtained clearance from OIRA. Phase 2 of the ARS added a questionnaire targeted to fathers and introduced biospecimen and environmental sample collections. Twenty-two of 37 study locations began biospecimen and environmental sample collection during the fourth quarter of 2011.

From July 2012 through December 2012, data collection at the seven Initial Vanguard locations will be conducted by a single contract research organization. This transition coincides with the expiration of the seven Study Center contracts and the gap until the award of new contracts for administration of the Vanguard (Pilot) Study. New contract awards are expected in September 2012 with data collection activities beginning in January 2013. For a period of 6 months, approximately 1,100 children will be followed via telephone or other remote data collection modes. The NCS intends to re-consent these participant families. While the number of Study visits varies by the age of the child, on average, each enrolled participant will be administered a single questionnaire by telephone. The questionnaire will be the age-appropriate visit, as approved by OIRA. All study locations involved in the NCS Vanguard Study will continue to follow Study participants enrolled at their study locations for the next two decades.

Table A.1.1 History of NCS Vanguard (Pilot) and Main Study Data Collection Activities

	Date Approved by OIRA	**Number of Study Locations**	**Approved Primary Data Collection Activities**	**Proposed Primary Data Collection Activities**
Vanguard (Pilot) Study				
Initial Vanguard Study	09/22/2008	7	Study visits and questionnaires from preconception to 24 months	*Re-consent of 1,100 participant families and continued follow-up of participants
Alternate Recruitment Substudy (ARS) (Phase 1)	07/23/2010	30; 15 study locations from the ARS are currently implementing biospecimen and environmental sample collection	*Pilot testing three recruitment strategies (Provider-Based Recruitment, Enhanced Household-Based Recruitment, Two-Tier High/Low Intensity Recruitment) *Minimal study visits and questionnaires from preconception to 24 months	*Discontinuation of recruitment for three ARS recruitment strategies *Continued follow-up of participants recruited during ARS Phases 1 and 2 *Additional post-birth biospecimen collections (Phase 2 only) *Physical measure collections
Alternate Recruitment	04/13/2011		Addition of biospecimen and	

	Date Approved by OIRA	Number of Study Locations	Approved Primary Data Collection Activities	Proposed Primary Data Collection Activities
Substudy (Phase 2)			environmental collections, father interview	
Provider-Based Sampling (PBS) Feasibility Study	Pending	3	N/A	*Addition of Provider-Based Sampling *No preconception data collection activities for PBS participants *No Father Interview for PBS participants *No biospecimen and environmental sample collection for PBS participants *No physical measure collection for PBS participants
NCS Main Study				
Main Study	Anticipated 2013	Unknown	Unknown	N/A

Table A.1.1 outlines the history of the NCS Vanguard (Pilot) and Main Study data collection activities between 2008 and the present. The table briefly describes OIRA clearance dates, number of study locations at each phase, primary data collection activities during each phase, and data collection activities proposed in this information collection request. Phase 2 expanded data collection activities (including sample and physical measures collections) will be performed by the following study locations:

Provider-Based Recruitment study locations (ARS): Durham County, NC; Hinds County, MS; Lamar County, TX; Schuylkill County PA; Wayne County, MI

Enhanced Household-Based Recruitment study locations (ARS): Baker County, FL, Cumberland County, ME; Cuyahoga County, OH; Polk County, IA; St. Louis, MO

Two-Tier High/Low Intensity Recruitment study locations (ARS): Baldwin County, GA; Cache County, UT; Davidson County, TN; Douglas County, CO; Westmoreland County, PA
The fifteen study locations conducting Phase 2 expanded data collection were selected based on several criteria including readiness to collect environmental samples and biospecimens, physical measures, and the father interview, quality of prior data submissions, and number of participants.

Preliminary Results from the ARS

The preliminary results indicate that each recruitment strategy differs in efficiency (the number of women contacted compared to the number enrolled) and that each strategy has different biases.

Overall, the Provider-Based Recruitment strategy was the most efficient with about 2 women contacted for each woman enrolled and the highest proportion of women who were enrolled during pregnancy. Details can be seen in Table A.2.1.

Table A.1.2: Overall Summary of NCS Recruitment Substudy as of June 14, 2012

Selected Measures from the Alternate Recruitment Substudy	Provider-Based Recruitment	Enhanced Household-Based Recruitment	Two-Tier High/Low Intensity Recruitment
A. Women eligible for contact	3600	27750	19350
B. Women Contacted for Pregnancy Screen (% of eligible)	3200(89%)	22050(79%)	19300 (99%)
C. Women Completing Screen (% of contacted)	2100 (66%)	20400 (93%)	15850 (82%)
D. Women Pregnant or Trying (% of screened)	1600(76%)	2600 (13%)	2800 (18%)
E. Women Enrolled (% of pregnant or trying)	1250(78%)	1600 (63%)	2250 (80%)
F. Babies Enrolled	850	750	900
Women contacted/women enrolled	2.9	13.8	8.6
Proportion of enrollees pregnant at the time of enrollment	89%	52%	50%

For Provider-Based Recruitment, about 175,000 addresses were pre-screened using an Address Lookup Tool to identify the 3,350 women potentially eligible based on residence in a Secondary Sampling Unit (SSU, or segments within a PSU) for the Provider-Based Recruitment strategy. The Address Lookup Tool only provides an approximate indication of whether a woman resides within an NCS SSU. About 66% of the women contacted for the Pregnancy Screener completed the pregnancy screen. The 34% difference between women contacted and women who completed the Pregnancy Screener was primarily due to additional women who were deemed ineligible for participation based on having an address outside an SSU.

Given that the ARS aimed to characterize recruitment strategies and its components that are effective in identifying, recruiting, and enrolling eligible participants into a population-based cohort study, and to determine the effect of how initial contact between the public and the Study influenced recruitment, the NCS used the preliminary data to conclude that sufficient data were collected to be analyzed to design next steps. Consequently, the NCS halted ARS recruitment (Provider-Based Recruitment, Enhanced Household-Based Recruitment, Two-Tier Recruitment) in February 2012.

NOTE: New Data Collections and Updates to the National Children's Study (NICHD)

Provider-Based Sampling Feasibility Study for the Vanguard (Pilot) Study

The NCS Program Office began in April 2011 a series of consultations including open public meetings to solicit input on the design of the Main Study using recruitment by health care providers. In the spring of 2012 the NCS Program Office integrated the advice and input to develop a proposal for a recruitment model that is based upon a layered cohort approach. The initial sampling frame would be based on geographic areas. Following selection of geographic areas using a probability based approach, hospitals that provided delivery services and birthing centers would be enumerated and listed within each selected area. From that list, again using a probability based approach, hospitals and birthing centers would be selected to recruit a birth cohort. In addition, prenatal care providers associated with the selected facilities would be listed to enroll a second cohort of pregnant women. The selection of prenatal providers and pregnant women would also use a probability based approach.

To better understand the potential efficiencies and processes of a prenatal care provider-based model and relate it to the proposed Main Study approach, the NCS proposes a new approach to eliminate the recruitment limitation of requiring participants to reside within small geographic SSUs, and instead, base the geographic eligibility on residing within the larger PSU. In addition, we propose using either the birth visit or the initial prenatal visit as a screening tool to allow for a uniform probability of selection of participants, and to target a decrease in the gestational age at recruitment for pregnant women when compared to the earlier NCS Vanguard Study Provider-Based Recruitment arm. Therefore, the NCS would like to improve upon the Provider-Based Recruitment strategy by screening potential participants by provider location, age eligibility, and residence in the sampled Primary Sampling Unit (PSU), confirmed pregnancy, and either scheduled with a prenatal care provider for an initial prenatal visit or present at a selected facility for birth (Provider-Based Sampling). <u>In this pilot, a Provider can be an individual (physician, midwife, nurse practitioner, or physician assistant), an office-based practice or a facility, including hospitals and birthing centers. We intend to assign office or clinic based practices that will enroll pregnant women in a prenatal cohort and hospitals and birthing centers that will enroll women during the perinatal period to separate strata.</u>

The NCS proposes to systematically assess the feasibility, acceptability, and cost of Provider-Based Sampling. In this strategy, a list of prenatal care providers who serve women residing in a specific PSU will be compiled using a variety of data sources, such as birth records and licensing information. In some cases, using the Provider-Based Sampling Frame Questionnaire, identified providers will supply practice characteristics and the measure of size (MOS) for their practice location(s). This information (practice characteristics and MOS) will be used in the systematic selection of providers from the larger list frame. Selected provider locations will be invited to serve as recruitment sites for the enrollment of pregnant women in the NCS. Procedures for recruiting pregnant women will be the same as those procedures that were fielded in the Provider-Based Recruitment (PBR) arm of the Vanguard Study Alternate Recruitment (ARS) Substudy. Data collected during the participant study visits will be the same as those approved by OIRA and implemented in the ARS, excluding preconception activities and Phase 2 expanded collection activities (biospecimen and environmental sample collection, physical measures collection, and the

Father Interview, see Table A.1.1). In the Vanguard (Pilot) Study Request for Renewal in 2013, we will request approval for sample collection, physical measures, and the Father Interview for the PBS cohort.

Developing the Sampling Frame

The NCS proposes to determine if adopting a provider-based sampling approach is feasible, and if such an approach could provide decreased cost, increased acceptability, and overall a more flexible model for NCS recruitment. Three additional study locations have been selected to pilot this approach in their respective Study Locations (PSUs). Based on information from the ARS, the NCS believes that three PSUs is the appropriate sample size needed to determine if the provider-based sampling approach is feasible and efficient. Use of three PSUs fits within NCS's budget and emphasis on improving efficiency in field operations, while imposing the minimum public burden to achieve the purposes of the feasibility study.

The following are examples of data sources that will be used to compile lists of prenatal providers:

1) Publicly-available datasets that list delivery hospitals, medical insurance providers, public clinics, academic medical institutions and professional organizations.
2) Birth records that include named "Birth Attendant" and "Birth Attendant Address," which may allow for a compilation of area prenatal care providers.
3) Publicly-available datasets from Web sites, phone directories, local medical society directories, to confirm provider practice location status (for example, has the provider retired, moved, or altered the focus of the practice?).

