REQUEST FOR OMB CLEARANCE

Recruitment Substudy for the National Children's Study, Phases 1 and 2

Part B only

B. Collection of Information Employing Statistical Methods

B.1 Respondent Universe and Sampling Methods

Inclusion and Exclusion Criteria

Inclusion and exclusion criteria for the Recruitment Substudy are comparable to those used in the Initial Vanguard Study. The following groups are eligible for inclusion as participants in the Recruitment Substudy:

- Women of the age of majority (typically, age 18) to 49 residing in a selected NCS geographic segment at the time of enrollment
- Men of the age of majority (typically, age 18) named by enrolled women during the pre- to neonatal period as their baby's father
- Children born to enrolled women
- Adult caregivers for enrolled children who have legal responsibility to authorize needed care for an enrolled child

Note that we propose to exclude women who are under the age of majority, regardless of pregnancy and emancipation status, for the purposes of the proposed Stage 1 and Stage 2 launch, anticipated to begin in July 2010 and April 2011, respectively.

Women must reside in a selected NCS geographic segment at the time of enrollment. From the Initial Vanguard Study experience, few women eligible based on residency will move outside of a selected segment during pregnancy. We propose to expand inclusion criteria to include enrolled women who move out of the selected segment to an area which is not a designated secondary sampling unit prior to the sample child's birth may be eligible to continue participation in the Recruitment Substudy. To remain geographically eligible, enrolled women must reside within 50 miles of the previous address that was initially located in the selected segment boundary. This will increase data available for methodological analysis without affecting generalizability of resulting data, because the Recruitment Substudy is not designed to yield representative data and, accordingly, sampling weights will not be created. This change in geographic eligibility is expected to increase sample size by a very small amount while maintaining good will with study participants.

If geographically eligible, women at any stage of pregnancy will be asked to enroll in the study. Pregnant women of the age of majority through age 49 at the time of screening are eligible for

enrollment into the study. Additionally, women between the age of majority and 49 years of age who are not pregnant but, at the time of screening, are determined to be at a high probability of later becoming pregnant, will be invited to join the study.

Women will be asked if we may contact the father of their baby to invite these fathers to participate in the study. Fathers of the age of majority will then be asked to enroll in the study. Enrolled mothers will also be asked to consent to enrolling their child in the study upon birth through the age of majority.

Women not residing in selected segments at the time of enrollment are not eligible to participate in the study. Women and fathers who are unable to understand NCS participation and grant informed consent will not be eligible to participate.

Primary Sampling Units

The sampling frame proposed for the Recruitment Substudy is the same as the frame used for the Initial Vanguard Study, with one enhancement, as noted, for the Two-Tier, High-Low strategy. As in the Initial Vanguard Study, the sampling design for the Recruitment Substudy uses a multistage clustered approach. In the first stage, 105 locations (generally corresponding to single counties) were randomly selected from all U.S. counties. The process for selecting these study locations was based on the intent to achieve statistically representative sample of children born in the United States during the enrollment period.

From these 105 study locations, or primary sampling units (PSUs), 30 were selected for implementation of this Recruitment Substudy. Each of the three recruitment strategies will be employed in 10 different study locations. As described above, study locations for each of the recruitment strategies are geographically and demographically diverse; however, they do not, and were not intended to, support generalizations to regions or the U.S. target population. See Tables B.1-B.3 (below) for a listing of study locations (PSUs) by recruitment strategy and study center.

Table B.1. Study Centers and Locations for Provider Based Recruitment

Study Center	Study Location
Arkansas Children's Hospital Research Institute	Benton County, AR
Brown University	Providence County, RI
Children's Hospital of Philadelphia	Schuylkill County, PA*
Michigan State University	Wayne County, MI ^
University of California, Davis	Sacramento County, CA
University of Mississippi	Hinds County, MS
University of North Carolina at Chapel Hill	Durham County, NC
University of Texas Health Science Center San Antonio	Bexar County, TX
University of Texas Southwestern Medical Center at Dallas	Lamar County, TX*
Yale University	New Haven County, CT

Table B.2. Study Centers and Locations for Enhanced Household Based Recruitment	
Study Center	**Study Location**
Saint Louis University	St Louis (city), MO
University of Washington	Grant, WA*
University of Iowa	Polk, IA
Maine Medical Center	Cumberland, ME*
University of Hawaii	Honolulu, HI
University of Arizona	Pinal, AZ
University of Miami	Baker, FL*
University of New Mexico	Valencia, NM
University of California, Irvine	San Diego, CA ^
Case Western Reserve University	Cuyahoga, OH ^

Table B.3. Study Centers and Locations for Two-Tier High-Low Intensity Recruitment	
Study Center	**Study Location**
Emory University	Baldwin County, GA*
Johns Hopkins University Bloomberg School of Public Health	Montgomery County, MD
Northwestern University	Cook County, IL ^
Tulane University School of Public Health	New Orleans Parish, LA
University of California at Los Angeles	Los Angeles County, CA ^
University of Colorado	Douglas County, CO
University of Minnesota	Ramsey County, MN
University of Pittsburgh	Westmoreland County, PA
University of Utah School of Medicine	Cache County, UT*
Vanderbilt University Medical Center	Davidson County, TN

NOTE: * Study locations selected as non-metropolitan for sampling purposes. ^ Urban Locations selected with sampling certainty due to population density.

Secondary Sampling Units

As in the Initial Vanguard Study, geographic segments are formed within study locations during the second stage of sampling. These segments comprise census blocks, or clusters of households roughly corresponding to neighborhoods. For the provider-based and enhanced household recruitment strategies, as was the case for the Initial Vanguard Study, approximately 10-15 of these segments will be selected within each location based on density of historical births. As in the Initial Vanguard Study, these secondary sampling units, or SSUs, are selected to yield a predicted 250 births per year per study location based on vital record data.

Specifically, the size of the secondary sampling unit is determined by the expected number of births over a four-year enrollment period, divided by the target enrollment, and divided by the expected response rate. This sampling interval determines the number of segments to be

selected. Since one segment will be selected randomly per stratum, the number of segments also determines the number of strata. The primary sampling unit is divided into that number of strata, and the boundaries of the strata are informed by Census data and physical geography and landmarks. Each stratum is split into the same number of potential segments, and each census block is assigned a segment. From each strata, one segment, or cluster of neighborhoods, is randomly selected.

Both the provider-based recruitment strategy and the enhanced household recruitment strategy employ the same two-stage sampling design employed with the Initial Vanguard Study; primary and secondary sampling units will contribute in the same way to the sampling frame. However, the two-tier high-low intensity strategy employs a somewhat different secondary sampling unit and a tertiary sampling unit as described below.

