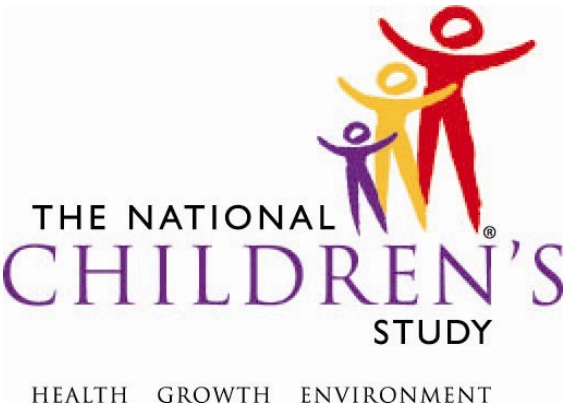

Supporting Statement B for

Pilot Study for the National Children's Study (NICHD)

OMB Re-Submission—August 29, 2008

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B. Collection of Information Employing Statistical Methods

B.1 Respondent Universe and Sampling Methods

The NCS Pilot Study will be conducted at the first seven study locations (Vanguard sites), and will consist of births that occur to eligible women in these locations from approximately July 2009 through June 2010.

A number of study and sampling design options were considered for the NCS (see Sample Design Options and other related documents available at http://www.nationalchildrensstudy.gov/events/advisory_committee/other_work_062004.cfm). There are advantages and disadvantages to each of the candidate approaches. However, after careful consideration and upon the advice of the NCS Federal Advisory Committee, a national probability sample of all U.S. births was chosen as the design that best fulfills the following goals:

- Collection of high quality, objective data to minimize measurement biases.
- Avoidance of selection biases and other biases that could lead to invalid inferences concerning exposure/outcome relations.
- Ability to capture the diversity of the U.S. population such that both the range and diversity of exposures and outcomes are represented.
- Ability to generalize results of the NCS to the U.S. population.

The selection of participants for NCS is based on a multistage probability design using an area frame. Sample size requirements for specific outcomes generated 100,000 births as the targeted number of participants. In particular, analyses of gene-environment and environment-environment interactions require analysis of specific subgroups; many of these resulting subgroup analyses are only possible with a large original sample. The sample sizes required for the specific study hypotheses vary but, in general, samples approaching the proposed 100,000 are required.

The first stage of sampling was the selection of primary sampling units (PSUs), which correspond to single counties or groups of contiguous counties. The second stage is the selection of smaller geographic areas (segments) from within the primary sampling unit. In general, these segments comprise city or suburban blocks or combinations of blocks and roughly correspond to neighborhoods. The third stage, which applies only to very densely populated segments, involves the selection of groups of households from within the segments.

As described in Part A, Section 2.1, the seven Centers included in the Vanguard Pilot represent a diverse set of PSUs included in the NCS, i.e., metropolitan/non-metropolitan, four Census regions, and certainty/non-certainty PSUs. The data collected during the Pilot phase will not be incorporated into the Main Study sample. The Vanguard Centers involved in the Pilot will continue to follow the initial Vanguard Pilot Cohort throughout the life of the NCS, and will begin to enroll Main Study participants concurrent with the other Wave 1 Main Study sites.

Appendix C.8 provides the detailed Sampling and Recruitment Plan for NCS.

B.2 Procedures for the Collection of Information

For the Vanguard Pilot, women will be enrolled into the NCS Pilot Cohort through a household enumeration and screening process that follows listing of households. Part of the Pilot also includes testing of a combined household listing and enumeration protocol, to be tested in the five Group 2 Vanguard Centers. Data collectors will list all dwelling units in the selected segments. Regardless of when the dwelling unit is listed (either prior or concurrently), listing data collectors will attempt to enumerate the household by speaking with a household member who is at least 18 years of age. All age-eligible women will be asked to complete the pregnancy screener, using Audio-computer assisted self-interviewing technology (A-CASI). Probability of pregnancy will be assigned based on their responses to the pregnancy screener: high, moderate, low, and no probability of pregnancy (see Appendix C.3.6). Pregnant women whose due dates are eligible (i.e., 6 months or more after the start of screening activities in that location) will be asked to enroll in the Study. Age-eligible women who are not pregnant will be assigned to a pregnancy probability group. Women with a high probability of becoming pregnant will be eligible for enrollment. Women with a moderate or low risk of pregnancy will be followed to determine if they become pregnant within the enrollment period for the Pilot Study. Study eligible women will complete the initial consent process either at the first pregnancy visit or at the first preconception visit.

Women with a high probability of pregnancy will be asked to schedule a time for study staff to visit her home to obtain consent, administer a questionnaire, collect environmental samples, biospecimens and physical measures, and return seven days later to collect environmental sampling equipment, self collected samples and self administered questionnaires. These women will then be called monthly (for up to four months) to determine if they become pregnant. Study staff will leave in-home pregnancy kits for the women to use to determine if they are pregnant.

