

DATE: December 21, 2011

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

FROM: CDR 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 Inclusion of Formative Research Projects

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

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).

B. Formative Research Projects

The two 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 OIRA 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	Respondent 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.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

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

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

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). All data collections will be performed by paid Study Center staffs, and therefore, would not impose burden upon nursery or hospital staffs.

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

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