Tertiary Sampling Units

In the two-tier high-low intensity strategy, the tertiary sampling unit is equivalent in target population density to the secondary sampling unit employed by the provider-based recruitment strategy and the enhanced household recruitment strategy (and the Initial Vanguard Study strategy). However, the secondary sampling unit in the two-tier high-low intensity strategy contains the tertiary sampling unit and, at maximum, 2 additional selected segments adjacent to each of the 10-15 selected tertiary sampling units. These "additional" segments contributing to the secondary sampling unit are selected by proximity to the tertiary sampling unit, target population density, and relevant political and social neighborhood boundaries. See Table B.4.

Table B.4. Comparison of Sampling Frame Characteristics by Recruitment Strategy

Recruitment Strategy	Primary Sampling Unit	Secondary Sampling Unit	Tertiary Sampling Unit
Initial Vanguard Study	Counties (Study Locations)	Census Blocks or neighborhoods (Segments)	NA
Provider-Based	Counties (Study Locations)	Census Blocks or neighborhoods (Segments)	NA
Enhanced Household	Counties (Study Locations)	Census Blocks or neighborhoods (Segments)	NA
Two-Tier High-Low Intensity	Counties (Study Locations)	Census Blocks or neighborhoods (Segments)	Census Blocks or neighborhoods (Segments)

NOTE: Shaded cells denote equivalence in population density.

The approaches proposed for the provider-based recruitment and enhanced household recruitment strategies do not require variation in the original sampling frame at the secondary sampling unit level. However, as described in detail below, the two-tier high-low intensity approach is designed to inform the Main Study of the optimal size of the secondary sampling unit to yield sufficient numbers of study-eligible pregnant women to meet NCS goals. Additionally, the two-tier high-low intensity approach to recruitment relies on a period of developing rapport with participants in a low intensity data collection experience, prior to inviting participants to engage in a higher intensity data collection experience. Both objectives particular to the two-tier approach, therefore, require a comparatively larger secondary sampling unit (roughly three times the size of the secondary sampling unit selected for the other recruitment strategies).

For each recruitment strategy, a list of all known households in the selected segments will be compiled. These households represent the dwelling units from which eligible participants will be recruited and, as such, form the base for determining if a woman may be geographically eligible for the study.

There are three ways that centers can compile household lists: 1) United States Postal Service (USPS) Listings; 2) Plat Maps; or 3) Conventional Listing. In the first option, USPS address lists are purchased from approved vendors. To date, we have found acceptable coverage of addresses by USPS lists in urban and semi-urban areas in the Initial Vanguard Study locations. However, rural areas, and areas experiencing significant, recent housing growth, may have much lower rates of coverage. The second approach, the Lot and Block Survey System, also referred to as the Recorded Plat Survey System, or Plat Maps, have also been used successfully to locate and identify land, particularly, in rural remote areas. The third approach, Conventional Listing, uses systematic, manual compilation of residential addresses in a given area. Trained field listers canvass selected segments, locate segment boundaries and then move systematically throughout the segment, compiling a list of all residential addresses. No contact with human subjects is necessary for listing. Conventional listing can be accomplished using either hard-copy or computer-based materials. Given the Initial Vanguard Study experience, centers are expected to make particular use of Plat Maps and conventional listing methods in rural segments or segments experiencing rapid housing growth.

B.2 Procedures for the Collection of Information

The NCS plans a phased rollout of the Recruitment Substudy. This phased launch features minimal study instruments initially to allow Recruitment Substudy centers to gain familiarity with data collection operations and logistics. Subsequently, all Recruitment Substudy strategies will employ additional and more robust (in length and complexity) instruments commensurate with those used in the Initial Vanguard Study. This Supporting Statement covers Phases 1 and 2 of the Recruitment Substudy.

Phase 1: Minimal Data Collection Effort, with Focus on Recruitment

At the anticipated July 2010 launch, data collection activities for all three recruitment strategies will be limited in the number of instruments and the complexity of each. Specifically, for the provider-based, enhanced household, and two-tier high intensity strategy, three prenatal interviews and one birth visit interview will be administered per participant: the Pre-Pregnancy Interview, the Pregnancy Visit 1 Interview, the Pregnancy Visit 2 Interview, and the Birth Interview. These instruments will be accompanied by informed consent materials, referred to as the Women's Informed Consent Form and Visit Information Sheets. The majority of items contained in these instruments were featured in the First Trimester Mother Instrument of the Initial Vanguard Study. Note that a Birth Visit, but not a Birth Interview, was part of the Initial Vanguard Study. However, the NCS would like to evaluate the Birth Interview as an option for the Main Study, and therefore this instrument is included in the Recruitment Substudy. Participants will also be asked to complete a brief self-administered questionnaire evaluating the data collection experience at the completion of the Pregnancy Visit 1 Interview and the Pregnancy Visit 2 Interview. See Table B.5.

These instruments are much briefer than instruments used in the Initial Vanguard Study (approximately 30 minutes each compared to approximately 3 hours each). No physical measures, biologic specimens, or environmental samples will be collected in Phase 1. Reducing the length of the instruments for the July 2010 launch is possible given the goals of the Recruitment Substudy: a) evaluate recruitment strategies and compare the effectiveness of those strategies; b) provide measures of study operations and logistics; c) evaluate item functioning of a small group of new measures that might inform Main Study instrumentation.

In Phase 1, the interview instruments will be administered in person for provider-based recruitment, enhanced household-based recruitment, and the high intensity tier of the two-tier high-low recruitment strategy. Alternate acceptable modes, such as telephone administration or secure web based administration, may be proposed in cases where participants are not available for in-person interviews. However, with the exception of the Birth Visit Instrument, which is preferred to be administered in a hospital setting, in-home administration is preferred for all other data collection events pertaining to the provider-based, enhanced household and two tier high/low recruitment strategies.

The low intensity tier of the two-tier high-low recruitment strategy will be administered by computer assisted telephone interviewing and self-administered questionnaire (either paper and pencil administration or secure web administration). In particular, for the low intensity participants, consent administration will be conducted by telephone. Study centers will be allowed the option of submitting: 1) a secure and reliable method of obtaining informed consent through a website interface; and 2) a telephone or secure and reliable website-administered data collection instruments. Proposals for these modes of administration will require review by the NCS Program Office and the NICHD Chief Information Officer in addition to regulatory approval prior to use. See Table B.6.