Women with a moderate probability of becoming pregnant will not be enrolled in NCS, but will be re-contacted approximately three months after the initial pregnancy screening to re-evaluate their probability of becoming pregnant. Women with the lowest probability of becoming pregnant will be contacted semi-annually by phone. It is anticipated that during the enrollment period, a woman's probability of becoming pregnant will not be stagnant. Data collection schedules will be modified based on the most current information on each individual's probability of pregnancy. Women with no probability of becoming pregnant will not be re-contacted.

Once women are pregnant, a 1st trimester home visit is planned. A visit in each of the 2nd and 3rd trimesters will occur in a clinical setting to enable the collection of study-sponsored fetal ultrasounds. Fathers of enrolled children will also be eligible for the Study, starting with the 1st trimester visit. However, if the mother does not want the Study to contact the father, she and her child will still be eligible for the Study.

At the time of birth, biologic specimens will be collected from the mother and baby. During the hospital stay other measures will be taken, including a neurological assessment. Medical records from labor and delivery, including the infant's hospital stay, will be abstracted. If it is not possible to collect certain measures prior to discharge, study staff will visit the mother and baby approximately one month after discharge. Brief telephone contacts with the mother are planned for 3, 9, 18, and 24 months after birth. At 6 and 12 months, in-person home visits are planned. At these visits, data will also be collected from the father (or the male partner living in the household). For a sub-sample of children enrolled in the Study, visits will also be made to child care settings for collection of environmental samples and observational data.

Data and information collected for NCS can be categorized into six broad types: questionnaire data, physical/medical examination data (e.g., blood pressure, ultrasounds, anthropometric measurements, etc.), biologic specimens (e.g., blood, urine, hair, saliva, etc.), environmental samples (e.g., dust, water, air,

soil, etc.), videos or still photographs (of the child), and medical chart abstractions. Appendix C.3 contains detailed tables providing specific measures to be collected at each planned contact. Participant questionnaires and data collection forms can be found in Appendices A.1 and A.2. In addition, brief evaluation questionnaires will be administered to selected health care providers and community leaders during the pilot (see Appendix C.9).

B.2.1 Informed consent

The NCS is primarily observational in nature and will have a low level of subject risk. Despite the minimal risk, however, many human subjects issues require consideration because of the duration and complexity of the research; the diversity of the participants; the collection of biologic, environmental, social and behavioral measures; and the creation of enduring data as well as biologic and environmental sample repositories with the potential for future studies not yet conceived. The informed consent plan for the study takes into account the various types of participants, and is tailored to address specific issues pertaining to each type. The types of participants who will require consent or assent include women at risk of becoming pregnant (pre-conception women), pregnant women (adolescents and adult women), biological fathers, other caregivers (such as mother's boyfriend and foster parents), and children.

Young women under the age of 18 will not be screened and will become part of the Study only if a household reporter reports that she is pregnant. Study centers are responsible for adhering to State laws on consent by a minor (e.g. some states may view pregnant teens aged 16 and over as emancipated minors, and therefore able to give consent). Parental consent will be required for any pregnant adolescents age 14 and younger. Women who are cognitively impaired or mentally ill are not eligible if they are not able to fully understand the requirements of the Study and grant informed consent.

At enrollment for the Pilot Study, participants will be asked to provide their informed consent for study participation. The NCS has developed an electronic consent tool to obtain signed informed consent from participants. This innovative approach to informed consent was designed to overcome some of the perplexing problems about informed consent documented in the literature. The primary goal of the video is to enhance prospective participants' understanding of the purpose of the study and all of the essential elements of informed consent. Because this is a new and innovative approach, an evaluation of this approach has been built into the NCS Pilot Study in order to determine whether this method will result in different study enrollment rates than using a more traditional hard-copy informed consent document. B.1.1 provides more details on the informed consent evaluation.

Once participants have provided their written consent, at each visit they will be given detailed information about what that specific visit will entail, and each activity they will be asked to perform. Data collectors will then request oral approval to continue, and will make note of any activities the participant does not wish to do. For telephone contacts, the same approach will be used (i.e., providing a detailed explanation of the contact activities and requesting oral consent to continue). The results of the oral consent for each contact will be tracked in the IMS.

Consent materials will be available in English and Spanish. Interpreters will be available for additional other languages. The consent plan also recognizes that pre-conception women may become pregnant and at that time will need to have additional consent obtained for continued participation in the study and permission obtained for participation of their infant in the Study. Fathers will also be consented prior to their participation in the Study. Appendix B.1 presents all consent documents for the visits covered by this clearance request. IRB approvals are pending (Appendix C.12).

