

**National Children's Study  
Federal Advisory Committee 27th Meeting  
January 26, 2011  
Natcher Conference Center, National Institutes of Health  
Bethesda, MD**

The National Children's Study (the Study) is led by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development of the National Institutes of Health (NIH) in collaboration with a consortium of federal government partners. Study partners include the National Institute of Environmental Health Sciences (NIEHS) of the NIH, the Centers for Disease Control and Prevention (CDC), and the Environmental Protection Agency (EPA).

**Welcome and Introductions**

*Carol Henry, Ph.D., Chair, National Children's Study Federal Advisory Committee (NCSAC),  
School of Public Health and Health Services, George Washington University*

Dr. Henry reviewed the highlights of the October 14, 2010, NCSAC meeting, which included the following:

- Summary of meeting and presentations posted to Study Web site
- Vanguard Study recruitment update
- Update on the Study
- Comments from the Director's Office, NICHD
- Comments from the Director's Office, NIEHS
- Qualification and validation of environmental assessments: considerations for analyte selection
- Developing the Third Edition of the American Academy of Pediatrics' *Pediatric Environmental Health* (Green Book)
- Overview of proposed NIEHS Gulf Long-term Follow-up Study: long-term follow-up of oil spill clean-up workers and volunteers
- Study informatics
- Tools and solutions for data capture
  - Pacific Northwest Center for the National Children's Study: informatics
  - NCS-Arkansas: open-source informatics solution
  - OpenClinica: an alternative for the Study
  - Research Electronic Data Capture (REDCap)
- Rapporteur's summary.

**National Children's Study Update**

*Steven Hirschfeld, M.D., Ph.D., Acting Director, National Children's Study, NICHD, NIH,  
Department of Health and Human Services (HHS)*

- **Overview.** The Study will examine the effects of the environment, as broadly defined to include factors such as air, water, diet, sound, family dynamics, community and cultural influences, and genetics on the growth, development, and health of children across the United States, following them from before birth until age 21 years. The goal of the Study is to improve the health and well-being of children and contribute to understanding the role

various factors have on health and disease. Findings from the Study will be made available as the research progresses, making potential benefits known to the public as soon as possible.

- **Leadership.** The Study leadership includes the NIH (NIH Office of the Director [oversight and scientific direction], the NICHD [lead operational agency], and the NIEHS), the CDC, and EPA.
- **Structure.** The Study is being implemented in several phases. All components and phases together form the Study. Current major components are the Vanguard Study, Main Study, and substudies.
- **Vanguard Study goals.** The Vanguard Study is designed to evaluate feasibility (technical performance), acceptability (impact on participants, Study personnel, and infrastructure), and cost (personnel, time, effort, and money) of Study recruitment, logistics and operations, and Study visits and Study visit assessments.
- **Projected timeline.** Data collection of the pilot/feasibility study (the seven initial Vanguard Centers) began in early 2009. The 30 Vanguard Centers implementing the alternate recruitment substudies began operations in October 2010. After analysis of the pilot data and plan and external scientific review, the Main Study is expected to begin operations in early 2011. There will be quarterly Congressional and scientific updates.
- **Alternate recruitment substudies status.** There are three alternate recruitment substudies: provider-based, two-tier high-intensity/low-intensity (Hi/Lo), and enhanced household. Infrastructure and communications and outreach are being developed. Initial data collection efforts will focus on questionnaires. Specimen and sample collection will be phased in over the coming months. The alternate recruitment study will provide an opportunity for cooperative learning and process improvement.
- **Informatics development and data standards.** Data field definitions, structure, relationships, and data tables are being developed centrally to address specific operational questions. The focus is on operational data elements to study feasibility, acceptability, and cost for the Vanguard Study. Data collection and transmission standards are conveyed to the Study Centers (primary contractors). The Study Centers are responsible for identifying, developing, or adapting if necessary, and deploying case management and data acquisition systems. All required data are transmitted per specifications to a central database at the NICHD. Study operational data elements (the concepts and data fields that describe Study operations) may serve as models for potential general data standards for operational data elements. Study architecture and standards align with the Data Document Initiative and the Clinical Data Interchange Standards Consortium. The Study will develop standardized informatics and data terminology.
- **Communications and outreach.** Communications and outreach activities will follow a decentralized model with Study locations initiating activities guided by general Study policies and messages. Each active Study location has a Web site linked to the Study public Web site. There will be targeted outreach to various populations. Additional community representatives will be incorporated into the Steering Committee.
- **Formative research.** Formative research is an essential component of the data-driven, evidence-based strategy for the Vanguard Study. Formative research projects are focused, time-limited activities for Study contractors to address specific technical or methodological questions. Two rounds of formative research requests in 2010 were initiated based on a gap analysis. Additional formative research opportunities are planned for the coming year. The Study has initiated several formative research projects that are limited in scope and duration

and are intended to augment the Vanguard Study to address specific technical questions and provide information on the acceptability, feasibility, and cost of the research. These formative research projects will provide data to explore new and potentially cost-effective approaches in many areas—including genetic, cognitive, and environmental assessments—that have not been previously evaluated from an operational perspective. Based on the results of these formative research projects, the Study can evaluate the types of research questions that would be feasible for the Main Study. Formative research topic areas funded in 2010 include:

- Real-time analysis of Study samples, specimens, and measurements
  - Study logistical analyses and improvements
  - Biospecimen collection and processing
  - Environmental sample collection and processing
  - Physical measures
  - Questionnaire development and validation
  - Study infrastructure development.
- **Compliance with the Federal Information Security Management Act of 2002 (FISMA).** FISMA requires a secure informatics environment for federal projects and activities. Because Study contractors are collecting data on behalf of the federal government, they must be FISMA compliant. The Study has implemented a program to achieve FISMA compliance at all Study locations. FISMA compliance has been challenging but achievable.
  - **Federated institutional review board (IRB) launch.** The federated IRB model was approved for implementation in July 2010. Three documents have been developed for the federated IRB: a compact outlining principles, processes, and performance goals; a memorandum of understanding; and a list of questions and responses. Other NIH programs and studies have expressed interest in adapting the federated IRB model. A presentation to the Secretary’s Advisory Committee for Human Research Protections was given on October 19, 2010.
  - **Federated IRB participation in the Study.** Of the 36 Study Centers, 17 have reliance on lead IRB (the NICHD Intramural IRB), 6 share responsibility with the lead IRB, and 13 have independent reviews with information sharing. The federated IRB implementation process in the Study and in other contexts is being systematically studied for process improvement. Additional membership from Study location hospitals, birth centers, and contract research organizations is expected.
  - **Office of Management and Budget (OMB) interactions.** Successful and collegial discussions have been under way with the OMB and its Office of Information and Regulatory Affairs regarding the Vanguard Study protocol and the alternate recruitment substudies. The OMB has provided multiple helpful suggestions and is motivated and supportive of the Study. Clearance for the alternate recruitment substudies was received in summer 2010. Clearance for formative research is pending new or additional formative research for 2011. See above where formative research projects are listed.
  - **A learning community.** The concurrent deployment of three different recruitment strategies plus a formative research program provides an exceptional opportunity for launching a learning community with structured and systematic training, feedback, process maps, process improvement, modeling, and simulations. The Study has adapted these approaches both

