National Children's Study
Federal Advisory Committee 17th Meeting
November 7–8, 2007
Westat Conference Center
Rockville, MD

This meeting was held in conjunction with the National Children's Study, which is led by a consortium of federal agency partners: the U.S. Department of Health and Human Services (DHHS), National Institutes of Health (including the National Institute of Child Health and Human Development [NICHD] and the National Institute of Environmental Health Sciences [NIEHS]), and the Centers for Disease Control and Prevention [CDC]), and the U.S. Environmental Protection Agency (EPA).

Day 1

Welcome and Introductions

Alan R. Fleischman, M.D., National Children's Study Advisory Committee (NCSAC) Chair; Medical Director and Senior Vice President, March of Dimes

Dr. Fleischman welcomed the NCSAC members and other participants to the 17th meeting of the NCSAC. He characterized the November 8 joint session of the NCSAC and the Steering Committee as a "monumental historic moment" for the Study .

Dr. Fleischman announced that he recently accepted the position of Medical Director and Senior Vice President of the March of Dimes. He will continue to serve as NCSAC chair and will continue his involvement with the Study in an advisory role.

Dr. Fleischman reviewed the functions of federal advisory committees as defined in the Federal Advisory Committee Act. The NCSAC's roles and responsibilities include providing specific advice and recommendations to the director of NICHD, the Study Director, and the Interagency Coordinating Committee (ICC). Dr. Fleischman reviewed the meeting's agenda and described the issues to be addressed by the Scientific Review, Ethics, and Community Outreach and Engagement Subcommittees during the breakout sessions.

Welcome and Brief Study Update

Peter C. Scheidt, M.D., M.P.H., Director, National Children's Study

Dr. Scheidt welcomed the NCSAC members and other participants at the meeting's opening session. He explained that the past year has been eventful and exciting. In February, Congress appropriated $69 million specifically for the Study . This funding was used to prepare for recruitment and enrollment at the Vanguard Centers, develop the information management system, and establish new Study Centers. For the coming fiscal year, the full House and full Senate mark-up of the President's 2008 budget includes $110.9 million for the Study. The major event for the past year was the solicitation and procurement for the next wave of Study Centers and locations. Contracts were awarded to 22 Study Centers to manage 26 locations. These

centers, together with the seven Vanguard Centers, will implement the Study in 33 locations in Wave 1. The awards of new Study Centers and the prospect of continued funding make the NCSAC's considerations and advice an important component of the Study's governance and management. The results of the NCSAC's deliberations will provide valuable input on the Study's implementation. In addition to answering questions posed to the Committee, the NCSAC may ask new questions and identify new issues to be considered.

Information Management System (IMS)

David C. Songco, Chief Information Officer, NICHD, NIH, DHHS

The Study's IMS has three modules: (1) support systems, (1) data capture and management systems, and (3) quality control and data delivery systems. The primary function of the IMS is to support the science behind the Study. Key elements of the IMS mission are to ensure security of data, privacy of information, and compliance with all federal, state, agency, and Study mandates and regulations. The IMS is being implemented by a team that will bring together the best in Study operations and information technology (IT) to support the current known Study requirements and management of the Study and its data over the next 25 years. The team is composed of the NICHD Tech Support Team, Booz Allen Hamilton, and Westat.

The Study's unique characteristics continue to drive the IMS vision. They include:

- National scope with dispersed site locations, IT infrastructures, and logistical challenges
- Extensive types of clinical and environmental data to be collected
- Long-term design considerations to support evolving Study operations and technologies
- Examination of many questions and high volatility of requirements
- Publicly available results as the Study progresses to facilitate information sharing while maintaining participant privacy
- Involvement of partners from multiple government agencies, as well as from public organizations and private companies to meet the needs of all stakeholder groups
- Use of state-of-the-art technology to provide the most accurate and reliable systems possible while taking advantage of information supplied by others (e.g., human genome).

The Study's IMS requirements are formed by the array of designed goals. The system must be:

- Flexible. The IMS must be able to accommodate continuously evolving requirements, including changing hypotheses, new scientific instruments, updated protocols, and new technologies. In addition, it must support the inevitable evolution of technology and functional requirements.
- Comprehensive. The wide range of environmental and health measures require the IMS to support an extensive range of data collection functions and technologies.
- Integrated. The IMS shall employ the most recent technological advances to meet the ongoing needs of the Study while ensuring seamless integration with multiple existing information sources.
- Accessible. Because there are multiple locations with differing levels of connectivity, the IMS must allow for reliable data collection even if the network is unavailable.
- Secure. The IMS must employ stringent security controls to prevent inappropriate information disclosure and possible data loss, while ensuring that the right information is provided to the right people.

- Private. A critical success factor for the IMS, beginning with participant recruiting and continuing throughout the program life cycle, is data privacy. The IMS must ensure data integrity for several decades, including inevitable technological evolution.
- User-focused and user-friendly. The IMS must be tailored to extremely diverse user populations, accommodate the objectives of multiple stakeholder groups, and support communication among all those involved in the Study.

As the Study evolves, the IMS will evolve with it to support the data that are collected for the pilot study, which begins in July 2008, and beyond. Site visits at the Vanguard Centers will provide additional information about Vanguard Center-specific IT needs and challenges. Lessons learned from the pilot study will be integrated into the IMS to support the main Study launch in 2009. The IMS will adjust to accommodate the evolution of technology and functional requirements.

NCSAC Discussion and Recommendations/General Discussion

- Elena Gates, M.D., asked about participant privacy and the use of personal identifiers. Specifically, she was concerned about personal identifiers stored on laptop computers and memory data storage devices such as USB flash drives. Mr. Songco explained that all participant data will be encrypted and that a two-factor authentication protocol will be required to access data. Sarah Knox, Ph.D., said no personal identifiers will be stored on laptop computers. A participant ID will be used, and both the data and transmission of data will be encrypted. Frank A. Chervenak, M.D., was concerned about identifying participants when data collectors are entering data in the home. Dr. Knox reiterated that the data and data transmission will be encrypted, and any data stored on laptops will be purged frequently and automatically.

Study Operations and Training of Research Staff

Elaine Eaker, Sc.D., Vice President, Westat

Dr. Eaker presented an overview of Study operations and implementation, Study Center and Coordinating Center communications, and training of research staff. She described the roles of the Coordinating Center and Study Centers, which will work together to produce new, generalizable knowledge. The Coordinating Center will assure valid and standardized data collection by developing and monitoring instruments, procedures, protocols, training modules, elements of the information systems, quality control, and communication structures. The Study Centers will implement protocols for standardized data collection, training, and quality control.

The Coordinating Center optimizes the collection of valid, generalizable data by (1) developing forms, questionnaires, instruments, equipment, and algorithms for data collection; (2) providing quality control procedures for checking, monitoring, and correcting the process; (3) providing an infrastructure for clear communication from and to the Study Centers; and (4) facilitating use of an overarching IMS. It is important that Study Center researchers and staff are trained on the IMS, that they understand it, and that they can use it. The Coordinating Center will perform quality control of IMS use and retrain as necessary. The Coordinating Center is responsible for building the IMS to be able to collect data in a standardized way, compile data from a multitude

of centers, analyze the data, and generate outstanding scientific findings that lead to health policy implications.

The Coordinating Center is sensitive to the needs for close interactions and communication with the Study Centers throughout the entire Study. Prior to data collection, the Coordinating Center will help the Study Centers understand the Study and develop and set up systems. As data collection begins, the Coordinating Center will help train staff and institute procedures. Throughout the Study, the Coordinating Center will present and communicate new protocols for each new phase of data collection. A Coordinating Center liaison will be assigned to each Study Center. The liaison will be the point-person for Study Center contacts and will triage communication through a variety of mechanisms. Incoming communications will be triaged to operations, technical experts, training, and information systems.