B.2.2 Quality control during the Vanguard Pilot phase

The first step in coordinating across Vanguard Centers is development of a comprehensive set of quality assurance (QA) and quality control (QC) procedures to which all sites must adhere, and documenting these procedures in the NCS Quality Assurance Process Plan (QAPP). The QAPP will ensure the collection, documentation and processing of accurate, reliable data. The procedures will reduce inter-examiner variability, reduce error, and ensure data quality. The components of the QAPP plan incorporate specific quality control procedures for training, site monitoring, data monitoring, equipment and calibration checks, and repository and laboratory standards and monitoring.

The Coordinating Center, in collaboration with the NCS Program Office, will use several approaches to assess adherence to and improvement of the QA and QC procedures. A large portion of the evaluative information regarding adherence and effectiveness of the procedures required in the QAPP will come from automated reports generated from the Information Management System (IMS). We propose that the IMS capture data regarding the following types of items and generate reports at an SC level, as well as across all locations:

- Protocol expectations and fulfillment by center and overall (e.g., results of observation reports addressing data collection, activities in labs and processing centers, activities at data capture centers)

- Data collection production trends and backlogs (e.g., response rates, started cases, not worked, resolved, etc., by date)

- System issues such as infrastructure reliability and availability (network, database) and requests for assistance from centers, type of request, and reason for request

Monitoring, reporting, and analyses of these results will allow the Program Office and the Coordinating Center to focus efforts to improve performance and quality in a cost-effective way – directing resources to addressing the most important issues.

As an additional method for assessing adherence to and improving the QA and QC procedures, the Coordinating Center will monitor the QA/QC activities through direct observation at each Vanguard Center as well as by repeating a subset of the QA/QC measures collected by each Center. Both these techniques are more costly than information gained through reports, but both also provide information not as visible in automated reports. Thus, the Coordinating Center will conduct direct observations and repeat measures of QA/QC assessment procedures on a small sample of cases, at each Center. Evidence of problems will trigger more on-site presence.

The QA/QC program begins with effective initial training and re-training of all study personnel at all locations in the appropriate areas of the protocol and procedures. Each study location will be responsible for ensuring that all local staff attend and successfully complete all required training. All Centers will keep the Coordinating Center informed as new personnel are hired, and will arrange for the appropriate training to be done. The QA/QC program includes refresher training, on a periodic basis, to introduce new procedures or to sharpen data collection skills. Remedial training will be required for personnel who do not meet acceptable performance standards as identified by QA/QC measures. Another key component of QA/QC program will be field audits performed by the supervisory staff from the local centers, the Program Office, and/or the Coordinating Center of all recruitment/enrollment and data collection activities. On a schedule to be established, supervisory staff will accompany data collection staff personnel as they perform recruitment/enrollment and data collection visits at participants' homes and clinic sites. They will observe adherence to the study protocol and procedures, and will initiate corrective action as needed. Examples of activities to be observed include: building rapport with subjects of interviews, the recruitment and consent process, appropriate collection of bio-specimens and

environmental samples, and appropriate processing of samples for shipment to the repository. Field audits of labs and repositories will involve the sending and tracking of "dummy" samples, and regular tracking of internal laboratory audits. The Study IMS will serve as the central system for QA/QC activities.

Lastly, the Program Office and the Coordinating Center will implement procedures to facilitate and improve their communications with the Vanguard Centers via a formal Communications Plan. Each center will have a Coordinating Center Liaison (CCL) who will serve as the hub of standard communication between the Coordinating Center Teams (operations, technical teams, etc) and the Vanguard Centers. Communication will go both ways. The CCL is the Coordinating Center contact person with whom the Centers can discuss questions about the study. This representative will respond to a question or request within 48 hours if s/he does not have the answer immediately available. The CCL will be responsible for consulting with Program Office and Coordinating Center staff to insure the Vanguard Center is given accurate information as quickly as possible.

Having a formal Communication Plan including persons directly and consistently responsible for handling communications between the Vanguard Centers and the Coordinating Center provides another mechanism for identifying issues or problems with implementing and or adhering to QA and QC procedures.

B.2.3 Pilot Study Evaluation Topics and Criteria

Monitoring of actual numbers relative to projected targets:

For the purpose of addressing the feasibility of the NCS study design, a negative count differential of 5% or greater at any of the seven sites will serve as indicator of a situation in need of further assessment that may require adjustments and potentially additional testing prior to the Main Study. Areas to be evaluated include:

- Counts of listed households by PSU, Group and overall compared to census counts for the same geography
- Counts of age eligible women overall, Group and by PSU compared to planned (also based on census data)
- Counts of pregnant women identified within first trimester versus later compared to planned (modeled using information from the National Survey of Family Growth, and migration data from the Current Population Survey)
- Counts of enrolled women overall, by Group and by PSU compared to planned
- Counts of births and enrolled births within each PSU compared to Vital Records (birth certificates) for the area.

