

**National Children's Study  
Federal Advisory Committee 21st Meeting  
May 26–27, 2009  
Hilton Washington DC/Rockville Hotel and Executive Meeting 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](#) (HHS) (including the [Eunice Kennedy Shriver National Institute of Child Health and Human Development](#) [NICHD] and the [National Institute of Environmental Health Sciences](#) [NIEHS] of the [National Institutes of Health](#) [NIH] and the [Centers for Disease Control and Prevention](#) [CDC]), and the [U.S. Environmental Protection Agency](#) (EPA).

**Day 1**

**New Members: National Children's Study Orientation**

Ten new members joined the National Children's Study Advisory Committee (NCSAC) in May 2009. They are:

- Ellen Wright Clayton, M.D., J.D.
- Elena Fuentes-Afflick, M.D., M.P.H.\*
- Bruce D. Gelb, M.D.
- Michael Furman Greene, M.D.\*
- Patricia O'Campo, Ph.D.
- Joan Y. Reede, M.D., M.P.H., M.B.A.
- Everett Rhoades, M.D.
- Melissa Tassinari, Ph.D.
- Thomas Ten Have, Ph.D., M.P.H.
- Michelle A. Williams, Sc.D., S.M., M.S.

*\*Did not attend*

Their orientation included an overview of the National Children's Study (the Study), a brief review of the Federal Advisory Committee Act (FACA), an overview of protocol development, and updates on the pilot study and Study Center activities.

**Welcome from the Chair of the NCSAC**

*Alan R. Fleischman, M.D., NCSAC Chair; Medical Director and Senior Vice President, March of Dimes*

Dr. Fleischman welcomed the NCSAC members, ex officio members, and other participants to the 21st meeting of the NCSAC. He reviewed the functions of federal advisory committees as defined in the FACA and the roles and responsibilities of the NCSAC. The NCSAC provides specific advice and recommendations to the NICHD Director, the Study Director, and the Interagency Coordinating Committee (ICC) regarding general direction and conduct of the Study, ethical issues, community engagement and consideration, and hypotheses and other

considerations of the Study. In addition, the NCSAC responds to specific requests for advice and recommendations by the NICHD Director, the Study Director, and the ICC.

Dr. Fleischman reviewed the minutes of the 20th NCSAC meeting on November 5–6, 2008.

Discussion topics and NCSAC recommendations were as follows:

- Informed consent
  - Informed consent brochures should be tested with potential participants.
  - Institutional review boards (IRBs) should be convened to develop consensus on wording on informed consensus materials.
- Data access
  - Study investigators should have a preferred role in accessing Study data.
  - The Study should reveal medically important findings and explain this clearly in the informed consent materials.
  - The Study should develop criteria for revealing findings to individuals and communities.
- Vanguard and Wave 1 activities
  - Participation in the Study need not remain confidential.
  - There is a need to track reasons for refusal to enroll and better understand what is motivating people to enroll or not enroll in the Study.
- Autism as an outcome
  - Real-time results from questionnaires should be shared with participants, and information about autism should be also shared.
  - The autism expert panel would benefit from broader expertise.
- Preterm birth as an outcome
  - There is a need for a better understanding of the relationship among many factors such as stress, depression, physical abuse, and substance abuse on adverse outcomes of pregnancy.
  - The NCSAC recognizes that cost constraints will limit measures, visits, and outcome assessments.
- Processes for scientific and protocol development
- Development of data collection protocol—working teams
- International Child Cancer Cohort Consortium.

### **Program Office Report**

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

**Funding and Outlook.** For fiscal year 2007, the Study received \$69 million, and for fiscal year 2008, it received \$110.9 million. Up to \$192.3 million is available for fiscal year 2009. The projected need for fiscal year 2010 is \$194.4 million.

**Program Office Staffing.** Geneticist Carol Kasten, M.D., joined the Program Office on a full-time basis on September 29, 2008. She is on detail from the National Cancer Institute. Julia Slutsman, Ph.D., joined the Program Office on January 1, 2009, as Senior Bioethicist. Interviews for a Senior Community Engagement Leader position are underway. Project officer/scientist positions are on hold pending Wave 3 procurements.