Training is determined by Study activities and staff role with flexibility allowing for variation in Study Center operations. To this end, the Coordinating Center is developing numerous training modules. Training will be direct (face to face), indirect (train the trainers), electronic, and via telephone. Other delivery modes will include videos, workshops, case studies, and webcasts. All data collectors will receive standard training on protocol and processes, cultural sensitivity and language, respect for the participant, moral conduct, and privacy and confidentiality. There are three special considerations for training: (1) risks that can potentially be detected as a result of the research protocol activities (for example, elevated blood pressure), (2) risks that are not associated with the research protocol (for example, excessive bruising on the child, observed excessive discipline), and (3) risks observed in the home. The data collectors will be trained to recognize risks that constitute "imminent dangers and serious harm" from those that are not. They will also be trained on protocols, procedures, and reporting for such risks, as well as the applicable local/state reporting laws and institutional review board (IRB) requirements.

NCSAC Discussion and Recommendations/General Discussion

- Antoinette P. Eaton, M.D., asked about the process of how risks will be considered, what the determinants will be, and who will make decisions on addressing risks. Dr. Eaker said the Coordinating Center and Study Centers are developing the processes. Although there may be local and regional differences on what risks are considered "imminent danger and serious harm," all data collectors will report their observations to their supervisors, who will make decisions based on protocols, procedures, and reporting requirements. It was acknowledged a national discussion is needed to develop consensus on a standardized approach for risk assessment, while allowing local/regional flexibility.

- Robert E. Chapin, Ph.D., asked about women who are screened for pregnancy but do not consent to participate in the Study. He mentioned the Yale Cultural Cognition Project, which describes how a person's world view influences risk perception. These perceptions need to be considered to maximize acceptance by people of widely differing value structures. Different people will view the risks of Study participation in different ways. Dr. Eaker commented that a pilot study of the informed consent process will help shed light on how risk is perceived.

- J. Ricardo Guzman asked whether undocumented immigrants and people without health insurance had been considered. Dr. Eaker noted that health insurance is not required to participate in the Study. Each Study Center is required to have local resources for referral of participants who require health care. The Study will not make diagnoses but will screen participants and make referrals as necessary, regardless of health insurance status. Dr. Scheidt said documentation is not required to participate in the Study. All individuals will be included if otherwise eligible.

- Given that there will be staff turnover over the years at the Study-Center level, particularly non-senior-level staff, Helen DuPlessis, M.D., M.P.H., asked what sort of monitoring, oversight, and ongoing quality controls will be employed. Dr. Eaker replied that turnover is a concern that can be addressed through the train-the-trainer model in which a supervisor is responsible for training new recruits. The Coordinating Center will oversee the quality control of the training, and there will be a protocol for monitoring quality. It is anticipated that much of the training and retraining of trainers will occur in the Study Centers. The Coordinating Center will also monitor the quality of data received from the Study Centers.

- Alexa Fraser, Ph.D., commented that a complex set of permissions is embedded in the IMS that limits data collection/input to only those individuals who are qualified and authorized to do so. System access requires password authentication. Data collectors who are not trained, certified, or assigned to a particular task will not be able to access the IMS.

- Michael Lebowitz, Ph.D., was concerned about the training and certification of Study interviewers and trainers of the trainers. He asked about the competence of these individuals as objective interviewers and culturally sensitive individuals. Dr. Eaker explained that Westat has extensive experience in conducting large, national in-home interviews. Westat is very familiar with issues and concerns with interviews. Westat has extensive experience in developing protocols and training staff how to implement and adhere to protocols. Dr. Eaker said that data quality depends on the quality of the data collectors. Westat has highly trained and experienced trainers. Data collectors are tested and recertified on a regular basis. If the data collector is not certified, then he or she cannot collect data.

- In response to Dr. Lebowitz's question, Dr. Eaker explained that Westat is participating in the pilot testing of Study instruments, developing the protocol, and developing the training modules. Westat is working closely with the Program Office and the IMS team. Westat is training the Vanguard Centers' staff.

- Myron Genel, M.D., asked for clarification on when enrollment will begin at the Vanguard Centers. Dr. Scheidt said enrollment for the pilot year, which will be implemented at the Vanguard Centers, will begin in summer 2008. The pilot will be initiated by two Vanguard Centers, and about 4 months later, the remaining five Vanguard Centers will implement it through the end of 2008. In 2009, the Vanguard Centers and new Study Centers will implement the full Study.

- David J. Schonfeld, M.D., asked how the Study will integrate new, evolving technologies, the extent to which data will be sent directly from data collectors to a central data center, and

the extent to which Study Centers will have ownership of the data they collect. Mr. Songco replied that the IMS team is assessing all possible technologies (for example, wireless devices) to connect Study participants, data collectors, Study Centers, and the Coordinating Center. The Study has a centralized data collection architecture, which allows direct data uploads into the data center at Westat. The data can then be transmitted back to the vanguard and Study Centers. Certain event data, such as those collected by parents or teachers, will be transmitted to the Coordinating Center over secure SSL/VPN (secure socket layer/virtual private network) connections via secure dial-ins. Data will be transmitted among vanguard/Study Centers, data collectors, business partners, external data sources, and the Coordinating Center through an encrypted VPN tunnel. Privacy and confidentiality will drive the Study, not the technology.

- Dr. Gates said the protocol must be standardized regardless of who is collecting data. Dr. Schonfeld commented that there must be a balance between data accessibility and data protection. Dr. Scheidt said the Study's data collection, transmission, and storage processes will ensure the confidentiality of data. James J. Quackenboss, M.S., said there must be certification, evaluation, and quality control to ensure a uniform collection of data. Dr. Gates commented that recertification of data collectors is essential to collecting quality data. Dr. Eaker explained that Westat is developing the training protocols, and there will be a balance between quality control and training. A protocol for spot checks has not yet been developed.

- Bruce Levin, Ph.D., asked about the possibility of a nonresponse rate of participants that is not random. He elaborated that potential participants may simply refuse to cooperate or reject participation at first contact. A systematic refusal may lead to biased representation. Dr. Eaker explained that the Coordinating Center will apply a protocol called refusal conversions for such situations. Dr. Fraser agreed that the Study needs a nonresponse plan.

Current Status of Study Centers

Ruth A. Brenner, M.D., M.P.H., Study Program Office, NICHD, NIH, DHHS

An estimated 30–50 Study Centers will oversee data collection of a representative sample of 105 locations. The Study will be implemented in three waves, with about 35 locations per wave. There will be a lag time of about 1–2 years between waves. Each wave will be reflective of the births in the United States, to the extent possible. The most recent procurement stated that offerers could submit proposals for data collection at one or more locations and that those locations could be implemented in any of the three waves.

The pilot study will be conducted in the seven vanguard locations. The second stage of sampling (defining and selecting segments) is complete in these locations. Current efforts focus on steps needed for implementation and engagement of relevant communities. However, many community and other assessments are on hold pending Office of Management and Budget (OMB) approval. Household screening is scheduled to begin July 1, 2008, in two pilot locations and November 1, 2008, in the remaining five pilot locations.

The new Study Centers are defining and selecting second-stage segments and developing plans for engaging communities in the Wave-1 locations. The centers will begin community

assessments following selection of segments and receipt of OMB approval. Household screening is scheduled to begin July 1, 2009.

The research plan has been reviewed by the Vanguard Centers, NCSAC, the ICC, and lead agencies. Public comment has been received and is being reviewed. The research plan is still under review by the National Academy of Sciences. The Study's Program Office will submit a "generic clearance" for formative research to OMB, which will allow the conduct of focus groups. A separate clearance will be submitted for the pilot study at the Vanguard Centers prior to submission of clearance documents for the full Study; this will allow an opportunity for modifications to the research plan prior to submission of the full Study.

Pilot Study Update

Kenneth C. Schoendorf, M.D., M.P.H., Study Program Office, NICHD, NIH, DHHS

The purpose of the pilot study is to field test the proposed procedures and instruments for the full Study. The Vanguard Centers will enumerate and screen the pilot study population, and women and infants will be enrolled in the first year after enumeration. The pilot study will be conducted about 1 year ahead of the full Study. In-person contacts before birth include the household enumeration and screening. Women with high probability of conception will be contacted by telephone at 1, 2, and 4 months. Moderate probability women will be contacted at 3, 6, and 9 months. Low probability women will be contacted every 6 months.