Identification of reasons why numbers might not meet targeted totals:

These analyses reflect a review of primarily qualitative data (other than response rates) which can then suggest potential reasons for problems. Results of these analyses may identify additional testing in order to fully diagnose and address issues. These analyses will continue throughout data collection on a regular cycle so the point in which a potential problem occurs will define whether any more focused testing that might seem necessary can potentially occur as part of the Group 2 Vanguard Centers, or whether we need to implement testing between the Pilot and Main Study.

- Comparison of cooperation rates for each data collection visit to expected rates (e.g. enumeration, pregnancy screening, T1, etc). In addition to this comparison, we will use the following methods to help identify potential reasons for deviations from the expected rates.

        - Interviewer debriefings
        - Reasons for refusals recorded by interviewers
        - Review of demographics of those who refuse after the enumeration visit
        - Relative contact patterns between each data collection attempt (e.g., timing between enumeration, pregnancy screening, consent, T1, monitoring calls, etc)
        - Review of various measures assessing awareness of the NCS and exposure to NCS outreach and engagement efforts - qualitative analyses of participant evaluation questionnaires and of the different methods (e.g., newsletters, cards) for communicating with participants included in the first phase of the Vanguard Centers.

    - Comparison of actual enrollment rates of pregnant women, births, and fathers to expected enrollment. The enrollment rate is defined as the count of pregnant women, mothers of babies, and fathers who sign the consent form, divided by all eligible for consent in each of those groups. We will use the following methods to help identify potential reasons for deviations from the expected rates.
        - Consent method evaluation – pregnant women only (see attached Study Plan for more detail)
        - Interviewer debriefings
        - Respondent provided reasons for not enrolling
        - Pregnant women only - Timing of consent request relative to pregnancy screener and enumeration for women identified as T1 eligible in the pregnancy screener.
        - Differences in enrollment of pregnant women by method of identification (e.g. pregnancy screener, pregnancy monitoring contacts, provider referral;)
        - Difference in enrollment of births by whether previous participant or identified by hospital, birthing center (no previous measures)
        - Differences in enrollment of fathers by the relationship status between the father and mother (e.g., married, partners, separated)
        - Review of various measures assessing awareness of the NCS and exposure to NCS outreach and engagement efforts - qualitative analyses of participant evaluation questionnaires and of the different methods (e.g., newsletters, cards) for communicating with participants included in the first phase of the Vanguard Centers.
    - Identification of potential sources of measurement error within the data collection visit/call
        - Recording and coding of a sample of interviews
        - Interviewer debriefings
        - Response pattern analysis, including review of interview completeness and item non-response by question

An overall response rate through birth of 75% is the goal for the Vanguard Pilot, as described in more detail in Section B.3 below. Though variation between Centers is expected, that will be used as the target for successful enrollment for each Vanguard Center. Based on standard power calculations (alpha error = 0.05, power = 0.80) the target sample size of 250 births per Center is adequate to formally identify a 10% decrease in response for each Center, not accounting for the clustering by segment. However, the qualitative and quantitative analyses described above will likely provide more useful initial information from the Vanguard Phase that will lead to revisions in the Main Study protocols.

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

A major goal of the NCS Pilot Study is to provide an indication of the response rates, as well as retention rates, which can be obtained for a study of this type, using the proposed procedures. This section describes the expected response rates for the NCS, and procedures that will be employed to encourage participants to enroll in the study and to retain them over the life of the NCS.

Estimated response rates—Response rates are an important and widely used indicator of survey quality. Response rates are computed as the ratio of the number of respondents to the number of eligible units, and may be weighted or unweighted. The unweighted rate, computed using the raw sample counts, provides a useful description of the success of the operational aspects of the survey. The weighted rate is computed by summing the weights (usually the reciprocals of the probabilities of selection) for both the numerator and denominator. Since the weights allow for inference of the sample data (including response status) to the population level, the weighted rate gives a better indication of the survey's success in representing the desired study population.

Thus, in order to compute response rates, it is necessary to define the unit of analysis and establish (at a minimum) definitions of eligible units and respondents. For the National Children's Study, the basic unit of analysis is a live birth. At the segment level, the number of eligible units is the number of live births occurring during the enrollment period to mothers who reside in the segment at the time of the birth; these counts will be obtained from Vital Statistics data. The availability of Vital Statistics will vary by Center, with some having almost immediate access to initial electronic birth records and others needing to wait for compilation by their State Vital Statistics Office. However, in order to define segments, all Vanguard Centers have had ongoing interaction with the relevant Vital Statistics offices; it is expected that all Centers should have access to preliminary segment-specific birth data in approximately 6 month intervals.

