U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
Centers for Disease Control and Prevention
U.S. ENVIRONMENTAL PROTECTION AGENCY

THE NATIONAL CHILDREN'S STUDY
HEALTH GROWTH ENVIRONMENT

DATE: September 9, 2011

TO: Dr. Margo Schwab, Dr. Julie Wise
Office of Management and Budget
Office of Information and Regulatory Affairs

FROM: Dr. Julia Slutsman
Ms. Colleen Lee

THROUGH: Dr. Steven Hirschfeld

SUBJECT: Request for Non-Substantive Change to National Children's Study, Vanguard (Pilot) Study (OMB Control #0925-0593, Expiration July 31, 2013) – Request for Measurement of Infant Race/Ethnicity and Inclusion of Formative Research Projects

CC: Dr. Sarah Glavin, Ms. Jamelle Banks, Ms. Seleda Perryman, Ms. Mikia Currie

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We request non-substantive change to the National Children's Study (NCS) Vanguard (Pilot) Study protocol approved as revised by the Office of Information and Regulatory Affairs (OIRA).

A. Changes to Vanguard Study Instruments

A.1 Measurement of Infants' Race and Ethnicity

We ask to include a mother-reported measure of race/ethnicity for infants enrolled in the NCS Vanguard Study. The measure (variable BC07B/ETHNICITY; BC007C/RACE) are the same as that approved by OIRA (7/22/2010) to measure adult race/ethnicity. These would be included in the Birth Interview (see highlight on page 5, Attachment A.1.1) and the Birth Instrument for Two Tier Low Intensity (see highlight on page 4, Attachment A.1.2). This information is necessary to comply with IRB reporting requirements at the time of continuing review.

The additional data collection described above represents very minimal additional burden; therefore, we do not request additional burden hours for these revisions. These changes will not affect recruitment and retention evaluation of the Vanguard Study protocol.

Attachments (2):
A.1.1 Birth Instrument for Enhanced Household, Provider-Based, and High Intensity
A.1.2 Birth Instrument for Two Tier Low Intensity

B. Formative Research Projects

The five proposed formative research projects described below (Table 1) align with the current scope of work for the NCS Vanguard Study. The NCS Vanguard Study is designed to assess the feasibility (technical performance and reliability), acceptability (impact on study participants and study infrastructure), and cost (level of effort, personnel, resources, and money) of recruitment, study visit measures, and study logistics to inform the NCS Main Study. Each of these proposed formative research projects would evaluate the methods to be considered for the NCS Main Study at minimal participant burden and cost when compared with direct implementation within the NCS Vanguard Study overall.

Additionally, these formative research projects do not feature aspects that would interfere with the comparison of recruitment and retention strategies described in the Alternate Recruitment Substudy of the NCS Vanguard Study. Language in the NCS Phase 2 Vanguard Study Supporting Statement A (approved by OMB on 4/13/2011) supports formative research recruiting either NCS Vanguard Study participants or their demographically similar peers.

Please note that all future requests for formative research clearance will use the agreed-upon template; the recent clarification of OIRA guidance occurred after the majority of this current request was formed and, therefore, we ask that the current format be acceptable for submission this last time.

