

NCS Formative Research Template for OIRA Clearance**TO BE COMPLETED BY STUDY CENTER:**

LOI #: LOI - - - -

Title of Formative Research: Collection of Circulating Fetal DNA from Maternal Blood and from Cervical Fluid

Participating Institutions: **University of Wisconsin, University of California—Irvine, Yale**

SME:

COTR: **Various**

Purpose of the Study: To develop robust methods for the detection, evaluation, and storage of fetal DNA in maternal blood and cervical fluid. This study will optimize fetal DNA yields from maternal circulation and from cervical fluid, provide measurements of fetal DNA collection, and assess the use of these samples for sequencing and other analyses within the NCS.

Benefit to NCS Vanguard or Main Study: This substudy will demonstrate the feasibility, acceptability, and cost associated with the storage and analysis of samples collected in the course of potential expanded NCS protocols which would enable large-scale sequencing of the human microbiome. Though it is not likely that microbiome research would be incorporated into the entire NCS cohort, a population-representative subset of several thousand participants at specific participating Study Center sites may eventually be included in microbiome research associated with the NCS.

Study Design: Study Centers will collect blood samples at up to four time points: pre-pregnancy, first trimester, third trimester, and post-delivery. At these time points, Study Centers will conduct only one blood collection, ensuring that enough blood is collected to fulfill the needs of both the Vanguard Study and this substudy. The approved NCS Vanguard Study (OMB #0925-0593; Expiration Date: 7/31/2013) protocol allows for blood sample collections at up to 2 prenatal study visits (pre-pregnancy, first trimester, and third trimester); therefore, additional burden will not be requested for blood sample collection for two of the four time points. Cervical fluid will be collected during the first or third trimester. In accordance with the Vanguard Study Phase 2 protocol, cord blood will be collected at birth; in approximately 30% of the sample, infant saliva will be collected in lieu of cord blood. Infant saliva will be collected by Study Center staff at the participant's regularly-scheduled postnatal follow-up exam. Following collection, samples will be shipped to Wisconsin, Pittsburgh, and/or Yale Universities for storage and analyses. Since the goal of this substudy is to establish the best methodologies for detecting, evaluating, and storing fetal DNA in maternal blood and maternal cervical fluid, it is not necessary that all participants contribute a complete set of samples. Participants will be invited to contribute the samples that they are willing and able to, with the goal of collecting a total of 200 of each type of sample. The attached consent will be customized for each participating Study Center, as appropriate. For IRB review purposes, the University of Wisconsin chose to combine the consent form for this substudy with the consent form for LOI2-BIO-20. This was done to minimize participant burden during the consent process since the vaginal samples for each substudy may be collected simultaneously. As applicable following consent, participants will be reminded of the samples that will be collected for this substudy, in addition to any Vanguard Study Phase 2 samples, at each visit.

Sample Size Calculation: We anticipate that we will be able to recruit enough participants for a total of 100 sets of samples across the two study locations for this methodological substudy. Based on prior experience with similar methodological studies, there will be statistical validity in assessing the feasibility of collecting these samples, and enough specimens to address the validity of the methodology. Additionally, a sample size of 100 participants will not overly burden the NCS Vanguard Study participants who are enrolled at the study locations that are participating in this formative study.

Target Respondents: This project will recruit NCS Vanguard Study participants (200 mothers and their infants) from Study Centers that are authorized to collect biospecimens either under the Original Vanguard protocol or the Expanded Phase 2 Vanguard Study protocol.

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Method of Recruiting: Study Center staff at Wisconsin and Irvine will invite NCS Vanguard Study participants to join this substudy during NCS Vanguard Study visits. There are no additional materials that will be used to aid recruitment into this substudy. Enrollment will continue until project-specific recruitment targets have been reached.

***Confidentiality:** Study Centers must abide by the terms of their Data Use Agreement, which should reference all formative research efforts involving the collection or management of NCS restricted-use data. All participating Study Centers will have approved Data Use Agreements and Security Plans prior to launch.

***IRB Approval:** Local IRB clearance for this activity has been obtained by all participating Study Centers. Please see attached IRB approval letters.

Incentives: Click here to enter text. We propose to offer participants a \$25 monetary incentive for each biospecimen collection visit that is not occurring as part of the NCS Vanguard Study Phase 2. If multiple biospecimens are being collected during a visit, participants will receive only one \$25 incentive for all biospecimens collected at that time. In the event that participants have provided a biospecimen (e.g., blood sample) for the Vanguard Study and must return to provide an additional amount for this substudy, we propose to offer a \$25 monetary incentive for the second visit, in addition to other monetary incentives approved for participants in the NCS Vanguard Phase 2. Additionally, we may choose to offer participants small, non-monetary NCS logo gifts following sample collection visits.

