REQUEST FOR OMB CLEARANCE

CONTINUATION OF NATIONAL CHILDREN'S STUDY VANGUARD (PILOT) STUDY DATA COLLECTION: STUDY VISITS THROUGH 60-MONTHS AND SIBLING BIRTH ENROLLMENT

PART B ONLY

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B. Collection of Information Employing Statistical Methods

B.1 Respondent Universe and Sampling Methods

The NCS Vanguard Study has enrolled approximately 5,000 children to-date. Children were eligible for enrollment if they were born to an enrolled woman who met pre-defined age and geographic criteria. Specifically, women were required to be of the age of majority (typically, age 18) and residing in a selected NCS geographic segment at the time of enrollment. Post-birthmothers (or other legally authorized representatives) were asked to consent to enrolling the child in the Study. Once children are enrolled in the Vanguard Study, their eligibility is no longer determined by their geographic residence. The Study will continue to follow these children if they move anywhere within the U.S., and internationally if the relocation is temporary. (Note that these policies are being tested in the Vanguard Study to determine whether tracking of participants internationally is effective and feasible.)

In addition to birth mothers and children, NCS participants also include fathers - both residential and non-residential – and other adult caregivers of the enrolled child. Fathers, if not already identified as a primary caregiver, are invited to participate upon agreement of the mother. All adults are asked to provide informed consent for their own participation in the Study. Anyone unable to understand NCS participation and grant informed consent will be considered ineligible to participate.

To date, children have been enrolled in 40 Study locations. NCS recruitment response rates – consolidated for all strategies — are shown in Table B1.1 below.

Table B1.1 NCS Vanguard Study Recruitment Rates	
Number of Eligible Women Identified for Screening	88,200
Percent Contacted to Screen	91%
Pregnancy Screener Completion Rate	88%
Percent Screened Identified as Pregnant /Trying to Conceive	16%
Percent Pregnant/Trying Enrolled in NCS	71%

These rates include women recruited for both pregnancy and pre-conception cohorts. Women found to be actively trying to conceive were initially enrolled in a pre-conception cohort and completed a single Study visit. However, if they did not eventually become pregnant by the end of active recruitment at their Study location their participation in the NCS ended.

Moving forward, all data collection activities completed by Regional Operations Centers (ROCs) will focus on families with children enrolled in the NCS, including any new births to women with a NCS child as described in section A2 “Initiation of a New Enrollment Cohort -Sibling Birth Cohort.” Note that no new families will be recruited into the NCS under this clearance; rather the enrollment of subsequently born siblings will serve to increase the Vanguard Study cohort size.

Characteristics of NCS Vanguard Study Cohort

During the transition of data collection activities from Study Centers to ROCs, participants enrolled in the NCS (with the exception of those recruited through the Provider-Based Sampling Substudy) were required to provide new informed consent to continue in the Study. Re-consent rates were high with more than 90 percent of women agreeing to remain in the Study with their enrolled child. Retention

rates have also been acceptable, and will likely increase with greater ability to provide precise estimates as data transitions are finalized and children age out of specific visit windows. The table below describes current retention rates of participants from enrollment to two endpoints: the Birth visit and the 12 month study visit. Updates to these tables can be provided as additional data are available.

		Retention Rates	
		Birth Visit	12-Month Visit
All Participants		**90%**	**74%**
Age			
	Under 25	**89%**	**69%**
	25 - 34	**91%**	**76%**
	35 +	**89%**	**77%**
Education			
	Less than high school	**91%**	**72%**
	HS graduate/some college	**89%**	**72%**
	College or higher	**93%**	**78%**
Ethnicity			
	Hispanic	**89%**	**73%**
	Non-Hispanic	**91%**	**75%**
Race			
	White	**91%**	**76%**
	African American	**90%**	**69%**
	Asian	**91%**	**73%**
	Other	**86%**	**76%**
	More than one race	**89%**	**72%**
Marital Status			
	Married	**92%**	**77%**
	Not married	**88%**	**70%**
Region			
	East	**92%**	**80%**
	Central	**88%**	**70%**
	South	**94%**	**74%**
	West	**88%**	**73%**

Additional detail on the demographic characteristics of women enrolled in the NCS Vanguard Study by recruitment group is provided below.