Table B.5. Study Instruments by Recruitment Strategy and Phase

Initial Vanguard Study Protocol	Phase 1					Phase 2				
	Initial Household	Provider-Based	Enhanced House-hold	Two-Tier High-Low Intensity		Initial Household	Provider-Based	Enhanced Household	Two-Tier High-Low Intensity	
				Low	High				Low	High
Household Enumeration	Household Enumeration	*Not Applicable*	Household Enumeration	*Not Applicable*	*Not Applicable*	Household Enumeration	*Not Applicable*	Household Enumeration	*Not Applicable*	*Not Applicable*
Pregnancy Screener	Pregnancy Screener	Provider-Based Pregnancy Screener	Pregnancy Screener	Low Intensity CATI Pregnancy Screener	Pregnancy Screener	Pregnancy Screener	Provider-Based Pregnancy Screener	Pregnancy Screener	Low Intensity CATI Pregnancy Screener	Pregnancy Screener
General Study Informed Consent Form**	Women's Informed Consent Form	Women's Informed Consent Form	Women's Informed Consent Form	Low Intensity Informed Consent Script	Women's Informed Consent Form	Women's Informed Consent Form	Women's Informed Consent Form	Women's Informed Consent Form	Low Intensity Informed Consent Script	Women's Informed Consent Form
Preconception (PI) and Visit Information Sheet (VIS)	Pre-Pregnancy Interview and VIS	Pre-Pregnancy Interview and VIS	Pre-Pregnancy Interview and VIS	Low Intensity Questionnaire	Pre-Pregnancy Interview and VIS	Pre-Pregnancy Interview and VIS	Pre-Pregnancy Interview and VIS	Pre-Pregnancy Interview and VIS	Low Intensity Questionnaire	Pre-Pregnancy Interview and VIS
Multiple Biospecimen Collections	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Maternal Blood and Urine Collection^	Maternal Blood and Urine Collection^	Maternal Blood and Urine Collection^	*Not Applicable*	Maternal Blood and Urine Collection^
Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script	Pregnancy Probability Group Follow-up Script
First Trimester (T1) and Visit Information Sheet (VIS)	Pregnancy Visit 1 Interview, SAQ, and VIS	Pregnancy Visit 1 Interview, SAQ, and VIS	Pregnancy Visit 1 Interview, SAQ, and VIS	Low Intensity CATI Questionnaire	Pregnancy Visit 1 Interview, SAQ, and VIS	Pregnancy Visit 1 Interview, SAQ, and VIS	Pregnancy Visit 1 Interview, SAQ, and VIS	Pregnancy Visit 1 Interview, SAQ, and VIS	Low Intensity CATI Questionnaire	Pregnancy Visit 1 Interview, SAQ, and VIS
Pregnancy Medical Care Log	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Pregnancy Health Care Log	Pregnancy Health Care Log	Pregnancy Health Care Log	Pregnancy Health Care Log	Pregnancy Health Care Log
Multiple Biospecimen Collections	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Maternal Blood and Urine Collection^	Maternal Blood and Urine Collection^	Maternal Blood and Urine Collection^	*Not Applicable*	Maternal Blood and Urine Collection^
Multiple Environmental Sample Collections	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Household Dust and Tap Water Collection+	Household Dust and Tap Water Collection+	Household Dust and Tap Water Collection+	*Not Applicable*	Household Dust and Tap Water Collection+
Father Informed Consent	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Father Informed Consent	Father Informed Consent	Father Informed Consent	*Not Applicable*	Father Informed Consent
First Trimester (T1) Father Interview and VIS	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Father Interview and VIS	Father Interview and VIS	Father Interview and VIS	*Not Applicable*	Father Interview and VIS
Second Trimester (T2) and Visit Information Sheet	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*
Third Trimester (T3) and Visit Information Sheet	Pregnancy Visit 2 Interview and VIS	Pregnancy Visit 2 Interview and VIS	Pregnancy Visit 2 Interview and VIS	*Not Applicable*	Pregnancy Visit 2 Interview and VIS	Pregnancy Visit 2 Interview and VIS	Pregnancy Visit 2 Interview and VIS	Pregnancy Visit 2 Interview and VIS	*Not Applicable*	Pregnancy Visit 2 Interview and VIS
Multiple	*Not Applicable*	*Not*	*Not*	*Not*	*Not*	Maternal	Maternal	Maternal	*Not Applicable*	Maternal

Table B.5. Study Instruments by Recruitment Strategy and Phase											
Initial Vanguard Study Protocol	**Phase 1**					**Phase 2**				
	Initial Household	**Provider-Based**	**Enhanced House-hold**	**Two-Tier High-Low Intensity**		**Initial Household**	**Provider-Based**	**Enhanced Household**	**Two-Tier High-Low Intensity**	
				Low	**High**				**Low**	**High**
Biospecimen Collections		*Applicable*	*Applicable*	*Applicable*	*Applicable*	Blood and Urine Collection^	Blood and Urine Collection^	Blood and Urine Collection^		Blood and Urine Collection^
Multiple Environmental Sample Collections	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Household Dust and Tap Water Collection+	Household Dust and Tap Water Collection+	Household Dust and Tap Water Collection+	*Not Applicable*	Household Dust and Tap Water Collection+

Table B.5. Study Instruments by Recruitment Strategy and Phase										
Initial Vanguard Study Protocol	**Phase 1**					**Phase 2**				
	Initial Household	**Provider-Based**	**Enhanced House-hold**	**Two-Tier High-Low Intensity**		**Initial Household**	**Provider-Based**	**Enhanced House-hold**	**Two-Tier High-Low Intensity**	
				Low	**High**				**Low**	**High**
Birth Visit (B1) and Visit Information Sheet (VIS)	Birth Instrument and VIS	Birth Instrument and VIS	Birth Instrument and VIS	*Not Applicable*	Birth Instrument and VIS	Birth Instrument and VIS	Birth Instrument and VIS	Birth Instrument and VIS	Low Intensity Questionnaire	Birth Instrument and VIS
Infant Medical Care Log and Instructions	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Infant and Child Health Care Log	Infant and Child Health Care Log	Infant and Child Health Care Log	Infant and Child Health Care Log	Infant and Child Health Care Log
Birth Visit Specimen Collections	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Cord Blood Specimen Collection	Cord Blood Specimen Collection	Cord Blood Specimen Collection	*Not Applicable*	Cord Blood Specimen Collection
3-Month Interview	3-Month Interview (Minimal)	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	3-Month Interview (Minimal)	3-Month Interview (Minimal)	3-Month Interview (Minimal)	*Not Applicable*	3-Month Interview (Minimal)
6-Month Visit Interview, SAQ, Diaries, VIS	6-Month Interview (Minimal)	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	6-Month Interview (Minimal)	6-Month Interview (Minimal)	6-Month Interview (Minimal)	Low Intensity Questionnaire	6-Month Interview (Minimal)
9-Month Phone Call	9-Month Interview (Minimal)	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	9-Month Interview (Minimal)	9-Month Interview (Minimal)	9-Month Interview (Minimal)	*Not Applicable*	9-Month Interview (Minimal)
12-Month Visit Interview, SAQ, Diaries, and VIS	12-Month Interview (Minimal)	Not Applicable	Not Applicable	Not Applicable	Not Applicable	12-Month Interview (Minimal)	12-Month Interview (Minimal)	12-Month Interview (Minimal)	Low Intensity Questionnaire	12-Month Interview (Minimal)
18-Month Phone Call and Child Food Questionnaire	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	18-Month Interview (Minimal)	18-Month Interview (Minimal)	18-Month Interview (Minimal)	Low Intensity Questionnaire	18-Month Interview (Minimal)
24-Month Phone Call	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	24-Month Interview (Minimal)	24-Month Interview (Minimal)	24-Month Interview (Minimal)	Low Intensity Questionnaire	24-Month Interview (Minimal)