Determining Measure of Size (MOS) and Selecting Provider Locations

We will determine MOS for each provider location using any or all of the following methods:

1) An initial postcard or letter mailing to each provider location, introducing the Study, alerting them to the fact than an NCS staff member will be contacting them, and providing NCS contact information.
2) Telephone calls to provider locations to further introduce the Study, explain the Provider-Based Sampling Frame Questionnaire, and identify the provider's preferred mode of questionnaire administration. Data collection modes may include telephone administration by field staff, in-person administration by field staff, a mailed self-administered questionnaire (SAQ), or a combination of these. During this process, Study Locations will begin building a relationship with each provider location.
3) Based on identified provider preferences, Study Locations will conduct in-person or telephone interviews with office managers, administrators, or prenatal care providers at each location to complete the Provider-Based Sampling Frame Questionnaire for each location. As needed, the Provider-Based Sampling Frame Questionnaire may be sent directly to provider practice locations for completion as a self-administered questionnaire (SAQ). Study location outreach staff to monitor receipt of questionnaires, and follow-up as necessary with the lead person of the provider location until all questionnaires are collected.

4) MOS (the estimated number of first prenatal care visits from women who reside in the sample PSU) for each provider location will be computed based on data obtained from the Provider-Based Sampling Frame Questionnaire, geocoding, and other available data sources.
5) Once the sampling frame is constructed and following probability statistical parameters (see Supporting Statement B. 1), we will select a subset of provider locations to invite to serve as recruitment locations for Provider-Based Sampling effort.

Recruiting Study Participants in the PBS

Recruitment of Study participants at the selected provider locations will follow the protocol and procedures developed for the Provider-Based Recruitment (PBR) arm of the ARS, as previously approved by OIRA. However, participants will not participate in preconception activities, and this new approach will not require screening of large numbers of addresses, as we would no longer need to identify women living in selected SSUs. Instead, potential participants will be screened only on age eligibility, residence in the sampled PSU (county), confirmed pregnancy, and appearance for an initial prenatal visit (Pregnancy Visit 1) using the Provider-Based Sampling Eligibility Screener. In some locations, medical records may be pre-screened to identify participants meeting these eligibility criteria. Post-enrollment, PBS participants will be administered the previously-approved Pregnancy Visit 1 instrument if appropriate and receive all subsequent Study Visits already in use in the ARS (excluding the Father Interview). Unlike earlier arms of the NCS Vanguard (Pilot) Study, PBS participants will not be enrolled prior to pregnancy and will not participate in preconception activities.

The recruitment goal for this feasibility study will be 250 births per PSU. Based on our experience from the Provider-Based Recruitment (PBR) strategy of the ARS, about 80% of identified eligible women agreed to enroll in the NCS. Assuming an 80% enrollment rate and an estimated attrition rate of 20% (from pregnancy loss and participant attrition through birth), we estimate that about 400 eligible women will need to be invited to participate in each PSU in order to achieve the desired number of 250 births per PSU in this feasibility study. Pilot testing Provider-Based Sampling will allow the NCS to understand the feasibility, acceptability, and cost of this recruitment approach, and will provide a comparison of response and retention rates between Provider-Based Sampling (PBS) and Provider-Based Recruitment (PBR).and to quantitatively establish the ability to recruit women more efficiently and economically using this approach.

Prior to posting a 60-day Federal Register notice for the Main Study, we will acquire at least 4 months of recruitment data using the Provider-Based Sampling Frame approach described above to meet the target of inviting 1,200 pregnant women across the three Study Locations to participate in the Study, enrolling 960 pregnant women at the first prenatal care visit. We estimate an 80% participant retention rate for pregnant women from the first prenatal care visit to the birth of the child, and assuming for this calculation that all of the enrolled women were enrolled in the prenatal stratum, resulting in approximately 750 births during the entire feasibility study. Note that the actual number of births is dependent upon the number of provider locations that agree to serve as recruitment locations for the PBS.

Through our experience in the Vanguard (Pilot) Study, we learned that ‘steady state’ in terms of stabilization of recruitment and early retention efforts was achieved in 9 months or less following initiation. Prior to posting a 30-day Federal Register notice for an OMB submission related to the Main

Study, we would have 6-8 months of data on recruitment and retention of participants through birth to assess success of this approach. These data, in combination with what is still being tested in the Vanguard (Pilot) Study, will add to our broader understanding of the drivers of early participant retention.

Supplemental Information and Biospecimen and Physical Measures Collections for the Continuing ARS

This ICR revision also covers the following activities associated with the NCS Vanguard Study:

1) Extend data collection for the children who have been recruited into the NCS Vanguard Study up to 30 months of age of the child by introducing the Core Questionnaire at the 30-Month Interview
2) Supplemental data collection designed to update and validate existing data collection include the introduction of validation questions for the 18-, 24-, and 30-Month Interviews, a revised Father Interview, and a new Nonrespondent Questionnaire.
3) Other previously-approved study assessment questionnaires have been modified based on feedback from field workers and are included in this information collection
4) Finally, physical measures that were initially approved for the Initial Vanguard Study (first seven study locations) and envisioned to eventually be added for the participants recruited through the Alternate Recruitment Substudy (30 study locations, excluding Two-Tier Low-Intensity participants) will be initiated at this point in time. Specifically, breast milk collection will be re-introduced at 1 and 3 months, and collection of infant urine, saliva, and blood will begin at the 6- and/or 12-month visits. At this time, biospecimen, environmental samples, physical measures, and the Father Interview will not be collected at the Provider-Based Sampling study locations. Further detail on these changes can be found in A.2 (Purpose and Use of the Information Collection) and B.2 (Procedures for the Collection of Information.

A.2 Purpose and Use of the Information Collection

The Initial Vanguard Study and the ARS have yielded valuable data and field experience regarding the robustness, participant and study infrastructure burden, and cost of piloted study visit measures. As the Study continues, the NCS Program Office has identified additional measures for piloting before consideration for implementation in the NCS Main Study. Among the piloted items is the Provider-Based Sampling Feasibility Study. The main goals of the Provider-Based Sampling Feasibility Study are:

1) To learn how to develop a list frame of providers. The specific details on the sources used for the lists of providers and how each Study Center involved in Provider-Based Sampling compiles this information will be used to provide information on the list frame development process.
2) To examine the efficiencies of recruiting pregnant women, including how early in pregnancy they can be recruited. This will help the NCS calibrate expectations for Main Study recruitment activities and the likelihood of collecting data on early prenatal exposures.
3) To generate data on cost.
4) To generate data on costs associated with developing sampling frames of providers, gaining cooperation of providers, identification and enrollment of participants, and implementation of Study Visits.

5) To establish participation rates of providers, including willingness to provide information requested by the Provider-Based Sampling Frame Questionnaire, and, if selected, to serve as a NCS recruitment location.
6) To compare the efficiency, demographics, quantity and quality of environmental exposure information and retention of populations of women perinatally with women recruited early in pregnancy.

The purpose of the overall proposed data collection is to obtain operational and performance data on processes, new measures, and study visit activities. In combination, the substudies encompassed by the Vanguard (Pilot) phase will be used to inform the design of the NCS Main Study. The Main Study will provide the data needed to evaluate exposure-response relationships.

Provider-Based Sampling Feasibility Study for the Vanguard (Pilot) Study

Provider-Based Sampling Frame Questionnaire: We will ask selected providers within the PSU to complete a brief questionnaire about their practice and their patient demographics. We will use information from this questionnaire to further develop the sampling frame and, in particular, will request the number of births attended by each practice or occurring at each facility as a measure of size (MOS) and information to be used in forming strata (e.g. geographic location of the study office, hospital or birthing center or demographic characteristics of the patient population).

Provider-Based Sampling Eligibility Screener: We will use this instrument to determine if a woman is eligible for participation for Provider-Based Sampling. Variables include the age of the potential participant, pregnancy status, county of residence, and whether or not the indexed visit is the first prenatal care visit. The instrument also captures demographic information to allow characterization of the population approached and comparisons of eligible and ineligible respondents.

Supplemental Measures for the Vanguard (Pilot) Study involving Study Visit Assessments Using a Core Questionnaire

We propose pilot use of a Core Questionnaire containing important variables designed to collect core data at every study visit from the time that the enrolled child is 6 months of age to the time the child is 5 years of age. Use of this instrument would allow consistent collection of housing characteristics and composition, neighborhood features, childcare arrangements, and healthcare utilization and access. Additional content of the Core Questionnaire includes sleeping patterns, medication assessment, and parental occupation and income. Along with this questionnaire, the respondent would complete age -or special topic modules (see 30-Month Interview Module). We propose piloting the Core Questionnaire at the 30-Month Interview. Results of this pilot will inform whether to incorporate the Core Questionnaire in existing and future visits.

Infant Race and Ethnicity: We ask to include a mother-reported measure of race/ethnicity for infants enrolled in the NCS Vanguard Study. The measures (variable BC007B/ETHNICITY; BC007C/RACE) are the same as that approved by OIRA (7/22/2010) to measure adult race/ethnicity. These would be included in the Birth Interview and the Birth Instrument for Two-Tier Low-Intensity. This information is necessary to comply with IRB reporting requirements at the time of continuing review.

30-Month Interview Module: We propose piloting the use of an age-specific module along with the Core Questionnaire at the 30-Month Interview. Constructs to be collected for this interview were developed with input from the study locations who offered expertise.

After collection of data from the 30-Month Interview, the NCS will analyze the feasibility, acceptability, and cost of this visit as a whole, as well as specific measures of mental health and neurodevelopmental outcomes. The age-specific modules include questions that measure constructs particularly relevant at that age. Some of these constructs are measured with a series of questions (such as parenting practices at a given age) while others are measured with previously validated assessment tools. Two instruments that have been chosen to obtain information about key dimensions in children's earliest development at the 30-month data collection are the Brief Infant/Toddler Social and Emotional Assessment (BITSEA), and the Infant-Toddler Sensory Profile. Both measures are completed by the parent/caregiver about the child. These measures were selected because they each uniquely obtain information about discrete aspects of child behavior, they are psychometrically sound, and they can be completed by the parent/caregiver on the basis of their observations about the child's typical behaviors. In addition, a third measure, the Brief Symptom Inventory-Revised (BSI-R), was chosen to obtain information about parent/caregiver mental health, which may contribute to, may moderate, or may alleviate children's problem behaviors (such as parental depression) that have been shown to negatively affect children's development. The BSI-R is completed by the parent/caregiver about his/her own mental health. A description of each of the selected standard assessments is provided below.