It is worth noting the confounding of response and *coverage*, the proportion of the target population that is covered by the survey population, in the calculation of the response rate described above. In most surveys, the denominator of the response rate is obtained or estimated from the sample itself. In NCS, this is not possible because the unit is defined at birth but nonresponse precedes the birth event; a woman pregnant who will later deliver an eligible infant chooses not to participate in the study. Because the calculation of the NCS unit response rate is based on a count of number of eligibles from an external source (Vital Statistics records), rather than from the NCS sample itself, the unit response rate will actually measure both response and coverage.

In simplest terms, respondents are those eligible units who complete the survey effort. However, this class is complicated by *partial completes*, units who respond to part of the survey request but not the entire request. (In the NCS, these may include, for example, children for whom birth data are available but preconception and prenatal data are not available.) Survey practitioners establish rules for handling partial completes that address which components, items, or sets of items must have been completed, or which "fenceposts" in the survey instrument(s) must have been reached, in order to classify a partial complete as a respondent. For the purpose of computing unit response rates for the NCS, response will be defined as the presence of data on the given child from the pregnancy and/or birth study phases. The NCS data collection effort includes, for each birth, collection of data through various components and questionnaires. Component and item response rates will be calculated based on the proportions of births eligible for the component/item who respond to the particular component/item.

An overall unit response rate of 75 percent is expected through birth, with variations among PSUs anticipated (e.g., in general, urban areas are expected to have lower response rates than rural areas). After birth, an attrition rate of about 2 percent per year is expected for the first 2 years. The goal of recruitment and retention efforts is to obtain a response rate that is as high as possible while maintaining high

standards for the protection of human subjects as volunteer respondents in the study. Building on the community engagement efforts and involvement of community members described above, a variety of strategies will be used to announce the NCS enrollment period. Examples include press releases, appearances on local television and radio shows, and other methods to increase community excitement and interest. Wherever possible, these activities will involve joint participation of Study staff and community members. The Vanguard Centers will work with the Coordinating Center and Program Office to identify, plan and implement outreach activities that are most appropriate for their location.

Community-level efforts to maximize response—Community engagement and outreach efforts will be an important component of overall efforts to promote the Study in the selected PSUs as well as nationally. These efforts will result in name recognition for the Study and a positive association between the Study goals and participation for respondents. The NCS is committed to working with communities in an effort to improve the health of America's children. Although observational in nature, the Study recognizes the need to involve both the national and local communities in planning and implementation. A partnership with each community will be formed to ensure mutual respect and the establishment of an ongoing relationship of reciprocity. A true collaboration between Study scientists and communities offers the hope of enhancing recruitment, retention, and participant satisfaction. Examples of ongoing community activities include establishing a community advisory board, partnering with other organizations to host events or forums, incorporating community leaders into the Center structure, and building referral networks between the Study and organizations, especially healthcare providers. Health care providers will be asked to support their patients who wish to be part of the NCS.

Field efforts to identify Study Eligible women—The Coordinating Center will provide each Vanguard Center with a preliminary list of dwelling units within the selected Study site segments. Advance letters will be sent to households in the targeted areas describing the Study and the upcoming screening activities (see Appendix B.2 for letters and study brochure). Data collectors will carry copies of the letters for households that either did not receive or misplaced their letters. The letters will be on co-branded letterhead for the NCS and the Vanguard Center. The letter will explain the study purpose, the importance of the respondent's participation in it and provide a toll free number and the NCS website (and a local VC website, if available) so that respondents can verify the Study's legitimacy.

Questions will also be asked about other dwelling units that may not be easily visible or obvious, and therefore may have been missed during the listing process. Residents of many dwelling units will be re-contacted over the four year Main Study period as part of the standard Study procedures. During the Pilot Study, we will identify the hidden dwelling units and recruit those households as well. Methods to discover and recruit hidden dwelling units will be evaluated as part of the Pilot Study. When possible the phone number will be obtained to facilitate future contacts with the household. Dwelling units that will not be followed as part of the routine study contacts, following the screening visit (e.g., no eligible women) will be re-contacted midway through the recruitment period to confirm that there have been no changes in the household composition. Much of the re-enumeration effort will be conducted by telephone, however it is estimated that approximately 25% of the dwelling units listed on the original listing will require a visit by Vanguard Center staff for re-enumeration.

As part of the household enumeration process, questions will be asked about the household reporter's race/ethnicity in order to provide data for nonresponse analysis. Also, if a household is not able to be reached for a complete enumeration, neighbors will be approached to obtain information about whether or not the household includes any age-eligible women. If two neighbors report no age-eligible women in the household, it will be closed out as not eligible and then scheduled to be re-contacted later during the screening period. If any neighbor reports indicate that there are age-eligible women present in the household, attempts to make contact with the household will continue.

