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: June 20, 2011

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

FROM: Dr. Jennifer Park

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 Alternate Modes; Participant-Collect Environmental Sample Instructions; 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. Alternate Mode of Administration

We ask that instruments approved for use in the Vanguard Study Phase 2 be administered in alternate modes as listed below (Table 1). Mode evaluation would assist in the development of efficient and less burdensome, but scientifically robust, data collection for the Vanguard Study and Main Study. With an anticipated recruitment of 2,500 to 3,000 participants, each with multiple encounters, we believe we will have sufficient sample size to examine mode effects statistically. There is no anticipated increase in participant burden.

Table 1. Proposed Alternate Modes of Instrument Administration, by Phase 2 Instrument

Item	Instrument Name	Initial Proposal		Proposed Change
		Mode	Clearance	Mode
1	3-Month Phone Call	CATI	1/19/2011	Plus In-Person/Web
2	9-Month Phone Call	CATI	1/19/2011	Plus In-Person/Web
3	18-Month Phone Call	CATI	4/13/2011	Plus In-Person/Web
4	24-Month Phone Call	CATI	4/13/2011	Plus In-Person/Web

1/CATI=Computer Assisted Telephone Interview.

B. Participant-Collect Environmental Sample Instructions
We ask that participant-collect environmental sample scripts and instructions be approved as part of the Phase 2 environmental sample collection mode experiment. As approved by OIRA on 4/13/2011, Phase 2 Study Centers will randomly assign environmental samples to be collected by participants or by interviewers, allowing for evaluation of the feasibility, acceptability, and cost of collection mode. At the time of OMB approval, only interviewer-collect scripts and instructions had been submitted for review. At this time, we ask that participant-collect scripts and instructions be approved. Text is consistent across interviewer-collect and participant-collect instruments. There is no anticipated increase in participant burden, as the burden estimate approved on 4/13/2011 reflects this activity.

Attachments (9): Proposed Phase 2 Participant Collect Environmental Sample
B.1 Environmental Tap Water Pharmaceutical (TWF) Participant Collect SAQ
B.2 Environmental Tap Water Pesticide (TWQ) Participant Collect SAQ
B.3 Environmental Vacuum Bag Dust (VBD) Participant Collect SAQ
B.4 Environmental Tap Water Pharmaceutical (TWF) Participant Collect Instructions
B.5 Environmental Tap Water Pesticide (TWQ) Participant Collect Instructions
B.6 Environmental Vacuum Bag Dust (VBD) Participant Collect Instructions
B.7 Environmental Tap Water Pharmaceutical (TWF) Sample Distribution Script
B.8 Environmental Tap Water Pesticide (TWQ) Sample Distribution Script
B.9 Environmental Vacuum Bag Dust (VBD) Sample Distribution Script

C. Formative Research Projects: LOI2-BIO-18; LOI2-PHYS-02; LOI2-PHYS-01, and LOI2-QUEX-14
The above-mentioned formative research projects 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 implementation across the NCS Vanguard Study.

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 (p.10, approved by OIRA on 4/13/2011) supports formative research efforts that involve recruiting either NCS Vanguard Study participants or their demographically-similar peers. Proposed incentives align with the OIRA-approved incentive structure for the Phase 2 Vanguard Study.

The purpose, mode(s) of data collection, rationale for inclusion, and total respondent burden hours in the NCS Vanguard Study for these formative research projects are summarized in Table 2 and described further below.