Demographic Characteristics of Enrolled Women		Total	Enhanced Household	Provider Based	Direct Outreach	IVC	PBS
		Percent within Demographic group	%	%	%	%	%
Ethnicity/Race	Hispanic	18.1	25.2	14.7	7.5	12.8	40.7
	Non-Hispanic White	57.5	52.6	53.4	73.8	60.3	33.9
	Non-Hispanic Black	12.2	10.6	20.3	12.5	4.1	16.0
	Non-Hispanic Other	9.5	10.3	5.9	5.9	16.4	9.3
	Missing	2.7	1.3	5.7	0.3	6.3	0.1
Age	Under 25	23.0	30.0	30.5	19.8	11.4	28.8
	25-34	57.1	56.0	48.4	63.6	58.2	54.7
	35-49	18.3	13.8	14.1	16.3	30.4	15.0
	50 and over	0.1	0.1	0.2	0.0	0.0	0.1
	Missing	1.5	0.1	6.9	0.3	0.0	1.3
Education	Less than high school	13.2	17.5	17.1	5.9	10.5	21.1
	High school / Some college	45.0	52.1	52.9	36.1	38.3	53.3
	College graduate or more	39.7	29.7	29.3	57.3	44.5	25.4
	Missing	2.0	0.8	0.7	0.8	6.7	0.2
Marital Status	Married	65.5	59.7	51.4	79.5	78.1	44.3
	Unmarried	34.1	40.0	48.4	20.2	20.8	55.7
	Missing	0.4	0.3	0.2	0.3	1.1	0.0

The final table describes the ethnicity and race of enrolled children.

Ethnicity/Race of Enrolled Children		Percent within Demographic Group
Ethnicity/Race	Hispanic	17.4
	Non-Hispanic White	59.5
	Non-Hispanic Black	11.6
	Non-Hispanic Other	2.3
	Missing	9.2
	Total	100.0

B.2 Procedures for the Collection of Information

This Information Collection Request (ICR) encompasses all data collection activities within the NCS Vanguard Study. The NCS proposes the establishment of Study visits for enrolled children at older ages (that is, 36 – 60 months), the initiation of a new enrollment cohort, revisions to already established Study visits, and two methodological substudies.

NCS Study visits are designed to maximize participant response and therefore allow for maximum flexibility. Instruments are generally developed for multi-mode administration and, unless specific method or mode requirements exist, may be completed in-person, by telephone, with secure web-based administration, or hard copy with a mailed questionnaire. Additionally, while we optimize the use of computer-assisted interviewing (CAI), we acknowledge the need for hard copy questionnaires to facilitate and promote response.

With this ICR, the NCS Vanguard Study will align all enrolled participants with a common protocol. Exceptions to this are highlighted in Supporting Statement A and occur when planning initial field tests of a particular measure or assessment that do not require the full sample size for later analyses. The requested frequency of all collections was carefully examined by the NCS Program Office and repeated measures only included when needed for key analyses, testing at specific age intervals, or alignment with other national or international studies.

To ensure the collection of high quality data, the NCS has defined processes and standards for critical components of the research process. Highlighted are (1) informed consent; (2) data collector training and oversight; (3) instrument development and informatics; (4) data review and monitoring; and (5) procedures for adverse event and other reporting.

Informed Consent

The NCS Vanguard Study uses a phased and ongoing informed consent process. Permission for participation must be granted for all enrolled adults and children prior to administration of Study visits. Adult participants, including mothers, fathers, or other primary caregivers, provide consent for their own participation. Adult participants are asked to provide both general consent to complete Study visits and questionnaires as well as consent to allow for the collection of biospecimens and environmental samples. Those who agree to provide biospecimens are also asked for permission to allow genetic analyses of collected specimens. These consents are documented with a hard copy signature page.

Permission for the enrolled child's participation is collected at two separate time points. Mothers, or another legally authorized representative (LAR) for the child, are first asked to provide written permission for the child's participation from birth to 6 months of age. Subsequently, at the time of administration of the 6 month Study visit, the mother or LAR is asked to grant permission for the child from 6 months of age until the Age of Majority. Consent is documented with a hard copy signature page in which the specific level of consent is documented, including whether biospecimens and environmental samples may be collected, and if so, whether genetic analyses of collected biospecimens are permitted.