Phase 2: Minimal Data Collection Effort Augmented with Selected Study Visit Assessment and Retention Measures

At the anticipated April 2011 launch, data collection activities conducted during Phase 1 among the 37 Vanguard Study Centers will continue with modest additions selected to test revised study visit measures and study logistics, and extension of the data collection effort from birth to age 24 months. As in the Phase 1 data collection, participants in the initial household, provider-based, enhanced household, and two tier high intensity recruitment strategies would receive three prenatal interviews and one birth visit interview. These instruments will be accompanies

by informed consent materials. Participants would also be asked to complete a brief self-administered questionnaire evaluating the data collection experience at the completeion of Pregnancy Visit 1 and 2.

In addition to the data collection activities used during Phase 1, Phase 2 would feature a woman participant blood and urine collection, tap water and dust collection, father interview, pregnancy and infant and child health care logs, and cord blood. See Table B.5. These study visit measures were revised based on field experience and would now benefit from testing in a large-scale field environment to inform Main Study content. Further, Phase 2 would extend Phase 1 data collection into infancy and early childhood. Extending the data collection effort from birth to age 24 months would allow further testing of how recruitment strategies may affect retention over time, as well as allow further testing of study logistics.

Similar to modes of administration proposed for Phase 1 implementation, interview administration would occur in person, by phone, direct mail, or secure web. See Table B.6.

NOTE: * A subset of items from the Household Enumeration Instrument may be administered to the Provider-Based Recruitment and the Two-Tier, High-Low Recruitment strategies as a mechanism for determining eligibility of a dwelling unit and identifying women that may be age-eligible to participate in the study.
**As discussed below, the Women's Informed Consent form will be administered to the Initial Vanguard Study participants subsequent to local IRB approval. This consent form has been approved by the NICHD IRB. The Women's Informed Consent Form would replace the General Consent and the Biological and Environmental Sample Consent forms as a way to reduce the burden and redundancy associated with current consent procedures that have emerged from field experience. See *Human Subjects Protections*, below.
^ Maternal blood and urine will be collected at two prenatal visits. We will first attempt to collect these specimens and samples at the Pre-pregnancy Visit and the Pregnancy Visit 1 visit; if the pre-pregnancy visit is not scheduled (a women is asked to join the study when already pregnant), we will attempt to collect these specimens at the Pregnancy Visit 1 and 2 visits. Additionally, if an enrolled woman declines to provide specimens at any two of the three visits, we will ask her to reconsider and request to obtain specimens up to and including the Pregancy Visit 2 visit. + Household dust and tap water collection will be collected at the Pregnancy Visit 1 and 2 visits.

Table B.6. Mode of Instrument Administration by Recruitment Strategy and Phase

Data Collection Event	Phase 1				Phase 2			
	Initial Household	Provider-Based and High Intensity	Enhanced Household	Low Intensity	Initial Household	Provider-Based and High Intensity	Enhanced Household	Low Intensity
Household Enumeration	In person	*Not Applicable*	In person	*Not Applicable*	In person	*Not Applicable*	In person	*Not Applicable*
Provider-Based Pregnancy Screener	*Not Applicable*	Telephone (Provider Only)	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone (Provider Only)	*Not Applicable*	*Not Applicable*
Pregnancy Screener	In person	In person (High Intensity Only)	In person	*Not Applicable*	In person	In person (High Intensity Only)	In person	*Not Applicable*
Low Intensity CATI Pregnancy Screener	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone, mail, web
Low Intensity CATI Questionnaire	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone, mail, web	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone, mail, web
Low Intensity	*Not*	*Not Applicable*	*Not*	Telephone with	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone with

Table B.6. Mode of Instrument Administration by Recruitment Strategy and Phase								
Data Collection Event	**Phase 1**				**Phase 2**			
	Initial Household	**Provider-Based and High Intensity**	**Enhanced Household**	**Low Intensity**	**Initial Household**	**Provider-Based and High Intensity**	**Enhanced Household**	**Low Intensity**
Informed Consent Script	*Applicable*		*Applicable*	direct mail information sheet*				direct mail information sheet*
Women's Informed Consent Form	In person	In person	In person	*Not Applicable*	In person	In person	In person	*Not Applicable*
Pre-Pregnancy Interview	In person	In person	In person	Direct mail, telephone, web	In person	In person	In person	Direct mail, telephone, web
Maternal Blood and Urine Collection^	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	*Not Applicable*
Pregnancy Probability Group Script	Telephone	Telephone	Telephone	Direct mail, telephone, web	Telephone	Telephone	Telephone	Direct mail, telephone, web
Pregnancy Visit 1 Interview, SAQ, and Visit Information Sheet	In person	In person	In person	*Not Applicable*	In person	In person	In person	*Not Applicable*
Pregnancy Health Care Log	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	Direct mail*
Maternal Blood and Urine Collection^	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	*Not Applicable*
Household Dust and Tap Water Collection+	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Participant Collect or Technician Collect~	Participant Collect or Technician Collect~	Participant Collect or Technician Collect~	*Not Applicable*
Father Informed Consent	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person, telephone , mail, web*	In person, telephone , mail, web*	In person, telephone , mail, web*	*Not Applicable*
Father Interview and VIS	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person, telephone , mail, web*	In person, telephone , mail, web*	In person, telephone , mail, web*	*Not Applicable*
Pregnancy Visit 2 Interview, SAQ, and Visit Information Sheet	In person	In person	In person	*Not Applicable*	In person	In person	In person	*Not Applicable*
Maternal Blood and Urine Collection^	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	*Not Applicable*
Household Dust and Tap Water Collection+	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	Participant Collect or Technician Collect~	Participant Collect or Technician Collect~	Participant Collect or Technician Collect~	*Not Applicable*
Birth Visit Instrument and Visit Information Sheet	In person	In person	In person	*Not Applicable*	In person	In person	In person	*Not Applicable*
Infant and Child Health Care Log	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	Direct mail*
Cord Blood Specimen Collection	*Not Applicable*	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	*Not Applicable*