There are two learning objectives associated with administration of the BITSEA, the Infant Toddler Sensory Profile and the Brief Symptom Inventory. The first objective is to obtain information about feasibility, acceptability and cost of administration of each of these tools within the context of the NCS. This will be assessed by looking at unit response rates, item response rates, and participant reactions to the various assessments (captured in interviewer comments and debriefings). The second objective is to determine whether responses obtained are consistent with what would be expected from the literature and in comparison with publisher norms.

- *Brief Infant/Toddler Social and Emotional Assessment (BITSEA)* - The BITSEA is a screening instrument designed to be completed by the parent/caregiver to identify children at-risk or currently experiencing social-emotional or behavioral problems, or delays in social-emotional competence. It assesses children's social-emotional competence, problem behaviors such as externalizing and internalizing behaviors, and behavioral and emotional dysregulation (such as sleep disturbances, eating difficulties, and negative emotionality). Social-emotional competence evolves over time and can be measured with the BITSEA beginning at 12 months. The NCS already includes the BITSEA as part of the 12-Month Interview. With this ICR, we propose including the BITSEA in the 30-Month Visit as well, to establish a trajectory of development for this construct. It is estimated that it will take the parent/caregiver approximately 10 minutes to complete this questionnaire.
- *Infant Toddler Sensory Profile* - The Infant/Toddler Sensory Profile is completed by the parent/caregiver measuring children's responses to sensory events in daily life. Young children's sensory processing can reveal sensitivities and difficulties that have been associated with the later diagnosis of ADHD and other learning disabilities. By 30 months of age, sensory responses may be consolidating into patterns of difficulties that have enduring effects on development,

particularly cognitive development. The Infant/Toddler Sensory Profile is estimated to take under 15 minutes for the parent/caregiver to complete.

- *Brief Symptom Inventory-Revised* - The Brief Symptom Inventory-Revised (BSI-R) is a 53-item inventory that covers nine symptom dimensions about the respondent: Somatization, Obsession-Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic anxiety, Paranoid ideation and Psychoticism; and three global indices of distress: Global Severity Index, Positive Symptom Distress Index, and Positive Symptom Total. We are interested in testing the BSI as a measure of parental mental health that could be administered during pregnancy and again during the child's early years. The BSI-R was chosen to be included at the 30-month data collection because parent/caregiver mental health functioning is an important contributor to young children's development and may mediate or exacerbate any difficulties that children may be experiencing. It is estimated that the BSI-R will require about 10 minutes for the parent/caregiver to complete.

Validation Questions for 18, 24 and 30 month: The administration of a validation questionnaire following a study visit is a well-established field practice designed to monitor interviewer performance and identify occurrences of data falsification. Questions have been added to the validation questionnaire that currently covers prenatal visits through 12 months. We propose addition of brief telephone-based questions that would be fielded to a random sample of each interviewer's cases after completion of the 18-Month, 24-Month, and 30-Month Interviews. Each set of questions would confirm the administration of a study visit, include one or two questions asked in the original instrument that should yield a consistent answer from participants, and allow participants the opportunity to provide additional feedback on the interviewer and the Study.

Nonrespondent Questionnaire: It is critical for the NCS to understand the characteristics and attitudes of enrolled women, those who withdraw, as well as those who choose not to enroll. This information may be used to revise our approaches to recruitment and will help the Study frame other systematic analyses of nonresponse bias. The Nonrespondent Questionnaire is designed to be interviewer-administered in-person, by telephone, via web, or by mail, and will collect information on why a participant chose to not enroll in or to withdraw from the NCS. The instrument will assess the impact of family and health care providers and key study characteristics (for example, biospecimen collection or sensitive questions) on the decision-making process. The instrument asks generally about the collection of biospecimens and allows the respondent an opportunity to provide unstructured comments and feedback to the NCS. Originally, this instrument was conceived to evaluate nonresponse across the ARS sites, but this purpose will be adjusted due to programmatic changes associated with Provider-Based Sampling. We will plan to revise this questionnaire after pilot data is collected (within the next year) to understand the impact of the Regional Operations Centers (for more information on Regional Operations Centers, please refer to A.15) and other program changes, including the addition of supplementary measures involving physical measurements and mother and child biospecimens collections.

Revised Father Interview: The results of consultations with experts in the field and an in-depth literature review have guided revisions to the Father Interview, which is administered before the child is born. The proposed revisions to the instrument now include measures of key social/personal resources and fathers' capacity, desire and attitudes towards engaging with mothers and children. We would like to

find out what impacts a father's personal resources, social network, and involvement will have on the health of the expecting mother and the development of the child. We would also like to evaluate their attitudes towards being involved as a father, and what effects those attitudes have on the health of the expecting mother and the development of the child. In total, we hope to identify factors that predict positive father involvement in the overall protection of maternal and child health. Feasibility of the additional measures in the revised interview will be assessed by quantitatively analyzing the relationships of these additional measures with the existing measures.

Revised 24-Month Interview: The 24-Month Interview is revised to include specific questions for parents about the social, behavioral, and neurological development of their child. These questions, in the form of a validated screening tool known as M-CHAT™, are geared specifically to identify characteristics of autism and autism-spectrum disorders. Although the instrument is under copyright, the instrument is free for use in research studies and can be downloaded from the Internet. The NCS intends to follow the M-CHAT instructions for use (https://www.firstsigns.org/downloads/m-chat.PDF). The proposed revisions increase the interview length from 30 to 35 minutes per respondent.

Tracing Questions Module

The NCS is developing a modular approach to conducting study visits. Tracing questions were removed from all study visits, and a tracing module was developed for administration at all study visits for all recruitment methods.

Administration of 3-, 9-, 18-, and 24-Month Interviews to Two-Tier Low-Intensity Participants: In July 2010, the NCS was approved to administer the Low-Intensity Questionnaire (Child-Focus) a total of four times between birth and 24 months of age of the child. Currently, data collections with child-specific questions for Low-Intensity participants are not occurring after birth because development of a specific instrument for Low-Intensity participants is still underway. Administration of the 3-, 9-, 18-, and 24-month interviews enables the NCS to ask child-focus questions of Low-Intensity participants. In addition to the 3-, 9,-, 18-, and 24-month interviews, the 6- and 12-month interviews are administered to High-Intensity participants. This ICR also proposes the collection of child physical measurements and mother and infant biospecimen for High-Intensity participants. For more information, please refer to "Supplemental Measures for ARS involving Physical Measurements" and "Supplemental Collections for ARS involving Biospecimens" in A.2.

Modular Consent and Visit Information Sheet (VIS) Administration: The NCS has proposed the merging of the existing written VIS and short informational script into a single multi-mode introductory Visit Information Script (VISCR), for consistency purposes, that can be read to participants during both in-person study visits and for all visits conducted via telephone. A Sample Collection VIS will be read to participants for visits that include collection of biospecimens, environmental sample collections, and physical measure collections, excluding the Birth Visit and the 1- and 3-Month breast milk collections. The Sample Collection VIS describes the visit sample and measure collection activities planned, and after the data collector reviews the information with the participant, a hardcopy of the Sample Collection VIS is left with the participant for reference. Participants who choose not to provide consent for a particular biological or environmental sample at a given visit, will be read the VIS Sample Refusal Reconsideration Script at subsequent visits in which that type of sample may be collected. For more information, please refer to B.2.1.

Participant Verification Questionnaire: The Participant Verification Questionnaire intends to improve data quality by confirming that participant contact information is correct. The questionnaire will ensure that study visits are being conducted with the correct consented participants.

Supplemental Measures involving Physical Measurements and Biospecimens for ARS

Supplemental measures involving Physical Measurements and Mother and Infant Biospecimen collections were originally in the Initial Vanguard Study. As discussed below, only a small number of collections were completed. When the Alternate Recruitment Substudy was initially proposed, the research goals (mentioned in "Alternate Recruitment Substudy Phases 1 and 2" in A.1) focused on determining efficiencies among different recruitment approaches. For this reason, these supplemental measures were not proposed in information collection requests for Alternate Recruitment Substudy Phases 1 and 2. In this information collection request, the NCS proposes to pilot the collection of these supplemental measures in order to determine the feasibility and acceptability of collection by type, quality of resulting analytic data, rates of consent for collection, and the impact on retention.

Supplemental Measures for ARS involving Physical Measurements

Physical Measures: Physical measures are measures of child anthropometry (for example, height, weight, and head circumference) and blood pressure signaling growth and maturation. These measures, obtained at the 6, 12-, and 24-month interviews will provide information on the potential early childhood indicators in the development of obesity, diabetes, premature puberty and a host of other health outcomes and diseases. Physical measures were collected at the 6-Month Interview in the Initial Vanguard Study; however, with the ending of Initial Vanguard Study in September 2010, a relatively small number of collections were completed. Physical measures were planned but never implemented at 12 months. Additional collections are needed to determine the feasibility, acceptability and cost of collection. Feasibility and acceptability of physical measurement collection will be assessed by rates of successful completion of physical measurement by type, quality of resulting analytic data, rates of consent for measurement collection, and impact on retention.

Supplemental Collections for ARS involving Biospecimens

Mother and infant biospecimens (listed below) will be collected among a subset of study locations participating in the three ARS arms (Provider-Based Recruitment, Enhanced Household-Based Recruitment, Two-Tier Recruitment) that currently have OIRA clearance. Fifteen of 30 ARS locations were selected for re-introduction of sample collection based on individual site readiness and quality of individual site prior performance. These biospecimen collections will provide information about preparation and infrastructure needed to carry out these collections in the NCS Main Study. Biospecimen and environmental sample collection will not take place in Provider-Based Sampling, as these activities do not address the main goals of the Provider-Based Sampling Feasibility Study, which, as mentioned earlier in this section and for purposes of this information collection request, are related specifically to recruitment. We plan to propose biospecimen and environmental sample collection for participants enrolled via Provider-Based Sampling in a future information collection request.

Breast Milk Collection 1 and 3 months: Breast milk was collected in the Initial Vanguard Study; however with the ending of the Initial Vanguard Study in September 2010, a relatively small number of collections were completed. Additional breast milk collection is needed to determine the feasibility, acceptability and cost of this type of collection. Feasibility and acceptability of specimen collection will be assessed by rates of successful completion of specimen collection by type, quality of laboratory analytic result data, rates of consent for specimen collection, and impact on retention. For more information, please refer to A.16.