To ensure that the informed consent process is active and ongoing, the NCS Vanguard Study supplements the written consent described above with an additional Multi-Mode Visit Information Script (MMVIS) administered at the start of each Study visit, which introduces the questionnaire(s) portion of the visit. The process is designed to inform participants of activities to be completed at a

particular visit and remind them that participation is voluntary and that they may skip questions and samples as they choose. The MMVIS is designed for administration either in-person or by telephone. For Study visits that include other data collection activities -such as biospecimens, environmental sample collection, and physical measurements - additional language is provided in a *Sample Collection VIS* which is created from a set of VIS specifications describing each specific data collection activity, its administration procedures, and possible risks. To complement the VIS, participants are read a reconsideration script at each visit which reminds them of their initial consent status for sample collections and offers the opportunity to take part on or refuse sample collection. If participants initially refused sample collection, but indicate willingness to provide samples at a particular visit, the initial consent will be re-administered and the new preference will be documented.

The table below maps proposed Consent materials with associated Study Visits.

Consent Materials	Study Visit
Pregnant Woman Consent	PV1, PV2
Adult Consent	1) Post-natal mother 2) Post-natal father 3) Post-natal new caregiver 4) Any adult participant requiring re-consent
Father & Parental Partner Consent	PV1, PV2
Parental Permission for Child's Participation – Birth to 6 Months of Age	PV2, PV1 if no time for PV2 visit, Birth, 3M if not obtained previously
Parental Permission for Child's Participation – 6 Month Visit to Age of Majority	6M, any subsequent visit if not obtained previously
Multi-Mode Visit Information Script	All visits
Sample Collection Visit Information Sheet Scripts	Pre-pregnancy, PV1, PV2, Birth, 6M, 12M, 24M, 36M, 48M, 60M
Reconsideration Instrument Child & Adult	Child: 12M, 24M, 36M, 48M, 60M Adult: Pre-pregnancy, PV1, PV2, 6M, 12M, 24M, 36M, 48M, 60M
HIPAA Authorization for Use and Disclosure of Health Information	Any visit – trigger-based
HIPAA Authorization to Obtain Bodily Fluids and Tissues	Birth
Authorization Form for Release of Child Death Certificate	Any post-natal visit – trigger-based
Authorization Form for Release of Parent/Guardian Death Certificate	Any visit – trigger-based
Authorization for Release of Health-Related Birth Certificate	Any post-natal visit

Data Collector Training and Oversight

The NCS developed a broad and comprehensive model for training field data collectors. We have implemented a multi-stage approach where training materials and programs are developed centrally by content experts and administered to ROC supervisory and training staff. ROC staff then subsequently train and certify their local data collection staff.

High-quality training is critical to success of NCS data collection and we have taken steps to ensure that trainings meet defined standards. First, in 2011, the NCS launched an introductory training program and resource toolkit designed to develop individual's skills as trainers. The curriculum - developed in consultation with the American Society for Training and Development – focused on how to organize, plan, and conduct trainings, respond to protocol revisions, and provide remedial and refresher instruction and evaluation. Materials were based on respected theories of adult learning,[1,2] such as offering multiple modalities for learning content and the need for active learning sessions. Attendees prepared and administered training modules, which were videotaped, and subsequently received one-on-one reviews with instructors.

Next, in February 2013, ROC supervisory and training staff members were required to attend an introductory training to the NCS. This curriculum, referred to as the NCS Building Blocks Training, provides an overview of the NCS, and sets standards, policies, and procedures for data collection efforts. Designed with separate curriculum for data collectors and trainers, the Building Blocks modules are designed to reinforce best practices for training, gaining participant cooperation, and data collection; emphasize the importance of correct administration of informed consent; and define criteria against which to evaluate both data collectors and trainers. Some modules were required to be completed via a web-learning system and others were administered as part of the in-person sessions. All attendees were evaluated based on their role in the Study; either administering a mock data collection or presenting a module as a trainer and, if successful, were certified. Those who did not certify were either offered an opportunity for remedial instruction and re-certification or not allowed to progress further in their role. Certified ROC supervisory and training staff members are permitted to serve as trainers for their local data collection staff. Data collectors who were certified are eligible to receive instruction and certification on domain-specific NCS modules. As successful completion of the Building Blocks curriculum is required of all newly hired staff, ROCs are responsible for holding ongoing sessions as needed.