Women who become pregnant will be contacted by telephone at 16 and 36 weeks. There will also be an in-home first trimester visit (T1), which will use several interview approaches (for example, computer-assisted personal interviewing, self-administered questionnaires) and cover an array of topics (for example, demographics, doctor visits, diet). During the T1 visit, environmental samples (for example, air, dust, water) will be collected. The women will be given a physical exam, and biospecimens such as blood, urine, hair, vaginal swabs, and saliva will be collected. Details on the timing and order of data collection for the T1 visit have not been finalized.

There will be two birth visits: at delivery in the hospital and about 24–48 hours later in the hospital or at home. Procedures for the birth visit will include biospecimen collection (for example, cord blood, placenta) and dysmorphology assessment. There will be three postnatal visits at 6 months (home), 12 months (home), and 36 months (clinic). The 6- and 12-month visits will include development assessments and child-parent interactions. There will be six postnatal telephone contacts up to 36 months.

NCSAC Discussion and Recommendations/General Discussion

- Dr. DuPlessis asked how the Study will handle women in the low-to-moderate probability groups who have an unintended pregnancy and elect to terminate their pregnancy. Dr. Schoendorf explained that women who become pregnant are not automatically enrolled in the Study. Women will self-report their pregnancy to the Study or report their pregnancy during a telephone interview. Women may become pregnant and not inform the Study. Women who

report pregnancy may elect not to enroll in the Study. There will also be women who enroll in the Study and then change their minds about their pregnancies.

- Dr. DuPlessis asked whether the Study had considered at-home and other out-of-hospital births. Dr. Schoendorf said that this group would comprise about 1 percent of Study births. At this time, an at-home protocol has not been developed, and there is a good chance that biospecimens may not be collected from these births. It is likely that the Study will miss some of the birth biospecimens for hospital births. Missed birth specimens will be collected at about 1 month of age.

- R. Gary Rozier, D.D.S., M.P.H., asked whether the Study has considered computer-assisted recorded interviewing. This approach allows the use of some sophisticated quality assurance techniques because the recording can be linked to the questionnaire schedule. This technology is being used by the U.S. Census Bureau. Interview recording could be used to monitor interviewer bias and ensure interview quality. It was noted that Westat is assessing the use of this technology as part of the quality control protocol.

- Dr. Rozier asked about the content of the interviews and questionnaires and process for developing the protocol. Dr. Schoendorf noted that several questions concern maternal oral health. Dr. Brenner explained the background of protocol development, including questionnaires, forms, and other data collection tools. The questionnaires and other data collection instruments have been developed up to age 6 months for the pilot study. The Vanguard Centers and new Study Centers will provide additional expertise and input on the data collection materials as the pilot study is refined and implemented. The research plan describes the domains that will be addressed but does not list specific questionnaires or instruments. OMB approval and IRB revisions will affect the final questions, which will then be made publicly available.

- Dr. Schonfeld asked about the relative emphasis given to psychosocial measures throughout the Study. There is a growing trend toward the belief in genetic predeterminism and a growing emphasis on biological measures as opposed to psychosocial influences. Genetic causes, physical environment, and social environment all contribute to child health and development. According to the Study's design and analytic plan, investigators will examine the relative contributions of these factors to outcome measures of interest. If the psychosocial measures are not very robust or are collected only on a subsample, the Study risks confirming that psychosocial factors are not as relevant as others. Dr. Schonfeld cited the daycare analysis as a substudy and the use of existing neighborhood-level data. He said that he had not seen a cost analysis of the relative amount of money being spent on collection of psychosocial variables versus, for example, environmental variables. Relative cost analyses for the different hypotheses could be used to ensure a balance among measures that will answer the different hypotheses equally. Dr. Brenner said an assessment of the interview components showed balance among psychosocial and other factors. Dr. Knox confirmed the balance, noting that time for collecting environmental samples was reduced in order to collect more psychosocial data. Dr. Brenner explained that the Study does not have the resources to follow each child to daycare and will therefore examine only a subsample. She said the Study has closely assessed the costs of the various components. To help reduce

costs, many environmental and biologic samples will be stored for future analysis. Observational measures such as parent-child interactions and other psychosocial measures will also be stored for future analysis. Dr. Schonfeld said the Study will be collecting neighborhood-level data.

- Dr. Scheidt noted that the Program Office and other protocol developers have worked hard to maintain a reasonable balance among measures of different domains. Because of limited resources, the Study is not able to include as many measures as investigators would like. The NCSAC can advise on gaps or missed opportunities in measures that are achievable. Based on cost analyses, the Study had to reduce the number of home visits and childcare settings, which reduce a number of psychosocial measures. Liliana J. Lengua, Ph.D., was impressed with the psychosocial measures and coverage of the constructs, provided they are measured well. Dr. Brenner clarified that the Study will collect data on daycare centers, but there will not be visits to all daycare centers.

- Dr. Lengua asked whether the Study had considered the possible risks of frequent telephone contacts to women in the high probability group who are having difficulty becoming pregnant and who are not yet enrolled in the Study. She suggested that repeated telephone contacts may be stressful. Dr. Schoendorf explained that, upon initial contact, women who have been trying to become pregnant for a while will be differentiated within the high probability group. If they continue to fail to become pregnant, contact will diminish over time. In all situations, the Study will be very sensitive to such issues. Women can decline participation in the Study at any time.

- Dr. Lebowitz commented that adjunct studies can fill in some of the gaps in questionnaires that the main Study is not able to cover.

- Dr. Genel asked how committed the Study is to sampling 100,000 children. He proposed that, budget permitting, the Study oversample with the expectation of finishing with 100,000. Dr. Brenner said the Study sample is based on 100,000 births. Dr. Scheidt said power calculations show that the hypotheses can be tested using 80,000–90,000 children. He acknowledged that unanticipated attrition or migration may lead the Study to expand or extend enrollment, if necessary, but probably not much beyond 100,000. The anticipated attrition rate is 2 percent per year over the course of the Study.

- Dr. Brenner said some of the questionnaire sources are listed in the research plan. The questionnaires for the pilot study were recently posted for Vanguard Center review, and when that review is complete, the questionnaires will most likely be posted for public review. The questionnaires for the main Study have not yet been developed. The OMB application will include questionnaires through age 2.

Informed Consent Update

Dr. Fleischman

Since the last NCSAC meeting in June 2007, the pregnancy and prepregnancy video consents have been revised. Written analogues of the video consents have been developed, which will be

studied in a pilot experiment. A video informed consent for fathers has been developed, the format of which is similar to the prepregnancy video consent. The pregnancy consent is an active video with embedded questions. The fathers and prepregnancy consents are static (that is, pictures) with a narrator but no embedded questions. The fathers and prepregnancy consents are shorter than the pregnancy consent. The pregnancy consent is the most comprehensive consent, and an assessment of comprehension is conducted in the middle of it.

Because the video consent process is a new way of obtaining consent, it needs to be evaluated in a rigorous manner. The Study, together with Coordinating Center scientists and input from the human subjects work group, has developed a strategy for a pilot consent experiment. The purpose is to compare the video consent with a written consent during the first trimester of pregnancy. A colorful, glossy, and attractive written consent brochure is being developed for this pilot experiment.

Subjects will be randomly assigned to either the video consent or written consent. The experiment's domains of interest are (1) rate of enrollment, (2) comprehension, (3) subjective experience of the Study, (4) retention/attrition rates, (5) clarity/level of detail, (6) length of time to administer, and (7) importance of consent materials in decision making. If the experiment reveals differential rates of enrollment, they would need to be explained. A power analysis of the experiment requires about 500 subjects in each arm.

The video informed consent for fathers was shown to the NCSAC and other meeting participants. Dr. Fleischman noted that this video has a male narrator, whereas the prepregnancy and pregnancy videos have female narrators. The video's relatively sophisticated technology allows some options in the presentation. A research assistant will watch the video with the father to be available to answer any questions.