Table 1. Candidate Formative Research Projects for Non-Substantive Change to the NCS Vanguard Study (OMB Collection # 0925-0593, Expiration 7/31/2013)						
Item	Project ID Number	Project Title	Purpose	Proposed Additional Information Collection	Rationale for Inclusion in Vanguard Study	Respon-dent Burden Hours
B.1	LOI3-BIO-02; -05	Prospective Analysis of Environmental Chemicals in Breast Milk	To determine the optimal schedule for breast milk sampling, evaluate levels and time trends in breast milk contaminant concentrations, and establish reference ranges in PBDE and BPA in human breast milk. ELISA methods for testing target environmental chemicals in breast milk would be evaluated.	Breast milk will be collected at 1, 2, 3, and 4 months postnatally.	The data collected will inform the processes for breast milk collections in the NCS Vanguard Study. Extant breast milk collected through the initial Vanguard Study is not suitable for these assays.	900
B.2	LOI2-PHYS-15	Visit Assessment Tool to Address Birth Defects and Dysmorphology	To develop and evaluate a standardized dysmorphology assessment instrument.	Photos, videos, and a brief physical assessment will be taken at birth, 6 month, or 12 month visits.	The data collected will inform the process for rigorously and efficiently assessing dysmorphology and birth defects in the NCS Vanguard Study.	225
B.3	LOI3-QUEX-01	Stress and Cortisol Measurement	To develop an optimized measure of self-reported maternal stress.	Blood, hair, urine, and saliva samples taken during pregnancy; self-reported stress scales and questionnaires during pregnancy and after birth. Time diaries and biologic measures assist with self-reported stress recall.	Data collected will inform the development of optimal item-reduced measures of stress for the NCS Vanguard Study.	2,800
B.4	LOI2-QUEX-05	Bayley-3 Short Form for the National Children's Study	To develop age-specific short forms of the Bayley Scales of Infant Development, Third Edition.	Mental and motor assessment given to children between 4 months and 44 months of age.	This project tests the feasibility, acceptability, and cost of a direct, short form assessment of early childhood development suitable for longitudinal measurement in the NCS Vanguard Study	324
B.5	LOI2-QUEX-13	Measuring Child Health Disparities	To assess the validity and stability of measures of health literacy, discrimination, parenting self-efficacy, and healthcare access, utilization, and quality.	Phase 1 will include cognitive interviews. Phase 2 will interview first-time mothers during pregnancy and again 6 months later; current mothers will be interviewed once.	Systematic measurement of mechanisms proposed to affect disparities in health care outcomes is lacking in the research literature. Data collected will identify robust and efficient measures to measure sources of child health disparities and develop process for the NCS Vanguard Study.	2,178

B.1. LOI3-BIO-02; -05: Prospective Analysis of Environmental Chemicals in Breast Milk
The NCS formative research project, LOI3-BIO-02; -05, aims to identify ideal specimen volume, collection timing, number of samples, and screening methods for discerning environmental chemicals in breast milk. The resulting technique and procedures would inform the NCS Vanguard Study protocol.

NCS Vanguard Study and non-NCS Vanguard Study mothers at less than three weeks postpartum who plan to breastfeed for a minimum of 2-4 months would be invited to participate in this project. NCS Vanguard Study mothers would be invited to join at the time of the birth visit; non-NCS Vanguard Study mothers would be recruited at the time of their well baby visit(s) to participating clinics. Enrollment will continue until 180 women have joined (see B.1.1 Exemplar Recruitment Flyer). After consent, participants will be trained on how to use the electric breast milk pump to be used for sample collection (the breast milk pump will be returned after the project is complete) and asked to complete a 10-minute health and infant feeding questionnaire. During follow up visits at one month, two months, three months, and four months, participants will be asked to provide 3-4 ounces of breast milk for screening. Breast milk collection will last approximately thirty minutes and will be done in the participant's home; participants may use hand expression, electronic breast pump loaned by the Study Center, or they may use their own pump. Field workers will then collect the samples and administer the health and infant feeding interview at each pickup visit.

Following the last sample collection, contaminant concentrations in breast milk over time will be compared to help determine the ideal sample type and timing of collection for estimating infants' exposure to environmental contaminants. Additionally, it will be possible to determine the minimum number of breast milk samples needed to estimate toxicant body burden, and a reliable, cost-effective enzyme-based immunoassay (ELISA) method for screening environmental chemicals in breast milk.

The additional data collection described above represents a minimal amount of additional burden (180 respondents X 1 hour/respondent X 5 events = 900 hours). This project would not affect comparisons of recruitment strategies. Language in the NCS Vanguard Protocol approved 4/13/2011 allows non-NCS Vanguard participants to join formative research activities. Incentive amounts are $25 per visit for the first contact; and a $50 incentive is proposed for the 5th contact. This incentive schedule is consistent with the Phase 2 Vanguard Protocol. Local IRB approval will be required prior to participant contact and documentation of that approval will be available upon request.
IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 900 hours

Attachments (8):
B.1.1 Exemplar Recruitment Flyer
B.1.2 Exemplar Screening Interview
B.1.3 Exemplar Breast Milk Collection Consent Form (for Non-NCS Vanguard Study Participants)
B.1.4 NCS Visit Information Sheet (for NCS Vanguard Study Participants)
B.1.5 Exemplar Collection Instructions
B.1.6 Exemplar Phone Script to Schedule Study Visits
B.1.7 Exemplar Interview
B.1.8 Protocol Summary (Excerpted from local IRB protocol)[1]

B.2. LOI2-PHYS-15: Visit Assessment Tool to Address Birth Defects and Dysmorphology

[1] IRB protocols as initially approved locally will be resubmitted upon OIRA clearance of the project, as appropriate.