centrally and in the field, particularly in the Hi/Lo recruitment substudy, to build an effective learning community.

- **Next steps.** The next steps are as follows:
  - Alternate recruitment substudies enrollment and data analysis
  - Continued analysis of data from initial seven Vanguard Study locations, including biospecimens and environmental samples
  - Gap analysis for formative research opportunities
  - New models for visit schedule
  - New models for visit assessments
  - Introduction of specimen and sample collection across all the Vanguard Study locations
  - Begin construction of framework and architecture for Main Study protocol and infrastructure.

## **NCSAC Discussion and Recommendations**

The group discussed the following topics and issues about the Study update:

- Patricia O’Campo, Ph.D., asked whether the Study will look at disparity issues; if so, which disparities, and how the disparities are defined. Dr. Hirschfeld said that disparities are a major focus of the Study. Disparities are definable (for example, economic, socioeconomic, access to health care, and educational opportunities). The Study will systematically examine as many dimensions of disparities as is feasible. The current emphasis of this examination is on pregnant women enrolling the Study, including maternal health care, and circumstances around birth. The Study will “front load” data collection from pregnant women and children because early events may be the most informative and have the largest gaps in knowledge.
- Jeffrey Krischer, Ph.D., asked for clarification on the Study’s geographically based sampling approach for a defined population, the sampling frames of the alternative recruitment substudies, and the definition of Study outcomes (that is, is health measured as the absence of illness?). Dr. Hirschfeld explained that the Study is adhering to a geographically based approach. The provider-based approach will screen and refer women, but only those women who live in the defined geographic areas are eligible. Dr. Hirschfeld further explained that health will not be defined simply as the absence of disease. The Study will address a number of health measures (for example, access to health care) in order to provide some objectivity to Study health outcomes.
- Jennifer Culhane, Ph.D., M.P.H., briefly described the provider-based recruitment approaches being studied in Montgomery and Schuylkill counties, Pennsylvania. She also defined a “segment eligible woman” and further elaborated on the geographically based sampling framework.
- Benjamin S. Wilfond, M.D., asked whether the issue of Study participants moving was considered when evaluating the priority of the sample frame. Dr. Hirschfeld noted that the Study’s sampling approach has been discussed for about 8 years, and there has been no consensus on the best approach. The Study is using a data-driven approach because past

performance cannot be used to predict future results. At this time, there are no plans to change the Study's geographically based sampling approach. However, depending on the data, adjustments may have to be considered at some time.

- Jonas Ellenberg, Ph.D., commented that many Study participants may move locally (that is, out of Study segments) and still be involved with their original Study Center. Participants who move a long distance may be in the geographic area of another Study Center.
- Ellen Silbergeld, Ph.D., asked whether the Study is on the right course in acquiring interpretable data and whether anything has been learned that may possibly change the Study's course or overall strategy. Dr. Silbergeld said she was concerned about the Study's ability to interpret in a meaningful way the data that are currently being collected in order to develop a feasible overall strategy.

### **Compensating Providers for Facilitating Recruitment Efforts**

*Julia Slutsman, Ph.D., Bioethicist, National Children's Study, NICHD, NIH, HHS*

Provider-based recruitment of participants is being used in the Vanguard Study as one of three key recruitment strategies in the alternate recruitment substudies and, to a more limited extent, in other recruitment approaches. The range of providers' roles in Study recruitment includes allowing Study Center field staff to have a presence in providers' offices, allowing Study Center staff to access medical records, informing patients of potential eligibility for Study participation, and facilitating an initial contact with a Study Center to begin the screening process. Providers will not administer informed consent, conduct screening, or conduct research activities.

There are three potential approaches to compensating providers:

- **Capitated monetary payments.** Capitated payment or "finder's fees" can be based on number of eligible participants referred or number of participants enrolled.
  - There is a potential for conflict of interest as providers' own financial interests can be pitted against their moral obligations to patients.
  - Although capitated payments are a controversial practice, they are not illegal. They are considered "unethical" by the American Medical Association (AMA) Council on Ethical and Judicial Affairs. If capitated payments are used in the Study, this practice should be disclosed to participants.
- **Monetary payments.** Monetary payments can be based on level of resources and effort expended and/or the volume of patients who live in Study segments.
  - It would be necessary to identify what is an appropriate index for payment amounts.
- **Nonmonetary incentives.** Nonmonetary incentives can take multiple forms, including provisions of content for Continuing Medical Education (CME) credits, stipends for travel to professional meetings or CME training, food, purchase of supplies, and branded giveaway items.

## **Prenatal Care Provider Recruitment in Montgomery and Schuylkill Counties, Pennsylvania**

*Jennifer Culhane, Ph.D., M.P.H., Principal Investigator, Children's Hospital of Philadelphia (CHOP) Study Center; Associate Professor of Pediatrics, University of Pennsylvania School of Medicine*

Dr. Culhane described the CHOP Study Center's experience of the prenatal care provider recruitment in two Study locations: Montgomery and Schuylkill counties, Pennsylvania. Montgomery County is one of the original Vanguard locations. The provider-based approach was developed as part of the original recruitment plan to supplement door-to-door enumeration.

Montgomery County has 390 annual segment births (out of about 10,000 annual births in the county), representing about 13,000 households. The county has 77 prenatal care provider practices, 230 individual practitioners, and 61 practice managers. The Study's goals for providers are to help publicize the Study, understand the importance of Study, facilitate participant recruitment, and support decision of patients' participation.