Training modules intended to cover the administration or collection of specific questionnaires, measures, or assessments are developed and administered centrally by Program Office domain teams and contractors. Trainings may address new measures, provide updates to Study protocol or procedures, or serve as a refresher training to reinforce standards and best practices. Depending upon the subject matter, these trainings may include any or all of the following modalities: remote webinars, training videos, on-line learning modules, or in-person, multi-day events. In general, large in-person training events are highly choreographed to include direct instruction, practice sessions, observation and evaluation, and certification. These training events are required for any planned collection of biospecimens, physical assessments, and environmental samples; and include instruction on preparatory activities and post-collection processing, storage, and shipping. Once certified by domain team experts, ROC supervisors and trainers are allowed to train and certify local data collection staff and are required to track and report the status of such trainings and certifications as part of their ongoing reporting deliverable.

Once data collection activities have begun ROC supervisors are expected to hold, at a minimum, weekly calls with individual field interviewers to identify issues and areas of concern, and provide strategic guidance. Interviewers based in a call-center facility may be monitored in other ways, including direct

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[1] Knowles, M. S. (1980). *The Modern Practice of Adult Education: From Pedagogy to Andragogy*. Englewood Cliffs: Prentice Hall/Cambridge.

[2] Bloom, B.S. *Taxonomy of Educational Objectives*, (1956). Allyn and Bacon Publishers, Boston, MA.

observation, and review of live or taped interactions with participants. Additionally, ROCs monitor data collector performance through detailed review of cases and interview data. Validation interviews also provide critical information on interviewer performance and help to identify instances of data falsification.

Instrument Development and Programming

NCS instruments, protocols, and procedures are designed centrally at NICHD with the input of subject-matter experts and the greater NCS community of contractors and stakeholders. Additionally, this ICR includes multiple assessments developed as part of the NIH Toolbox. Details related to the construction, validation, and norming of these measures for children as young as 3 years of age are available at www.nihtoolbox.org.

To ensure quality and consistency of data collection, all instruments are designed with standardized variable names, question text, response categories, skip patterns, range checks, and interviewer and programmer instructions. Data layouts are available for each instrument and for all operational data that describe the process of collecting the data, and specify required formats, labels, and code frames. Most importantly, the data layouts specify handling of various types of item nonresponse distinguishing between legitimately missing data versus those missing in error.

Proposed New Instruments

This ICR includes three new instrument modules developed specifically for the NCS as part of the Study's formative research portfolio. These include the (1) Retrospective Pregnancy Questionnaire; (2) Post-Natal Father Questionnaire, and (3) Cultural Values battery. The design and development process for each instrument is described below.

The **Retrospective Pregnancy Questionnaire** (RPQ) was developed in collaboration with RTI. All protocols and materials used in the cognitive testing were reviewed and approved by the RTI Institutional Review Board (IRB). If approved, this instrument will only be administered to a small subset of the Vanguard cohort. Specifically, only women enrolled in the proposed Sibling Birth Cohort will be asked to complete it. While modeling to predict the number of likely pregnancies among already enrolled women, the NCS anticipates no more than 500 babies will result from this effort. This estimate is reduced from the original requested burden.

Cognitive testing was conducted in Atlanta, GA, and Raleigh-Durham, NC. Potential participants completed a screening questionnaire to ensure that they met the eligibility requirements. Fewer than 10 participants were administered each of the six questionnaires and PRA approval was not sought. Women who were under the age of 18 at the time of the screening, had not given birth in the past 6 months, or were currently or previously enrolled in the National Children's Study were not eligible to participate in the cognitive testing. The screening questionnaire also collected demographic information from potential participants, including age, race, ethnicity, education, and household income. Women were recruited at Women, Infants, and Children (WIC) Supplemental Nutrition Program clinics, Hispanic maternal health clinics, and at church day care centers and other community locations. Additional participants were recruited through word of mouth and snowballing efforts, wherein willing participants referred other local women who had given birth in the past six months. The NCS made a concerted effort to recruit and enroll women from diverse races, ethnicities, and socioeconomic backgrounds. Participants received a $10 monetary incentive.