Table B.6. Mode of Instrument Administration by Recruitment Strategy and Phase								
Data Collection Event	Phase 1				Phase 2			
	Initial Household	Provider-Based and High Intensity	Enhanced Household	Low Intensity	Initial Household	Provider-Based and High Intensity	Enhanced Household	Low Intensity
3-Month Interview (Minimal)	Telephone	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone	Telephone	Telephone	*Not Applicable*
6-Month Interview (Minimal)	In Person	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	*Not Applicable*
9-Month Interview (Minimal)	Telephone	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone	Telephone	Telephone	*Not Applicable*
12-Month Interview (Minimal)	In Person	*Not Applicable*	*Not Applicable*	*Not Applicable*	In person	In person	In person	*Not Applicable*
18-Month Interview (Minimal)	Telephone	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone	Telephone	Telephone	*Not Applicable*
24-Month Interview (Minimal)	Telephone	*Not Applicable*	*Not Applicable*	*Not Applicable*	Telephone	Telephone	Telephone	*Not Applicable*

NOTE: *Alternate acceptable modes are proposed for approval. See *Minimal Data Collection Effort*. ~ Random assignment of participant collect or technician collect modality. ^ Maternal blood and urine will be collected at two prenatal visits. We will first attempt to collect these specimens and samples at the Pre-pregnancy Visit and the Pregnancy Visit 1 visit; if the pre-pregnancy visit is not scheduled (a women is asked to join the study when already pregnant), we will attempt to collect these specimens at the Pregnancy Visit 1 and 2 visits. Additionally, if an enrolled woman declines to provide specimens at any two of the three visits, we will ask her to reconsider and request to obtain specimens up to and including the Pregancy Visit 2 visit. + Household dust and tap water collection will be collected at the Pregnancy Visit 1 and 2 visits.

B.2.1 Informed Consent

Procedures For The Recruitment Strategies (Except Low Intensity)

The same consent process used in the Initial Vanguard Study will be used for participants in the provider based recruitment, enhanced household based recruitment and the high intensity tier of the two-tier, high-low intensity recruitment strategy.

Women participants will be administered consent in the same manner and using the same informed consent forms that have been approved by the NICHD IRB and OMB for Phase 1 (Appendix A). Men identified by the enrolled pregnant as the father of their baby and when the pregnant women allow the Study to contact, will be administered consent using the form approved by NICHD IRB. Women will be asked to provide consent for childrens' participation. Additional Visit Information Sheets (tailored to the content of each visit and, on an as needed basis, other informational materials) have been developed for participants in each of these recruitment strategies particular to the content of each phase. These information sheets will inform participants that data collection activities may be expanded throughout the course of

their participation. However, expansion of the data collection activities will not exceed the level of respondent burden of Initial Vanguard Study participants.

Procedures For The Low-Intensity Arm

A new telephone informed consent script will be used for participants in the low intensity effort of the two-tier high-low intensity recruitment strategy, as research participation in this effort will involve only completion of self-administered or telephone based questionnaires and will not involve face to face interviews and observations, physical measurements or samples at any time throughout the Recruitment Substudy. This Low Intensity Informed Consent Script will be administered through telephone, mail, and via a secure internet site. The telephone consent script is included as Appendix A2.

The consent script will describe to participants that they can expect to receive periodic questionnaires delivered through mail, telephone, or secure web instruments, that the study will follow children born to women participating in the study for 21 years, and that the study may at a later date invite geographically eligible participants to enroll in higher intensity data collections, for which they would go through an additional, separate informed consent process (that is, the same consent process described above for the Initial Vanguard Study and the provider-based, and the high intensity recruitment strategies). Participating women will be mailed the NCS Low-Intensity Visit Information Sheet, which describes the information conveyed in the in the telephone informed consent script, to maintain for their personal records.

The NCS has been granted approval by the NICHD IRB (the study's IRB of record) of a waiver of documentation of informed consent for the low intensity tier participants. The NICHD IRB concluded that the consent evaluation meets the regulatory requirements for a waiver of documentation of informed consent as described in CFR §46.117 (c).

Of all the women participating in the low intensity data collection, only those who reside in the subset of neighborhoods comprising the tertiary sampling unit will be offered the invitation to participate in the high intensity data collection. This invitation will be offered by mail or by telephone. If women decline the invitation, they may still participate in low intensity data collections. If the women accept the invitation and give their consent for high intensity data collections (using the same procedures), they will no longer be asked to participate in low intensity data collections (self-administered or telephone based questionnaires). Over time, participants may wish to cease participating in high intensity data collections. If so, the study will offer them the opportunity to continue with the study by receiving low intensity data collections, and notify them that they may return to high intensity data collection as their preferences dictate. Participants may fully withdraw from the study at any time by giving verbal or written notification of their intent, and may decline any particular data collection event or component.

B.2.2 Quality Control

Informatics Model

The Initial Vanguard Study utilized a centralized model of data management where NCS case management systems and data capture systems utilized the same approach throughout the Vanguard study centers. This centralized approach is common in large scale data collection, even in multi-center studies. In the Initial Vanguard Study experience, it was determined that data capture systems and case management systems used successfully by other studies did not meet the particular needs of a study as complex and dynamic as the National Children's Study. Therefore, a new solution was sought.

The NCS Program Office proposes to use a facilitated decentralization model to support informatics in the Recruitment Substudy. Like in the Initial Vanguard Study, the NCS Program Office will continue to develop evaluation questions and plans; data fields, tables and relationships; formatting and transmission standards; a central data archive; and specifications and guidelines for data security, participant confidentiality, and regulatory compliance. Distinct from the centralized model, however, the facilitated decentralization model allows study centers under contract with the NCS to select case management systems, data acquisition platforms, and as appropriate, data collection tools to acquire data whose content, format and security requirements have been established by the NCS Program Office. All data systems are certified and accredited per the Federal Information Security Management Act of 2002 (FISMA) and related regulatory compliance. All data specifications are consistent with international standards (for example, the Clinical Data Interchange Standards Consortium (CDISC) and the National Cancer Institute cancer Bioinformatics Grid (caBIG).

The facilitated decentralization model encourages the use of open-source, non-proprietary data capture and case management systems. It builds on local study center expertise with existing systems. In practice, NCS study centers have proposed a short list of open-source systems, with collaboration in architecture and programming planned among study centers proposing like systems. It also allows a systematic evaluation of the feasibility, acceptability, and cost of various data capture and case management systems to inform the Main Study. Systematic comparison of data is possible due to the harmonization of data specifications and terminology established by the NCS Program Office, being also consistent with existing international standards.

Although offering many advantages, a decentralized model also poses challenges, particularly in the area of IT security and compliance. While the recruitment evaluation will follow the same standards of confidentiality applicable to the Initial Vanguard Study, the decentralized model puts the primary responsibility on the individual study centers to implement, assess, and maintain the security controls that are necessary to assure the confidentiality and integrity of participant data. The NCS Program Office supplements this self-assessment with on-site inspections.