Data collection procedures to maximize response—To insure that field staff are able to encourage eligible women for participation in the NCS, staff will be hired who are enthusiastic, outgoing, and able to follow study protocols and to work independently. Experience as a data collector is not necessary as all staff will be thoroughly trained on all NCS data collection procedures, using standardized training developed by the Coordinating Center and Program Office. During training, trainers and supervisors observe trainees to insure they understand and can successfully implement all study protocols. All staff must be certified for their position, which involves successful completion of training and a written exam. If any data collectors seem to be having difficulty during or after training with any of the study protocols, additional training will be provided.

All Site Office staff, including field staff, who have contact with participants, will be trained on refusal avoidance and gaining cooperation techniques. Knowledgeable, well-trained staff can enthusiastically and accurately explain the NCS to participants and answer questions they may have about the study. Staff will be provided with frequently asked questions (FAQs) and responses to be able to respond to specific questions participants may have about participating in the NCS. Staff will be trained to address common concerns and objections participants may have, such as statements in which participants express they do not have time to be part of the study or think the data collector is a salesperson. The NCS advance letter and brochure; the enumeration, pregnancy screening and telephone verbal consents; and the written and video informed consents explain the purpose and goals of the NCS, risks and benefits of participating, and the time involved and types of data to be collected. They also explain that participation is voluntary and that participants can refuse to participate in any activity in the NCS and still be included in the study.

The NCS also has developed letters to promote cooperation for each data collection event (e.g., enumeration, pregnancy screening). These will be sent to participants who refuse to participate. Study Centers will send these letters to participants and then recontact them to attempt to gain their cooperation. Supervisors also have the option of assigning certain data collectors to attempt to gain participants cooperation, after a participant has refused. For example, some data collectors may be better at gaining cooperation for enumeration and others may be more proficient at gaining cooperation for another data collection event. As the NCS progresses, the NCS will continue to recontact participants who have refused to participate in a particular study event, unless requested to discontinue contact. Participants who withdraw from the NCS will receive a letter thanking them for their participation up to that point and providing contact information for the study should they decide to rejoin the NCS at a later time. Participants may not want to participate in a data collection event, but months or years after may decide to be included in a later data collection event.

Each staffer will report to his or her supervisor weekly to discuss response rates and any unusual situations he or she may have encountered, including refusals and households or participants the data collector is unable to contact. For example, supervisors will be able to run reports with the number of cases for each result code (e.g., completed, not yet worked, refused) by data collector and by segment to inform their discussions with the data collectors. If any data collector has an unacceptable rate of refusals or non-contacts, the supervisor will work with him or her to determine the next steps, including providing additional training and refresher training, as needed. The Coordinating Center will work with each Site Office to help them implement procedures to improve response rates as well.

Accounting for movement into and out of selected Study segments—Some women will move into sampled segments after the segments have been screened (and prior to the re-contacts discussed above). Since all children born to women living in the sampled segments are eligible, other mechanisms are needed to identify and recruit these women. A supplemental mechanism is to recruit eligible women (those living in the sampled segments) through providers of prenatal care, birthing centers, and hospitals. In addition to increasing the study's ability to cover the mobile population that otherwise would be missed, this supplemental recruitment strategy also provides another opportunity to encourage participation from

women who previously chose not to participate in the study when contacted during the household screening. While this method is useful in reducing non-response and undercoverage, it does not provide full data during the prepregnancy and early pregnancy data collections and is thus viewed as a supplemental approach. The Pilot Study will allow analyses of how much this recruitment method affects response rates. These women will also receive a late entry data collection module. We will evaluate if this module will provide sufficient information to continue to recruit women who are past their first trimester of pregnancy.

A certain percentage of women who are eligible will move during pregnancy and during the first year of the child's life. Pregnant women who move out of their original PSU to an area which is not a designated PSU will not be eligible for participation in the study. If a move is made after the birth of the child, that child will be followed for all scheduled visits either by the nearest Study Center or by the CC. Some moves by pregnant women and children into their own or other PSUs may trigger "re-visits" to collect environmental specimens. If she has not notified the Study center or CC, the study will undertake tracing efforts. The Study Centers will conduct initial tracing activities, including re-visiting homes to determine if the woman has moved and tracking returned mail for new address information. The CC will trace any women that the Study Centers have not been able to locate, using emergency contacts and Internet (and other) sources.

All retention and tracing methodologies will be implemented for the Pilot Study as described below. The rate at which respondents move, especially the number who move out of study segments, will be closely monitored to better inform tracking and tracing efforts for the Main Study. This will help determine the number of women who will need to be followed by the CC, rather than a VC or other Study Center.