NCSAC Discussion and Recommendations/General Discussion

- Dr. Levin asked whether consent is required for the participants in the pilot experiment. Dr. Fleischman replied that IRBs will be asked to waive an additional written consent for the pilot, but the women will be informed that they are being asked for consent to enroll in the Study and that the consent will be in one of two formats.

- In response to a question from Dr. Gates, Dr. Fleischman explained that the content of the video and written consents will be the same. Pilot participants will be asked questions at the end of each consent "presentation" to evaluate comprehension and measure the participants' impressions.

- In response to a question from Dr. Levin, Dr. Fleischman said the primary outcome is differential enrollment. One hypothesis is that the more a person knows about the Study, the less she will be inclined to participate. Therefore, if the video is more informative, it will decrease enrollment. The pilot will attempt to explain the reasons for differential enrollment, if there is any.

- Dr. DuPlessis asked whether those participants who use video consent will receive a written document to keep after they have consented. Dr. Fleischman said these participants will receive what is basically a transcript of the video. Language in human subjects regulations specifies that Study subjects be given a written document. The Study is exploring whether a DVD can be substituted for written documents for participants who use the video consent.

- Mr. Guzman asked whether there was any discussion about using different male voices to ask the questions throughout the video. Dr. Fleischman replied that there was discussion about the voices in both the English and Spanish video consents about perceptions of ethnicity and country of origin. Mr. Guzman suggested using a different man's voice for each question.

- Virginia Delaney-Black, M.D., M.P.H., a public participant, asked how the Study will address IRB requirements and if specific language be included in consents (for example, waivers). Dr. Fleischman said anything that is required by local IRBs will be inserted into the video consents, and the technology allows tailored modifications. The Study will attempt to convince IRBs that local idiosyncratic approaches are not required.

Ethics Subcommittee Report

Myron Genel, M.D., Chair, NCSAC Ethics Subcommittee; Professor Emeritus of Pediatrics, Yale University School of Medicine

Incentives and Gifts of Appreciation. The subcommittee addressed three questions:
- What criteria should be used for nonmonetary gifts of appreciation for adults (mothers and fathers), infants, and children?
- By what process should these decisions be made?
- Is it acceptable to give different gifts at different sites?

The subcommittee agreed on/recommended the following:
- Issues of incentives and gifts of appreciation should be further explored, refined, and discussed at future NCSAC meetings.
- The term "tokens of appreciation" is preferred over "gifts of appreciation."
- Tokens of appreciation should be of modest monetary value.
- The purpose of tokens is to enhance or reinforce participants' relationship to the Study.
- The gift should somehow be connected to the Study through some form of an insignia, logo, or statement.
- More generous gifts could be allowed on a significant occasion such as a participant's birthday.
- There should be a defined process to provide national study guidelines on acceptable tokens of appreciation.
- All gifts must be vetted within the community as part of the community engagement process.
- All gifts must be approved by the local IRB.
- Different sites should be allowed to have different tokens of appreciation.

Cord Blood Banking. Participants may wish to (1) privately bank cord blood solely for future use by their family or (2) voluntarily donate their cord blood to a public bank. The subcommittee addressed two questions:

- What does the subcommittee recommend the Study do in each of these cases?
- What should participants be told before arriving at the hospital for their deliveries?

The subcommittee agreed on/recommended the following:
- Study participants should be informed of their cord blood banking options at the time of initial consent.
- Cord blood banking options should be fully explained at the third trimester visit.
- The absolute need for a specific donation to a public bank is relatively modest.
- Donations to private banks should be neither encouraged nor discouraged.
- Explanatory material given at initial consent and at the third trimester visit should be shared with the woman's health care providers.
- The community should be actively engaged to solicit input and comments on banking cord blood.
- Women who decide to donate cord blood for public or private use should not be excluded from the Study.
- Participants should be encouraged to donate their cord blood to the Study.

NCSAC Discussion/General Discussion

- Dr. Genel explained that the gifts of appreciation will be given in addition to compensation such as reimbursement of expenses and modest incentives for participation.

- Dr. Gates clarified that one of the purposes of tokens of appreciation is team building.

- According to Dr. Chervenak, there would no impact on the well-being of children with cancer if the 100,000 Study participants did not donate cord blood to public banks. At the same time, Dr. Gates reported that the subcommittee felt there was not much benefit from private cord blood banks. Dr. Levin noted that the subcommittee could not agree on the precise language to inform participants of these two situations.

- Dr. Lengua said there are restrictions on donations to public banks. She asked whether blood that is rejected by a public bank can be returned to the Study. It was acknowledged that protocols for collecting, aliquoting, and storing would have to match those of the Study. Knowing a public bank's criteria in advance could prevent rejection and preclude the need to recapture a sample.

- Issues on use of cord blood as it pertains to stem cell research were discussed.

NCSAC Recommendations

- The NCSAC recommended that (1) the Study allow tokens of appreciation, setting broad guidelines for them and allowing local site to tailor their approach; (2) incentives be approved by local IRBs or vetted in some fashion; and (3) different sites be allowed to have different tokens of appreciation.

- The NCSAC formally recommended that at the third trimester visit, for those sites that have public blood banking available to women, there be a carefully crafted explanation as part of the process of informing women about what will happen in labor and delivery. All options will be described to the women so that they may be able to make an informed choice about donating cord blood to the Study, private blood banks, or public blood banks. Private banking may have more cost than gain but NCS researchers should not actively discourage it. The value of cord blood in the Study should be emphasized.

Scientific Review Subcommittee Report

David J. Schonfeld, M.D., Chair, NCSAC Scientific Review Subcommittee; Professor of Pediatrics, Cincinnati Children's Hospital Medical Center

The subcommittee addressed three questions pertaining to the samples that are available after use by the Study to address core hypotheses:

- Given that there are going to be stored biospecimens and environmental samples and given that there will be proposed adjunct studies for other uses of the remaining samples, what criteria and methods should be recommended for the Study to consider for the use of these scarce finite resources?
- By what process should these decisions be made?
- What process should be used for continual scientific review of the research plan?

The subcommittee proposed three overarching principles for the use of banked specimens for adjunct studies:

- Adjunct studies should be important, making maximal contribution to the public health of children. Although the Study's goal is to contribute to the overall public health, proposed adjunct studies of competing local interest will be considered.
- Use of samples by adjunct studies will need to be weighed favorably against the future potential value of samples. If an adjunct Study is approved that requires access to archived samples, those samples would not be available to be used for other adjunct studies or other expansions of the protocol.
- Samples should only be used if that use is consistent with the consent process and the spirit of the Study.

The subcommittee proposed four major guiding principles for the selection of adjunct studies. Highest priority should be given to adjunct studies that:

- Offer new and better ways to answer a core hypothesis or hypotheses
- Allow expansion of a core hypothesis or hypotheses based on analyses completed to date
- Take maximum advantage of unique characteristics of the Study (for example, depth of variables, large representative sample of United States) and are a good fit with the Study.
- Allow the same analysis to answer more questions and provide a "maximal return on investment."

The subcommittee proposed additional relevant but less important principles for the selection of adjunct studies. Adjunct studies should:

- Be national in scope and used for international comparisons
- Require a large *n*

- Be a small enough *n* that it can be easily accommodated or replicated with another subsample
- Be a quality control substudy (for example, stability of samples over time)
- Meet other needs of an agency or sponsor.

The proposed process for selection of adjunct studies includes complementary reviews by a Sample Oversight Group and an Adjunct Study Review Group. The Sample Oversight Group would evaluate the issues regarding the specimens (for example, amount available, amount requested, good use of the samples). The Adjunct Study Review Group would examine the quality and actual purpose of the adjunct study. These two groups would provide feedback to the Program Office. After a proposed adjunct study was approved by the Program Office, there would be subsequent, and more rigorous, scientific review by potential funders of the study if external funding is sought. The subcommittee was concerned about rigorous scientific review of proposed adjunct studies that were privately funded.