Each study center and the NCS Program Office Data Warehouse will be required to complete a security plan, a privacy impact assessment, and a risk assessment. All of these documents will be submitted to the NCS Mission Assurance Team and NICHD CIO for review and approval. After their security plan is approved, each study center will conduct a security control assessment in order to evaluate of the adequacy of applicable NIST 800-53 controls protecting the study center's information system(s), underlying infrastructure, and physical location. Any deficiencies discovered in the assessment, along with corrective actions and their scheduled completion dates, will be documented in the Plan of Action & Milestones (POA&M). The results from the assessment and the resulting POA&M will also be submitted to the NCS Mission Assurance Team and NICHD CIO for review and approval. In certain circumstances, it may be necessary for the NCS Mission Assurance Team to physically perform the security control assessment, or to require the study center to submit evidence to verify their assessment results. Once the Security Control Assessment is complete and the submitted documentation and POA&M are approved, a Memorandum of Understanding (MOU) is drafted and signed by the CIO and Study Center Approving Authority. With all necessary artifacts submitted and approved, an Authority to Operate (ATO) is granted by the NICHD CIO. Completion of these documents will also be monitored by the NCS Program Office. No data collection will take place prior to completion of the ATO.

Due to the decentralized nature of the Recruitment Substudy, it is imperative that robust procedures are in place to provide adequate oversight of study center security operations, as well as to ensure the quality of artifacts necessary to maintain compliance with the federal law and related regulatory compliance. All POA&Ms will be monitored on an ongoing basis to ensure that deficiencies are remediated in a timely manner. Any remediation actions taken or any other changes to a study center's operations, procedures, systems, and/or facilities will require a modification to their security plan and subsequent approval by the NICHD CIO. Following the initial authorization, the study centers will assess key security controls (including management, operational, and technical controls) on an ongoing basis during continuous monitoring. These assessments will be reviewed by the NCS Mission Assurance Team and the NICHD CIO on a routine basis.

Data Management Quality Assurance Process

Quality Control and Quality Assurance (QA/QC) procedures and metrics have been included in each component of the Recruitment Substudy. As related to data collection and data management, the QA/QC effort is focused on three major task areas, including instrument development/design; interviewer training and oversight; and data monitoring. Each task area is described below.

<u>Instrument Development</u>

All study instruments were designed centrally at NICHD for implementation by the study centers. Instruments were designed with standardized variable names, question text, response

categories, skip patterns, range checks, and interviewer and programmer instructions. Adherence to these requirements is mandatory, and their implementation will be monitored through a variety of methods, including, but not limited to, site visits, remote access to Computer Assisted Interviewing (CAI) systems, attendance at interviewer training sessions, and interviewer debriefing sessions.

Interviewer Training and Oversight

Study centers will be provided guidance on interviewer recruitment, training and ongoing monitoring. Centrally developed training materials have been provided for specific tasks, and site visits are planned to monitor training sessions at local study centers. Study centers are required to track and report the various trainings and certifications completed by individual interviewers, as well as the frequency and outcome of validation calls to participants aimed at identifying potential falsification of study data. Study center supervisory staff are expected to hold, at a minimum, weekly calls with individual field interviewers to identify issues and areas of concern, and provide strategic guidance.

Data Monitoring

Monitoring and analyses of operational and study data will occur on an ongoing basis at both local study centers and centrally at the NCS Program Office. The NCS has (and will continue to) develop standardized file layouts for all data collected for the Recruitment Substudy. Study centers will be required to transform their "raw," production-level data to meet these common specifications. 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, or "missingness," distinguishing between legitimately missing data versus those missing in error.

The NCS will conduct ongoing reviews of these transformed data, comparing "national" and study center-specific outcomes against expected values. The centralized review will occur through the development of standardized reports as well as ad hoc queries. Standardized reports will be made available to study centers to assist in their field monitoring efforts and any resolution of known issues or concerns. Examples of operational data to be examined include, but are not limited to, characteristics of contact attempts; refusal conversion patterns; interviewer-effects on recruitment; and questionnaire timing data. As needed or on a schedule still to be determined, the NCS Program Office will conduct audits of "raw" production data that have not yet been transformed to meet NCS specifications, and all programming code developed to complete such transformation s.

Adverse Event and Other Required Reporting

The National Children's Study Program Office has implemented monitoring and reporting procedures to ensure that human subject protections are followed, participant confidentiality is

maintained, and study protocols are implemented correctly. Within this structure, study centers 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 incidents reported by NCS study centers at least once per week (or more frequently, depending on the nature of the event and associated regulatory requirements). The NCS Program Office reports adverse events systematically in accordance with guidance from the Office of Human Research Protections to the NICHD IRB and to the iSMOC for their review.

NCS study centers are also expected to report adverse events to their local IRB(s) in accordance with local reporting requirements. Should study centers sign the Memorandum of Understanding to join the (IRB) Federation, they will retain the responsibilities of reporting adverse events to the IRB of record. Depending upon their level of participation as a member of the Federation, study centers will report adverse events either to the NICHD IRB or the appropriate local IRB. In reporting adverse events, study centers do not ask additional questions of study participants; therefore, the NCS does not request permission for additional respondent burden hours for this activity.

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

Community Outreach And Engagement

Each recruitment strategy will employ a community outreach and engagement plan that benefits from core content generated centrally from the NCS Program Office, employs themes reflecting recruitment strategy enrollment approaches, and is adapted to fit local interests and needs. This framework will allow systematic comparison of message themes and locally-determined media use across recruitment strategies and substudy locations, while maintaining consistency in core NCS content.

Core NCS content includes the presentation of the purpose, goals, design, and management of the study. This content will be used consistently throughout outreach and engagement activities across recruitment strategies. Message themes will be customized for each of the three recruitment strategies to emphasize aspects of enrollment most particular to a given recruitment approach. All study locations are expected to use of media and community activities, tailored to local circumstances, to increase public awareness of the NCS and aid with recruitment of participants. These methods will include but will not be limited to messages transmitted through local media (for example, newspapers, radio, and television), distribution of various NCS materials (for example, brochures, question and answer sheets, and newsletters), and secure use of electronic modes, such as Internet and social media. Table B.7 summarizes the community outreach and engagement plan by recruitment strategy.

Table B.7. Community Outreach and Engagement Plan by Recruitment Strategy			
Recruitment Strategy	**Core Content**	**Message Theme**	**Conveyance**
Initial Vanguard Study	NCS Program Office	General	Locally-determined*
Provider-Based	NCS Program Office	Relationship with Care Provider	Locally-determined*
Enhanced Household	NCS Program Office	Relationship with Community	Locally-determined*
Two-Tier High-Low Intensity	NCS Program Office	Self-Determination	Locally-determined*

NOTE: * Permits comparison of primary media use methods.