At each stage in data collection, starting with the first participant contact, contact information that will be important for long-term tracking of the participant will be collected. At this time, in addition to documenting the participant's first and last name, we also will collect the participant's birth date, current telephone numbers (home, cell, and work), and email address. Additionally, name and contact information on two family members or friends who do not live with the participant will be collected. The participant's Social Security number may be collected to assist with long-term tracing efforts and records searches (e.g., National Death Index). All contact information will be updated at each subsequent in person contact.

Many types of mailings will be sent to participants throughout the study, which include data collection forms, birthday cards, newsletters, appointment reminders, and thank you letters. These periodic mailings are important either for data collection or as a way to maintain contact with the participant through the course of the NCS. In this context, however, they also can be viewed as an important strategy for locating participants. Returned mail will trigger follow-up tracing to obtain the participant's new residence and contact information. All study mailings will be sent first class with forwarding address service requested.

When a study participant moves and the provided contact information and directory assistance prove to be inadequate to locate her, the Coordinating Center and the Study Centers each will take the lead on different aspects of tracing.

Study Center staff will follow up on leads provided by the alternative contacts. Local WIC programs, health departments, and physician offices may be contacted. Contacts also may be made with neighbors of the participant at the last known address, apartment managers, employers, local post offices, voter registration offices, and tax assessor's offices.

The Coordinating Center will take the lead on national level tracing efforts. The list that follows illustrates some of the sources the Coordinating Center will use to locate participants who are not located at the local level:

- **U.S. Postal Service.** A cost-effective means of tracing is to use post office files for address verification. This method involves mailing an address or list of addresses to request the last known address of the subject. These cards or letters are stamped "Address Correction Requested."

- **National Change of Address (NCOA) Database.** The NCOA is operated by private businesses licensed by the U.S. Postal Service. The licensees, using address-matching software, standardize the list of addresses they receive. They retain change of address for a 3-year period. When matches are found, they provide a new address.

- **Private Companies for Address and Telephone Matching.** Companies such as Telematch will be used to find telephone numbers that are missing or found to be incorrect. Reverse match service provides addresses when telephone numbers only are available. Telematch also will be used for Electronic Directory Assistance.

- **Other Database Sources.** MetroNet and Axxiom are examples of this type of resource. They provide access to several databases, including the National Consumer Database, change of address files, and the Regional Bell Operation Companies electronic directory assistance databases. Based on name and address, these resources provide standardized address, telephone numbers, and changes of address. They also provide names, addresses, and phone numbers of up to 30 neighbors. This service may prove useful for women who move first out of the segment and then a second time in an area not well covered by an NCS Study Center.

- **Credit Bureaus.** Credit bureaus will be used to confirm that a person is alive or to obtain a last known address. Recent laws have increased security on this information and made it less accessible as a tracing resource, however.

- **State Department of Motor Vehicles.** Some states allow access to these files for in-state tracing of individuals or groups of individuals.

- **Social Security Administration (SSA).** Through an interagency agreement, a search can provide all demographic data on selected Social Security numbers. The SSA also offers a service that either verifies a subject is living or indicates the subject is deceased, providing a date and place of death (presumed living search). NIH does not yet have this type of agreement in place, but we would anticipate that as the children age it will become valuable and will be obtained.

- **National Death Index (NDI) search.** The NDI, established by the National Center for Health Statistics (NCHS), is a central computerized index of death record information on file in state vital statistics offices. NCS will use it for comprehensive searches of death records for children, mothers, and fathers.

For the Main Study, NIH anticipates using the NCOA as one of many tools to locate sampled children who have moved. This process requires submitting the name and address of the child (parent) as input to the NCOA register. We have looked into the possibility of using NCOA to identify women who have moved *into* the sampled segment, but we can see no way by which this can be done, given the NCOA input requirements. However, we do plan to submit the names and addresses for all households in the sampled segments to identify those who have moved *out*, which will help locate addresses which now

contain a new potentially eligible woman (recognizing that we may have limited information for households in which no eligible women reside). Therefore, we will use the results of NCOA movers (and movers identified by other means, e.g., returned mail) to target addresses that would likely have new residents, and they will be followed up using standard means.

Additional strategies for maximizing response—Other elements for achieving a high response rate include developing and implementing a training program that prepares the data collectors for the survey tasks; implementing appropriate data collection procedures; being sufficiently flexible to accommodate respondents' requests; and implementing sound management and quality control procedures. Factors that specifically influence individuals to participate include the following:

- *Obtaining cooperation*—During training, all data collectors will be monitored, evaluated, and provided with instant feedback on their performance to eliminate interaction patterns or demeanor that might be detrimental to achieving cooperation.

- *Flexibility in scheduling data collection contacts*—Data collection activities for the study will be scheduled to coincide with the hours people are most likely to be at home, and to accommodate participants' schedules. Data collection visits and telephone calls can also be broken up into shorter time periods, if needed, in order to accommodate participants' schedules.