**Procurements.** In September 2008, contracts were awarded to 27 Study Centers for 39 new Wave 2 Study locations. Twelve of these contracts were awarded to new Study Centers. The awards were announced on October 3 and included a briefing upon their request to the Congressional Study Interest Group, a media telebriefing, and a stakeholders' telebriefing. In 2009, contracts will be awarded for (1) a biospecimens and samples repository and (2) a laboratory for analyzing unstable environmental samples. The Study has an interim repository through an existing NICHD contract. Final negotiations are under way for the Study repository, with contract award by July. A short-term interim subcontract for an environmental laboratory is in place through the Data and Clinical Coordinating Center. The request for proposals for the environmental laboratory is being revised for posting by June, with contract award in 2010. There will be no solicitations for Wave 3 locations in 2009.

**Cost and Budget Issues.** On March 23, 2009, NICHD Director Duane Alexander, M.D., released a statement regarding the Study's cost and budget issues. The statement explained that the initial cost projections in 2001–2002 were rough and conceptual. They were not specific and included direct costs only. There was no accounting for inflation. Subsequent sampling and various other protocol decisions increased costs. There was no planning or discussion with the Office of Management and Budget (OMB), HHS, and NIH when the Study was not specifically funded in the President's budget. For fiscal year 2010, the prospects for inclusion of Study funding in the President's budget resulted in realistic budget planning that was not previously possible. For the fiscal year 2010 budget cycle, current estimates of options from \$3.4 billion to \$6.9 billion were presented to NIH leadership. A decision was made to incorporate a 1-year "pause" on implementing Wave 1 and Wave 2 locations to allow full evaluation of the Vanguard pilot study. The Vanguard locations will proceed as originally planned. Program Office staff will prepare cost projections for a "full protocol" (pilot protocol expanded to all Study locations) and a "core protocol" that is revised based on the Vanguard experience. The main Study protocol will be revised based on Vanguard Center input and pilot study experience over the next year. The revised protocol will be reviewed for scientific merit and ability to address directives in the Children's Health Act of 2000. In January 2011, Wave 1 locations will begin recruitment and enrollment activities according to the new protocol.

**Pilot Study.** There are seven Vanguard locations, which are divided into two groups. Group 1—Duplin County, NC, and Queens, NY—began data collection in January 2009. Group 2 began data collection in April 2009. Group 2 locations are Montgomery County, PA; Lincoln, Pipestone, and Yellow Medicine counties, MN, and Brookings County, SD; Orange County, CA; Salt Lake County, UT; and Waukesha County, WI. The second stage of sampling, which involves selection of geographic areas (segments) within counties, was completed in November 2007. The listing of households in selected segments (about 7,000–15,500 households per location) was completed in October 2008. Enumeration of residents in households began in January 2009 for Group 1 and in April 2009 for Group 2. About 8,000 households have been enumerated to date. The pilot study will screen about 3,000 potentially eligible women. Informed consent is currently administered only to women in the first trimester of pregnancy. Informed consent will eventually include the nonpregnant and high and moderate probability of pregnancy groups. With regard to data collection, first trimester home visits have begun. The Study's first birth is due at the end of July 2009.

**Working Teams.** The primary method for obtaining input on protocol development from the Study Centers is through working teams. There are 6 operational/overarching working teams (with 32 Study Center members) and 12 scientific domain working teams (with about 70 Study Center members). Each team includes a chair from the Program Office and a co-chair from a Study Center or the Data and Clinical Coordinating Center. There is a rotating membership for Study Centers. The working teams conduct general examinations of hypotheses and trajectory of measures in the existing protocol. They have made several specific recommendations that have led to protocol revisions. Two Wave 2 Study Center members will be added to each working team. The working teams will continue to work through the 1-year pause.

**Key Committees.** Since November 2008, the Steering Committee and Executive Steering Committee have expanded. A Data Access and Confidentiality Committee (DACC) has been established and is finalizing policies. An Adjunct Studies Review Committee has been established. It began receiving proposals in September 2008, and it held its first meeting in October 2008. A Specimen Oversight Committee has been established and held its first meeting in October 2008. An Independent Study Monitoring and Oversight Committee (iSMOC) has been established and will hold its first meeting in June 2009.