Sensitive Questions: We will not ask sensitive questions as a component of this study.

Proposed Project Schedule: We will begin this project upon receipt of all regulatory approvals.

Data Collection Burden:

Estimates of Annual Hour Burden -- Generic Substudy: LOI2-BIO-24, "Collection of Circulating Fetal DNA from Cervical Fluid"

Data Collection Activity	Type of Respondent	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Hours Per Response	Estimated Total Annual Burden Hours
Consent	Pregnant Women	200	1	0.08	16
Blood Sample Collection	Pregnant Women / Mothers	200	2*	0.17	68
Cervical Fluid Collection	Pregnant Women	200	1	0.17	34
Cord Blood Collection	Infant	140	0**	0.00**	0
Saliva Collection	Infant	60	1	0.17	10
TOTAL		400			128

* To be completed before project proposal is submitted for OIRA clearance.

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Annualized Cost to Respondents -- Generic Substudy: LOI2-BIO-24, "Collection of Circulating Fetal DNA from Cervical Fluid"

Data Collection Activity	Type of Respondent	Estimated Number of Respondents	Estimated Number of Responses per Respondent	Hourly Wage Rate	Respondent Cost
Consent	Pregnant Women	200	1	\$10.00	\$160.00
Blood Sample Collection	Pregnant Women / Mothers	200	2*	\$10.00	\$680.00
Cervical Fluid Collection	Pregnant Women	200	1	\$10.00	\$340.00
Cord Blood Collection	Infant	140	0**	\$10.00***	\$0.00
Saliva Collection	Infant	60	1	\$10.00***	\$100.00
TOTAL		400			\$1280.00

*The NCS Vanguard Study protocol already includes pre-pregnancy, first trimester, and third trimester blood collections. At these time points, Study Centers will conduct only one blood collection, ensuring that enough samples are collected to fulfill the needs of both the Vanguard Study and this substudy; therefore, additional burden hours will not be requested for blood sample collection for two of the four time points when blood is collected.

**The NCS Vanguard Study protocol already includes cord blood collection. Therefore, additional burden hours will not be requested for cord blood sample collection for 140 of the 200 respondents.

*** The allotted hourly wage rate accounts for the mother's time associated with the data collection activity.

Please check here after ensuring that all calculations have been verified

Estimated Costs: Staff Hours: 256 hours.
Supervisor Hours: 64 hours.

Attachments: Exemplar consent form, Exemplar IRB protocol, IRB approval letter. Note: The consent will be customized for each participating study center and target population, as appropriate, and approved by the local IRB prior to use.

Please check here after ensuring that the OMB #: 0925-0647 and Expiration Date: 01/31/2015 date have been inserted as first-page headers on each proposed instrument.

Please check here after ensuring that the following OMB burden statement has been inserted as a first-page footer on each proposed instrument.

Public reporting burden for this collection of information is estimated to average [SC insert estimated response time] minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments

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regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-0647*). Do not return the completed form to this address.

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Appendix 1. Maximum NCS Incentives, by Study Activity and Impact on Participants (Approved by OMB 1/5/12)

Data Collection Activity Characteristics	Initial NCS Vanguard Study	NCS Recruitment Substudy and Formative Research		
		Phase 1	Phase 2	Formative Research
Time for encounter	3 hours	0.5 to 1 hour	0.5 to 1 hour	0.5 to 1 hour
Sensitivity of questions	Sensitive, including sexual activity	Few sensitive questions	Few sensitive questions	Few sensitive questions
Physical measures	Yes	No	No	Yes*
Environmental specimens	Yes	No	Yes	Yes*
Biospecimens	Yes	No	Yes	Yes*
Participant observation	Yes	No	No	No
Monetary incentive, per visit	\$100	\$25	\$25 for the group of study questionnaires, plus \$25, in total, for any bio-specimens collected during a contact and, where appropriate for environmental specimens	\$25, in total, for any bio-specimens collected during a contact. For questionnaires, or any environmental specimens - up to \$25 when deemed necessary
Non-monetary incentives (tote bags, post its, key chains, etc.)	<u>In addition to the monetary incentive</u> , non-monetary incentives valued at \$25 or less may be offered to participants	<u>As an alternative to the monetary incentive</u> , NCS logo gifts valued at \$25 or less may be offered to the participants in lieu of cash or local incentives not exceeding \$25 in value and deemed non-coercive by local IRBs	<u>In addition to the monetary incentive</u> , NCS logo gifts valued at \$25 or less may be offered to the participants if these are deemed acceptable by local IRBs	<u>Instead of monetary incentives</u> , NCS logo gifts valued at \$25 or less may be offered to the participants if these are deemed acceptable by local IRBs