The NCS formative research project LOI2-PHYS-15 will develop and evaluate a standardized dysmorphology assessment instrument (DAI). To accomplish this, the study will define the normal variations of physical characteristics and create a valid and reliable assessment tool for use in the field. Following the development of the DAI, Study Centers will develop a training module for field examiners, and will compare assessment reliability and validity across examiners to validate the assessment tool. Pre-piloting of the assessment with 9 or fewer infants has informed procedures to be used in this formative research project.

NCS Vanguard Study participants will be invited to join the project at the scheduled NCS Vanguard Study birth visit, the 6 month visit, or the 12 month visit. Non-NCS Vanguard Study participants who are demographically similar to NCS Vanguard Study participants, but who are not geographically eligible to participate for the Vanguard Study, will be recruited from collaborating nurseries as a complementary convenience sample until the desired overall sample size of 300 infants is reached (see B.2.1, Exemplar Recruitment Flyer (Non NCS Vanguard Participants)). After consent, photographs of the infants' face, hands, and feet will be taken from 100 infants at birth, from another 100 infants at 6 months, and from another 100 infants at 12 months of age. Ten-second videos will also be taken of each infant's face and diapered body. A brief physical exam of infants will also be performed by trained researchers. These images and exams will be evaluated using the DAI. A five-minute questionnaire will be used to assess participant satisfaction with formative research project procedures. The image collection and physical assessment will take about half an hour to complete for each participant. This additional data collection represents a minimal amount of burden (300 respondents X .75 hours/respondent X 1 event = 225 hours).

This project would not affect comparisons of recruitment strategies. Language in the NCS Vanguard Protocol approved 4/13/2011 allows non-NCS Vanguard participants to join formative research activities. An incentive of $25 will be offered to participants for joining this project; the amount is consistent with the OMB approved incentive structure for the Phase 2 Vanguard Study.

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 225 hours

Attachments (6):
B.2.1 Exemplar Recruitment Flyer (Non-NCS Vanguard Study Participants)
B.2.2 Exemplar Dysmorphology Assessment Consent Form (for Non-NCS Vanguard Study Participants)
B.2.3 NCS Visit Information Sheet (for NCS Vanguard Study Participants)
B.2.4 Exemplar Participant Experience Survey
B.2.5 Protocol Summary (Excerpted from local IRB protocol)[1]
B.2.6 IRB Approval Letters

B.3. LOI3-QUEX-01: Stress and Cortisol Measurement
The NCS formative research project LOI3-QUEX-01 proposes to use Item Response Theory (IRT) to develop an optimized, item-reduced measure of self-reported maternal stress that is supported empirically through convergent validity analysis of stress biomarkers and biologic measures. Additionally, key moderators of stress biomarkers will be evaluated to inform efficiency and quality of measurements during pregnancy. Development of a scientifically robust, IRT-optimized maternal stress measure would more efficiently measure chronic stress, would not require biomarker collection, and would thereby reduce burden for participants and Study costs.

A convenience sample of 700 women who are demographically similar to NCS Vanguard Study participants, but who are not geographically eligible to participate in the Vanguard Study, will be invited to join. Participants must be age of local majority or older and less than 20 weeks pregnant with a singleton birth. Local advertising in collaborating clinics will be used to recruit participants; enrollment will continue until sample size targets are met.