Preparation for prenatal care provider recruitment included updating a database of all providers, updating a database of all practice managers, mailing letters of support from the director of the Montgomery County Health Department to all individual practitioners in 2009, and hiring a dedicated staff-physician liaison. Implementation included:

- Identifying multi-practice organizations and individual practices
- Having one-on-one meetings with practice managers (that is, the "gatekeepers")
- Individualizing procedures for multi-practice organizations and individual practices
- Hosting multiple "educational dinners" for practice managers.

A single model was developed for corporate practices. The steps for the model included:

- Monthly data acquisition by the practice
- Identification of segment-eligible new patients by ZIP Code
- Transmittal of address list to the Study Center
- Address geocoding by the Study Center, tagging eligible records, and sending list back to the practice
- Practice call to eligible participants to get phone consent for Study contact
- Study staff follow-up with eligible participants who agree to Study contact.

Three models were developed for individual practices in Montgomery County:

- **Model I.** Potential participants are identified by ZIP Code. Once identified, the practice discusses the Study with potential participants. Potential participants are responsible for contacting the Study Center, or the potential participant signs a consent form to allow researchers to approach for research. The potential participant's contact information is sent to the physician liaison by phone or e-mail.
- **Model II.** The practice identifies potential segment-eligible participant by ZIP Code. The Study Center confirms eligibility through the Study management system. The practice allows Study Center staff to approach eligible participants on site at next their scheduled visit.
- **Model III.** The practice displays or dispenses literature only.

Model I (submit contact information) is being used in 35 individual practices, model II (onsite Study Center staff) is being used in 5 practices, and model III (literature only) is being used in 37 practices.

The 9-month data for potential eligible participants identified through prenatal care providers are as follows.

- Addresses submitted 3,633
  - Not eligible 3,456
  - Eligible 177
    - Already participating 29
    - Already refused 9
- Eligible for consent 123
  - Refused 16
  - Pending 70
  - Moved or delivered 6
- Phone consent to approach 47
  - Pending 10
  - Moved 1
  - Pregnancy loss 3
  - Refused 17
  - Consented 16

Lessons learned from prenatal care provider recruitment in Montgomery County are as follows:

- Preparation for prenatal care provider collaboration takes at least 6–8 months.
- Model II was the most successful model.
- Model III was the least successful model. The Study Center continues to encourage Model III practices to transition to submission of addresses and onsite consents.
- Dinner meetings with practice administrators were very helpful in gaining cooperation.
- No practice has been paid for participation because no practice has accepted the offer of payment.
- Flexibility in approach is essential—each practice is unique.
- A Health Insurance Portability and Accountability Act (HIPAA) waiver to approach preparatory to research would help tremendously.

Schuylkill County has 384 annual segment births. The county has 3 prenatal care provider practices, 12 individual practitioners at 5 locations, and 3 practice managers. Of the 3 practices, practice 1 sees 70 percent of all pregnancies, practice 2 sees 30 percent, and practice 3 sees 1 per month. Unlike in Montgomery County, the Study Center plans on reimbursing for practice staff effort to determine eligibility and acquire HIPAA waivers: \$20,000 per year for HIPAA waivers and \$60,000 per year for physician consent.

### **Explanation of HIPAA Waivers**

In a brief discussion after Dr. Culhane's presentation, Dr. Slutsman explained that under HIPAA, in the context of research, there are two mechanisms for physicians/practices to transfer

identifiable patient information to entities that are not part of the same covered entity under HIPAA (for example, from a prenatal care practice to the CHOP Study Center). (1) A patient may sign a consent authorizing the physician/practice to send identifiable information to another entity such as the CHOP Study Center. (2) A privacy board or IRB at a covered entity makes a determination and gives permission to waive the HIPAA requirement for the authorization.

### **Compensating Providers in Wayne County, Michigan**

*Nigel Paneth, M.D., M.P.H., Principal Investigator, Michigan Alliance for the National Children's Study (MANCS) Study Center, University Distinguished Professor, Departments of Epidemiology and Pediatrics and Human Development, Michigan State University*

Dr. Paneth explained that the MANCS Study Center is on the brink of implementing provider-based recruitment in Wayne County. Data have not yet been collected. Recruitment begins the week of February 1.

The Study cannot conduct research without extensive collaboration and cooperation with providers in the communities in which the Study operates. Although this collaboration and cooperation is important for the entire Study, it is particularly important for provider-based recruitment. Due to its geographically based sampling approach, the Study cannot choose which clinicians to work with. Study Centers must follow participants to any clinic in which they get prenatal care and to any hospital in which they deliver. Therefore, the Study Centers have no leverage over the practitioners to help the Study. Practitioners' primary concern is that the Study not interfere with the established routines to practice medicine. Study Centers must work out what will motivate practitioners to work with the Study.

Wayne County had 344 segment births in 2010. These births were delivered by more than 250 providers in 150 clinic settings. The births can be delivered in any of 26 hospitals, several of which are not in Wayne County. In preparation for recruitment, the Study Center has contacted more than 100 provider clinics and about 20 hospitals. Provisions arrangements have been made with about 60 clinics and with 16 hospitals, accounting for 70–80 percent of segment births. There is diversity among the clinics with regard to location (for example, inner city and suburban) and race, ethnicity, language, and socioeconomic status of patients. The clinics vary in the daily volume of patients; the number of segment women they serve; the amount of space available to accommodate research staff; access to the Internet; level of training of staff; dependence on nurses, physicians, and other health care providers; experience with clinical research; and willingness to participate in the Study. Although generally interested and cooperative, the clinics remind the Study Center that medical care comes first, they will have to make some sacrifices in time and risk of loss of income by participating. Only one clinic and one hospital have refused to participate. One clinic has not returned phone calls, and one hospital insists that its IRB review the Study's protocols. Due to a lack of quorum at its last quarterly meeting, the hospital IRB has not reviewed the protocol.

The Study's Independent Study Monitoring and Oversight Committee (iSMOC) recommended that provider incentives not include capitation-based monetary incentives but should include a uniform menu of incentive options across all locations. Dr. Paneth said the term "incentive" is a misnomer. Practitioners in Wayne County are not seeking an incentive; they are seeking to be

reimbursed fairly and equitably for the time, effort, and inconvenience of accommodating the Study's research. The term "uniform menu" may not fully recognize the diversity of locations in which participants must be recruited. The Study must come up with some sort of reimbursement policy for all kinds of practitioners. The policy should be tailored to each different and location-specific barrier.