Costs and effectiveness of these approaches, particularly for minority engagement, will be evaluated systematically. For example, preliminary data from at least one study center in the Initial Vanguard Study suggest that current outreach and engagement practices may not be effective in reaching some age-eligible women of Asian ethnicity; this and other related findings will inform approaches used in the Recruitment Substudy. Other questions of interest include:

- How do local travel costs associated with outreach events vary across recruitment strategies?
- What were the dates, costs, and geographic targeting of outreach and media campaigns?
- What is the cost per delivered message in media campaigns (exact or approximate)?
- What is the size of the targeted population of the media campaign?
- What is the yield of responses from particular media campaigns?
- What is the cost in time for community outreach efforts (both contractor and volunteer labor)?
- Does increased frequency of media messages result in increased response by interested individuals?
- Does varying the type of media message result in increased response by interested individuals?
- Are particular outreach efforts more or less successful with persons with particular demographic traits (race, ethnicity, age, marital status, primary language, employment, or education)?
- Are particular outreach efforts associated with more effective retention? For instance, participants encountered through a provider might be retained in the study better than participants recruited through a household visit.

Other Methods to Promote Response and Deal with Nonresponse

The experience of the Initial Vanguard Study has yielded several important "lessons learned" that have informed the design and implementation of the proposed Recruitment Substudy. The study centers have learned that using the same data collectors to interact with households over time builds rapprort and promotes response. For this reason, field staff should be cross-trained to administer multiple instruments and visits. Obtaining supplementary contact information (such as cell phone numbers), varying callback days and times, and setting up each subsequent

meeting at the preceding visit have also proved successful strategies. Finally, the experience of the Initial Vanguard study also demonstrated that professionalizing enumeration staff – and employing different staff with different skills and characteristics for enumeration compared to interviewing – can promote successful responses. These findings have informed all strategies proposed for the Recruitment Substudy, as appropriate.

B.4 Tests of Procedures or Methods to be Undertaken

The analytic aim of the Recruitment Substudy is a quantitative description of the feasibility, acceptability, and cost of three discrete participant recruitment strategies (Phase 1), the association of recruitment strategies with retention outcomes, and testing of selected study visit measures that have been revised based on Initial Vanguard Study experience (Phase 2). Overarching research questions, and research questions specific to particular recruitment strategies, were presented in Part A of this supporting statement (see *Research Goals* and *Study Design and Methods*, respectively). This section describes the decision rules that form the basis of the evaluation plan for the Recruitment Substudy.

Phase 1 Evaluations: Recruitment and Retention

Recruitment

Feasibility will be evaluated in terms of recruitment and retention of participants. Recruitment goals will not target a particular response rate or a particular number recruited. Instead, the outcome of interest is the defining the maximal and steady state rates for each of the recruitment strategies in identifying eligible women, successfully gaining their consent, and successfully collecting data throughout pregnancy and including birth. For these purposes, the "steady state" rate is defined as three consecutive months of approximately the same rate.

Accordingly, outcomes that will be used to assess recruitment include:

- The rate at which the study learns of potentially eligible women, which will occur through a variety of sources dependent on the recruitment schema.
- The rate at which the study can successfully contact these potentially eligible women.
- The rate at which the study determines the dwelling unit eligibility and the pregnancy screening eligibility of these women.
- The rate at which eligible women consent to entering the study after being contacted and screened for eligibility.

For the Main Study, a customized recruitment strategy may be required for different types of study locations. The Recruitment Substudy experience, along with other extant data and resources, will help guide the choice of recruitment strategies for the Main Study.

Retention

A key goal for the NCS Main Study is to obtain information on the health and developmental outcomes of subjects as they move through adolescence and early adulthood. To answer many of the central 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 Recruitment Substudy. Retention of participants from visit to visit will be carefully monitored.

Specifically, the NCS will monitor:

- The proportion of age-eligible women not pregnant at initial contact who consequently become pregnant and agree to join the study.
- The proportion of consented women who participate in at least one data collection study visit.
- The proportion of women enrolled during pregnancy and participating in all data collection visits through the birth of a child that is enrolled into the study.
- The proportion of women who receive a pre-birth data collection visit that also receive a successful birth visit.
- The proportion of women enrolled during pregnancy and participating in all data collection visits through age 24 months of the child that is enrolled

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. For instance, women not planning to become pregnant are of interest to the study, and yet identification with the study may not appear as salient to this group.

Two areas of retention are particularly important for generating recommendations for the Main Study's design—retention of women in pre-pregnancy and during pregnancy. The NCS is distinct among longitudinal child cohort studies in that it aims to collect environmental exposure data prior to pregnancy and during pregnancy. It is because of these aims that the study design does not draw from a birth certificate sampling frame, which is a simpler and less costly method of identifying women to enroll in a generalizable, large-scale study. In large part, then, the extent to which these three strategies successfully retain women pre-pregnancy and during their pregnancy will drive their recommendation for use in the Main Study.

Acceptability will be evaluated in terms of selection bias and respondent burden. All recruitment strategies may introduce selection bias, but it is important to understand the nature and extent of this bias given key research objectives and, accordingly, inform any necessary adjustments to the Main study design so that research objectives are well met. The NCS is a study of the effects of the environment on children, and many relevant environmental exposures occur either before or during pregnancy. Thus, it is important to inform the Main Study design by identifying any bias in the stage of pregnancy when women enter the study and participate in their first data collection. The Recruitment Substudy will track the distribution of women who are enrolled before they are pregnant, during pregnancy, or at or around the birth event. The Recruitment Substudy will also record and examine the distribution of gestational

age at the time of consent and at the time of first study visit for data collection, as these early data collections are important for understanding exposures during pregnancy.

It is essential to recruit a broad range of enrollees to the Main Study so that the NCS can provide valid information about the population of births in the United States. Further, the receptiveness of particular women to particular recruitment strategies may be associated with demographic factors, such as race, ethnicity, age, marital status, primary language, employment status, and level of education. The Recruitment Substudy will examine the demographic and general medical characteristics of screened and recruited women and compare those characteristics among the three recruitment strategies, and, as measures permit, the cohort for theInitial Vanguard Study. Additionally, these distributions will be compared to population level data such as U.S Census or birth data for the geographic region.

As described above, respondent burden and impact on study center and Program Office infrastructure will be evaluated as well. All else being equal, methods that reduce respondent burden will be given priority over methods that reduce impact on study infrastructure.

Evaluation of cost will consider level of effort, equipment and materials for data collection. Study centers and the NCS Program Office will track these data; the NCS Program Office will evaluate the combined data. Evaluation will consider stationary or repeated costs, and investment in infrastructure that may reduce costs in the Main Study. Cost alone will not be the basis for retaining or rejecting a recruitment strategy.