Infant Urine Collection at 6 and 12 months: Infant urine was collected at the 6-Month Interview in the Initial Vanguard Study, with the ending of the Initial Vanguard Study in September 2010, a relatively small number of collections were completed. Infant urine collection was planned but never implemented at 12 months. Additional urine collection is needed to determine the feasibility, acceptability and cost of this type of collection at these ages. Feasibility and acceptability of specimen collection will be assessed by rates of successful completion of specimen collection by type, quality of laboratory analytic result data, rates of consent for specimen collection, and impact on retention. For more information, please refer to A.16.

Infant Blood and Saliva Collection at 12 months: Infant blood and saliva collections were planned for the 12-Month Interview in the Initial Vanguard Study, but never implemented. Additional infant blood and saliva collections are needed to determine the feasibility, acceptability and cost of these types of specimen collections at this age. Feasibility and acceptability of specimen collection will be assessed by rates of successful completion of specimen collection by type, quality of laboratory analytic result data, rates of consent for specimen collection, and impact on retention. For more information, please refer to A.16.

Changes to 6-, 12-, and 24-Month Study Visits from a Consent Perspective

In the currently approved collection, the NCS gathers data via questionnaire only for the 6-, 12-, and 24-month study visits. Participants provide consent for their own involvement and permission for their children's participation in the NCS in stages. Participating mothers provide written consent for their own participation when they join the Study. Mothers (or other legally authorized representative (LAR)) provide their written permission for children's participation at two separate time points. First, the mother or LAR is asked to provide written permission for a child's participation from birth through 6 months (using either the *Birth Visit Information Sheet (sample collection)* or the *Birth Visit Information Sheet (no sample collection)*) parental permission forms. Prior to the administration of the 6-month data visit, the NCS administers the *Parental Permission for Child's Participation* (6-months through Age of Majority) to the mother or the child's legally authorized representative. This form requests written permission for the NCS to collect information and samples involving enrolled children from six months through the child's age of majority. The parental permission mentions that parents and guardians will be provided with descriptions of the data collection activities to be conducted during a particular visit at the start of that visit. As described in B.2.1, the NCS has used a series of visit-specific visit information sheets (VIS) for administration during in-person visits that involve questionnaire and/or specimen collection.

In the proposed information collection request, all visits which involve questionnaire administration, including the 6-, 12-, and 24-month visits, begin with the reading of the *Multi-Mode Visit Introductory Script* (VISCR). The VISCR describes what questionnaire topics will be covered during the visit, indicates incentives, provides an avenue for study participants to ask questions, and discusses the voluntary nature of participation. For visits where specimens will be requested, there are visit-specific written sample collection visit information sheets (VIS) describing the specimen collection requested of each participant at that visit. The respective VIS is administered directly after the VISCR. Documentation of consent for participation in specific specimen collections is not a part of VIS administration, consent or dissent for specific collections is provided verbally. When applicable, a VIS Sample Refusal Reconsideration Script for data collections that can be captured at one of multiple visits, is administered as part of the VIS administration to recognize that participants may choose not to provide specimens during the initial Study informed consent administration, but may choose to provide the specimen at a subsequent visit. The language of the script can be administered to caregivers of enrolled children as well as adult participants. Specifically new to this information collection request, NCS requests collection of child biospecimen and physical measures starting at 6 months of age of the child (in addition to data collection from questionnaires). As described above, the 6-, 12-, and 24-month visits include a reading of the Multi-Mode Introductory VISCR followed by reading and distribution of a hard copy Sample Collection VIS describing the specific sample collection and other procedures that will take place during the visit. Further details are mentioned in B.2.1.

Elimination of Data Collection during Preconception

In February 2012, the NCS halted recruitment for the three ARS arms, ending the follow-up of non-pregnant women for inclusion of what will become known as the preconception cohort of the Vanguard Study. In the ARS, two different screening tools were used in order to identify women who were likely to become pregnant. Now that recruitment has ended, the analysis on this study aspect is underway. In the Provider-Based Sampling Feasibility Study, the objectives are to define the feasibility, acceptability and cost of constructing a provider list frame, recruiting providers, and recruiting women early in pregnancy from providers. As the providers in this feasibility study will only recruit pregnant women, the NCS will no longer need to collect information from participants prior to pregnancy for the following data collection activities resulting in a reduction in respondent burden:

- Pregnancy Screener (Two-Tier Low-Intensity)
- Healthcare Provider Questionnaire
- Household Enumeration Instrument
- Low-Intensity Consent Script
- Pregnancy Screener (Provider-Based Recruitment, Enhanced Household, Two-Tier High-Intensity)
- Low-Intensity Invitation to High-Intensity Script
- Non-pregnant Women's Informed Consent
- Pre-Pregnancy Interview
- Biological and Environmental Sample Collection (at preconception)
- Pregnancy Probability Group Follow-Up Script
- Low-Intensity Questionnaire (Non-Pregnant)
- Pregnant Women’s Informed Consent (Provider-Based Recruitment, Enhanced Household, Two-Tier ONLY)

A.3 Use of Information Technology and Burden Reduction

Information technology solutions will be used, as appropriate, to limit respondent burden. This may include incorporation of previous information into the interview process, computer-assisted telephone interviewing, and information management solutions to ensure that the proper study components are administered at the appropriate times. Forms and questionnaires that are given to participants will be developed in user-friendly formats to reduce the time they take to complete.

Title II of the E-Government Act of 2002 requires federal agencies to conduct privacy impact assessments (PIAs) before developing or procuring information technology (IT) systems that collect, maintain, or disseminate personally identifiable information (PII). In 2007, NIH released Manual Chapter 1745-1, "Privacy Impact Assessments," which reinforces the Department of Health and Human Services (HHS) requirement for PIA completion, and details NIH employee roles and responsibilities in support of this process.

PIAs provide a documented process, the purpose of which is to identify and protect employee and public citizens' PII; and it ensures that the government has considered necessary safeguards for the PII passing through or being collected, maintained, or disseminated in its systems. The NCS must effectively manage participant safety while preserving data integrity and availability to carry out NCS activities. To do so, privacy risks associated with NCS systems are documented by having field contractors complete PIAs and include risks in the system plan of action and milestones (POA&M). The NICHD Chief Information Officer exercises appropriate oversight of contractors in carefully reviewing PIA information.

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

Before the planning and initiation of the NCS was launched, an inventory and review of longitudinal studies was conducted. The review examined whether the study goals could be addressed without embarking on an entirely new study. The systematic review of all available longitudinal cohort studies found no study capable of answering the questions and concerns that led to the proposed National Children's Study regarding potential long-term effects in children from environmental exposures.

In addition, a systematic review was conducted to assess the information available to inform the experience of the Vanguard (Pilot) Study with respect to recruitment and retention. The review found that there was insufficient information to enable the NCS to determine the feasibility, acceptability, and cost of alternate recruitment strategies for enrollment of pregnant women into the NCS. The literature on recruitment and retention strategies in epidemiological and clinical research did not include sufficient research on recruitment into studies that were comparable to the NCS in size, length, longitudinal design, scope of coverage, diversity of participants, and types of information requested. Nonetheless, lessons from other studies were identified and incorporated into the Alternate Recruitment Substudy design. This collection is built upon the Alternate Recruitment Substudy outcome showing that provider-based recruitment is the most efficient means of identifying and enrolling eligible women into the NCS. However, provider-based sampling is a logical option that remains untested and has the potential to improve recruitment at a lower cost. Additionally, selected NCS Vanguard (Pilot) study visit assessment measures are continually revised based on data from the field. These revised measures now require testing before implemented responsibly in the NCS Main Study. User acceptance testing

complements, but does not adequately replace, use and evaluation of measures in a large-scale data collection environment.

A.5 Impact on Small Business and Other Small Entities

We anticipate minimal impact on small businesses (for examples, health care providers such as physicians, nurses, and others) due to a relatively low amount of burden. 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

The schedule for collection of longitudinal data from NCS participants has been planned to coincide with important time periods for environmental exposures and developmental milestones for children. Women will be identified and enrolled in the earliest stages of pregnancy, so that early maternal and fetal exposures can be measured. Understanding how these contacts with study participants affect response rates and retention rates over time, particularly during the infancy and early childhood years, as well as data quality, will be essential to inform the methodology for the Main Study.

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

Comments in Response to the Federal Register Notice

The 60 day Federal Register Notice regarding the Provider-Based Sampling for the NCS Vanguard (Pilot) Study was published on pages 4569-4571 of the Federal Register on January 30, 2012. One comment was received in response to that notice. The commenter questioned the value of the National Children's Study overall and suggested that the NCS be eliminated. The comment is reproduced below in its entirety:

our govt is getting entirely too nosy. the fat cat bureaucrats in skanky corrupt washinton dc. want to manage out kids bodies, instead of parents and now they seem to want to m anage our kids minds. it is time to downsize this out of control agency. this agency seems to find parents unacceptable. the budget for this proposal should be zero. this is invasive govt at work. the taxpayers of america do not want to be taxed to pay for this. this survey is not helping america, where l out of 2 americans are living in poverty. they are overtaxed to pay for the wastefulness of this agency.

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

(a) *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.

Efforts to Consult Outside Agencies:

Strategic advice and oversight is also provided by independent advisors through several groups as described below. Some of these committees are independent of the NCS; other committees comprise the NCS Program Office, study location staff, and independent advisors.

The Steering Committee consists of Principal Investigators from study locations as well as community representatives and provides first-level scientific guidance to the National Children's Study. It is the arbiter of issues referred to it by the Program Office, the Principal Investigators, and the Executive Steering Committee. It is empowered to make protocol modifications that do not change the direction or cost of the study, subject to confirmation by the Program Office. The full Steering Committee meets face-to-face twice a year. Interim meetings by conference call are scheduled as needed.

The National Children's Study Federal Advisory Committee (NCSAC), constituted under the Federal Advisory Committee Act, meets quarterly to provide strategic advice and recommendations to the Director of the National Institutes of Health, the Director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, and the Director of the National Children's Study regarding critical aspects of the study. These meetings are open to the public.

The National Children's Study Federal Consortium consists of partner agencies with an interest in maternal child health, the environment, education and other topics. The Federal Consortium consists of about 20 Agencies and Departments and meets every 6 months to explore partnering and consultative opportunities, data sharing opportunities and technical advice and input on broad scientific topics.