In the near term, the MANCS Study Center is asking practitioners to (1) review the addresses of women in prenatal care to determine eligibility; (2) according to HIPAA rules, ask the provider or staff member to communicate with the patient to permit the Study Center to contact the patient directly; and (3) talk to eligible patients about the Study, provide information, and contact potential participants in the practice. Each of these activities takes time away from providing medical care to patients.

The MANCS Study Center has not finalized any overall reimbursement strategy. For larger clinics or clinic systems, the Study Center is considering paying a negotiated percent effort of a clinic staff member to coordinate recruitment activities. Clinics may be reimbursed separately for each activity. For some clinics, a reasonable solution might be a single capitation-based fee to fairly, equitably, and honestly cover the time and work for each potential participant. This approach has not been proposed in any Wayne County setting. The opposition to capitation-based monetary incentives stems from the possibility of harm to research participants should they be steered by clinicians receiving such payments into clinical trials of potentially toxic drugs. Such harm is inconceivable in the purely observational Study. The concerns about capitation should be viewed in terms of the potential harm it might do. However, capitation is being used in many other NIH initiatives such as the Community Clinical Oncology Program.

Dr. Paneth recommended the following:

- Begin all interactions with practitioners by telling them that the Study Center's goal is not to impose a specific solution, but to work with them to develop a way of doing research without interfering with their practice routines.
- Assure providers that the Study Center is committed to not having the practice lose money or lose patients because of Study research activities.
- Enumerate and quantify each and every task by each and every member of the staff that is required to accommodate the research needs of the Study.
- Work out a way of equitably reimbursing the practices for their time, by using the going hourly rate for comparable services in clinical work.
- Feel free to use appeals to generosity of community spirit and commitment to scientific discovery to motivate practitioners, but do not make the mistake of relying on them or thinking they are sufficient to sustain work that will take place over several years.

## **NCSAC Discussion and Recommendations**

José F. Cordero, M.D., M.P.H., served as "champion" for this discussion. The group discussed the following topics and issues about compensating providers:

- Bruce D. Gelb, M.D., asked about the differences in success of consent between provider-based recruitment (about 50 percent) and door-to door screening (about 70 percent) in

Montgomery County. Dr. Culhane explained that 177 pregnant eligible women were identified through prenatal care providers; 123 of the 177 were not previously known to the CHOP Study Center. Many of these women may have refused participation during door-to-door screening and simply did not get into the phone system. Women identified through prenatal care providers are probably not more likely to refuse than women identified through door-to-door screening. Most likely, they have already refused once (that is, they were part of the 10 percent that would not participate in the very beginning).

- Dr. Ellenberg asked whether the Study Center understood why the 123 women were not previously known. Dr. Culhane said some of the 123 women could have moved into Study segments after the door-to-door screening (for example, a turnover of residence or a daughter moving home) or the household refused enumeration or refused pregnancy screening. Dr. Paneth noted that it is challenging to ascertain something that is so delimited in time such as pregnancy just by making one household visit. Recruiting at prenatal care providers is a better overall strategy because there is better provider buy-in. Other studies have shown that this strategy yields about 60–70 percent agreement to participate.
- Jessica Graber, Ph.D., commented that, given the response rate from household screening, it may be unlikely that such a large proportion of the women identified as eligible for consent were refusers at initial screening. Enumeration and pregnancy screening may not have been completed at some households and therefore the women simply did not make it into the phone system. The issue is determining what happened if enumeration and screening were completed. More information is needed to adequately assess this approach. Dr. Paneth said Vanguard legacy data indicate that the number of births identified through household screening constitutes about 20 percent of all births occurring with segments. Household screening is missing pregnancies because the households are screened only once. To more accurately ascertain pregnancies by household screening, the household would have to be screened every 2 or 3 months. There needs to be more consistent follow-up of dwelling units.
- Dr. Culhane agreed to further examine the 123 eligible-for-consent cases to determine why they were not previously identified and report the findings to the NCSAC.
- Dr. Hirschfeld said the iSMOC recommended that provider compensation be encouraged but a compensation mechanism that could be perceived as coercive should not. He noted the AMA's position on capitated payments. The NCSAC meeting is the only public forum for discussing the issues of provider compensation. The NCSAC's discussions, informed comments, and perspectives will be publicly available. They will be integrated into the recommendations of other entities to help determine the Study's position on provider compensation.
- Dr. Wilfond commented that the iSMOC may not have been fully aware of the pragmatic issues of implementing provider-based recruitment and the need for provider compensation. Members of the iSMOC may not have the same experiences as Study investigators. Dr. Wilfond said that "coercion" is an appropriate term only when somebody is being threatened. If the Study does not pose a threat, then coercion is not an issue.

- Dr. Silbergeld said coercion includes circumstances that are such that people are persuaded to do something against their better interest. Coercion is not simply something that implies or is restricted to threat. Coercion is a complicated issue.
- Dr. Wilfond noted that provider compensation should be an inducement to participate. Compensation is in the interest of physicians and should motivate participation.
- Dr. Hirschfeld explained that the potential harm to Study participants is the loss of privacy. Once a person is identified as a Study participant, there is an assumption that the person's private information is available in Study archives, which could be targeted by someone seeking information about a person. The Study is protecting identification of segments in order to protect identification of participants. If participation is viewed as a liability, an issue is whether a trusted person such as a physician would refer a potential participant if it was not in that person's best welfare.
- Dr. Gelb said the Study has no fiscal interest in asking physicians to enroll their patients. The Study is not in the business of making money, unlike pharmaceutical companies that are asking physicians to help with recruitment. Therefore, the ethical issues of provider compensation are different for the Study than for a drug or treatment study.
- Dr. Silbergeld said the issue of benefit is secondary. Observational studies can carry risks to participants, not practitioners. The primary issue is whether, through inducements to the practitioner, a person may end up participating who in some way should not or may experience an increased risk.
- Dr. Slutsman said the AMA's statement is largely in the context of clinical research. There are concerns that undue incentives for referral may bend eligibility criteria thus leading to greater risk for people who should not have been referred for clinical research. The question for the Study is whether physician referral increases risks to participants and whether referral limits a potential participant's ability to give an informed, voluntary consent.
- Dr. Paneth said it is standard practice to compensate physicians for activities and tasks performed in the course of doing clinical research. This compensation includes capitation fees. Dr. Paneth asked whether the Study's provider compensation is different from compensation in clinical research. Dr. Hirschfeld said that in some contexts capitation fees can be correlated with or dependent on a given outcome (for example, consent). Compensating providers based on the number of consents would be different than compensating them for time and effort.
- Dr. Moyer noted that the iSMOC was clearly opposed to the concept of "finders' fees" (for example, those in industry-sponsored drug studies). The iSMOC was not universally opposed to the concept of compensation, provided it is equitable across providers. Compensating for screening and referral is different than offering finders' fees.
- Dr. Krischer commented that his impression is that the household survey and phone data bank are incomplete with respect to case ascertainment. An issue of incentive and