The subcommittee recommended the following review process for the selection of adjunct studies that would use stored samples:
- Scientific review and sample availability review should be conducted within the study.
- Reviewers should include outside experts, "inside" experts (for example, Study Center principal investigators [PIs]), and ad hoc reviewers based on scientific review expertise needed.
- Reviews should be timely.

With regard to issues related to continued review of the research plan, the subcommittee recommended the following:
- Research plan review should include continued involvement of the NCSAC.
- The Study should create a scientific review committee (with input from Study Center PIs) that would include interested NCSAC members as well as other researchers.
- The Study should facilitate public input, including input from the scientific community.
- The Study should reconsider development of a detailed research plan in 3-year blocks but should have a longer term vision beyond these blocks and plan accordingly.

NCSAC Discussion/General Discussion

- In response to a question from Dr. DuPlessis, Dr. Scheidt explained that the National Academy of Sciences has been contracted for a single overarching review of the entire research plan. Although the Academy could conduct future reviews, the process is expensive and slow and is not required for the 3-year reviews required by OMB. Allen Dearry, Ph.D., commented that periodic review by the Academy would be worthwhile and would lend public credibility and accountability to the research plan.

- Dr. Lebowitz proposed that the research plan review process be standardized in some way. Review of the protocol could also be standardized and could benefit from public input and comments from outside scientific experts.

- In response to a question from Dr. Levin, Dr. Schonfeld noted that the amount of samples collected (for example, the amount of blood drawn) is the amount anticipated for use by the

Study for the measures already proposed. Although the Study will not bank large amounts of samples, there will be limited amounts of extra samples. Dr. Scheidt clarified that the Study is obligated to preserve samples for potential future studies. Many core hypotheses require specimens to be available near the end of the Study.

- Given that the Study's IMS will have an inventory-tracking system for stored samples, Dr. Levin proposed that inventory information be made available to potential researchers before they propose adjunct studies. Potential researchers will know beforehand how much of a particular sample is available.

- Dr. DuPlessis said the Study must address financial disclosure and conflict of interest issues of outside reviewers who serve in an ad hoc capacity on the Sample Oversight Group and Adjunct Study Review Group.

Recommendations

The Scientific Review Subcommittee recommended that the NCSAC accept the three overarching principles for the use of banked specimens for adjunct studies and the four major guiding principles for the selection of adjunct studies that will use banked specimens:

- Offer new and better ways to answer a core hypothesis or hypotheses
- Allow expansion of a core hypothesis or hypotheses based on analyses completed to date
- Take maximum advantage of unique characteristics of the Study (for example, depth of variables, large representative sample of United States) and are a good fit with the Study.
- Allow the same analysis to answer more questions and provide a "maximal return on investment."

- The Scientific Review Subcommittee recommended that the process for selection of adjunct studies include complementary reviews by a Sample Oversight Group and an Adjunct Study Review Group. The complementary reviews would involve requests to access the samples as well as the quality of the proposed study. These two groups would provide feedback to the Program Office. Rigorous scientific review will be required to determine a proposed adjunct study's merit before stored samples would be released. Reviewers should include outside experts, "inside" experts (for example, Study Center PIs), and ad hoc reviewers based on scientific review expertise needed.

- The Scientific Review Subcommittee recommended that there be a continual ongoing review of the research plan. Reviews would occur at least every 3 years and include longer range evaluations. Interested members of the NCSAC will review drafts of the revised research plan as part of the ongoing review process. The interested members can comprise an NCSAC subcommittee or can serve as individuals on an ad hoc basis. Ongoing review of the research plan should be relatively inexpensive (that is, less expensive than the National Academy of Science review), timely, and "external" but should include experts who are familiar with the Study.

Day 2: Joint NCSAC and Steering Committee Session

Welcome and Introductions

Dr. Scheidt

Dr. Scheidt welcomed the attendees to the second day of the 17th NCSAC meeting. In particular, he welcomed NCSAC members, PIs and co-PIs from the new Study Centers, and other members of the Steering Committee. The purpose of this joint session was to familiarize the NCSAC and Steering Committee with each other and to further familiarize these two entities with the Study's progress. The Study's promotional video was shown.

Update on the National Children's Study: Study Director's Report

Dr. Scheidt

Dr. Scheidt provided an update on the Study's status. In 2007, Congress appropriated $69 million for the Study. This was the first appropriation specifically for the Study. For fiscal year 2008, there are no funds for the Study in the President's budget. However, the full House and Senate mark-ups of the President's budget include $110.9 million for the Study. At this time, the outlook for the Study is relatively good, thanks in large part to the many individuals and groups who have worked so hard to make the Study a reality. In addition to the funding, the second major event for the Study was the awarding of contracts for 22 Study Centers and 26 Study Locations in Wave 1. In an effort to make the sample more representative, a small procurement is planned to target a few locations to supplement the current Wave 1. Other planned upcoming procurements are for Wave-2 centers and locations, the repository, and laboratory (or laboratories) for environmental samples and biospecimens—all pending future funding.

Dr. Scheidt reviewed the Study's governance and management structure and described the following key entities: ICC, NCSAC, Program Office, Steering Committee, Coordinating Center, and Data Safety Monitoring Committee, which is not yet constituted. Over the past year or so, the role of the ICC has shifted from planning to broad oversight of the Study's major activities. The NCSAC, which was chartered in 2002, has continued to review Study activities and provide advice to the director of NICHD and the Study Director. The NCSAC meets two or three times a year. The Program Office, which was established in 2003, provides the day-to-day scientific and operational management of the Study. The Steering Committee was formed shortly after contracts were awarded for the initial seven Vanguard Centers. The Steering Committee is composed of Vanguard and Study Center PIs and co-PIs, as well as federal scientist representatives from the ICC and Program Office. The Steering Committee is responsible for the primary scientific deliberations about the conduct of the Study. The Coordinating Center, which was established when the Vanguard Centers were, provides data management capability and overall clinical coordination of the Study Centers. The Data Safety Monitoring Committee will monitor data and give advice based on Study findings.

Because of the major changes in Study activities and funding, the Program Office has been organizationally relocated directly under the Office of the Director, NICHD. The Program Office currently has 11 federal staff members. The Program Office is actively recruiting for Study

Center project officers; scientific experts for the protocol, implementation, and analyses; and repository and laboratory project officers.

Broad scientific review of the proposed plans and protocols for the Study is extremely important. These reviews have been conducted by a variety of sources. The research plan was first reviewed by the ICC and then by the NCSAC. From June to September 2007, the research plan was posted for public comment. These comments are still being compiled and undergoing review. The research plan is currently being reviewed by scientists at EPA, CDC, NICHD, and NIEHS. In April 2007, the Study contracted with the National Academy of Sciences to peer review the research plan. The review is being conducted by the Academy's Committee on National Statistics; Board on Children, Youth, and Families; and Board on Population Health. Study representatives met with the review panel in September to address the panel's questions and concerns and provide additional documentation. The panel's second meeting is in November. The panel will issue a preliminary report in January or February 2008; the final published report is due in April 2008.

The Study constitutes a key step in crossing the frontier of health challenges for children in developed countries. The Study will be poised to answer important questions about the possible effects of various environmental exposures as well as possible environmental causes and contributions to various child conditions and diseases. The Study offers a key step in the application of modern genomics to human health. It will provide an unprecedented resource for child health research. However, there have been a number of challenges to this bold initiative, including funding, reconciling the diverse scientific interests, and sampling strategy. Several lessons have been learned so far: (1) Broad input and inclusion is messy and inefficient but essential for planning a large multipurpose research project; (2) defining hypotheses is important for scientific credibility and for planning; and (3) research organizations will respond to create strong innovative centers to conduct the Study.

With regard to potential threats, funding is an ever present overriding challenge in planning and managing a costly large cohort study. High recruitment and retention with this sample and approach are unproven, vulnerable, and critically important. The large size and complexity of the Study may overwhelm it no matter what happens. It is unknown whether the government can respond with necessary infrastructure and support. Finally, consents, acceptance, and approvals (for example, from OMB and IRBs) are major challenges.