The Independent Study Monitoring and Oversight Committee (iSMOC) monitors National Children's Study data and the safety of study participants. The responsibilities of the iSMOC are to:

- Monitor human subject safety through review and evaluation of accumulated study data
- Review study conduct and progress
- Make recommendations concerning continuation or modification of the study.

During the study, the iSMOC will review data regarding procedure-related adverse events; unanticipated problems involving risks to subjects or others; adherence to the protocol; factors that might affect the study outcomes or compromise the data (for example, protocol violations, losses to follow-up, breach of subject confidentiality); and barriers to study progress or completion (such as slow enrollment, new data or findings, other milestones, change in resources, rate of endpoint accumulation). The iSMOC will recommend appropriateness of notification and referral of individual participants for significant abnormal findings on testing of stored samples. The committee consists of 5 to 10 individuals not associated with the study. Committee membership reflects the disciplines and clinical specialties necessary to interpret study data and to evaluate subject safety.

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 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 Initial Vanguard Study and the Alternate Recruitment Substudy. Participants agreeing to provide biospecimen samples will be offered a monetary incentive or equivalent not exceeding $25. Compensation amounts will be addressed specifically in IRB submissions for each pilot. Small gifts of appreciation for participation may be provided to participants. These may include items such as t-shirts, tote bags, and are intended as tokens of appreciation.

Table A.9. Maximum NCS Incentives, by Study Activity and Impact on Participants				
Data Collection Activity Characteristics	**Initial NCS Vanguard Study**	**NCS Recruitment Substudy, Provider-Based Sampling, and Formative Research**		
		Phase 1	Phase 2 and Provider-Based Sampling	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	Instead of monetary incentives, 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 IRBs	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

A.10 Assurance of Confidentiality Provided to Respondents

The Provider-Based Sampling Feasibility Study for the National Children's Study, NICHD will follow the same procedures and standards of confidentiality applicable to the Vanguard (Pilot) Study. Study data collected will be safeguarded closely and actions will be taken to protect participant confidentiality. Participants will be informed about the Certificate of Confidentiality (attached) granted to NCS to protect data from involuntary disclosure. The study locations, 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 locations will implement all federally required study-related confidentiality and data security procedures. All NCS Program Office staff, NCS study location 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 Information Security and Privacy 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 the Office of Personnel Management requirements.

To further assure confidentiality of participant data, the study will employ rigorous methods to provide security for personal identifying information. Each field contractor, support contractor and the NCS Program Office 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 field contractors and support contractors complete the self-assessment of their security plans, the NICHD Chief Information Officer will review all study center security plans to determine the contractor's authority to operate. Frequent and regular monitoring visits will assist in compliance with these terms.

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 questions that may be contained in 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. Fathers or other family members will not be contacted without mothers' agreement. All study questionnaires that would be proposed 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 Vanguard (Pilot) 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 Estimates of Hour Burden Including Annualized Hourly Costs

Estimates of annualized hour burden and annualized cost to respondents are laid out in Tables A.12-1 and A.12-2, respectively. The total number of estimated respondents is 31,082 annually. The total number of annual burden hours is 22,791. The estimated total annual respondent cost is $229,804.

By data collection activity, the number of estimated respondents varies based on two factors – the recruitment schema that are administered the data collection activity (for example, more participants receive the 18-Month Interview than the 12-Month Interview, because it is administered to Two-Tier Low-Intensity participants), as well as the retention estimates between study visits (for instance, we estimate 95% participation retention between the 12- and 18-month study visits).

The frequency of response varies by data collection activity. For instance, the tracing interview is a module which is administered at every study visit; therefore, the frequency response is 13, whereas the Pregnancy Visit 1 Interview is administered only once.

The average burden per response was determined by timing instruments and applicable files (for example, visit introductory scripts) that impose burden and the average burden per response for sample and physical measure collections are estimates based on field experience.

In general, study visits range between 15 minutes and 1 hour. Burden associated with biospecimen and environmental sample collection and physical measures collection differ based on what samples are collected (for instance, measuring blood pressure at 12 months only takes 10 minutes per respondent, while collecting blood, saliva and urine at 12 months takes 55 minutes).

Estimates of the total annual respondent cost for the collection of information use the appropriate wage rate categories. For individuals, the wage rate is $10.00 per hour. For health providers (OB/GYN) that receive the Provider-Based Sampling Frame Questionnaire, the wage rate is $101.13 per hour.

The cost of contracting out or paying outside parties for information collection activities is included in A.14.

LEGEND
PB: Provider-Based Recruitment
EH: Enhanced Household-Based Recruitment

TT-HI: Two-Tier Recruitment, High Intensity
TT-LI: Two-Tier Recruitment, Low Intensity
PBS: Provider-Based Sampling

NOTE: Instruments or recruitment strategies in **bold** represent new collection.

A.12 - 1 Estimates of Hour Burden

Table A.12.A Estimated Hour Burden for Vanguard (Pilot) Study Respondents, Prenatal to 30 Months of Age of the Child

Data Collection Activity	Type of Respondent	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Per Response (in hours)	Estimated Total Annual Burden Hours
Screening Activities					
Provider Based Sampling Eligibility Screener (PBS)	Pregnant Women	3,125	1	20/60	1,042
Provider Based Sampling Frame Questionnaire (PBS)	Healthcare Providers	50	1	25/60	21
Continuous Activities					
Nonrespondent Questionnaire (PB, EH, TT-HI, TT-LI, PBS)	Pregnant Women, Mothers or Fathers	480	1	5/60	40
Validation Interview - **up to 30 Months** (PB, EH, TT-HI, TT-LI, **PBS**)	Respondents	1,268	1	5/60	106
Participant Verification (PB, EH, TT-HI, TT-LI, PBS)	Pregnant Women, Mothers or Fathers	2,320	1	5/60	193
Tracing Interview (PB, EH, TT-HI, TT-LI, PBS)	Respondents	1,167	13	10/60	2,528
Pregnancy Activities					
Low-intensity Questionnaire (Found Pregnant) (TT-LI)	Pregnant Women	173	1	15/60	43
Pregnancy Visit 1 Interview (PB, EH, TT-HI, **PBS**)	Pregnant Women	2,018	1	35/60	1,177
Pregnancy Visit 2 Interview (PB, EH, TT-HI, **PBS**)	Pregnant Women	1,817	1	25/60	757
Biological and Environmental Sample Collection - Prenatal (PB, EH, TT-HI)	Pregnant Women	1,456	2	60/60	2,913

Table A.12.A Estimated Hour Burden for Vanguard (Pilot) Study Respondents, Prenatal to 30 Months of Age of the Child

Data Collection Activity	Type of Respondent	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Per Response (in hours)	Estimated Total Annual Burden Hours
Pregnancy Health Care Log (PB, EH, TT-HI, **PBS**)	Pregnant Women	1,615	1	20/60	538
Father Interview (PB, EH, TT-HI)	Alternate Caregiver	818	1	35/60	477
Birth-Related Activities					
Birth Visit Interview (PB, EH, TT-HI, **PBS**)	Mother/Baby	1,141	1	20/60	380
Low-intensity Questionnaire (Birth-focus) (TT-LI)	Mother/Baby	432	1	15/60	108
Postnatal Activities					
Infant Feeding Log (PB, EH, TT-HI, **PBS**)	Mother/Baby	1,106	1	20/60	369
Biological Sample Collection - Mother/Baby (PB, EH, TT-HI)*	Mother/Baby	761	4	22.5/60	1,141
3-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Baby	1,518	1	20/60	506
6-Month Interview (PB, EH, TT-HI, **PBS**)	Mother/Baby	1,066	1	30/60	533
Physical Measures - Child Anthropometry (6-,12-,24-Month) (PB, EH, TT-HI)	Baby/Child	701	3	20/60	701
Physical Measures - Child Blood Pressure (12-,24-Month) (PB, EH, TT-HI)	Baby/Child	675	2	10/60	225
9-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Baby	1,428	1	10/60	238
12-Month Interview (PB, EH, TT-HI, **PBS**)	Mother/Baby	1,003	1	50/60	836
18-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Child	1,316	1	30/60	658
24-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Child	1,251	1	35/60	729
Core Questionnaire (PB, EH, TT-HI, TT-LI, PBS)	Mother/Child	1,188	1	30/60	594
30-Month Visit Interview (PB, EH, TT-HI, TT-LI, PBS)	Mother/Child	1,188	1	55/60	1,089

Table A.12.A Estimated Hour Burden for Vanguard (Pilot) Study Respondents, Prenatal to 30 Months of Age of the Child

Data Collection Activity	Type of Respondent	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Per Response (in hours)	Estimated Total Annual Burden Hours
Total, Vanguard (Pilot) Study		**31,082**			**17,943**
Total, Formative Research					**4,847**
Grand Total		**31,082**			**22,791**

*Postnatal biospecimen sample collections take place at 1 (breast milk – mother), 3 (breast milk - mother, 6 (infant urine), and 12 (infant urine, blood, saliva) months. We anticipate 3,044 responses (collections) per year over the three-year period (total: 9,132). As demonstrated in B.2, we anticipate that we will collect samples from approximately 3,850 mothers and children from September 2012 – July 2013. This period will represent the bulk of biospecimen sample collections for this age group. We do anticipate being within the requested burden over the three-year period.