**Affiliated Planning Activities.** The Study is planning activities with a number of organizations, including Autism Speaks, the March of Dimes, the Society of Toxicology, the Teratology Society, the Special Olympics, and SPAN (Study of Puberty Across the Nation).

**NCSAC Recommendations.** The Program Office has addressed or is addressing in an ongoing manner all NCSAC recommendations from previous meetings.

### **NCSAC Questions, Comments, and Discussion**

- Dr. Rhoades noted that a possible source of bias would be the question of informed consent by pregnant women who are younger than 18 years. He asked whether such a woman can give consent for her child's participation in the Study. Dr. Scheidt said that in most states, a pregnant minor can give consent for her child, but the laws are state-specific. There is an inherent bias in the recruitment of teenage participants because women who are younger than 18 years and who are not pregnant are not eligible for the Study. The Study will, however, enroll pregnant teenage mothers through referrals from prenatal care providers.
- Helen DuPlessis, M.D., M.P.H., asked what types of formative research and assessments can be conducted during the pause period. Dr. Scheidt explained that the Study submitted two applications to the OMB. One was for a bank of hours to conduct formative research such as focus groups, small surveys, and methods development. The other application was for the pilot phase of the Study. Applications have recently been submitted to the OMB from several Vanguard Centers to conduct formative research during the pause, and other applications are being prepared. Wave 1 and Wave 2 Study Centers are not yet approved to carry out the Study because the protocol not been approved by the OMB.
- Ana V. Diez-Roux, M.D., Ph.D., M.P.H., asked what components and factors are driving the excess costs and what the process is for cutting costs. Dr. Scheidt said the main cost drivers

are data collection activities and the infrastructure. It is costly to send two people to conduct a home visit and spend half a day collecting data and to have follow-up visits to collect samples and specimens. The infrastructure for the many Study locations is also costly because each location requires an associated Study Center, with extensive facilities and personnel. Other cost drivers are the Study's sample size ( $n = 100,000$ ) and geographically based household screening approach. About 14,000 households must be contacted for every 1,000 live births. Modeling and cost simulations are being used to estimate the savings in a variety of scenarios (for example, deleting certain measures). The Vanguard Centers' experience will determine what approaches are feasible and where the protocol should be revised. Working teams will provide input to the cost-cutting process.

- Dr. Fleischman commented that the Study's original costs estimates were based on direct costs and did not include indirect costs.
- Carol Henry, Ph.D., said that when considering cost issues it is important to emphasize the Study's overall value and unique potential for understanding factors affecting health and development. Ultimately the Study will be a worthwhile investment because of the saving in health care costs. Dr. Henry asked whether cost savings of adjunct studies have been estimated. Dr. Scheidt said cost projections of adjunct studies have been made. Approaches for cutting costs include reducing the number of home visits and reducing the number of costly data collection activities. Reducing the number of home visits will reduce participant burden and may help with recruitment and retention.
- Dr. Clayton commented that there are many regulatory and ethical issues regarding teenage pregnancies and informed consent, and these issues can be complicated. She asked about the members of the DACC. She also asked whether the data repository is maintained by the federal government. She noted that the certificate of confidentiality is not always valid for data held by the federal government. Issues for protecting the confidentiality of data can be complicated. Dr. Scheidt said the data repository will be under contract to a nonfederal facility. Membership of the DACC is posted on the Study's Web site. Jennifer Park, Ph.D., a senior scientist in the Program Office, chairs the DACC.

### **Interagency Coordinating Committee Report**

*Marshalyn Yeargin-Allsopp, M.D., ICC Chair; Medical Epidemiologist, Developmental Disabilities Branch Chief, National Center on Birth Defects and Developmental Disabilities, CDC*

The ICC is composed of representatives from HHS (the NICHD, the NIEHS, and the CDC) and the EPA. The ICC oversees broad Study issues, promotes interagency collaboration, ensures that the mission of the Study is maintained over time, and ensures that Study goals reflect the scientific priorities of the NICHD, the NIEHS, the CDC, and the EPA. Each lead agency has an essential role to play in the Study, and the Study will play a role in fulfilling each agency's mission.