Dr. Scheidt finished his presentation by briefly reviewing media activities for the announcement of new Study Centers, media responses to this announcement, activities and events since the last NCSAC meeting, and upcoming symposia and conferences that Study representatives will attend.

Introduction to the New Study Centers and Locations: Session 1

Brookings County, SD, and Yellow Medicine, Pipestone, and Lincoln Counties, MN (BYPL). This Study Location is large (2,555 square miles), sparsely populated (21 persons per square mile), and very rural. In 2003, there were about 9,000 women age 18–36. In 2006, there were 583 total resident births, with about half occurring outside the four counties. The Study

Location has a relatively stable population, a strong sense of community, and diverse communities. About 96 percent of the population is non-Hispanic White. Median household income is about $34,000. Challenges to the study in this location include the travel distances, low population density, inclement weather, and working with four county health departments and two state health departments. South Dakota State University with Children's Medical Center of Cincinnati and the University of Cincinnati comprise the BYPL Vanguard Center for this location.

Salt Lake County, UT. This Study Location is urban high desert. The population is relatively young (median age of 30.5), and families are generally large. In 2006, this county had a total population of 978,700, about 19 percent of whom were women age 18–44. The population density is 1,211 per square mile. The birth rate is relatively high (19.4/1,000); 22 percent of births are to Latinas. Median household income is $52,900. About 85 percent of the population is White; about 15 percent is Hispanic or Latino (of any race). Environmental challenges include 11 National Priority ("Superfund") Sites and 3 Brown Field Projects. Air quality is compromised by the "stagnant bowl" effect. The county has a unique disease surveillance system. The University of Utah is the Vanguard Center for this location.

Cache County, UT. This Study Location is a very rural, high-altitude, desert region. The population is relatively young (median age of 24.6), and families are generally large. In 2006, the total population was 98,662, about 23 percent of whom were women age 18–44. The population density is 88 per square mile. The birth rate is relatively high (23.3/1,000); 11.5 percent of births are to Latinas. All births are linked to the Utah Population Database. Median household income is $52,900. About 94 percent of the population is White; about 9 percent is Hispanic or Latino (of any race). Ethnic, cultural, and religious considerations include a fearful and distrusting undocumented community due to a 2006 immigration raid. Environmental challenges include winter inversions, with high levels of particulate matter, and ongoing drought conditions. The University of Utah is the Vanguard Center for this location.

Honolulu County, HI. This Study Location is predominantly metropolitan. It has a population of 905,266 living in a 600-square-mile area. The population is racially diverse: 47 percent Asian; 23 percent Caucasian; 19 percent mixed, predominantly Hawaiian; and 9 percent Native Hawaiian or Pacific Islander. The median income is about $51,500, with 10 percent of the population living below poverty. There are about 13,000 births per year. Involvement of community leaders and advocates is crucial to the success of the study in Honolulu County. At least 21 different languages are spoken in the county. Because the population is racially integrated, determining race and ethnicity will be challenging. Assessing diet will also be challenging. The diet of Native Hawaiians is 80 percent complex carbohydrates and 12 percent protein. About 80 percent of the Filipino diet originates from Spain. This location's Study Center is led by the University of Hawaii at Manoa and includes Kaiser Permanente; Johns Hopkins University; and University of California, Irvine.

Marion County, WV. This largely rural county has a total population of 56,598, with 183 individuals per square mile. The county has a history of mining and farming, and it has two Superfund sites, both with coal-tar waste. The county ranks 10th in the state for water toxicants. The population is 95 percent White/non-Hispanic. In 2005, there were 635 live births. About 26

percent of households have children younger than age 18. Of the households with children, 21 percent are below the poverty level. The median household income is $28,626. Based on national comparisons, Marion County has more families in poverty, more individuals with less than a high school education, lower rates of college education, and lower median household incomes. Recruitment will target all women in the county. Among county residents, there is extreme apprehension for outsiders. The Allegheny Consortium (University of Pittsburgh and University of West Virginia) is the Study Center for Marion County.

Westmoreland County, PA. This largely rural county has a total population of 367,635, with 361 individuals per square mile. It has a history of farming, railroads, and mining. The population is 96 percent White/non-Hispanic. There were 3,367 total live births in 2005. About 5 percent of households have children younger than age 5. Of the households with children, 11 percent are below the poverty level. The median household income is $43,323. Community interest will be developed through messages of study importance, descriptions of incentives, and study materials that clearly describe the purpose of sample collections and procedures. Community ownership and connection will be developed through advisory committee representation, partnership with providers, monthly telephone calls, and clinical referrals when needed. The Allegheny Consortium (University of Pittsburgh and University of West Virginia) is the Study Center for Westmoreland County.

Hinds County, MS. Mississippi is the fourth most rural state in the nation. It has a population of 2.8 million, 37 percent of which are African American. Half of the state's African Americans live in rural areas. African Americans in Mississippi are at an increased risk of dying prematurely, developing major chronic diseases, and experiencing poorer health care compared with other ethnic groups. The state ranks poorly on many health indicators; for example, it has the highest percentage of deaths from cardiovascular disease (30 percent above the U.S. rate) and the highest prevalence of diabetes and obesity. The infant mortality rate in Mississippi is 3 times higher than the national average, and African-American infants are 2.7 times more likely to die before age 1 than White infants. The higher infant mortality rate in Mississippi is due to prematurity, and low birth weight is 10 times higher among non-Whites than Whites. The University of Mississippi is the Study Center for this location.

New York City (Queens), NY. Queens is one of five boroughs of New York City. In 2000, the population was 2,229,379, living in 112.2 square miles. Queens is the most ethnically diverse county in the United States; 152 different languages are spoken. About 46 percent of its residents were born outside the United States, coming from more than 100 countries. About 52 percent of its residents speak a language other than English at home (45 percent Spanish). Of the babies born in Queens, 71 percent have foreign-born mothers. About 24 percent of Queens' residents receive some sort of public assistance; about 15 percent live below the poverty level. Community engagement will include meetings with and presentations to community organizations, borough leadership, health care providers, and hospitals. The Queens Vanguard Center is a consortium led by the Mount Sinai School of Medicine and includes Columbia University Mailman School of Public Health, New York City Department of Health and Mental Hygiene, University of Medicine and Dentistry of New Jersey, and Columbia University Department of Obstetrics and Gynecology.

Nassau County, NY. Nassau County is located on Long Island and is contiguous with Queens. It is a largely suburban county. In 2000, it had a population of 1,334,544. About 23 percent of county residents speak a language other than English. The population is significantly older than it was 20 years ago, and it is becoming far more ethnically, racially, and economically diverse. The county is the richest county per capita in New York State, with a median income of $78,762, but there are pockets of communities in significant poverty. There are about 16,000 births per year. The Nassau County infant mortality rate (4.9/1,000) is lower than both the national rate (7.0/1,000) and the New York State rate (5.9/1,000). Within the county, there are disparities among the 3 hospitals and 56 villages. Community engagement activities to date include regular conference calls with New York State, Nassau County, and New York City departments of health. The New York–New Jersey Study Center is a consortium led by Mount Sinai School of Medicine that includes Columbia University College of Physicians and Surgeons and School of Public Health, University of Medicine and Dentistry of New Jersey, Environmental and Occupational Health Sciences Institute, and Battelle Memorial Institute.

King County, WA. King County is the 13th most populous county in the United States and the most populous county in Washington. The county encompasses a large (2,000 square miles) and geographically diverse region that includes urban, coastal, alpine, and agricultural areas. In 2006, the population was about 1,835,300; the population density is about 917 individuals per square mile. In 2005, there were 22,680 births to county residents. The Pacific Northwest Center for the National Children's Study will implement the Study in King County. The Study Center is a consortium of the University of Washington (Schools of Medicine, Public Health and Community Medicine, and Nursing), Fred Hutchinson Cancer Research Center, and King County Public Health Department.