compensation is the goal of establishing an unbiased sample. Provider-based recruitment seems to be inadequate. Past experience has shown significant provider biases in identifying for potential referral. Dr. Krischer asked whether compensation and incentives can be structured to overcome provider biases. For provider-based recruitment, the most effective model is placing a Study staff member in the practice. Providers are more likely to refer if there is a perception of benefit. Monetary incentives may not be large enough to change provider referral behavior.

- Dr. Culhane explained that provider-based recruitment is incomplete in Montgomery County as of now. Because 37 practices are not yet participating, the coverage is not yet full. She agreed that the phone center is incomplete. Monetary compensation is not an issue because the small amount of money being offered is not worth the effort to process the payments. One approach to compensation is payment for identifying segment eligible women, not payment for consent.
- Dr. Paneth said some Wayne County providers are paid \$1 for each name run through an address-matching algorithm. Unlike some other studies, the Study does not compensate for enrollment. Although practitioners play a modest role in recruitment and enrollment, they want a system that can be integrated into their practice so that it does not interfere with medical care.
- Dr. Wilfond remarked that the Study could collect empirical data from Study participants who were recruited through providers to ascertain whether they were pressured into enrolling. Data can also be collected on the actual risks of people being identified as living in a segment or being enrolled (for example, people who self-identify their enrollment).
- Dr. Hirschfeld said the Study will collect data to look at real versus theoretical risks.
- Dr. Cordero summarized the key discussion points as follows:
  - The Study must clarify whether payments to providers are recruitment fees or compensation for time and effort
  - The Study must clarify whether compensation or reimbursement is linked to the number of consents versus the number of potential participants who are identified.
  - The Study's policy is that monetary payments are compensation for time and effort and is not contingent on the number of consented participants.

Dr. Cordero noted the diversity of compensation approaches used in other NIH studies. To meet the many challenges of recruitment, Study Centers should have flexibility in their approaches to provider compensation.

### **Provision of Educational Materials to Potential Study Participants**

*John Moye, M.D., Senior Scientist; Director of Laboratories and Repository, National Children's Study, NICHD, NIH, HHS*

The Study is considering whether to provide publicly available information about health and safety to potential participants, consistent with the NICHD's mission to promote health and well-

being of children and families. Examples of public educational materials are those for the NICHD's Back to Sleep Campaign.

The iSMOC met on December 7, 2010, and discussed the concept of provision of educational materials to potential Study participants. Two issues were discussed: (1) whether these materials constituted an intervention or (2) whether the Study was obligated to provide materials because of the NICHD's mission. The iSMOC considered ethical, statistical, and Study design issues. The iSMOC drafted a report, which was conveyed to the Director, NICHD and the Study's Acting Director.

In its December 9, 2010, report, the iSMOC:

- Endorsed the concept that health and safety information (such as NICHD's Back to Sleep Campaign to prevent sudden infant death syndrome) should be provided to potential participants
- Recommended that provider incentives should not include capitation-based monetary incentives but should include a uniform menu of incentive options across all Study locations (for the provider-based recruitment strategy substudy).

### **NCSAC Discussion and Recommendations**

Everett Rhoades, M.D., served as "champion" for this discussion. The group discussed the following topics and issues about the provision of educational materials to potential Study participants:

- Sheila Newton, Ph.D., said the issue of providing educational materials to potential Study participants has been discussed by the Interagency Coordinating Committee (ICC). The ICC's general range of opinions is similar to that of the iSMOC. The ICC recognized that pregnant women, as a class, receive much health information. There may be competing priorities among the state and federal agencies regarding which materials to provide as well as competing agency policies. The issue is not whether to give information but what type of information should be given.
- Dr. Rhoades asked whether the risks of providing materials should be weighed against the benefits. He noted that the mandate of science to educate may be a fallacy.
- Dr. Wilfond commented that there is a growing body of literature on researchers' obligations to provide ancillary care. Obligations may depend on the research setting, capabilities, and available resources. The question is not whether there are obligations but how to fulfill those obligations. There should not be the assumption that education is always good or that the information provided is appropriate.
- Dr. Culhane said providing materials to potential participants would probably not have a big effect. Many materials are widely available. She asked why the Study would want to pick a few materials to distribute to potential participants. Distributing materials is not the Study's "business." She noted that the Montgomery County Health Department required Study staff

to distribute locally chosen public health information to all segment households. The Study Center emphasized that these educational materials are in no way a substitute for health care.

- Dr. Rhoades asked whether educational materials should be provided as an intervention. He noted that there may be a potential risk of misinformation for some individuals in some circumstances.
- Dr. Hirschfeld clarified that whatever the Study does would not be limited to participants only. The receipt of information would not be a condition of enrollment. The Study wants to engage communities, not just individuals. There will be a broad message on the benefits of research and how research findings affect public health policy.
- Dr. Henry asked what the desired outcomes from providing educational materials would be and how would the impact be measured.
- Dr. Newton said the ICC's discussions of materials were in the context of healthy pregnancies, babies, and childhood. If the Study wanted to inform about benefits of research for communities, the public information materials would not need to be about pregnancy and children's health.
- Dr. Rhoades asked whether an educational effort could be considered part of Study recruitment and operations.
- Dr. Hirschfeld said that the purpose of providing educational materials to communities is to raise awareness about the Study.
- Dr. Ellenberg noted that if the information that is provided is effective in eliminating a health problem (for example, sudden infant death syndrome), then the cohort is no longer representative of the United States. Educational effectiveness would become an intervention that could impact on the nature of the Study's cohort.
- Edward Sondik, Ph.D., said the provision of educational materials could have a confounding effect on the cohort and also be an intervention with communities. It might be possible to delink provision of educational material from the Study by having NICHD conduct distinct activities in communities. In order to keep people participating in the Study, it is more important to give feedback on Study findings. Dr. Sondik also said that the Study's purpose is to monitor, not intervene, and it should avoid any activities that can be perceived as interventions.
- Dr. Hirschfeld explained that, as part of its mission, NICHD disseminates evidence-based findings as widely as possible. If the behavior of the Study cohort is influenced by NICHD information, the issue then becomes whether NICHD should avoid disseminating information to the cohort—information that is disseminated to other communities across the country.