Phase 2 Evaluations: Selected Study Visit Measures

Study Visit Measures

The Initial Vanguard Study yielded valuable data and field experience regarding the robustness, participant and study infrastructure burden, and cost of piloted study visit measures. The NCS Program Office has reviewed study visit measures across a range of domains and identified items that a) are acceptable; b) should be improved; or c) should be replaced with alternatives.

Given these analyses, selected measures have been revised to improve feasibility, acceptability, and cost as described below.

Household Dust and Tap Water Collection

In Phase 2, tap water samples will be evaluated for an array of analytes. In the Initial Vanguard Study, tap water samples were collected by study field staff from 10 percent of study participant homes with water supplied by a community water supply system, and from all homes with water supplied by a private well. The samples collected from homes supplied by a community water system were analyzed for two disinfection by-products—trihalomethanes (THMs) and haloacetic acids (HAAs). The samples collected from homes with a private well were analyzed for volatile organic compounds (VOCs). Although the collection and analysis of

these samples provide an opportunity to assess the feasibility, acceptability, and scalability of tap water sample collection for these analytes, it does not provide sufficient information about other chemical contaminants in drinking water. In consultation with scientists from the United States Geological Survey (USGS), we will expand tap water analysis to a greater number of chemicals, such as pesticides and pharmaceuticals, and attempt to relate these results to USGS water quality data to increase the informative value of tap water sample collection. Additionally, in the Initial Vanguard Study, water samples were collected by trained Study Center field staff. In Phase 2, each Study Center will randomly assign some samples to be collected by participants to test the feasibility, acceptability, and cost of self-collected tap water samples.

In the Initial Vanguard Study, four house dust samples were collected by study field staff; three wipe samples and a vacuum dust sample. One wipe sample from each home was analyzed for pesticides. The other two wipe samples were stored, to be analyzed for semi-organic compounds and inorganic compounds. The vacuum samples were stored, and planned to be analyzed for allergens and endotoxin. In Phase 2, one vacuum bag sample is planned as a way to improve ease in sample collection. The vacuum bag sample would be analyzed for organic compounds, molds, allergens, endotoxin, metals, and other contaminants. Additionally, the vacuum bag will provide a large amount of dust that can be stored for future analysis. Additionally, Phase 2 will randomly assign vacuum bag collection as collected by the participant or by the field staff to evaluate the feasibility, acceptability, and cost of self-collected household dust using this method.

Cord Blood and Maternal Blood and Urine Collection

We propose to reintroduce cord blood collection in Phase 2 to evaluate the feasibility, or scientific quality, of the collection with revised equipment. Cord blood was collected in the Initial Vanguard Study using a cord blood bag that contained liquid citrate phosphate dextrose (CPD) as an anti-coagulant. This collection matrix results in laboratory analysis challenges because of 1) the inability to make lipid measurements as CPD is not an acceptable anticoagulant for the commercial kits used for the assays; and 2) the large dilution effect from varying amounts of blood, sometimes very low volume of blood, being collected in the bag with the liquid anti-coagulant. In Phase 2, we would use a newly developed bag with dry ethylenediaminetetraacetic acid (EDTA) as the anti-coagulant.

Maternal blood and urine are core collections for the NCS Vanguard and Main Studies. Inclusion of these collections will allow comparison of specimen collections across recruitment strategies. In addition, biospecimen collections will provide participants with an NCS visit experience more closely mirroring the anticipated Main Study experience, which will inform retention analyses and Study Center infrastructure evaluations.

Pregnancy Health Care Log and Infant and Child Health Care Log

We propose to reintroduce a Pregnancy Health Care Log and and Infant and Child Health Care Log in Phase 2 to evaluate the feasibility, or scientific value, of revised forms. A Pregancy Health Care Log and Infant and Child Health Care Log were incorporated in the Initial Vanguard Study. As part of analysis of study visit measures, the logs were reviewed to improve their utility scientifically and logistically. The revised logs specifically require inserting data regarding contact information for the source of care, the purpose of which is to facilitate locating medical records. This content is not present in the original logs. The medical record is generally considered the credible reference for health-related information. For the Main Study, it will be essential to locate and abstract selected medical records for the analysis of key data elements. By reintroducing the revised logs in Phase 2 of the Vanguard Study, we will be able to evaluate the extent to which the revised content assists our ability to locate participant medical records (with the consent and authorization of participants), or if this content would benefit from further revision.

Additionally, as it is essential to incorporate, within the NCS database, information about the source of care, the revised logs are also anticipated to reduce participant burden by formalizing real time documentation, thus reducing the effort and time to obtain that information by interview or questionnaire.

Father Interviews

We propose to reintroduce a minimal visit father interview in Phase 2 to evaluate acceptability of the instrument as it may vary by mode of administration. The Initial Vanguard Study featured a father interview at two prenatal data collecting events, each about one hour in length. Results from the Initial Vanguard Study indicated that response rates for eligible, consented fathers was lower than desired (about 50% at first trimester). Accordingly, we propose to offer alternate modes of administration of the father instrument to improve acceptability as measured by item nonresponse, and time to return the completed instrument. Paper-based (direct mail), phone, and web-based modes would be offered to father participants. Phone administration of the father interview would take place only after approval of a father telephone informed consent script (forthcoming).

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

The sampling and data collection strategies proposed for the Recruitment Substudy have been presented to, and benefited from, comments received from staffs from several federal agency representatives, advisory and research groups including: representatives from the Census Bureau, the National Center for Health Statistics (NCHS), the National Center for Education Statistics (NCES), the National Cancer Institute (NCI), and EPA attending the NCS Recruitment Methods Meeting [November 2009]; the Institute of Medicine's Committee on Pediatric Health and Health Care Quality Measures [December 2009]; the NCS Advisory Committee [January 2010 and April 2010]; the Committee on National Statistics (CNSTAT) of the National Research

Council (NRC) [May 2010]; representatives from the Office of Management and Budget, the Administration for Children and Families, NCES, NCI, EPA, and NIEHS attending the NCS Retention Methods Meeting [June 2010]; the NCS Interagency Coordinating Committee, comprising EPA, CDC, NIEHS and NICHD [monthly meetings]; Westat, NORC, and Battelle [as needed]. In addition, other statisticians and/or individuals from statistical agencies participate on NCS advisory committees. Each of the NCS study centers is also staffed with appropriate statistical expertise. Each study center will obtain birth certificate data for their local area and will review these data for consistency with the results of the Initial Vanguard and Recruitment Substudy.

Organizations involved in collecting and/or analyzing NCS Recruitment Substudy data are listed at http://www.nationalchildrensstudy.gov/newsannouncements/announcementsupdates/announcements/Pages/LOIfeb2010.aspx.