A.12 - 2 Annualized Cost to Respondents

Table A.12.B Estimated Cost for Vanguard (Pilot) Study Respondents, Prenatal to 30 Months of Age of the Child

Data Collection Activity	Type of Respondent	Estimated Total Annual Burden Hours	Hourly Wage Rate	Estimated Total Annual Respondent Cost
Screening Activities				
Provider Based Sampling Eligibility Screener (PBS)	Pregnant Women	1,042	$10.00	$10,417
Provider Based Sampling Frame Questionnaire (PBS)	Healthcare Providers	21	$101.00[1]	$2,104
Continuous Activities				
Nonrespondent Questionnaire (PB, EH, TT-HI, TT-LI, PBS)	Pregnant Women, Mothers or Fathers	40	$10.00	$400
Validation Interview - **up to 30 Months** (PB, EH, TT-HI, TT-LI, **PBS**)	Respondents	106	$10.00	$1,057
Participant Verification (PB, EH, TT-HI, TT-LI, PBS)	Pregnant Women, Mothers or Fathers	193	$10.00	$1,933
Tracing Interview (PB, EH, TT-HI, TT-LI, PBS)	Respondents	2,528	$10.00	$25,281
Pregnancy Activities				

Table A.12.B Estimated Cost for Vanguard (Pilot) Study Respondents, Prenatal to 30 Months of Age of the Child

Data Collection Activity	Type of Respondent	Estimated Total Annual Burden Hours	Hourly Wage Rate	Estimated Total Annual Respondent Cost
Low-intensity Questionnaire (Found Pregnant) (TT-LI)	Pregnant Women	43	$10.00	$432
Pregnancy Visit 1 Interview (PB, EH, TT-HI, **PBS**)	Pregnant Women	1,177	$10.00	$11,774
Pregnancy Visit 2 Interview (PB, EH, TT-HI, **PBS**)	Pregnant Women	757	$10.00	$7,569
Biological and Environmental Sample Collection - Prenatal (PB, EH, TT-HI)	Pregnant Women	2,913	$10.00	$29,127
Pregnancy Health Care Log (PB, EH, TT-HI, **PBS**)	Pregnant Women	538	$10.00	$5,382
Father Interview (PB, EH, TT-HI)	Alternate Caregiver	477	$10.00	$4,770
Birth-Related Activities				
Birth Visit Interview (PB, EH, TT-HI, **PBS**)	Mother/Baby	380	$10.00	$3,802
Low-intensity Questionnaire (Birth-focus) (TT-LI)	Mother/Baby	108	$10.00	$1,080
Postnatal Activities				
Infant Feeding Log (PB, EH, TT-HI, **PBS**)	Mother/Baby	369	$10.00	$3,688
Biological Sample Collection - Mother/Baby (PB, EH, TT-HI)	Mother/Baby	1,141	$10.00	$11,411
3-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Baby	506	$10.00	$5,061
6-Month Interview (PB, EH, TT-HI, **PBS**)	Mother/Baby	533	$10.00	$5,331
Physical Measures - Child Anthropometry (6-,12-,24-Month) (PB, EH, TT-HI)	Baby/Child	701	$10.00	$7,014
Physical Measures - Child Blood Pressure (12-,24-Month) (PB, EH, TT-HI)	Baby/Child	225	$10.00	$2,250
9-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Baby	238	$10.00	$2,381
12-Month Interview (PB, EH, TT-HI, **PBS**)	Mother/Baby	836	$10.00	$8,360
18-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Child	658	$10.00	$6,582

Table A.12.B Estimated Cost for Vanguard (Pilot) Study Respondents, Prenatal to 30 Months of Age of the Child

Data Collection Activity	Type of Respondent	Estimated Total Annual Burden Hours	Hourly Wage Rate	Estimated Total Annual Respondent Cost
24-Month Interview (PB, EH, TT-HI, **TT-LI, PBS**)	Mother/Child	729	$10.00	$7,295
Core Questionnaire (PB, EH, TT-HI, TT-LI, PBS)	Mother/Child	594	$10.00	$5,940
30-Month Visit Interview (PB, EH, TT-HI, TT-LI, PBS)	Mother/Child	1,089	$10.00	$10,890
Total, Vanguard (Pilot) Study		**17,943**		$181,331
Total, Formative Research		**4,847**		$48,473
Grand Total		**22,791**		$229,804

[1]The hourly wage rate for an OB/GYN is $101.13 (http://www.bls.gov/oes/current/oes291064.htm).

A.13 Estimate of Other Total Annual Cost Burden to Respondents or Record keepers

NCS participants will be reimbursed for any expense resulting from their participation in the NCS in alignment with Table A.9. There are no additional costs associated with acquiring, installing, or utilizing technology and systems. In turn, there are no capital and start-up costs and there are no costs associated with operation and maintenance and purchase of services.

A.14 Annualized Cost to the Federal Government

The proposed information collection is estimated to cost about $71,904,774 per year over a three-year period. The annualized cost to the federal government is based on budgetary data for task orders that include costs of information collection, design, development, tests, printing forms, mailing list compilation and maintenance, mailing or enumeration, editing, coding, tabulation, analysis and publication of results. Salary and travel costs associated with project development, implementation, and monitoring are incorporated into the annualized cost to the federal government.

A.15 Explanation of Program Changes or Adjustments

This section describes program changes that are the result of deliberate Federal government action.

As noted in A.1 and A.2, the NCS halted ARS recruitment (Provider-Based Recruitment, Enhanced Household-Based Recruitment, Two-Tier Recruitment) in February 2012, eliminating the need for further screening and preconception data collection, which comprised the bulk of respondent burden in the Vanguard (Pilot) Study. This resulted in significantly decreased burden to the public. Currently, the NCS is approved for 159,966 annualized burden hours. In this information collection request, the total annualized hour burden for the ARS is approximately 15,000 annualized burden hours.

This request for revision proposes the addition of a Provider-Based Sampling Feasibility Study component of the Vanguard (Pilot) Study, supplemental measures involving Study Visit assessments, supplemental measures involving physical measurements, and supplemental collections involving biospecimens. These information collections, revisions of instruments, physical measure implementation, and biospecimen collections will evaluate the feasibility, acceptability, and cost of study design elements to inform the Main Study.

The NCS intends to use a modular approach for Study Visit assessments. The Core Questionnaire (described in A.2) is intended to be administered at multiple study visits, and will be piloted at the 30-month visit. A modular approach will also be instituted for the informed consent process (described in B.2.1.) and the Tracing Interview (described in A.2). In the long term, we anticipate that the modular approach mentioned above will result in reduced administrative burden as well as the potential for reduced participant burden.

To date, child physical measures have not yet been collected into the Vanguard (Pilot) Study. This collection will impose a relatively small amount of burden on the public. In addition, the re-introduction of child biospecimen collection into the Vanguard (Pilot) Study will also represent a relatively small amount of burden on the public.

To accommodate Department of Health and Human Services data standards for the Affordable Care Act Measures, the NCS has proposed a plan to incorporate questions on ethnicity, race, sex, primary language / language spoken, and disability status into existing Study Visit assessments that are asked of mothers, fathers, children, and primary caregivers, and range from before the child is born until 5 years of age. Upon finalization of this plan, this will result in a minimal public burden increase.

As mentioned in A.1, data collection at the seven Initial Vanguard Study locations will be conducted by a single contract research organization starting in July 2012. This transition has been planned to coincide with the expiration of Study Center contracts and the award of new contracts for administration of the Vanguard (Pilot) Study. For a period of 6 months, approximately 1,100 children will be followed via telephone or other remote data collection modes. This will not affect burden to the public.

NCS Proposed Implementation of the Data Collection Standards Pursuant to Section 4302 of the Affordable Care Act

The Affordable Care Act (ACA) includes several provisions aimed at eliminating health disparities in America. Section 4302 requires the Secretary of the Department of Health and Human Services (DHHS) to establish data collection standards for race, ethnicity, sex, primary language, and disability status. The law requires that, once established, these data collection standards be used, to the extent practicable, in all national population health surveys. In response to this statutory requirement, the NCS has proposed an implementation strategy that complies with the guidance standards for race, ethnicity, sex, primary language and disability status. For the current participants types (mother, father, primary care giver, and child) the inclusion of necessary questions has been incorporated into the following visits as outlined in Table A.15: (1) Pregnancy Visit 1, (2) Father Interview, (3) Child at birth, (4) Child at 60 months, (5) Primary Caregiver, and (6) Child ages 6 years of age and over. Currently, the oldest children in the NCS

are approaching 30 and 36-months of age. The *NCS Proposed Implementation of the Data Collection Standards Pursuant to Section 4302 of the Affordable Care Act* was submitted to DHHS in March 2012 and approved on April 13, 2012.

Table A.15 NCS Proposed Implementation of the ACA Data Collection Standards

	Participant Types = Mother, Father, Child, Primary Caregiver Interview Time Points = Pregnancy Visit, Father Interview, Birth Visit, 60-Month Visit					
HHS Data Standard	Mother	Father	Child at Birth	Child at 60 months (5 years)	Primary Caregiver*	Child (ages 6 and over)
Ethnicity	Pregnancy Visit 1	Father Interview	Birth Visit (Mother will respond on behalf of child)	Mother or Primary Caregiver on behalf of the child	60-Month Visit	**
Race	Pregnancy Visit 1	Father Interview	Birth Visit (Mother will respond on behalf of child)	As above	60-Month Visit	**
Sex	Pregnancy Visit 1	Father Interview	Birth Visit (Mother will respond on behalf of child)	As above	60-Month Visit	**
Primary Language/ Language Spoken	Pregnancy Visit 1	Father Interview	NA	Child may answer if questions are in plain language	60-Month Visit	**
Disability Status	Pregnancy Visit 1	Father interview	NA	Child may answer # 1-5 if questions are in plain language	60-Month Visit	**

* If the primary caregiver is not the mother or the father at the 60-month visit, a new consent would be signed for the primary caregiver who would answer the questions about themselves. ** Visit Schedule and Instrumentation for this age group have not yet been developed

Future Transition to Regional Operating Centers

As noted in Solicitation Number NIH-NICHD-NCS-SBSS-2012-07 (National Children's Study Vanguard 2.0), the NCS will establish an NCS Vanguard Study Regional Operations Center (ROC) Network, which will consist of 4 Regional divisions of 10 current Study Locations based on geography: Central, East, South and West Regions. The goals of the solicitation will be to implement the next phase of the NCS Vanguard Study with a focus on the activities of data collection and evaluation, participant retention, study visit development and assessment and formative research on methods to address specific questions or needs. We anticipate that this transition will not adversely impact burden to the public. Further details on the solicitation are available online: https://www.fbo.gov/index?s=opportunity&mode=form&id=78a04a4e4845cef6339be27662eb935a&tab=core&_cview=1.

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

Information collection for Phase 1 of the Alternate Recruitment Substudy of the Vanguard (Pilot) Study began in November 2010. Table A.16a describes the key evaluation questions for the Phase 1 recruitment strategies and retention measures with regard to feasibility, acceptability and cost (when applicable) of these collections. Phase 2, which began in the fourth quarter of 2011, added a questionnaire targeted to fathers and introduced biospecimen and environmental sample collection. Key evaluation questions for Phase 2 with regard to information collections, environmental and biospecimen collection and physical measures collection are described in Table A.16b. Key evaluation questions with regard to sampling, recruitment, and retention for the Provider-Based Sampling approach are described in Table A.16c.