**The NICHD.** The Children's Health Act of 2000 directed the NICHD to conduct a national longitudinal study of environmental influences on children's health and development. As a

result, the Study will help fulfill two elements of the NICHD's mission: to ensure that every person is born healthy and wanted and that all children have the chance to fulfill their potential to live healthy and productive lives free from disease or disability.

**The NIEHS.** The NIEHS's mission is to reduce the burden of human illness and disability by understanding how the environment influences the development and progression of human disease. The Study presents an opportunity to synergize with other complementary efforts at the NIEHS (for example, the Exposure Biology Program/Genes, Environment, and Health Initiative and the Centers for Children's Environmental Health and Disease Prevention Research). Study hypotheses overlap with existing NIEHS research priorities and will provide future opportunities to capitalize on environmental and biological samples to better understand gene-environment interactions and epigenetic underpinnings of health and disease.

**The CDC.** The Study is relevant to the CDC's health impact goals to:

- Provide data to define the nature and extent of the health problems facing infants, children, and adolescents, including health disparities
- Provide new information regarding the impact of environmental and genetic factors on child health and development
- Evaluate exposure-outcome relationships in order to inform prevention research across the life stages
- Establish reference ranges to evaluate environmental chemical exposures in mothers, infants, and young children
- Assess effectiveness of public health efforts to decrease exposure to specific chemicals and known risk factors
- Translate public health research findings into best practices for communities.

**The EPA.** The Study will help the EPA to (1) assess the effects of environmental exposures on children's growth, development, and disease including the consequences of fetal exposures; (2) evaluate community-level cumulative risks; and (3) evaluate consequences and effectiveness of regulatory decisions. EPA is helping the Study examine possible exposure "validation" designs (for example, nested substudies).

**New Administration.** The ICC will lead the effort to inform the new administration about the Study. ICC members have briefed (or plan to brief) new agency leadership about the Study and the benefits of the Study to each agency with the goals of making the Study a cornerstone of the administration's health and environment policies, engaging the administration in promoting the Study to the American people, and improving coordination on children's health at the federal level.

**ICC Accomplishments in 2008-2009.** The ICC advised the Program Office on cost-saving measures, served on the working teams and committees, identified agency scientists to serve on working teams, served as liaisons between the ICC and Steering Committee and Executive Steering Committee, and represented the Study to the members' respective agencies and at scientific meetings.

**ICC Projected Activities for 2009–2010.** The ICC will continue to be the “big picture” face of the Study, participate in evaluation of the Vanguard pilot phase, and advise the Study Director and Program Office regarding cost-cutting measures.

## **NCSAC Questions, Comments, and Discussion**

- Michael D. Lebowitz, Ph.D., asked what the ICC is doing to raise money for the Study. Marshalyn Yeargin-Allsopp, M.D., explained that because they are federal scientists, ICC members cannot raise money. They can, however, work within their respective agencies to generate support and funding for the Study. She noted that the lead agencies funded the Study’s planning phase.

## **Obesity: Challenges and Opportunities**

*David S. Ludwig, M.D., Ph.D., Division of Endocrinology, Director, Optimal Weight for Life Program, Children’s Hospital of Boston; Associate Director, Clinical and Translational Research Unit; Associate Professor, Pediatrics, Harvard Medical School; Associate Professor, Nutrition, Harvard School of Public Health*

Dr. Ludwig addressed three questions:

- How will obesity affect the future health of the current generation of children?
- What are the biological, behavioral, and environmental determinants of body weight?
- What areas merit further investigation?

Since the mid 1980s, the prevalence of obesity in the United States has been increasing rapidly. Prevalence has increased in adults and children, with some ethnic groups (for example, African Americans and Hispanics) showing higher prevalence in certain age groups.

In adulthood, obesity reduces life expectancy and causes about 100,000 deaths per year. Excessive weight causes more than 300,000 deaths per year. Childhood obesity may decrease life expectancy by 2–5 years or more by 2050. There are many complications of childhood obesity, affecting the brain, heart and blood vessels, lungs, digestive tract, bones and joints, and hormones. There are psychosocial consequences as well. Adults who were overweight during adolescence complete fewer years of school (particularly women), have higher poverty rates (particularly women), and are less likely to be married (both women and men).