- Melissa Tassinari, Ph.D., asked for clarification on whether materials are disseminated not by the Study to participants but by participating agencies to communities at large. The agencies' activities would be distinct from the Study's activities.
- Dr. Hirschfeld said there are two models: (1) the delinked model described by Dr. Tassinari and (2) acknowledging that the Study is recruiting and providing educational materials.
- Dr. Wilfond said that because the provision of educational materials is probably a modest intervention, it might be acceptable. The dissemination of materials by NICHD is another opportunity to engage communities with the Study. If the materials influence people's decision to participate in the Study, then that would be a good influence.
- Dr. Rhoades made two observations. (1) What distinguishes a participant from a subject is that a participant begins participation before any tests are done; the moral imperative to engage is greater than the need to provide more educational materials. (2) Providing materials is a unidirectional education; the Study should also be learning from the communities.
- Dr. Newton commented that providing materials can ensure a baseline in the Study communities is similar to the baseline in other communities that have access to the same materials. Additional information dissemination to Study communities may not be incrementally great.
- Dr. Wilfond said it would be helpful to get input from community advisory boards (CABs) about the provision of educational materials.
- Dr. Hirschfeld said the Study will not seek input from Study Centers and CABs until the issues of providing materials are discussed by the NCSAC. If the provision of educational materials is acceptable to the Study Centers and communities, the Study would develop a structured program that would allow data collection on the activities.
- Dr. Henry said community-based approaches would be valuable in helping to understand community awareness and acceptance and learn about the behavioral issues of childrearing.
- Dr. Newton noted that having materials tailored to communities' exposures of interest are more likely to affect behavior simply by communicating the information and would more likely be a confounder.
- Dr. Culhane said the Study should be clear to CABs about the nature and boundaries of their input. CABs can help to get community buy-in and develop strategies to get to potential participants. The CABs should understand that the Study is not asking for input on the protocol. The Study should not ask for input that cannot be acted upon.
- Dr. Rhoades said communities are interested in their data and Study findings. They are interested in how their data and findings compare with other communities.

- Dr. Hirschfeld said the topic of providing feedback has been discussed, and the Study has been encouraged to provide feedback on individual and community levels. The current focus is whether the Study should provide generic information to individuals and communities.
- Dr. Sondik said another approach to disseminating information would be to have a 1-800 number that people could call if they have questions or need information about childrearing. He also said it would be valuable to understand the type of information the communities get and how they use the information compared with communities that do not get information and are not part of the Study.
- Dr. Rhoades noted that disseminating information to communities will be an ongoing process for the Study. This information will be more than just educational materials.
- Dr. Hirschfeld said the Study will continue to explore whether educational materials will be provided to potential participants and their communities.
- Dr. Krischer said that because the purpose of educational materials is to effect change, their provision has the potential for biasing the Study and should not be further explored. He noted that any time a study influences the outcome that is measured it creates a bias.
- Dr. Henry noted that there are differences between clinical studies and observational studies. There can be severe consequences if an observational study is aware of some information (for example, about lead exposure) and it is not shared with participants. Sharing such information is a confounder, but researchers must share the information.
- Dr. Tassinari commented that dissemination of educational materials would be a major undertaking for the Study that would have to be conducted over the next 25 years. There is a possibility of information overload. Information from federal agencies carries a certain weight and may be more influential than other materials. Dr. Tassinari said information dissemination may not be the Study's role.
- Dr. Rhoades summarized the NCSAC's discussion: (1) dissemination of educational information is a moral imperative for health-related activities, but it may not be an appropriate role for the Study; (2) there are concerns about whether educational information would be a confounder or introduce bias; and (3) the Study should proceed cautiously and deliberately with its exploration of providing educational materials.
- Dr. Wilfond said, when considering its options, the Study could develop a limited scope of materials and be selective in what is provided.

## **Report of the Working Group on Legacy Vanguard Data**

*Jonas Ellenberg, Ph.D., Professor of Biostatistics, Department of Biostatistics and Epidemiology, Associate Dean of Research Program Development, University of Pennsylvania School of Medicine*

As a result of discussions of the presentation of Vanguard Study data at the October 14, 2010, NCSAC meeting, a working group of NCSAC members was formed to develop recommendations on new table shells for presenting data. The working group members were Dr. Ellenberg; Dr. Silbergeld; Joan Y. Reede, M.D., M.P.H., M.B.A.; Dr. Rhoades; Michael Lebowitz, Ph.D.; and Michelle A. Williams, Sc.D., S.M., M.S. Available working group members met via conference call to examine the proposed table shells. The working group then made recommendations to the Study's Program Office.

## **Vanguard Study Recruitment Data Update and Presentation Plans for Legacy Vanguard Data**

*Brian Haugen, Ph.D., Senior Scientist (Analysis and Evaluation), National Children's Study, NICHD, NIH, HHS*

In advance of the working group establishment, the Program Office proposed table shells to meet NCSAC member requests for more information about the flow of participants, how calculations are made, and Study Center variability. Following the working group's recommendations, the Program Office made the following adjustments: (1) removed two proposed table shells, (2) added one proposed "summary" table, and (3) added a glossary. Dr. Haugen presented 10 table shells. His presentation is posted on the Study's Web site.

Dr. Haugen listed the following next steps:

- Enhance glossary to provide more information about the disposition/status codes that contribute to high-level categories (ineligible, other nonresponse, refusal)
- Enhance table shells to provide more detailed categories, where appropriate
- Conduct qualitative analysis of reported race "other" responses
- Ensure response rate calculations follow American Association for Public Opinion Research standards.

## **NCSAC Discussion and Recommendations**

The group discussed the following topics and issues about Vanguard Study recruitment and enrollment:

- Dr. Silbergeld asked how the efficacy rate of a particular recruitment strategy could be determined and therefore be able to interpret with confidence the enumeration, screening, and consent data and then compare the data with other studies. Dr. Hirschfeld said several surrogates are being used to estimate birth rates within a segment and then, based on the number of women identified and the number of identified women who enrolled, get an estimated proportion of the efficiency of any recruitment method.