Table A.16a: Measures Being Computed for the ARS, Phase 1, with Timetable

RECRUITMENT STRATEGIES			
Key Evaluation Question		Data Source/ Questionnaire	Frequency of data reporting
FEASIBILITY			
1	How effective is the recruitment strategy per location and per schema?		
	a. Number of women to be contacted for screening per month	N/A	Monthly
	b. Number eligible women contacted by study per month	N/A	Monthly
		N/A	Monthly
	c. Number eligible women consented per month	Consent	Monthly
	d. Distribution of women enrolled while preconception, during pregnancy, or at birth	Pregnancy Screener	Monthly
		Birth Visit	Monthly
		Consent	Monthly
	e. Distribution of gestational ages at consent and first study visit	Pregnancy Screener	Monthly
		Consent	Monthly
		Study Visit questionnaires	Monthly
	f. Monthly enrollment rate of babies among all eligible women with due date in that month	Pregnancy Screener	Monthly
		Consent	Monthly
		Birth Visit	Monthly
	g. Birth visits (full & partial complete) among women receiving at least one pre-birth study visit	Study Visit questionnaires	Monthly

Table A.16a: Measures Being Computed for the ARS, Phase 1, with Timetable			
2	Is the population recruited representative of the target population?		
	a. Race	Pregnancy Screener	Monthly
	b. Ethnicity	Pregnancy Screener	Monthly
	c. Age (DOB)	Pregnancy Screener	Monthly
	d. Marital Status	Pregnancy Screener	Monthly
	e. Primary language	Pregnancy Screener	Monthly
	f. Employment	Pregnancy Screener	Monthly
	g. Education	Pregnancy Screener	Monthly
3	How effectively do outreach and media campaigns reach eligible women?		
	a. What was primary source for entry?		Monthly
	b. What were the number of and types of ways women heard about NCS?	Pregnancy Screener	Monthly
	c. Principal media sources including print, broadcast, internet, social media	To be addressed through formative research*	Monthly
ACCEPTABILITY			
4	How does retention vary by recruitment strategy?		
	a. Number retained to first visit vs. total consented	Study Visit questionnaires	Monthly
		Consent	Monthly
		Follow-up calls	Monthly
	b. Retention across all study visits	Study Visit questionnaires	Monthly
		Consent	Monthly
		Follow-up calls	Monthly
	c. Percent "movers"	Consent	Monthly
		Follow-up calls	Monthly
5	Are the reasons for participation and nonparticipation comparable across the three recruitment strategies?		
	a. Evaluate reasons given for nonparticipation	To be addressed through formative research*	Monthly

Table A.16a: Measures Being Computed for the ARS, Phase 1, with Timetable			
	b. Evaluate reasons given for participation in the study	To be addressed through formative research*	Monthly
	c. Respondent reactions to study assessments	Study Visit questionnaires	Monthly
COST			
6	What is the cost per recruited participant?		
	a. Total number of consented participants	Consent	Monthly
	b. Total study cost	Field contractor invoice	Monthly
	c. Calculated cost per consented participant	See Note	
7	How do local travel costs vary across recruitment schema?		
	a. For each PSU_ID, sum weekly STAFF_MILES from Weekly Staff Expense Table	Field contractor will furnish data	Monthly
8	How do total charged administrative and field staff hours vary across recruitment schema?		
	a. Administrative hours	Field contractor will furnish data	Monthly
	b. Field staff hours	Field contractor will furnish data	Monthly
9	How does total charged time for scientific staff vary across recruitment schema? (Cost of scientific staff as function of recruitment schema)	Field contractor invoice	Monthly
10	What were the dates, costs, and geographic targeting of outreach and media campaigns? (Need to capture the media outreach process for each schema type)	Field contractor will furnish data	Monthly
11	What is the cost per delivered message in media campaigns (exact or appropriate)? (Need to capture the media outreach process for each schema type)	Field contractor will furnish data	Monthly
	a. What is the size of the targeted population of the media campaign?		
	b. What is the yield of responses from media campaign?		
12	What is the cost in time for community outreach efforts (both contractor and volunteer labor and incentives)? (Cost of contractors and volunteers used in community outreach efforts)	Field contractor will furnish data	Monthly

Table A.16a: Measures Being Computed for the ARS, Phase 1, with Timetable			
13	What is the cost for instrument development and IMS infrastructure?	Field contractor will furnish data	Monthly
*Note: All analysis will be done by PSU and by recruitment schema, using reports submitted by the field contractors.			

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
RETENTION MEASURES			
1	How effective is the data collection strategy per location and per schema?		
	a. Number of participants to be contacted for data collection per month	Study Visit questionnaires	Monthly
	b. Number participants contacted by study per month	Study Visit questionnaires	Monthly
	c. Number participants with completed data collections per month	Study Visit questionnaires	Monthly
2	How effectively are participants retained per location and per schema?		
	a. Percent Pregnant women who agree to enroll their child(ren)	Consent	Monthly
	b. Percent enrolled children whose families help complete at least one post-birth data collection (for example 3, 6, 9, 12, 18, or 24 month visits)	Study Visit questionnaires	Monthly
	c. Percent enrolled children whose families help complete at least one post-birth and in-person data collection (for example 6, 12, 18, or 24 month visits)	Study Visit questionnaires	Monthly
	d. Percent enrolled children whose families help complete at least on in-person visit in each of the first two years of life (for example, the 6 or 12 month visit in year 1,	Study Visit questionnaires	Monthly

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	and either the 18 or 24 month visit in year 2)		
	e. Distribution of child ages at each study visit	Study Visit questionnaires	Monthly
3	Is the subset of participants retained representative of the target population? Are there particular demographic groups that are retained at lower rates? Are there particular modes of data collection that have better completion rates among poorly retained groups?		
	a. Race	Pregnancy Screener	Monthly
	b. Ethnicity	Pregnancy Screener	Monthly
	c. Age (DOB)	Pregnancy Screener	Monthly
	d. Marital Status	Pregnancy Screener	Monthly
	e. Primary Language	Pregnancy Screener	Monthly
	f. Family Income	Pregnancy Screener	Monthly
	g. Education	Pregnancy Screener	Monthly
4	Are the reasons for completion and non-completion of study visits comparable across the three recruitment strategies?		
	a. Evaluate reasons given for non-completion	Formative research	Per work assignment deliverable schedule
	b. Evaluate reasons given for completion in the study	Formative research	Per work assignment deliverable

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
			schedule
	c. Respondent reactions to study assessments	Formative research	Per work assignment deliverable schedule
ENVIRONMENTAL SAMPLES			
FEASIBILITY			
1	Does the vacuum bag method of household dust collection yield a stable sample for initial and future analysis?		
	a. Stability of organic compounds, molds, allergens, endotoxins, metals	Prenatal Data Collection Visits	Monthly
	b. Quality of shipped sample from participant	Prenatal Data Collection Visits	Monthly
2	Can pesticides and pharmaceuticals be detected in tap water collected by the NCS?		
	a. Detection rates	Prenatal Data Collection Visits	To be determined
	b. Stability of the sample	Prenatal Data Collection Visits	To be determined
ACCEPTABILITY			
3	Does the vacuum bag method of household dust collection reduce participant burden (in comparison to wipe, dust plate, and vacuum bedside methods)?		
	a. Rate of unit non response	Prenatal Data Collection Visits	Monthly
	b. Time to return sample	Prenatal Data Collection Visits	Monthly
4	Is participant collection of household dust preferred over data collector collection?		
	a. Unit non response	Prenatal Data Collection Visits	Monthly

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	b. Time to return sample	Prenatal Data Collection Visits	Monthly
	c. Quality of shipped sample from participant	Prenatal Data Collection Visits	Monthly
5	Will participant-collected tap water be more acceptable to participants than technician- collected tap water?		
	a. Unit non response	Prenatal Data Collection Visits	Monthly
	b. Time to return sample	Prenatal Data Collection Visits	Monthly
	c. Quality of shipped sample from participant	Prenatal Data Collection Visits	Monthly
COST			
6	Is the vacuum bag method of household dust collection more cost effective (in comparison to wipe, dust plate, and bedside vacuum methods)?		
	a. Cost of vacuum bag shipping	Phase 2 Prenatal Data Collection Visits	Monthly
	b. Cost of wipe, dust plate, and bedside vacuum method	Initial Vanguard Study Data	Monthly
PREGNANCY HEALTH CARE LOG AND INFANT HEALTH CARE LOG			
FEASIBILITY			
1	Will the health care logs enable location (and thus abstraction) of medical records?		
	a. Location item response	Prenatal Data Collection Visits	Monthly
	b. Matching of location with secondary health care data source	Extant data	Monthly
2	Will the health care logs yield accurate medical information at an acceptable		

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	burden to participants?		
	a. Participant responses to acceptability questions	Prenatal Data Collection Visits	Monthly
	b. Rate of item non response	Prenatal Data Collection Visits	Monthly
BIOSPECIMENS			
FEASIBILITY			
1	Will the revised cord blood bag featuring dry EDTA as the anticoagulant result in improved specimen for environmental chemical measurements and reduced dilution effect when compared to the initial cord blood bag featuring liquid anticoagulant?		
	a. Environmental chemical measurements	Birth Data Collection	Monthly
	b. Dilution effect	Birth Data Collection	Monthly
2	Will the collection procedures and transport of breast milk provide a specimen suitable for analysis?	Postnatal Data Collection Visits	Monthly
3	Will the collection procedures for infant urine provide a specimen in sufficient amount for analysis?	Postnatal Data Collection Visits	Monthly
4	Will the collection procedures and transport of infant saliva provide a specimen suitable for analysis?	Postnatal Data Collection Visits	Monthly
5	Will the collection procedures for infant blood, urine, and saliva provide a specimen suitable for analysis?		
	a. Quality of laboratory analytic result data	Postnatal Data Collection Visits	Monthly
ACCEPTABILITY			