This protocol involves two in-person visits at collaborating health centers and a series of self-administered measures that will take place in the participant's home. At the first visit, after screening and consent, blood, urine, and hair samples will be collected for cortisol measurement. The procedure for saliva self-collection will be demonstrated. Participants will then be asked to complete a demographic and health interview, a contact form, and a stress survey. Participants will then receive training on the ecological momentary assessment. The heart rate measuring device will be demonstrated, and time diary completion will be reviewed. After the first in-person visit, participants will be asked to self-collect saliva samples from home and mail them for analysis. Time diaries and heart monitoring will continue to complete the ecological momentary assessment. The take home packet of additional stress measures will be completed by participants. Approximately 12-14 weeks after the first in-person visit, a second in-person visit will be scheduled. Participants will be asked to provide blood, urine, and hair samples; the time diary and the take home packet will be collected and the second stress survey will be administered. Participants will be asked to self-collect and mail a second saliva sample. Project researchers will complete the enrollment survey and postnatal survey by way of medical record abstraction, with participant consent, outside of the in-person interview.

The purpose of this project is to develop a short-form measure of prenatal stress that is robust, efficient, and cost-effective. To do this, it is necessary to administer multiple items and collect multiple samples repeatedly. Accordingly, the estimated burden is approximately four hours per participant for both visits and home self-administration, combined. The incentive schedule approved for NCS formative research is up to $25 for up to one hour of contact and up to $25 for collection of samples. For this formative research project, we propose offering an incentive of $50 after completing each of two in-person visits, including sample collections, and an additional $25 after returning each of two self-collected saliva samples. This additional data collection represents a modest amount of burden (700 respondents X 2 hours/respondent X 2 events = 2,800 hours).

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 2,800 hours

Attachments (12):
B.3.1 Exemplar Recruitment Flyer
B.3.2 Exemplar Screening Tool
B.3.3 Exemplar Stress and Cortisol Consent form
B.3.4 Exemplar Participant Contact Information Sheet
B.3.5 Exemplar Medical Record Abstraction Form
B.3.6 Exemplar Demographics and Health Interview
B.3.7 Visit 1 Stress Questionnaire
B.3.8 Take-Home Questionnaire Packet
B.3.9 Visit 2 Stress Questionnaire
B.3.10 Stressful Life Event Schedule (SLES) Checklist
B.3.11 Exemplar Postpartum Medical Record Abstraction Form
B.3.12 Protocol Summary (Excerpted from local IRB Protocol)[1]

B.3.13 IRB Approval Letters

B.4 LOI2-QUEX-5: Bayley Scales of Infant Development, Third Edition, Short Form

The NCS formative research project LOI2-QUEX-5 will explore the feasibility, acceptability, and cost of age-specific short forms of the Bayley Scales of Infant and Toddler Development Third Edition (BSF-3), a standardized assessment of young children's cognitive, language, and motor development for use at child age 6-, 12-, 18-, 24-, and 36 months. The short form, if robust, would substantially reduce participant burden and field costs by reducing time in the field and field training. Psychometric analyses were conducted to identify items from the BSF-3 to be included in the short form, and administration and scoring procedures have been reformulated for maximum feasibility in the field. The short form of the BSF-3 has been pre-tested with 9 participants within the proposed age ranges, and results from this pretesting will inform the proposed formative research project.

A convenience sample of 300 participants who are demographically similar to NCS Vanguard Study participants, but who are not geographically eligible to participate in the Vanguard Study, will be recruited into this formative research study (see B.4.1, Exemplar Flyer). Enrollment will continue until recruitment targets have been met. Parents responding to the flyer will be asked to provide limited demographic information about the child (for example, sex of child age, household composition, and socio-economic status) during a short phone screener. The demographic information will be used in the psychometric analyses to rule out differential item functioning and differential test functioning potentially associated with demographic factors. The estimated time for the child's participation is 50 minutes, on average.

This project would not affect comparisons of recruitment strategies. Language in the NCS Vanguard Protocol approved 4/13/2011 allows non-NCS Vanguard participants to join formative research activities. An incentive of $25 will be offered to participants for joining this project; the amount is consistent with the OMB approved incentive structure for the Phase 2 Vanguard Study. This additional data collection represents a minimal amount of burden (300 respondents X 1.08 hours/respondent X 1 event = 324 hours).