- *Gaining cooperation*—For each case in which the respondent refuses to participate in the study, the data collector will complete a Non-Interview Report. The report will capture information about key characteristics of the refusing respondent and the stated reason(s) for refusing to participate. The field supervisor will review these reports to decide whether refusal conversion should be attempted and, if so, how to customize the approach to address the potential respondent's concerns. One approach may include sending a letter to gain cooperation (see Appendix B.2.3).

- *Translation of documents and use of interpreters*—For the pilot, study materials will be available in English and Spanish and interpreters will be provided for respondents who cannot complete the data collection in English or Spanish.

Efforts to maximize retention during follow-up period—Participant retention begins with regular contacts and appropriate incentives (monetary and non-monetary) over time. Participants will be contacted regularly during the study (every 2 to 3 months during pregnancy, every three months through age 1 of the enrolled children; every 6 months through age 24 months of enrolled children) either in-person or by telephone. The study will also send appropriate greeting cards, such as birthday cards, and newsletters designed for participants. Another key item for ensuring participant retention is providing participants with relevant, useful information. It is planned that participants will be provided with a Report of Findings. This report will be provided at the time of the in-person visit that will include physical measures such as height, weight, and blood pressure. (see Appendix C.11).

Nonresponse bias analysis—The NCS has a very specific response population with an excellent administrative data set that will be utilized in a way that is different from most household surveys for nonresponse bias analysis. The eligible population for the NCS is births, and the administrative data set is the birth records of resident births. In the NCS we plan to compute an overall response and coverage rate as the ratio of the number of children born who have participated in the NCS protocol and reside in the sampled segments at time of birth to the number from the birth records in the segments. This computation will be done for all births and by a variety of characteristics such as child characteristics (low-birth weight, race, location of the child) as well as characteristics of the parents (age, marital status, etc). We intend most of our nonresponse analyses to be based on these data because they are most pertinent to our

target population and the administrative data is expected to be of very high quality. The key is linking the births in the study to the vital records data set and we believe this linkage will be very strong.

Other data will be collected, including neighbor characteristics and type of dwelling unit, that may affect respondent participation. Most of these data are currently captured in our enumeration process and are in those data collection instruments. The neighborhood data collection is a separate activity that is being piloted and is addressed in our responses elsewhere. All of these data can and will be used in assessing nonresponse bias, but we expected it to be of more limited value because it is ecological or aggregate data for the segment or housing unit. With a relatively rare characteristic such as a birth, these data are often not very useful for estimating response propensities that are most appropriate for this study. For example, an area of high income that could be characterized in the paradata as having limited access (and lower than average response rates for the enumeration) might also have very few births per household. The major advantage of using these data for nonresponse bias is that it will be available sooner than the birth records data.

B.4 Test of Procedures or Methods to be Undertaken

The first year of data collection in the Vanguard Center locations is considered the initial Pilot Study for the full NCS. In addition, the seven Vanguard Centers will serve as a platform to introduce and pilot test the methodologies and procedures that will be refined and implemented throughout the study. The purpose of the proposed data collection is to pilot test all data collection methodologies for the NCS from household enumeration through the time when enrolled children reach 24 months of age.

Study participants will be consented at the time of study enrollment—that is, at the time of their initial NCS visit. (See Appendix B.1 for the informed consent documents.) Two different presentations of the informed consent are planned for the Pilot Study - a video version and a hard-copy version to determine the effect of the consent process—video vs. hard copy—on enrollment. Prior to administering consent at the first trimester pregnancy visit, participants will be informed that there are two different methods and that the computer will assign them to one or the other procedure. If they agree, they will be randomly assigned to receive either the video or the hard-copy. Participants who do not agree to let their consent method be randomly assigned will receive the hard-copy consent as a standard procedure. At every visit, participants will be provided with a Visit Information Sheet, providing the details of all activities planned for that visit, and informing them of the risks and benefits of participation in the visit.

Pregnant women enrolled in the NCS will be asked to record basic information from each visit to a health care provider on a “Medical Care Log” (Appendix A.2.1.e). A sub-sample of pregnant women with broadband Internet access will be randomly selected and asked to complete a web-based data collection tool (currently under development) that collects the same information as the hard copy. A woman choosing not to participate in this evaluation will be provided the paper version of the Medical Care Log. Information on participant satisfaction with the two methods will be collected.

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

The use of statistical sampling methods is critical to this study. The PO and the CC have developed the sampling plan for this survey as described in Appendix C.8, using standard statistical methods. The CC (Westat) and NICHD are also responsible for selecting the sample, and carrying out the analyses. NICHD has consulted with Lester Curtin, from the National Center for Health Statistics, CDC, and J. Michael Brick, from Westat, on the development of the sampling plan for the selection of the agencies and the selection of the participants, as well as the survey methodology for the survey.

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