Of the 75 women asked to participate, 6 refused, 15 were ineligible, and 54 completed the interview. The participants were aged 18 to 40 years, with a mean age of 27.4 and a median age of their infants were 1 week to 6 months old, with a mean age of 3.0 months and a median age of 3.0 months. There was no apparent clustering of demographic characteristics by testing module, with one exception: by design, six of the women who were interviewed with the medications instrument (one of six instruments in the RPQ) had infants who were 1 month old or younger. Most women were white (21) or African-American (28). One woman was multiracial and four either refused the question or felt that none of the race categories were appropriate. All 12 women who completed the interview in Spanish considered themselves Hispanic.

For testing purposes the RPQ questions were divided into six instruments; each requiring 20 minutes or less to complete. Each instrument included general instructions to assist the participant in understanding the cognitive interview process, the interview questions, and scripted interviewer probes. A bilingual language methodologist translated each new or modified question into Spanish, and a second methodologist reviewed the translations. Each participant completed one instrument (which was composed of one or more modules). Staff conducted the interviews using scripted cognitive interviewing protocols. The interviewer also asked spontaneous probes as needed to explore specific responses. Except for a self-administered module designed to collect potentially sensitive data, the interviewer read the instrument questions out loud, following up with probes as needed.

Women could generally answer questions confidently and without difficulty when the questions were clearly defined and about topics central to their lives or pregnancies. Three types of questions were most problematic, including (1) questions about situations that could change over the course of pregnancy, such as living situation and household composition; (2) questions that asked for information the woman did not have direct knowledge of, such as the details of pesticide application; and (3) questions that required recall of activities that may not have seemed important at the time or were of short duration, such as taking over-the-counter cold medications. Revisions were made based on these results.

The **Post-Natal Father Questionnaire** was developed in collaboration with Battelle. Historically, not all fathers were eligible to complete a father-specific questionnaire. During the Initial Vanguard Study, pregnant women were asked to identify the father and provide permission for the NCS to contact and attempt to interview him. During the ARS phase, only 15 Study Locations were allowed to conduct similar interviews with fathers during the pregnancy period. (This was approved as part of the ARS Phase 2 ICR in April 2011). As a result, the NCS has only sparse data from the fathers of enrolled children recruited as part of the ARS. Furthermore, formal engagement of fathers in the data collection process is important for retention of families.

The development of the Post-Natal Father questionnaire was a multi-stage process that included gathering information from past research (literature and surveys); consultation with experts; cognitive interviewing; a small pilot test; and revisions to survey questions based on the test results. Cognitive interviews were conducted with a total of adult fathers (N = 9) recruited in and around major metropolitan areas in the Midwest and West regions of the United States. Informed consent was obtained from all participants. The purpose of the cognitive testing was to ensure that the proposed questions and response categories in newly-added questions were being interpreted as intended by respondents.

Subsequently a questionnaire was finalized to conduct a pilot test of the full telephone interview under actual survey conditions. This provided a final check on the feasibility of the questionnaire items and response categories, as well as a good estimate of respondent burden. A 30-minute telephone interview was conducted with a total of nine (9) fathers of young children using the revised instrument. Participants, all of whom were adult fathers age 18 or older, were recruited in and around major metropolitan areas in the Midwest and West regions of the United States. Participants were asked a few brief questions on their comprehension and evaluation of the survey instrument. Interviewers also provided input on any questions that were difficult for the participants to answer. The final NCS Father Post-Natal Questionnaire provides an instrument to conduct a brief 20-minute telephone interview to collect information relevant to child health and development during early childhood from fathers of diverse backgrounds (for example, race, ethnicity, socioeconomic status, age).

The **Cultural Values** battery that may eventually be tested in the Vanguard Study was developed in collaboration with Battelle. The goal was to develop a scale that can be used with all ethnic groups and that does not pose a burden on respondents (e.g., a scale of approximately 12 items). Battelle developed a multidimensional measure of cultural values was developed using qualitative techniques. It was decided that the questionnaire should include measures for the dimensions of Individualism/Collectivism, Machismo, Interpersonal Relations, and Time Orientation with three to four questions on each dimension. Although qualitative techniques were used to develop the scale and final questionnaire, the NCS relied heavily on relevant literature for item selection.