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 324 hours

Attachments (6):
B.4.1 Exemplar Flyer
B.4.2 Exemplar Consent
B.4.3 Telephone Screener
B.4.4 Assessment Description
B.4.5 Protocol Summary (excerpted from local IRB protocol)[1]
B.4.6 IRB Approval Letter

B.5 LOI2-QUEX-13: Measuring Child Health Disparities

The Children's Health Act mandates the NCS to conduct a systematic evaluation of health disparities in children's development. Robust measures of mechanisms for observed health disparities are not well established in the research literature. The NCS formative research project LOI2-QUEX-13 will assess the feasibility, acceptability, and cost of specific health literacy, acculturation, and discrimination measures for use in a large scale observational study such as the NCS.

A pre-pilot of this study (in less than 9 mothers) informed the cognitive testing design for proposed health literacy, acculturation, and discrimination measures. A convenience sample of 60 women demographically similar to, but not geographically eligible for, the NCS Vanguard Study will be invited to participate in cognitive testing; a brief demographics questionnaire will also be administered. Cognitive testing represents a minimal amount of burden (60 respondents X 1.3 hours/respondent X 1 event = 78 hours).

Upon conclusion of cognitive testing and subsequent revision of project instruments and logistics, a convenience sample of 1,400 women demographically similar to, but not geographically eligible, for the NCS Vanguard Study will be invited to participate in the second phase of this project. Local advertising will be used to enroll women until desired sample targets are met. Approximately half of this sample will comprise mothers of children ages five and younger. The remainder of the sample will comprise first-time pregnant mothers. The full sample will receive the instrument battery comprising demographic, health literacy and education, acculturation, and discrimination measures. The instrument will be administered a second time six months after the initial interview for participants recruited during pregnancy only.

The proposed sample size is necessarily large to present precision in comparison for key race and ethnic groups of interest. Because we wish to validate instruments across population subgroups of African Americans, Asians and Pacific Islanders, Latino Caribbean or Central Americans, Latino Mexicans, and Caucasians, the sample size is comparatively large. For instance, the newest Vital Sign, a short measure of health literacy compared to the S-TOHFLA, has not been tested in these populations. To compare percent agreement across population subgroups requires a subgroup of 250 of interest and 250 of non-Hispanic whites to yield a power of 97% to detect a difference in percent agreement given population levels of agreement of 72% to 85%, two tailed alpha of 0.05. Sample size targets of ethnic subgroups can be achieved through extensive research and community networks already established by participating NCS Study Centers.

Phase 2 represents a modest amount of additional burden justified by power analysis calculations ((700 respondents X 1 hour X 1 event) + (700 respondents X 1 hour X 2 events)) = 2,100 hours. This project would not affect comparisons of recruitment strategies. Language in the NCS Vanguard Protocol approved 4/13/2011 allows non-NCS Vanguard participants to join formative research activities. An incentive of $25 will be offered to participants at each of two visits for joining this project; the amount is consistent with the OMB approved incentive structure for the Phase 2 Vanguard Study.

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 2,178 hours

Attachments (10)
B.5.1 Exemplar Recruitment Flyer
B.5.2 Exemplar Cognitive Interview Phone Screener Script
B.5.3 Exemplar Consent for Cognitive Interview
B.5.4 Exemplar Cognitive Interviewing Guide
B.5.5 Exemplar Interview Phone Screener Script
B.5.6 Exemplar Consent for First-Time Mothers
B.5.7 Exemplar Consent for Mothers with Children Age 0-5
B.5.8 Exemplar Interview
B.5.9 Protocol Summary (Excerpted from Local IRB Package)[1]

B.5.10 IRB Approval Letters

Table 2. Respondent Burden Table for Candidate Projects (OMB Collection # 0925-0593, Expiration Date 7/31/2013)							
Item	**Formative Research Project Number**	**Project Title (Abbreviated)**	**Type of Respondent**	**Number of Respondents**	**Responses per Participant**	**Hours per Response**	**Total Hour Burden**
B.1	LOI3-BIO-02; -05	"Breast Milk"	Mother	180	5	1.00	900
B.2	LOI2-PHYS-15	"Dysmorphology"	Infant/Child	300	1	0.75	225
B.3	LOI3-QUEX-01	"Stress & Cortisol"	Mother	700	2	2.00	2,800
B.4	LOI2-QUEX-5	"BSF-3"	Infant/Child	300	1	1.08	324
B.5	LOI2-QUEX-13	"Health Disparities"	Mother	1,478	1	1.47	2,178