Investigators have assessed many variables in studies of the obesity epidemic, including genetic factors, early life influences, diet, environmental toxins, physical activity, and psychosocial considerations. Dietary changes have been dramatic and largely adverse. Many studies have focused on diet quality, including total energy intake and consumption of macronutrients, micronutrients, fatty acids, carbohydrates, sugar-sweetened beverages, and fast foods.

In general, conventional obesity treatments in adults have proven to be ineffective, and most pediatric obesity interventions result in small changes in relative weight or adiposity and substantial relapse. Dietary approaches focused primarily on macronutrient ratio have little evidence of efficacy. Alternative approaches focused on nutrient quality merit greater attention.

Studies of environmental toxins related to obesity have focused on several endocrine disruptors, including polybrominated diphenyl ethers (flame retardants), diethylstilbestrol, bisphenol A (plasticizer), heavy metals, solvents, organophosphate pesticides such as DDT, phthalates, dioxins, and polychlorinated biphenyls. These studies have shown the following:

- Bisphenol A at environmentally relevant doses inhibits adiponectin release from human adipose tissue explants.
- Daily exposure of rats to penta-BDE for 4 weeks significantly alters metabolism of isolated adipocytes.
- Tributyltin chloride (TBT) induces the differentiation of adipocytes *in vitro* and increases adipose mass *in vivo*.
- Lipophilic environmental contaminants accumulated in adipose tissue dysregulate gene expression profile.

Reduced physical activity has contributed to the obesity epidemic. Adolescents spend more than 6 hours per day in sedentary pursuits (television, computer, video games, and so on), less than 1.5 hours per day in any kind of physical activity, and only 12 minutes per day engaged in vigorous activity. In one study, among 16- to 17-year-old girls, half reported doing no physical activity of any kind outside of gym class. Alternative approaches that aim to increase physical activity throughout the day need to be considered.

There are several psychosocial considerations related to the obesity epidemic. A “toxic environment” has been created that emphasizes profit over public health. For example, the food industry spends \$12 billion each year to influence the eating habits of children, overwhelmingly for junk food. Food marketing to children has potential effects on diet quality. Other psychosocial considerations are stress, family structure, parenting practices, and communicable influences.

Dr. Ludwig concluded his presentation by describing a transgenerational perspective of the causes and outcomes of adult and childhood obesity. The obesity epidemic will have a catastrophic societal impact, increasing health care costs, decreasing economic productivity, increasing human suffering, and shortening life expectancy. The National Children’s Study is designed to improve our understanding of the etiology of obesity and holds great potential at improving obesity trends.

### **Childhood Obesity: What Can the National Children’s Study Contribute?**

*Sarah A. Keim, Ph.D., M.A., M.S., Associate Study Director for Operations and Logistics,  
National Children’s Study*

The Study has five priority outcome areas, one of which is obesity and diabetes. The Study has several strengths that facilitate the study of childhood obesity: large sample size (which facilitates the ability to assess gene–environment interactions), longitudinal design, repeated measures starting *in utero*, diversity of exposures, and clustered sampling approach. Five National Children’s Study hypotheses focus on obesity:

- Intrauterine growth restriction is associated with risk of central-body obesity and insulin resistance in offspring, independent of body mass index (BMI).

- Impaired maternal glucose metabolism in pregnancy is related to the risk of obesity and insulin resistance in offspring.
- Breast milk feeding compared with infant formula feeding is associated with lower risk of obesity and insulin resistance.
- Consumption of a high glycemic load diet in childhood is associated with obesity and subsequent insulin resistance.
- Geographic area of residence is associated with exposure to factors that increase the risk of obesity and decrease access to protective factors.

Challenges to studying childhood obesity include (1) burden and frequency of visits and (2) logistics and cost. Measures must be field-ready, field-able everywhere, and inexpensive.