Bexar County, TX. This Study Location is in South Texas. San Antonio is the county seat. In 2000, the population was 1,392,931; the population density was 1,117 individuals per square mile. Of the 489,000 households in the county, about 36 percent have children younger than age 18. About 29 percent of people in the county are younger than age 18. The racial/ethnic composition includes 69 percent White (Hispanic and non-Hispanic), 7.2 percent Black, 1.6 percent Asian, 0.8 percent Native American, 0.1 percent Pacific Islander, and 17.8 percent other. About 16 percent of the county's residents live below the poverty line. Challenges for individual participants include high percentages of Medicaid births, single mothers, and late prenatal care. Organizational challenges include a competitive health care marketplace, neighborhoods not linked to doctors or hospitals, and fragmentation of care. The Study Center for this location is a consortium led by the University of Texas Health Science Center at San Antonio. The consortium includes University Health System, Christus Santa Rosa Hospital System, Metropolitan Health District, independent school districts, and a variety of community organizations.

The National Children's Study Community Engagement Panel

Juanita Sims Doty, Ed.D., Senior Outreach Advisor, NICHD, NIH, DHHS

This panel was convened to discuss the study's community outreach and engagement (O&E) efforts thus far and identify areas of future efforts. Dr. Doty explained that the Study, the director of NICHD, and other NICHD leadership place a high value on community engagement and

recognize the importance of community engagement to the success of the study. In addition, the NCSAC has emphasized the importance of community O&E, which is critical to successful recruitment and retention. The panel discussed not only what communities could do for the study but what the study could do for communities. The panel also discussed the level at which community leaders can, or will be able to, participate in the decision-making processes of the study. Dr. Doty served as the panel moderator.

The National Children's Study Efforts in Community Engagement

Kate (Costella) Winseck, M.S.W., Study Outreach and Communications Coordinator, NICHD, NIH, DHHS

Collaboration with communities can provide unique perspectives and a wealth of information that can be incorporated into study design and implementation. Community engagement can consequently enhance recruitment and retention of participants, help produce valid and meaningful results, and increase participant satisfaction. Because research questions require the same data collection across sites from the national sample, the study cannot follow a strict community-based participatory research model. The study will, however, address big public health issues that mesh with community concerns. The study's philosophy regarding community O&E was made clear in the criteria stated in the requests for proposals for the vanguard and Study Centers.

The study's community O&E efforts will provide information to participating communities; enlist support of state, regional, and local entities; identify potential community-specific barriers to recruitment and retention; and establish and maintain a firm foundation for successful recruitment and retention of study participants and associated data collection activities. Community O&E helps ensure an ethical approach to the study as well as a better understanding of the study by individuals and the larger community. Community members can voice the local perspective which can be helpful to researchers as they navigate the uniqueness of each community and engage local media.

To date, the study has conducted a variety of outreach activities at both national and local/county levels, including focus groups, consultations, workshops, tools development, and media outreach. Many national organizations have been actively involved in promoting and supporting the study. The Vanguard Centers have been conferring with community advisory boards (CABs), conducting needs assessments, planning community engagement, and engaging health care providers.

Current issues and activities include bridging national and local efforts (for example, National Association of County and City Health Officials), developing new illustrations and design themes for public materials, revising the national Web site, branding study materials with local information, and standardizing outreach materials across Study Centers versus Study Center customization.

Overview of the Community Outreach and Engagement Team

Chris Cronk, Sc.D., Co-PI, Waukesha County, Wisconsin, Vanguard Center; Medical College of Wisconsin

The O&E Team (originally the Recruitment and Retention Team) was formed in April 2006 by the Program Office and Coordinating Center. The team's agreed-upon charge is to ensure that participant and community interests, perspectives, and needs affecting recruitment and retention are represented and used in planning and implementation of the study. Team members and contributors include representatives from the Vanguard Centers, the Program Office, the Coordinating enter, lead federal agencies and two community representatives from the Steering Committee. The team has gathered, interpreted, and communicated community perspectives, developed documents and outreach materials, and reviewed proposed study processes. These efforts have produced a variety of products and documents, a materials and activities database, and a library of conference presentations. One of the key documents is the Community Outreach and Recruitment and Retention Overview (also called "Overarching Document"), which presents the guiding principles and practices for community O&E.

Although there have been successes thus far in implementing the O&E charge, challenges remain. The Vanguard Centers have formed and are using CABs with a range of purposes and functions. However, not all CAB functions have been meaningfully implemented. All Vanguard Centers shared plans and developed recommendations for community needs assessments. However, few needs assessments have been completed due to lack of approvals (for example, from OMB and IRBs). The Vanguard Centers improved materials by providing input on issues such as cultural propriety and readability. The study's segment announcement policy presents a unique issue of balancing community outreach needs and confidentiality. The Vanguard Centers will be challenged to develop and implement specific policies that create a dynamic tension between research and community orientation.

The O&E has developed several guidance documents to share ideas and provide information about key community-related issues potentially useful for other working teams and Study Centers. Topics include health care, community O&E, segment characterization, noncash incentives, and translation recommendations. Additional guidance documents are in progress. Formats of guidance documents are primarily spreadsheets/grids, statements, and bullet points. Recent O&E Team discussions and efforts include approaches to sensitive data, community input on study operations, and barriers to full community engagement.

Vanguard Centers O&E Organization, Activities, and Testimonials

Suzette Baez VanderBeek, M.P.H., Site Coordinator, Queens Vanguard Center; Mount Sinai School of Medicine

Ms. VanderBeek provided overviews of O&E organization, activities, and testimonials for the seven Vanguard Centers. Key aspects of these Vanguard Centers' community O&E are as follows:

- **Queens, NY.** Team leaders are from the Mount Sinai Medical Center and the New York City Department of Health and Mental Hygiene. The community engagement team has consulting agreements with several community partners and includes the Northern Queens Health

Coalition, Clergy United for Community Empowerment, and the Addabbo Family Health Center. The team has met with the borough president and borough community boards. A unique invitation event was held in November 2006.

- **Waukesha County, WI.** Three entities provide input to the core management team: a community outreach team, a medical outreach team, and a CAB, which has been built to include a broad range of expertise, perspectives, and community connections. Medical outreach to obstetricians, family practitioners, and pediatricians has included meetings with individual practices and physicians, development of a "Practice Partners" plan, and meetings with community hospital IRB chairs and administrators.
- **Orange County, CA.** The Orange County outreach organization includes the Children and Families Commission, a community outreach team, a health professional and hospital outreach team, and a CAB. There is a shared responsibility among local partners. The community outreach team meets biweekly, maintains a contact database and conducts media monitoring, gathers quantitative and qualitative information on segments, and meets with local officials and school readiness coordinators.
- **BYPL Counties, MN/SD.** Community engagement has involved state, tribal, and city governments; hospitals, clinics, and health care providers; cooperative extension and public health agencies; county social service agencies; preschools and schools; community-based organizations; media partners; and major employers.
- **Montgomery County, PA.** The community outreach team for this Vanguard Center includes the Montgomery County Health Department, Montgomery County Health Collaborative Boards, and a CAB. Ongoing activities include weekly conference calls, "windshield surveys," regular CAB meetings, attendance at county health collaborative board meetings to update the community about the study and gain community response to study plans, and clinic site visits.
- **Salt Lake County, UT.** Key community members and officials include mayors and city managers, who are the gateway to identifying ethnic communities, churches and other faith-based organizations, community organizations, and land-use history. Other members are neighborhood watch coordinators, city councilpersons, and Latter-day Saints stakeholders. The goal is to have these key community members serve as study advocates in their communities.
- **Duplin County, NC.** This Vanguard Center uses a community involvement model that provides multiple avenues for community O&E. The community outreach team is led by a community advisory group that receives input from key stakeholders and persons of influence. The community advisory group meets bimonthly, directs feedback and access to study investigators and staff, and is the "face of the study" to the community. The community advisory group has self-governance with a chair and vice-chair.

Report from the Director's Office, NICHD

Duane F. Alexander, M.D., Director, NICHD, NIH, DHHS

Dr. Alexander thanked the NCSAC for its continuing service and welcomed Vanguard Center representatives and PIs from the new, Wave-1 Study Centers. The number of people involved with the study has grown significantly over the past year or so and will continue to grow as new Study Centers are brought on board and the study is implemented in all 105 locations. Dr.