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
6	Will the introduction of maternal blood and urine collection decrease retention in the recruitment substudy?		
	a. Unit non response	Prenatal Data Collection Visits	Monthly
	b. Item non response	Prenatal Data Collection Visits	Monthly
	c. Retention over time	Prenatal Data Collection Visits	Monthly
7	Will the re-introduction of maternal breast milk decrease retention?	Postnatal Data Collection Visits	Monthly
	a. Consent rate	Postnatal Data Collection Visits	Monthly
	b. Completion rate (by time point)	Postnatal Data Collection Visits	Monthly
	c. Retention over time	Postnatal Data Collection Visits	Monthly
8	Will the collection of infant blood, urine, and saliva decrease retention?	Postnatal Data Collection Visits	Monthly
	a. Consent rate	Postnatal Data Collection Visits	Monthly
	b. Completion rate (by type)	Postnatal Data Collection Visits	Monthly
	c. Retention over time	Postnatal Data Collection Visits	Monthly
FATHER INTERVIEWS			
ACCEPTABILITY			
1	Will the mode of administration improve father response rates?		
	a. Mode of administration (web, phone, or	Pregnancy Visit 1	Monthly

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	SAQ)	Father Interview	
	b. Unit non response	Pregnancy Visit 1 Father Interview	Monthly
	c. Item non response	Pregnancy Visit 1 Father Interview	Monthly
	d. Time to return	Pregnancy Visit 1 Father Interview	Monthly
2	Will offering father interviews improve pregnant women's response rates? Retention rates?		
	a. Father consent rate	Pregnancy Visit 1 Father Interview	Monthly
	b. Father response rates	Pregnancy Visit 1 Father Interview	Monthly
	c. Pregnant women's response rate (named father)	Women's Consent	Monthly
	d. Pregnant women's retention rate over time	Prenatal and Postnatal Study Visits	Monthly
3	What impact does a father's personal resources, social networks, and involvement have on the health of the expecting mother and the development of the child?		
	a. Father's personal resources	Father Interview	Monthly
	b. Father's social resources	Father Interview	Monthly
4	What impact does the father's desire and attitude towards engaging with the mother and child have on the health of the expecting mother and the development of the child?		
	a. Father's desire and attitude towards being involved as a father	Father Interview	Monthly

Table A.16b: Measures Being Computed for the ARS, Phase 2, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
CORE QUESTIONNAIRE			
FEASIBILITY			
1	Will the Core Questionnaire enable the continuous collection of specific data throughout the Study?	30-Month Visit	Monthly
PHYSICAL MEASUREMENTS			
FEASIBILITY			
1	Will the recordings from infant / child blood pressure data collections be suitable for analysis?	Postnatal Data Collection Visits	Monthly
2	Will the height and weight data be suitable be suitable for analysis?	Postnatal Data Collection Visits	Monthly
ACCEPTABILITY			
3	Will the introduction of infant / child physical measurements decrease retention in the Alternate Recruitment Substudy?		
	a. Consent rate	Postnatal Data Collection Visits	Monthly
	b. Completion rate (by type)	Postnatal Data Collection Visits	Monthly
	c. Retention over time	Postnatal Data Collection Visits	Monthly

Table A.16c: Measures Being Computed for Provider-Based Sampling, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
SAMPLING MEASURES			
FEASIBILITY			

Table A.16c: Measures Being Computed for Provider-Based Sampling, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
1	Can a sampling frame of prenatal care providers be constructed?	Extant Data	Monthly
		Stratified Probability Proportional to Size (PPS) sampling design	
		Provider-Based Sampling Frame Questionnaire	
		Computed Measure of Size	
2	Is the feasibility of construction of the sampling frame consistent across the three study locations? If not, what factors contribute to success of failure?	Stratified Probability Proportional to Size (PPS) sampling design	Monthly
		Computed Measure of Size	
		Study Visit Questionnaires	
		Prenatal Data Collection	
		Birth Data Collection	
3	Are the measures of size of the number of first prenatal care visits sufficiently reliable for an efficient sample design? If not, what alternative measures can be used?	Computed Measure of Size	Monthly
		Consent	
		Pregnancy Visit 1	
		Birth Data Collection	
4	Of providers selected into the sample, what proportion agrees to participate? Is this proportion comparable across the three study locations? If not, what factors are associated with rates of participation amongst providers in completion of the	Subset of selected providers at each study location invited for participation	Monthly
		Number of participating provider locations at each	

Table A.16c: Measures Being Computed for Provider-Based Sampling, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	frame questionnaire?	study location	
5	What is the percentage of providers willing to provide information requested by the PBS Frame Questionnaire?	Provider-Based Sampling Frame Questionnaire	Monthly
RECRUITMENT MEASURES			
FEASIBILITY			
1	How effective is the Provider-Based Sampling approach as a method of recruitment?		
	a. The rate at which the study learns of potentially eligible women through the participating provider	Provider-Based Sampling Frame Questionnaire Extant Data	Monthly
	b. The rate at which the study can successfully contact potentially eligible women	Provider-Based Sampling Eligibility Screener Computed measure of size from the Provider-Based Sampling Frame Questionnaire	Monthly
	c. The rate at which the study can complete the screening for eligibility	Provider-Based Sampling Eligibility Screener	Monthly
	d. The rate at which eligible women consent to entering the study after being contacted and screened for eligibility	Provider-Based Sampling Eligibility Screener Consent Pregnancy Visit 1	Monthly
	e. The distribution of gestational age at time of enrollment of pregnant women	Consent Pregnancy Visit 1	Monthly
	f. Participation rates of women contacted for enrollment post delivery;	Field contractor will furnish data	Monthly
	g. The percent of women unavailable due to birth complications	Field contractor will furnish data	Monthly

Table A.16c: Measures Being Computed for Provider-Based Sampling, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	h. The percentage of women unavailable due to early discharge from hospital.	Field contractor will furnish data	Monthly
	i. Ease of access to potential participants to describe the Study and attempt enrollment	Field contractor will furnish data	Monthly
	j. Differences in the efficiencies in recruitment between prenatal care providers and birth providers	Field contractor will furnish data	Monthly
	k. Differences in the quality and quantity of prenatal exposure data collected retrospectively versus prospectively	Field contractor will furnish data	Monthly
	l. Differences in the demographics of women enrolled at prenatal care provider locations versus birth providers	Field contractor will furnish data	Monthly
	m. Differences in the feasibility of collecting perinatal samples retrospectively versus prospectively	Field contractor will furnish data	Monthly
COST			
2	What is the cost per recruited participant?		
	a. Total number of consented participants	Consent	Monthly
	b. Total study cost	Field contractor invoice	Monthly
	c. Calculated cost per consented participant	See Note	
3	How do local travel costs vary across recruitment schema?		
	a. For each PSU_ID, sum weekly STAFF_MILES from Weekly Staff Expense Table	Field contractor will furnish data	Monthly
4	How do total charged administrative and field staff hours vary across recruitment schema?		
	a. Administrative hours	Field contractor will furnish data	Monthly
	b. Field staff hours	Field contractor will furnish data	Monthly
5	How does total charged time for scientific staff vary across recruitment schema? (Cost of scientific staff as function of	Field contractor invoice	Monthly

Table A.16c: Measures Being Computed for Provider-Based Sampling, with Timetable			
Measure	**Key Evaluation Question**	**Data Source/ Questionnaire**	**Frequency of Data Reporting**
	recruitment schema)		
6	What were the dates, costs, and geographic targeting of outreach and media campaigns? (Need to capture the media outreach process for each schema type)	Field contractor will furnish data	Monthly
7	What is the cost per delivered message in media campaigns (exact or appropriate)? (Need to capture the media outreach process for each schema type) a. What is the size of the targeted population of the media campaign? b. What is the yield of responses from media campaign?	Field contractor will furnish data	Monthly
8	What is the cost in time for community outreach efforts, inclusive of both contractor and volunteer labor and incentives?	Field contractor will furnish data	Monthly
9	What is the cost for instrument development and IMS infrastructure?	Field contractor will furnish data	Monthly
RETENTION MEASURES			
FEASIBILITY			
1	How feasibly can Provider-Based Sampling retain participants?		
	a. The proportion of consented women who participate in at least one data collection study visit	Consent Study Visit Questionnaires	Monthly
	c. The proportion of women enrolled during pregnancy and participating in all data collection visits through the birth of a child that is enrolled into the Study	Consent Pregnancy Visit 1 Pregnancy Visit 2 Birth Visit	Monthly
	g. The proportion of women who receive a pre-birth data collection visit that also receive a successful birth visit	Consent Pregnancy Visit 1 Pregnancy Visit 2 Birth Visit	Monthly
	k. The proportion of women enrolled during pregnancy and participating in all data collection visits through age 30 months of the child that is enrolled	Consent Study Visit questionnaires	Monthly

*Note: All analysis will be done by PSU and by recruitment schema, using reports submitted by the field contractors.

Prior to posting a 60-day FR notice for the Main Study (projected January 2013), we will acquire at least 4 months of recruitment data using the Provider-Based Sampling approach described in this information collection request to meet the target of inviting 1,200 pregnant women, enrolling 960 eligible women at the first prenatal care visit. Estimating an 80% retention rate from the first prenatal care visit to the birth of the child, and assuming for this calculation that all of the enrolled women were enrolled in the prenatal stratum, this would result in approximately 750 child births over the course of the entire Provider-Based Sampling Feasibility Study. As noted in B.2, we expect that on average about 5 eligible women would be invited per provider location (approximately 20 per PSU) per month. Over the recruitment period, we expect 20 eligible women to be invited at each provider location, resulting in 400 pregnant women to be invited per PSU (1,200 total).Prior to posting a 30-day FR notice for the Main Study, we would have 8-9 months of recruitment and retention data to assess success of this approach. The Vanguard (Pilot) Study would continue to inform the Main Study visit design following the end of recruitment for Provider-Based Sampling. Please refer to Table A.16.d for more details for the Provider-Based Sampling Feasibility Study project time schedule.

Table A.16.d: Provider-Based Sampling Feasibility Study Project Time Schedule

Activity	**Time Schedule**
Fielding of Provider-Based Sampling	Immediately after OMB approval
Provider-Based Sampling recruitment period end date	At least 4 months after OMB approval
Analysis of Provider-Based Sampling recruitment data	1-6 months after OMB approval
Analysis of Provider-Based Sampling retention data through birth of the child	1-12 months after OMB approval
Submission of the 60-day Federal Register (FR) notice for the Main Study	7 months after OMB approval
Submission of the 30-day FR notice for the Main Study	9-10 months after OMB approval

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.