The Study will use the following measures in pregnancy: International Physical Activity Questionnaire (preconception), time and activity (first and third trimesters), anthropometrics (preconception, first and third trimesters, maternal, and paternal), food frequency questionnaires (preconception, first and third trimesters), and biospecimens.

Fetal and child measures (to 1 year) will include fetal growth (second and third trimesters), anthropometrics (birth, 6 months, and 12 months), time and activity (6, 9, and 12 months), infant feeding questionnaires (1, 6, and 12 months), breast milk (1 month), and biospecimens.

### **Questions, Comments, and Discussion**

- Dr. Ten Have commented on the importance of collecting data on geographical differences in obesity, race/ethnicity, and socioeconomic status. Dr. Keim said this type of data will be collected in the earliest phases of the Study.
- Dr. Henry noted that because the biospecimens will be stored and not analyzed immediately, there will be delays in the reporting of findings from biospecimens. Dr. Keim said that information collected through questionnaires will be analyzed in real time.
- Carol Kasten, M.D., asked Dr. Ludwig to identify the three most optimal biospecimens (for example, DNA, RNA, hormones, and single nucleotide polymorphisms) and critical collecting times for genetic analyses related to obesity. Dr. Ludwig replied that there are no specific optimal biospecimens or collection times. Platforms such as metabolomics allow multidimensional assessments, and modern informatics can be used to elucidate some fundamental biologic principles.
- Janet Currie, Ph.D., commented that the presentations highlight the potential value of linking Study data with data from other sources. Long-term outcomes (for example, morbidity and mortality related to obesity) of Study participants could be linked to childhood environmental exposures.
- Marion J. Balsam, M.D., asked whether there are data about vegan or vegetarian diets and obesity. Dr. Ludwig said that there are no data on this topic for children, but there are adult data on

vegan diets and diabetes risk. There are some data on the effects of qualitative aspects of diet on blood pressure, cholesterol levels, and heart rate.

- Dr. O’Campo asked whether the state of the art of diet questionnaires has improved enough to adequately address diet quality issues, particularly for children. Dr. Keim answered that collecting diet information is challenging and that there are opportunities to improve and validate questionnaires and dietary assessment instruments. Technological developments may provide useful tools in the future. Dr. Ludwig noted that early childhood questionnaires are completed by parents, but collecting data on diet and food frequency for adolescents is particularly challenging. Dietary assessments for adults can be labor-intensive.
- Dr. Diez-Roux said the Study’s investigations of obesity will provide a valuable platform for evaluating natural experiments (for example, interventions in communities and schools). Data linkages for such evaluations need to be established early in the Study.
- Liliana J. Lengua, Ph.D., asked whether the Study has hypotheses for the mechanisms that account for socioeconomic and racial disparities in obesity. According to Dr. Keim, none of the Study’s obesity-related hypotheses currently address these disparities. However, the Health Disparities Working Team is developing some hypotheses that could focus on the mechanisms of disparities in obesity.
- Dr. Clayton said electronic purchase records from grocery stores could provide insight into children’s diets. Proximity of grocery stores to participants’ homes and the type/quality of the stores could also provide insight into diets. Grocery chains offer a potential public–private partnership.
- Dr. Reede asked whether the Study will make distinctions among ethnic subgroups. Diets vary across subgroups, often depending on country of origin. She asked how the Study will capture dietary diversity across subgroups. Dr. Keim said the Nutrition Working Team is exploring, for example, augmentation to the food frequency questionnaire given to women during pregnancy in an effort to capture important dietary items that are specific to a Study location. Dr. Fleischman asked how the Study is assessing the depth/specificity of race, ethnicity, and culture. Dr. Schoendorf explained that the Study will follow current OMB standards for race and ethnicity, which allow self-reporting of more than one choice. Self-reported race/ethnicity must be collapsed into one of five categories: White, Black or African American, Hispanic or Latino, Asian, native Hawaiian or other Pacific Islander, and American Indian or Alaskan Native. The Study will ask questions about the parents’ and grandparents’ birth place, as well as languages spoken at home.
- Dr. Gelb asked about the Study’s efforts to coordinate with other—including international—studies on obesity. Dr. Ludwig noted that several countries collect detailed obesity-related information, and the Study should be able to add to the overall knowledge gathered by those countries.