A multi-phase development approach was used beginning with detailed reviews of the literature to identify existing acculturation and cultural values scales (along with their psychometric properties and data source) that may be used (or adapted for use) in measuring acculturation and cultural values across racial and ethnic groups. Next, focus groups were designed and conducted to gather information from mothers and fathers from diverse ethnicities regarding their perspectives on the four cultural values domains, the specification of the domains, and the potential questionnaire items. The focus groups consisted of two-hour discussions about the draft subscales that were conducted separately with mothers and fathers in the NCS St. Louis office during May 2011. The Mother Focus Group included eight mothers of diverse ethnicities (non-Hispanic African American, Columbian, Mexican, Asian (Indian), Italian, and non-Hispanic white) and with different education levels (high school degree or GED, and Bachelor's degree). The age range of the mothers participating in the focus group was 18 to 44 years. The Father Focus Group included two African American fathers, a Chinese American father, a Puerto Rican father, and two non-Hispanic white fathers (n=6). The education levels present in the Father Focus Group ranged from less than high school to post-graduate degree, and ages ranged from 21 to 74. Participants in each focus group provided their perspectives on the four cultural domains, the specification of the domains, and the potential questionnaire items. Participants were asked to identify the items within a subscale that were most important or relevant to their parental role and to pregnant women. In addition, participants were asked to identify items that were confusing or did not make sense, as well as to note any questions that might be missing but which should be asked or items which were particularly effective in capturing a concept.

Next, cognitive interviews were conducted to ensure that the proposed questions and response categories were being interpreted as intended by diverse respondents. Interviews were conducted in St. Louis with four mothers and five fathers. The mothers' ages ranged from 25 to 37, included a mix of ethnicities (Asian, non-Hispanic African American, South American, and non-Hispanic White) and varied education levels (Associates/Trade degree, some college, and post-graduate schooling). The fathers' ages ranged from 26 to 40 and also included a mix of ethnicities (Filipino, non-Hispanic African

American, Cuban, and non-Hispanic White) and varied education levels (less than high school degree, high school degree or GED, and Bachelor's degree). During the two-hour in-person cognitive interviews, the interviewer collected information from the participant on each subscale by asking him/her to read the survey questions and to think out loud when answering the survey questions. The interviewer then also asked specific questions about each item in each subscale related to the participants' understanding and comprehension of the item, difficulty in answering the survey question, any confusing or unclear parts, and their confidence in answering the question. The interviewer also asked participants which items in the section best reflect or represent the concept of interest, as well as overall questions on the purpose of the survey items, any items particularly difficult to answer, or any they recommend to drop.

Lastly, to test the instrument under actual survey conditions, provide a final check on the feasibility of the subscale questions and response categories, and provide an estimate of respondent burden. The revised set of scale items was pretested through a pilot survey involving a 30-minute in-person interview with three fathers and six mothers (all 18 years or older). Participants were recruited from the St. Louis metropolitan area. The pilot sample was diverse in terms of ethnicity, marital status, education, and income. The average age of participants was 37.3 years.

Informatics

The NCS Vanguard Study continues to develop and test several informatics options. The NCS approach to informatics has been informed by several trends, including the use of open, modular, and flexible architecture, the leveraging of standards-based terminologies and transmission specifications, interoperability, and established development communities. Overall, this approach fosters innovation while adapting to the ever-evolving field of informatics. Each ROC has been paired with a unique informatics provider (or "hub") that is charged with providing all data collection, case management, and data review tools, and hardware. Each IMS hub has been certified and accredited per the Federal Information Security Management Act of 2002 (FISMA) and meets all regulatory compliance standards. To support NCS data collection, hubs use standardized instrumentation and specifications developed by the Program Office to program individual systems. ROCs and IMS hubs work collaboratively to conduct user-acceptance testing of instruments, and ensure all data collectors are trained on using the software to conduct Study events.

Program Office Data Review and Monitoring

In addition to the summary and case-level data reviews undertaken by the ROCs, the Program Office conducts ongoing monitoring of data submissions to evaluate quality and completeness of all submissions. Centralized review of data focuses on cooperation rates for Study visits and key individual items. Contracting Officer Representatives with oversight of the ROCs also hold biweekly calls with each contractor to review current progress. Production reports developed by the PO and completed by the ROCs help inform these discussions. These reports provide highly granular descriptions of the effort at each Study location, tracking rates of re-consent activities, cases requiring locating and tracing efforts, and participation and completion of individual Study visits by mode.