Table 2. Candidate Formative Research Projects for Non-Substantive Change to the NCS Vanguard Study (OMB Collection # 0925-0593, Expiration 7/31/2013)					
Project ID Number	Project Title	Purpose	Proposed Additional Information Collection	Rationale for Inclusion in Vanguard Study	Respondent Burden Hours
LOI2-BIO-18	Placenta Studies: Cell Collection, Banking, and Morphology Assessment	To evaluate the parameters that will yield useful and reproducible data from placenta and cord blood.	Cord blood and placental collection during birth visit.	The data collected will inform the processes for cord blood and placental collection and storage in the NCS Vanguard and Main Study.	154
LOI3-PHYS-02	Evaluation of Ulnar Length Measurement	To evaluate ulnar length as an anthropometric measure compared to body length/height and to identify the training and conditions under which these measures are most reliably taken.	Height, weight, ulna, arm span, tibia, and lower leg length of mothers, and their children at birth to age 5	The data collected will inform the process for collecting robust and reliable anthropometric measures in the NCS Vanguard and Main Study.	1,000
LOI3-PHYS-01	Lung Function Among Children 1-8 Years	To assess and compare tools for measuring pulmonary function in children and adults, including spirometry.	Raw, FeNO, and spirometry measurements for children aged 1-8 years and their mothers.	The data collected will inform pulmonary measurements in different age groups of children enrolled in the NCS Vanguard Study and Main Study.	450
LOI2-QUEX-14	Improving Dietary Assessment in Pregnant Women and Children	To systematically compare feasibility, acceptability and cost of the Automated Self-Administered 24-hour Recall (ASA24) method and the NCS Food Frequency Questionnaire (FFQ) method.	Automated Self-Administered 24-hour Recall (ASA24) and the NCS Food Frequency Questionnaire (FFQ)	The data collected will inform the most scientifically robust and efficient measure of diet for mothers and children for use in the NCS Vanguard and Main Study.	638

C.1. LOI2-BIO-18: Placenta Studies: Cell Collection, Banking, and Morphology Assessment

The NCS formative research project LOI2-BIO-18 will evaluate the parameters that will yield useful and reproducible data from placentas and cord blood being collected as part of the Vanguard Study. Of critical importance is to know how the quality of the collected placental tissue will affect recovery of stem cells from cord blood, placenta, and umbilical cord samples, RNA and DNA, assessment of placental morphology, and the detection of metals and other contaminants in these biospecimens.

There was considerable variation in the time that placentas were shipped from Initial Vanguard collection sites to the Placental Processing Site, ranging from 1-6 days. Additionally, there was variability in the ways in which the tissue is handled and processed at Initial Vanguard Center hospitals prior to shipment. Variability in processing has raised questions regarding how the different methods of specimen processing might affect the results of specimen analysis. This formative research study is important for establishing the gold standard as well as “minimal acceptable conditions” appropriate for

sample collection and preservation for future use of these tissue resources for stem cell banking, genetics, environmental analyses, and morphology/pathology.

For this project, Study Centers will pilot test the collection protocol by collecting 42 placentas, umbilical cord samples, and cord blood samples from mothers not geographically eligible for the NCS Vanguard Study. For the subsequent stage of this formative research study, Vanguard Centers will collect an additional 240 placentas, umbilical cord segments, and cord blood samples from NCS Vanguard Study participants. Following collection, samples will be shipped to a central processing site, where the samples will be examined for an assessment of morphology/pathology. For the morphology portion of the study, an additional 335 NCS placentas will be examined. The additional data collection described above represents a minimal amount of additional burden (617 respondents X 0.25 hours/respondent X 1 response(s) per respondent = 154 hours). An incentive of $25 will be offered to participants for joining this project; the amount is consistent with the OIRA-approved incentive structure for Phase 2 of the NCS Vanguard Study.

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 154 hours

Attachments (2): Proposed Instruments Supplemental to the Approved Vanguard Study Phase 2 Protocol
C.1.1 Exemplar Consent Form (for Non-NCS Vanguard Study Participants)
C. 1.2 Birth Visit Information Sheet (only for NCS Vanguard Study Participants joining LOI2-BIO-18)

C.2. LOI3-PHYS-02: Evaluation of Ulnar Length Measurement

Reliable field measurement of length and height of infants and young children is difficult to ascertain using standard methodology. The NCS formative research project LOI3-PHYS-02 will test the reliability of measuring ulnar length, arm span, and lower leg length as a means to calculate the length and height of infants and young children. Additionally, the study will map the correlation between ulnar length, arm span, and lower leg length in children to currently approved anthropometric measurements by age, sex, and race/ethnicity. Specifically, the project will determine if reproducibility and accuracy of limb measures is greater than infant length board measurements, and whether measurements taken using a segmometer are in agreement with other methods. The study will also evaluate the cost effectiveness and ease of lay training in segmometer use for these measurements.