- Dr. Lebowitz noted that factors affecting diet and obesity include region of origin, extent of acculturation, duration of residence in the United States, socioeconomic status, and rural or urban location.

## **Independent Study Monitoring and Oversight Committee Update**

*Jack Moye, Jr., M.D., Director of Laboratories and Repository, National Children's Study*

The National Children's Study research plan specifies that a data and safety monitoring board (DSMB) consisting of 5–10 individuals not associated with the Study be created to review data periodically. According to the research plan, the DSMB will:

- Have expertise in biostatistics, epidemiology, environmental toxicology, pediatrics, genetics, psychology, social determinants of health, ethics, and other appropriate disciplines
- Report to the Study Director and review standard process data such as accrual rates and adverse events and possibly other appropriate aspects of Study data as determined by the Study Director and the Steering Committee
- Alert the Steering Committee if data become available that might require participants to be informed about the finding.

In addition, the research plan specifies that an ethics advisory committee (a subcommittee of the Federal Advisory Committee to the Study) be established to review relevant situations at the request of the Study Director or Steering Committee.

In 2008 a planning group was created within the Program Office to implement the formation of this body, which, to more accurately reflect its charge, was renamed the Independent Study Monitoring and Oversight Committee (iSMOC). Selection of committee members is near completion, a draft charter for the committee has been developed, and an initial committee meeting is planned for June 8, 2009. The committee will be chaired by Leon Gordis, M.D., Ph.D., professor emeritus at Johns Hopkins School of Public Health. Committee members and their areas of expertise are as follows:

- William McIlvane, Ph.D., developmental psychology
- Daniel O. Hryhorczuk, M.D., M.P.H., environment/toxicology
- Barnett Kramer, M.D., M.P.H., epidemiology/prevention
- Jean McEwen, J.D., Ph.D., ethics
- Roberta A. Pagon, M.D., genetics
- Bernard Guyer, M.D., M.P.H., maternal and child health
- J. Christopher Carey, M.D., obstetrics–gynecology
- Bonita F. Stanton, M.D., pediatrics
- Greg J. Duncan, Ph.D., social determinants of health
- Jane Alexander, B.S.Ed., Study participant representative
- Jean J. Schensul, Ph.D., community representative.

A committee member with expertise in statistics has not yet been named.

## Questions and Comments

- Dr. Fleischman asked for clarification on the rules for a DSMB versus the rules for a federal advisory committee. Dr. Moye explained that a DSMB such as the iSMOC has more flexibility than does a federal advisory committee. The iSMOC is not a public committee and can convene closed-door sessions, FACA requirements are not applicable, and there are no geographical or ethnic distribution requirements. Members of the iSMOC are selected on the basis of specific expertise.

## Autism Followup Report

*Gitanjali Taneja, Ph.D., Senior Scientist and Study Center Project Officer, National Children's Study*

There are several broad Study hypotheses related to neurodevelopment and behavior. They focus on nonpersistent pesticides and poor neurobehavioral and cognitive skills, prenatal infection and neurodevelopmental disabilities, gene–environment interactions and behavior, and impact of media exposure on child health and development.

The Study will assess autism through the core protocol and adjunct studies. The core protocol includes screening the entire sample (for example, using the Modified Checklist for Autism in Toddlers [M-CHAT]—administered at 18 and 24 months via phone interview—as well as information on medical procedures and vaccines), nested case control studies, and studies of genes (for example, epigenetic, genomewide association studies). Adjunct studies could follow identified cases throughout the Study and could include increased screening for a segment of the population.

In early 2008, the Study was approached by Autism Speaks concerning possible collaboration. Autism Speaks, a not-for-profit corporation formed in 2005, is dedicated to increasing awareness about the growing autism health crisis and raising funds for critical autism research.

A multidisciplinary expert panel was convened in fall 2009. The panel consists of epidemiologists, pediatricians, behavioral scientists, toxicologists, and environmental scientists. Panel members represent academic institutions as well as federal agencies. The panel will examine the Study's research protocol as it relates to autism and provide input into development of the Study Protocol and possible adjunct studies.