Adverse Event and Other Required Reporting

NCS has implemented monitoring and reporting procedures that meet or exceed all requirements of various oversight bodies, including the Office of Human Research Protections (OHRP), the NICHD IRB, and the NCS Independent Study Monitoring and Oversight Committee (iSMOC) to ensure that human subject protection regulations are followed, participant confidentiality is maintained, and study protocols are implemented correctly. Within this structure, ROCs are responsible for reporting to the NCS PO using a standard format within 24 hours of knowledge of serious adverse events, unanticipated

problems, suspected or confirmed confidentiality breaches, or failure to obtain legally effective consent. The NCS Program Office then adjudicates and responds to all incidents reported at least once per week (or more frequently, depending on the nature of the event and associated regulatory requirements).

B.3 Methods to Maximize Response Rates and Deal with Nonresponse

To promote high response rates, the NCS Vanguard Study utilizes known best practices to tailor retention approaches to the individual participant. Many of these are based on the theories of social exchange and reciprocity as put forth by Don Dillman.[3] This work stresses the importance of topic salience, minimization of burden, and maximization of flexibility for response.

In addition to providing flexible options for participating, including multiple modes of Study visit administration and scheduling interviews to meet individual schedules and needs, the NCS employs strategies and practices found to be successful in other longitudinal studies. For example to demonstrate our appreciation participants are provided with small monetary and non-monetary incentives.

Nonresponse can be minimized through the caliber and training of the data collection staff. The NCS has charged data collection contractors with hiring experienced field and telephone interviews who are responsive to participants and able to collect data of the highest quality. These data collectors must be able to adapt their approach to best meet the needs of individual respondents. For example, the timing or method of contact may be very different for a father than for a grandparent who is a primary caregiver. Additionally, during the transition of data collection contractors, the ROCs have hired many NCS-experienced interviewers who already have relationships and rapport with enrolled participants.

Interviewers and supervisors strategize about the best way to work each case; reviewing past case histories to determine the best times to contact someone for an appointment and identifying any special considerations for the case. To facilitate these attempts, the NCS collects detailed tracing information from participants – including cell phone numbers and email addresses – to enhance our ability to make subsequent contacts.

If a participant refuses, there are effective strategies to gain their cooperation. ROCs utilize highly trained interviewers – refusal converters – who use known techniques to make a case for participating. One of the most effective strategies is simply letting the case "rest" for a few weeks. Often times, refusals are simply a reflection of a given moment in time and not a long-term reaction. An effective refusal converter will understand what questions to ask to identify core concerns and take steps to address these issues. However, some participants will continue to refuse and their decisions are respected. Data collectors will always leave open an opportunity for later participation and communicate that future involvement will be welcomed.

The conduct of ongoing sample maintenance activities is also critical to reducing unit nonresponse. The NCS has developed extensive policies and guidelines for tracing and locating participants who have moved. We ask participants to provide detailed contact information for themselves and others in their lives. We also utilize change-of-address services available from the United States Postal Service and commercial databases that maintain individual-level information. As needed, data collectors may

[3] Dillman, Don A. 1978. Mail and Telephone Surveys: The Total Design Method. New York: Wiley-Interscience.

conduct in-person locating efforts to identify those who are most difficult to reach. All NCS tracing and locating activities have been approved by the NICHD IRB and were developed to ensure confidentiality protections are not violated.

NCS ROCs participate in multiple collaborative improvement networks, including one specifically focused on participant retention. The charge of this group is to highlight existing or potential problems and identify the range of associated factors. Based on this inventory, brief tests are developed and executed using a Plan-Do-Study-Act cycle. Sequential tests build on earlier outcomes and can help refine our procedures. The retention-focused network has developed tools to identify risk factors for retention and whether they are universal or specific to a given Study location or population. These efforts enhance NCS efforts to tailor approaches to the unique characteristics of each participant.

The NCS Vanguard Study reports cooperation rates for specific study visits or assessments. Specifically, we calculate the number of participants who fully or partially complete a visit or assessment, divided by the total number eligible for administration.

B.4 Tests of Procedures or Methods to be Undertaken

Overarching research questions and research questions specific to this information collection were presented in Part A of this supporting statement. This section describes our plan for ongoing evaluation.