For this project, Study Centers will recruit an approximate total of 1,500 infants and children up to age 5. Participants will include NCS Vanguard Study participants, and persons who are demographically similar to NCS Vanguard Study participants, but who are not geographically eligible for the Vanguard Study. Infant length board (or stadiometer), and segmental length measurements will be taken during the first visit. At a second visit, dual energy x-ray absorptiometry (DXA) will be used to verify accuracy of segmental measurements. This additional data collection represents a modest amount of burden (1,500 respondents X 0.33 hours/respondent X 2 response(s) per respondent = 1,000 hours), which could lead to improved reliability of anthropometric measurement in children. An incentive of $25 will be offered to participants for joining this project; the amount is consistent with the OMB approved incentive structure for Phase 2 of the NCS Vanguard Study.

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 1,000 hours

Attachments (5): Proposed Instruments Supplemental to the Approved Vanguard Study Phase 2 Protocol

C.2.1 Exemplar Flier (for Non-NCS Vanguard Study Participants)
C.2.2 Exemplar Consent Form (for Non-NCS Vanguard Study Participants)
C.2.3 Exemplar Demographic s (for Non-NCS Vanguard Study Participants)
C.2.4 Exemplar Measurement Form
C.2.5 Visit Information Sheet (for NCS Vanguard Study Participants)

C.3. LOI3-PHYS-01: Tools for Screening Pulmonary Function in Children Ages 1-8 Years
The NCS formative research project LOI3-PHYS-01 will assess the feasibility, acceptability, and cost of tools to measure pulmonary function in children 1-8 years of age. The study will measure lung function in toddlers and pre-school children by measuring spirometry, airway resistance (Raw), and exhaled nitric oxide (FeNO) using technologies that are accurate and easy to perform. Additionally, the study will assess the reproducibility of utilizing these measurements between multiple sites. The study will also evaluate the correlation between Raw, FeNO, and spirometry measurements in children.

Since Raw and FeNO do not require patient cooperation outside of measuring normal breathing rates, these measurements can be performed on toddlers and preschool children. These tests can also be performed across age groups, including older children and adolescents. However, the relationship between measurements of resistance and flows has not been well-established. Taking simultaneous measurements of Raw and FeNO, and subsequent spirometry measurements will allow an assessment of whether Raw and FeNO can be performed accurately in children younger than previously studied, whether the measurements are correlated with each other, and whether they have predictive value for lung function later in childhood and in adolescence.

A total of 450 mothers and their children aged 1-8 years will be recruited into this formative research study. Both NCS Vanguard Study participants as well as persons who are demographically similar to NCS Vanguard Study participants, but who are not geographically eligible to participate for the Vanguard Study, will be invited to participate in this project. At the initial visit, an eligibility screener will be administered. Then, after consent, the child's parent will answer a demographic, general health, and respiratory questionnaire. Airway resistance, exhaled nitric oxide, and a conventional spirometry tests will be administered. (Spirometry will only be measured in children older than 4 years of age.) Approximately one week after the first visit, a health screener will be administered and the respiratory tests will be repeated. At a third visit, approximately three weeks after the second visit, the health screener and the respiration tests will be repeated, and an exit survey to gauge participant burden will be administered. This additional data collection represents a modest amount of burden (450 respondents X 0.33 hour/respondent X 3 response(s) per respondent = 450 hours). An incentive of $25 will be offered to participants for joining this project; the amount is consistent with the OMB approved incentive structure for Phase 2 of the NCS Vanguard Study.