Alexander congratulated the new Study Centers for being selected to join the study, which will require enthusiasm and the capacity for hard work.

Dr. Alexander acknowledged Dr. Fleischman for his help, guidance, and dedication to all aspects of the study. Dr. Fleischman has been involved with the study since its inception and has led the work in informed consent and ethics. As a pediatrician, Dr. Fleischman has knowledge of all aspects of children's health and development, which has been a valuable asset to the study. More important, he has served as chair of the NCSAC. Although Dr. Fleischman has left the New York Academy of Medicine to join the March of Dimes as Medical Director and Senior Vice President, he will continue as NCSAC chair and intermittent study advisor. Dr. Alexander thanked Dr. Fleischman for all he has done for the study.

Much work has been done to get the study to where it is today, but an enormous task lies ahead, particularly in 2008. The study received $69 million in funding in 2007, and was able to award contracts for the Vanguard Centers and the Wave-1 Study Centers and begin planning for the next waves of Study Centers. In the next phase, the Vanguard Centers will begin the pilot study and start recruiting participants in summer 2008. The new Study Centers will be integrated into study operations, including community O&E and recruitment activities, which will begin in 2009. As these activities ramp up, the study will solicit for and implement Wave 2 and prepare for Wave 3. Completing Wave 3 will bring the study to full capacity, including activation of all 105 locations. In addition, the study will implement laboratory and repository activities in 2009.

The study must continue community O&E and ensure that data handling is at full capacity. Reviews of the protocol and research plan must be included in 2009 activities. Completion of the National Academy of Sciences' review of the research plan is next. Because the study is so important, represents such an investment, and offers a one-time opportunity, reviews by expert advisors will help ensure that the study can be as good as possible with the resources available. The Program Office is currently recruiting additional staff. Dr. Alexander asked the meeting participants to recommend individuals—particularly those with prior federal government experience—who can provide expertise to the study.

Dr. Alexander reported that the $69 million appropriation was spent in fiscal year 2007. In the fiscal year 2008 budget, both the House and Senate included $110.9 for the study. Congress is still negotiating the final budget before submitting it to the President. Congress is supporting the study in other ways. A Capitol Hill briefing was held to announce the awards of the Wave-1 Study Centers. The briefing was cohosted by Congresswoman Doris Matsui (D-CA) and Congressman Chris Smith (R-NJ), both of whom have strongly rallied behind the study. Congressman Smith is particularly interested in the relationship of autism and environmental exposures. Dr. Alexander said that as people learn about the study, enthusiasm and support have been building around the country. For example, his recent presentation to the American Academy of Pediatrics was positively received.

Community Outreach and Engagement Subcommittee Report

Helen DuPlessis, M.D., M.P.H., Chair, NCSAC Community Outreach and Engagement Subcommittee; Harbor/UCLA Medical Center

The subcommittee addressed three questions:

- How can the study optimize community O&E at the new Study Centers?
- How can the study best use what has been learned from the Vanguard Center experience?
- To what extent can/should the study standardize community outreach efforts across sites to ensure scientific consistency?

The subcommittee identified the following themes:

- The study is not designed as community-based participatory research.
- The distinction between community engagement and community outreach may not always be appreciated, which results in misperception about the expected scope of O&E activities and tension in balancing the allocation of time, energy, and resources among different activities.
- The success of the study depends largely on the effectiveness of community engagement.

The subcommittee defined two terms:

- *Community outreach* is the provision to a specific population of education, information—and where appropriate, counseling and referrals—related to a specific service or activity.
- *Community engagement* is the process of working collaboratively with groups of people who are affiliated with or united by at least one common characteristic (for example, geography, culture, special interest, profession, similar situation, race/ethnicity).

To date, the study has focused on primarily on community outreach and communication—critical activities that overlap with community engagement but are somewhat subsumed under community engagement. However, outreach and communication are not sufficient to address community engagement needs and activities.

To optimize community O&E at the new Study Centers and learn from the Vanguard Centers' experience, the subcommittee recommended the following:

- The study should encourage completion of and access to the guidance documents.
- The O&E "Overarching Document" should be reviewed and approved by the O&E Team and the NCSAC.
- A learning collaborative model should be used to provide a structured approach to improving community O&E.
- The study should identify and provide technical assistance on community engagement.
- A mechanism should be put in place to monitor the effectiveness of community O&E.

With regard to standardizing community outreach (and engagement) efforts across sites, the subcommittee recommended the following:

- Community O&E principles should be standardized but allow flexibility.
- The principles should include the following:
  - Be clear about the purpose and goals of the study.
  - Build trust and cultivate key relationships in each community.
  - Become knowledgeable about the community.

  - Partnering is necessary for participation (health improvement).
  - Respect and be aware of the diversity in each Study Center and Vanguard Center population.
  - Mobilize the assets and develop the capacities and resources of the community.
  - Community O&E requires long-term commitment by the engaging organizations and partners.
- Expectations for O&E should be specified, including but not limited to the following:
  - Begin O&E activities early in the study process.
  - Identify key leaders (representing organizations with longevity) whose relationships should be cultivated.
  - Use "champions" who represent key communities.
  - Use paid staff who are representative of the diversity in the community.
  - Avoid excessive use of unpaid community volunteers.
  - Specify the charge to and functions of CABs.
- Study and Vanguard Centers should have flexibility to tailor efforts to community needs.
- Expertise in working with various cultures, races, and ethnicities should be located within each Study Location.

The subcommittee posed the following additional questions for NCSAC consideration:
- How can the community be incorporated into adjunct studies?
- How can community concerns be incorporated into protocol implementation?
- How can/should community expectations be managed?

NCSAC Discussion and Recommendations/General Discussion

- Mr. Quackenboss clarified that, by definition, adjunct studies involve a portion of the Study cohort, utilizing individually or in combination, any of the following: the Study participants, their biospecimens, their environmental samples. Community-level studies of data already collected on environmental factors or exposures that are community concerns are not adjunct studies. Alternative funding sources should be sought for such community-level studies.

- Michael Bracken asked about the tension between the huge effect of working with communities and families (that is, the Hawthorne effect) and the evolution of communities and change in populations such that the study's families are no longer representative. Dr. Fleischman explained that the NCSAC has been discussing this issue from its first meeting, and the Program Office, ICC, and other study planners have addressed the issue directly. The study's commitment to community O&E is both the right thing to do and the smart thing to do. The Hawthorne effect has been acknowledged, but the study's ultimate success still depends on community O&E, which will be continuous. Limits to community O&E will be dictated by the research plan. However, the process by which the study implements the research plan is subject to local flexibility to meet the needs of communities. It was further acknowledged that the Hawthorne effect cannot be avoided, but the study will be able to collect objective exposure data that will have been collected in real time on each child.

- Jonas H. Ellenberg, Ph.D., asked whether the NCSAC has considered methods for measuring the success of community O&E, for example: Is the study recruiting as expected? Is the study

retaining participants as predicted? How will the study evaluate the success of these activities? Dr. DuPlessis replied that the subcommittee recommended that a mechanism be put in place to monitor the effectiveness of community O&E efforts. The subcommittee discussed certain indicators but did not make any recommendations other than that the topic should be further addressed by either the O&E Team or other working group.

- Bonny Specker, Ph.D., explained that soon after its contract award, the BYPL Vanguard Center began informing the media and engaging communities. At this time, the Vanguard Center is experiencing a "backlash" from too much community engagement. The media and communities are tired of being engaged, and both are asking when the study will begin. Dr. Specker said the timing of community O&E is very important. She cautioned against engaging communities too early in the process.

- Neil Halfon, M.D., M.P.H., commented that the trajectory of the study's community O&E should be improving over the enrollment period. The study should not only be measuring effectiveness but should be developing and applying continuous improvement tools. There should also be continuous improvement of the tools.

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

01/25/08

Date

Alan R. Fleischman, M.D.
Chair
National Children's Study Federal Advisory Committee