- With regard to Shell 2, Dr. Tassinari asked whether the table provides enough information so that the 61 percent household enumeration completion rate for Vanguard location 2 serves as a flag or whether the data are captured with enough caveats that the rate is not a concern. Dr. Haugen said the Program Office is aware of the particular reasons why the completion rate for Vanguard location 2 is low. The reasons were related to the particulars of that location and are plausible within the context of the Study. Dr. Hirschfeld said the Study has different early warning systems, and the data tables are part of the system. Data will be analyzed more frequently, which will provide better information for the early warning systems.
- Dr. Hirschfeld explained that for parameters being examined, the Program Office is looking at performance in the field and data outliers. With a historic reference frame, the Program Office will be better able to examine and interpret data from the 30 Study locations. The Program Office will also be conducting internal consistency analyses. Because data collection is operationally oriented, the Program Office should be able to understand signals through process maps of the operations and identify where problems are occurring. Another analytical tool is the use of data simulation to anticipate data trends.
- Dr. Wilfond said that if the Study is viewed as a continuous improvement activity and not as a clinical trial with prior assumptions, then the Study will only know what to do next by analyzing data and identifying outliers. Dr. Wilfond proposed that the third column in Shell 2—Household Enumeration Completed—be moved two columns to the right.
- For Shell 2, Dr. Henry proposed separating “refusal” from “other nonresponse.”
- With regard to Shell 3, Dr. Ellenberg asked whether the reasons for refusals could be parsed out for the next NCSAC meeting.
- In Shell 3, Dr. Sondik proposed that the number of women who became ineligible at consent (for example, due to a change in pregnancy status) be presented separately from the number women who lost eligibility because they moved out of a segment.
- With regard to Shells 4a and 4b, Dr. Henry asked whether the Study Centers were exploring “other nonresponse,” “refusals,” and “withdrawals.” Christina Park, Ph.D., clarified that only the women who withdrew or moved out of the segments were clearly out of the Study. Women categorized as “other nonresponse” and “refusals” were still technically in the Study.
- Dr. Ellenberg proposed using the “Concord” approach to present data in a tree or flowchart. He also proposed indenting subsets of data elements within the tables. Dr. Haugen said some schematic and treelike flow diagrams are being developed.
- With regard to Shell 6, Dr. Krischer asked whether a “multiple” category could be used. Dr. Hirschfeld noted that race and ethnicity data collection forms have been revised to be consistent with the U.S. Census forms and will use the “multiple” category. Shell 6 data are from older data collection forms. The Study will continue to align with data standards.

- Dr. Henry reiterated the preference to separate the data from women who became ineligible due to change in pregnancy status from women who became ineligible because they moved out of a segment. She proposed showing these data by race and ethnic group.
- Dr. Hirschfeld said the Study will follow Consolidated Standards of Reporting Trials when reporting and publishing data.
- Dr. Sondik said “withdrawal” in Shell 5b should be specifically defined because it is not the same as in other tables. Shell 5b is actually multiple tables that should be broken up with indents or presented as a tree.
- Dr. Ellenberg noted that the household-based sampling supplements the provider-based sampling approach. This two-stage approach is the right way to go.
- Dr. Tassinari asked whether there will be new shells for data on children. Dr. Haugen said there are already shells from the legacy Vanguard data for children that have had 3- and 6-month visits. Shells are being developed for the 9- and 12-month visits.

### **Meeting Summary by NCSAC Member**

Dr. Tassinari summarized the meeting as follows:

- The Study update is valuable information for the NCSAC and provides an appropriate introduction for the meeting.
- The Study is an integrated system of activities.
- The upcoming activities of implementing the Main Study and the data that will be available in the next year will be an exciting time.
- The Vanguard Study will lead the Main Study by 2½–3 years. This period may be sufficient, but Study leadership and other entities will have to monitor the progress and success of the Vanguard Study.
- The infrastructure that is being developed for the Study will be useful beyond just the Study (for example, Study Centers’ compliance with FISMA and creation of the federated IRB).
- The presentations by Study investigators Drs. Culhane and Paneth were informative about the realities of provider compensation.
- Issues of and data from provider compensation should be further explored.
- The identification of potential participants not identified through household enumeration and screening should be further investigated. Identification of these women shows that the provider-based recruitment could be a successful augmentation to the household enumeration and screening approach.
- HIPAA obligations and requirements were considered. Further discussions are needed on challenges and potential hurdles of HIPAA with regulations.
- Provider compensation is an essential element of provider-based recruitment, but compensation is not necessarily monetary. Study Centers will have to find ways to work with providers and ensure that their engagement is fulfilling.
- The discussion of the provision of educational materials was interesting. The NCSAC is in agreement that the one of the reasons for conducting the Study is to improve health, and

disseminating information is part of the Study's entities' missions. The Study needs to balance education against confounding or biasing data and maintain the rigors such that the data are interpretable. How this balance is achieved and who handles it needs to be determined. Stakeholders and communities need to be involved in solutions.

- The NCSAC agreed that the new formats for presenting data are much improved and informative about past activities.
- The NCSAC agreed that the reasons for participants' refusals, withdrawals, and loss of eligibility due to change in pregnancy status and moving should be further explored.

## **NCSAC Membership Transitions**

Michael Greene, M.D.; Thomas Ten Have Ph.D., M.P.H.; and Dr. Tassinari commented on their experience as NCSAC members. Dr. Green said that 2 years is too short a term to provide the Study with the best use of NCSAC members' advice. More time is needed to learn about and understand the issues facing the Study. He proposed 4-year terms. Dr. Ten Have thanked the Study leadership for the opportunity to serve on the NCSAC. Dr. Tassinari agreed with Dr. Green about term length and expressed thanks for the opportunity to serve. The 2-year term length does not allow the Study to fully tap the use of NCSAC members' experience. She proposed that the Study engage the NCSAC more than four times a year. Departing NCSAC members are as follows:

- Elena Gates, M.D.
- Dr. Greene
- Dr. Lebowitz
- Dr. Tassinari
- Dr. Ten Have.