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 450 hours

<u>Attachments (8): Proposed Instruments Supplemental to the Approved Vanguard Study Phase 2 Protocol</u>
C.3.1 Flyer (for Non-NCS Vanguard Study Participants)
C.3.2 Exemplar Screening Form
C.3.3 Exemplar Consent Form (for Non-NCS Vanguard Study Participants)
C.3.3 Exemplar Contact Information Sheet (for Non-NCS Vanguard Study Participants)
C.3.4 Visit Information Sheet (for NCS Vanguard Study Participants)
C.3.6 Exemplar Demographic and Health Questionnaire

C.3.7 Exemplar Visit Screener
C.3.8 Exemplar Exit Survey

C.4. LOI2-QUEX-14: Improving Dietary Assessment in Pregnant Women and Children
The NCS formative research project LOI2-QUEX-14 will systematically compare feasibility, acceptability, and cost of the Automated Self-Administered 24-hour Recall (ASA24) method and the NCS Food Frequency Questionnaire (FFQ) method to inform the NCS Vanguard Study and the NCS Main Study design. Additionally, scientific robustness of proposed measures by acculturation status will be evaluated.

Utilization of the Web-based ASA24 tool may reduce participant burden and improve accuracy in participant response compared to the paper-based NCS FFQ. Additionally, if ASA24 can be keyed by the respondent rather than a data collector (for example, upon receipt of a mail-in reminder), the web-based ASA24 would be a more cost efficient method than the mail-in NCS FFQ. Suitability of both measures by acculturation status will inform measurement of key outcomes for the NCS.

The ASA24 is a standardized measure developed by the National Cancer Institute and is available at http://riskfactor.cancer.gov/tools/instruments/asa24/ for use without copyright fees; the NCS FFQ was approved for use in the NCS Initial Vanguard Study on 9/22/08. Upon enrollment into the project (Contact 1), participants will be trained on how to complete the ASA24, food record diaries, FFQ, and the acceptability questionnaire. Participants will be asked to complete the acculturation questionnaire. At Contact 2, participants will be asked to complete an ASA24, a food record, and an acceptability questionnaire. At Contact 3 (one month from Contact 2), participants will be asked to complete an ASA24 and a food record. At Contact 4, (one month from Contact 3), participants will be asked to complete an ASA24, a food record, the NCS FFQ, and a second acceptability questionnaire. At Contact 5 (immediately after Contact 4), participants will return their hard copy questionnaires and food records. Accuracy of the ASA24 and the NCS FFQ will be compared with food records. Burden will be evaluated by acceptability questionnaires and time to complete each measure. Acculturation status will be compared to measure responses. This additional data collection represents a modest amount of burden (150 respondents X average 0.85 hours/respondent X 5 response(s) per respondent = 638 hours). Incentive amounts are $25 per visit for each of the first 4 contacts; a $50 incentive is proposed for the 5th contact, estimated at about 80 minutes. This incentive schedule is consistent with the Phase 2 Vanguard Protocol.

IRB Approval for participating Study Centers: Yes
Total Requested Participant Burden: 638 hours

<u>Attachments (10): Proposed Instruments Supplementing the Approved Vanguard Study Phase 2 Protocol</u>
C.4.1 Informed Consent Exemplar
C.4.2 ASA24 protocol
C.4.3 ASA24 Instructions
C.4.4 Food Record
C.4.5 Food Portion Guide
C.4.6 Food Diary Instructions
C.4.7 NCS FFQ
C.4.8 Acculturation Questionnaire
C.4.9 Initial Acceptability Questionnaire
C.4.10 Second Acceptability Questionnaire

Table 3. Respondent Burden Table for Candidate Projects (OMB Collection # 0925-0593, Expiration Date 7/31/2013)						
Formative Research Project Number	**Project Title (Abbreviated)**	**Type of Respondent**	**Number of Respondents**	**Responses per Respondent**	**Hours per Response**	**Total Hour Burden**
LOI2-BIO-18	"Placentas"	Mother (Child)	617	1	0.25	154
LOI3-PHYS-02	"Ulnar Length"	Mother/Infant/Child	1,500	2	0.33	1,000
LOI3-PHYS-01	"Pulmonary Measurement"	Mother/Child	450	3	1.0	450
LOI2-QUEX-14	"Dietary Assessment"	Mother/Child	150	5	0.85	638