Key evaluation questions during this continued phase of the Vanguard Study concern the feasibility, acceptability, and cost (when applicable) of data collection operations and processes to assess and understand if each visit, components of individual visits, and individual data collection instruments work to capture the desired information and can be scaled up for the Main Study. In addition, to answer critical scientific questions it will be essential to retain a sample of sufficient size throughout the course of the Main Study. Determining expected rates of retention of participants through pregnancy to birth and beyond is a key part of the analytic plan for the Vanguard (Pilot) Study. Retention of participants from visit to visit will be carefully monitored. Retention challenges and solutions will likely vary by the nature of the visit, the length of time between visits, and the participant's stage in the study cycle. Additional planned evaluations specific to this ICR are detailed below.

Race and Ethnicity Questions. As noted in SSA, in the 36 month Study Visit the NCS is tailoring the format of Race and Ethnicity questions by mode of administration, while still maintaining fidelity to OMB and HHS requirements. To determine the impact of this structure, the NCS will evaluate any impact item nonresponse and data quality.

Biospecimen Collections. This ICR includes the addition of new and previously approved biospecimens to Study visits. The NCS will evaluate any impact of adding collections for participants who were historically not asked to provide them, or those with multiple children enrolled and experience variation across children regarding which specimens were collected at which visits.

Participant Motivation Questionnaire, to be administered at 48 month visit, will be evaluated on individual response distributions to understand participant's experience in the Study and what motivates them to continue participation. **Participant Satisfaction Questionnaire** responses will also be analyzed to help determine the acceptability of the various components of Study Visits.
The Sibling Birth Cohort will enroll sibling births from NCS mothers' subsequent pregnancies with a primary goal of collecting preconception data and data early in pregnancy, during critical periods of development. This has an important implication for developing a design feasible for collecting pre- or

peri-conception data given the Vanguard Study results to date which indicate that current methods of enrolling pre-conception women and collecting pre-conceptional data are extremely difficult and cost-prohibitive. The NCS will determine whether subsequent pregnancy data along with the data already collected on the family environment from the NCS index child can serve to provide peri-conceptional data.

Statistical goals of two methodological experiments involving incentives are to test the impact of incentive variation on data collection cooperation rates, data quality, and costs. This will help develop an effective incentive structure that enhances long-term retention and data collection compliance for this longitudinal Study. Experiment #1 will test the impact of the amount and timing of monetary incentive (Early Bird bonus vs. no Early Bird bonus) at each data collection event on participant retention and cooperation rates. Experiment #2 will test the impact of different incentive conditions and their timing of delivery to participants on response to a mailed Self-Administered **Tracing Questionnaire**. The current NCS Vanguard Study cohort of approximately 5,000 families/children will be randomly allocated into experimental groups – 4 groups of 1,250 participants each in Experiment #1 and 5 groups in Experiment #2 with sample size of 1,666 in one group and 833 in the other 4 groups.

The key outcome metrics – retention rates and Study Visit cooperation rates in Experiment #1 and SAQ completion rates in Experiment #2 – will be compared among these experimental groups overall and by key demographic subgroups. The differences in rates between various experimental groups and subgroups will be tested for statistical significance. Since the majority of the NCS participants are expected to be in both experiments, multivariate regression analyses will also be performed to adjust for being in various arms of the other experiment and to account for the time period or specific Study Visit at which the participant participated in these experiments. The effect of Tracing Questionnaire administration and its completion by participants on the Study retention rate will also be assessed independent of the stated analyses for these two experiments.

B.5 Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

The data collection activities and protocols described in this ICR have been presented to and benefited from comments received from staff from several federal agencies, advisory committees, and scientific experts. Federal agencies consulted include but are not limited to the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention, the Environmental Protection Agency, the Census Bureau, the Bureau of Labor Statistics, the National Institutes of Health (NIH) including the Division of Epidemiology, Statistics, and Prevention Research (DESPR) at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Institute of Environmental Health Sciences, and the National Human Genome Research Institute (NHGRI). Specific scientific input received during development of individual measures is highlighted in the associated descriptions in Supporting Statement A, Section 2. Lastly, the protocol is provided to NCS contractors for their review and input. Contractors include Study Center principal investigators and affiliated researchers, as well as statistical and other subject matter experts from contract research organizations.

Once approved data collection activities will be conducted by NCS Regional Operations Centers: NORC at the University of Chicago, Westat, and Northwestern University. Each organization has also provided review and comment on included measures and assessments.