## **NCSAC Members**

Wilma Brakefield-Caldwell, R.N., Public Health Nurse Administrator

Maria Cancian, Ph.D., University of Wisconsin-Madison

José F. Cordero, M.D., M.P.H., University of Puerto Rico

\*Ana V. Diez-Roux, M.D., Ph.D., M.P.H., University of Michigan

Jonas H. Ellenberg, Ph.D., University of Pennsylvania Medical School

\*Elena Fuentes-Afflick, M.D., M.P.H., University of California, San Francisco

\*Elena Gates, M.D., University of California, San Francisco

Bruce D. Gelb, M.D., Mount Sinai School of Medicine

Michael Furman Greene, M.D., Massachusetts General Hospital

Carol J. Henry, Ph.D., NCSAC Chair, George Washington University School of Public Health and Health Services

Jeffrey Krischer, Ph.D., University of South Florida

Alma M. Kuby, M.A., M.B.A., Survey Methodologist

\*Michael D. Lebowitz, Ph.D., University of Arizona

Patricia O'Campo, Ph.D., University of Toronto

\*Joan Y. Reede, M.D., M.P.H., M.B.A., Harvard Medical School

Everett Rhoades, M.D., University of Oklahoma Health Sciences Center

Ellen Silbergeld, Ph.D., Johns Hopkins University Bloomberg School of Public Health

Melissa Tassinari, Ph.D., DABT, Center for Drug Evaluation and Research, U.S. Food and Drug Administration (FDA)

Thomas Ten Have, Ph.D., M.P.H., University of Pennsylvania School of Medicine

Benjamin S. Wilfond, M.D., University of Washington School of Medicine

\*Michelle A. Williams, Sc.D., S.M., M.S., University of Washington School of Public Health

*\*Did not participate*

### **Ex Officio Members**

\*Allen Dearry, Ph.D., NIEHS, NIH, HHS

\*Alan E. Guttmacher, M.D., NICHD, NIH, HHS

Edward J. Sondik, Ph.D., M.S.Hyg., CDC, HHS

\*Kevin Y. Teichman, Ph.D., Office of Research and Development (ORD), EPA

*\*Did not participate*

### **Designated Federal Official/Executive Secretary**

Kate Winseck, M.S.W., NICHD, NIH, HHS

### **ICC Members**

Amy Branum, M.S.P.H., National Center for Health Statistics, CDC, HHS

Adolfo Correa, M.D., Ph.D., National Center on Birth Defects and Developmental Disabilities, CDC, HHS

Sally P. Darney, Ph.D., ORD, EPA

\*Michael Firestone, Ph.D., Office of Children's Health Protection, EPA

Kimberly Gray, Ph.D., NIEHS, NIH, HHS

Steven Hirschfeld, M.D., Ph.D., NICHD, NIH, HHS

Mary E. Mortensen, M.D., M.S., National Center for Environmental Health, CDC, HHS

\*\*Sheila A. Newton, Ph.D. (chair), NIEHS, NIH, HHS

\*\*James J. Quackenboss, M.S., ORD, EPA

\*Marshalyn Yeargin-Allsopp, M.D., National Center on Birth Defects and Developmental Disabilities, CDC, HHS

*\*Did not participate*

*\*\*Represented agency's Ex Officio member at this meeting*

### **Program Office Members**

Marion J. Balsam, M.D., NICHD, NIH, HHS

Ruth A. Brenner, M.D., M.P.H., NICHD, NIH, HHS

Andrew M. Briggs, (contractor), NICHD, NIH, HHS

Margot T. Brown, Sc.D., NICHD, NIH, HHS

Danielle Cloutier (contractor), NICHD, NIH, HHS

Jessica E. Graber, Ph.D., NICHD, NIH, HHS

Brian J. Haugen, Ph.D., NICHD, NIH, HHS

Carl V. Hill, Ph.D., M.P.H., NICHD, NIH, HHS

JoEllen Jay (contractor), NICHD, NIH, HHS  
Carol H. Kasten, M.D., NICHD, NIH, HHS  
Nicole Kramer (contractor), NICHD, NIH, HHS  
Scott Lewis, NICHD, NIH, HHS  
Maria Lopez-Class, Ph.D., M.P.H., NICHD, NIH, HHS  
Eric Lorenzo, Ph.D., NICHD, NIH, HHS  
John Moye, Jr., M.D., NICHD, NIH, HHS  
Nancy Parfitt Hondros, NICHD, NIH, HHS  
Christina H. Park, Ph.D., NICHD, NIH, HHS  
Jennifer E. Park, Ph.D., NICHD, NIH, HHS  
Nicole Pultar (contractor), NICHD, NIH, HHS  
Julia Slutsman, Ph.D., NICHD, NIH, HHS  
Gitanjali S. Taneja, Ph.D., NICHD, NIH, HHS  
Maureen R. Wildman (contractor), NICHD, NIH, HHS

### **Observers and Other Participants**

Anjene M. Addington, Ph.D., M.P.H., Booz Allen Hamilton Inc.  
James Baumberger, American Academy of Pediatrics  
Arthur M. Bennett, B.E.E., M.E.A., Consultant, NICHD, NIH, HHS  
Richard A. Chestek, Ph.D., Booz Allen Hamilton Inc.  
Jennifer Culhane, Ph.D., M.P.H., University of Pennsylvania School of Medicine, Children's  
Hospital of Philadelphia  
Angela DeBello, M.A., National Opinion Research Center (NORC) at the University of Chicago  
Sarah Garnett, Price Waterhouse Cooper  
David L. Hubble, Westat  
Linda M. Katz, M.D., M.P.H., Center for Food Safety and Applied Nutrition, FDA  
Juergen A. Klenk, Ph.D., Booz Allen Hamilton Inc.  
Janice Machado, M.B.A., Westat  
John McGrath, Ph.D., NICHD, NIH, HHS  
Nigel Paneth, M.D., M.P.H., Michigan State University  
Jin-Young K. Park, Ph.D., Center for Food Safety and Applied Nutrition, FDA  
Susan Schechter, NORC at the University of Chicago  
Branka Sekis, Social and Scientific Systems, Inc.  
James P. Shannon, P.E., RTI International  
Michael D. Sinclair, Ph.D., NORC at the University of Chicago  
Andrew Westdorp, Social and Scientific Systems, Inc.

*I hereby certify that, to the best of my knowledge, the foregoing minutes are accurate and complete.*



March 17, 2011

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Date

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Carol J. Henry, Ph.D.  
Chair  
National Children's Study Federal Advisory Committee