The expert panel held its kick-off meeting in November 2008 and created two subcommittees:

- Autism Diagnosis and Assessment, cochaired by Dr. Yeargin-Allsopp and Craig J. Newschaffer, Ph.D.
- Etiology and Environmental Exposures, chaired by Irva Hertz-Picciotto, Ph.D., M.P.H.

The subcommittees have met several times each. Their discussions focused on:

- Importance of early identification of children with autism spectrum disorder, including early screening and follow-up and clinical confirmation at 36 months
- Interest in adding a general developmental screener
- Medical records collection, including cost considerations and a possible subcohort study

- Interest in gathering adequate biospecimens and environmental samples.

The subcommittees will continue to meet. An additional subcommittee will be formed on best practices for informing families about children who screen positive for an autism spectrum disorder. The expert panel will prepare a report that contains suggestions for the Study Protocol.

### **Questions, Comments, and Discussion**

- John L. Butenhoff, Ph.D., asked about the funding of the expert panel. Dr. Taneja replied that Autism Speak funds the panel's activities. The panel members are volunteers and are not compensated for their work. Dr. Scheidt clarified; the Study cannot legally fund or support these activities. The federal government has certain prescribed procedures for seeking advice. The Study cannot solicit advice from organizations such as Autism Speaks.
- Dr. Currie asked whether there will be a developmental screener. Dr. Taneja explained that the Vanguard Centers protocol includes a list of about 20 items that are developmental milestones. The items are from the Denver Developmental Assessment. If there is a recommendation to use a full developmental screener, the recommendation will be evaluated by working teams. Dr. Yeargin-Allsopp noted that the use of a checklist versus a full assessment has been questioned. The use of a standardized instrument to screen development is being discussed. Dr. Scheidt said the Bayley Scales of Infant Development will be used at 1 year of age.
- Dr. Clayton commented that autism screening will change the natural history of the disease because of the greater chance of early identification and intervention. In essence, the Study is not strictly observational. She asked whether the Study is planning to use electronic medical records. Dr. Balsam explained that one of the Study's information technology contractors has been actively monitoring the state of the art of electronic health records and personalized health records. The Study faces challenges due to the complexity of aggregating data; issues of privacy, confidentiality, and data security; and third-party access. There is the possibility that data collected from personalized health records could be skewed in terms of quantity and quality because certain populations might be more likely to have such records. The Medical Event Data Working Team is examining the use of medical logs, how they interface with interviews and questionnaires, and how well they are used. This working team is also examining certain aspects of electronic medical records. Dr. Taneja acknowledged that revealing findings of positive screens will change what is observed, but the Study is ethically bound to inform parents of positive screens.
- Dr. Henry asked whether the Study has developed criteria or principles for involving nongovernment organizations and accepting partnerships, especially special interest and not-for-profit groups. Dr. Scheidt said the Study's relationship with Autism Speaks is not a partnership. The organization is simply providing input. A number of other organizations are also providing input. Such input, as well as proposals and ideas, is passed on to working teams and evaluated for significance and value to the Study. Dr. Henry proposed that the process be clearly described and posted publicly.

- Dr. Lengua noted that the involvement of Autism Speaks is a good opportunity to have the protocol reviewed by independent autism experts. She said there should be an equal level of input and scientific review for other Study outcomes such as obesity.
- Dr. Gelb said the definition of autism spectrum disorder has been a moving target. It has been revised several times. Much of what is called the “autism epidemic” may actually reflect the changes in definition. It is likely that the definition will continue to change as the Study moves forward.
- Maria Cancian, Ph.D., commented on the importance of linking Study data with administrative records or other data sources such as health records and grocery purchases. Data linkage may create challenges to the consent process. There may be cost savings if permission for data linking is given early in the Study.
- Dr. Lebowitz said autism spectrum disorder may be multiple diseases that are lumped into a single broad category. The sensitivity of current instruments may not be able to discriminate among the diseases within the spectrum. Dr. Taneja said the autism expert panel has been discussing this issue and has been focusing on the 36-month screening and the instruments that can be used to confirm cases with a clear specific diagnosis.
- Dr. Balsam clarified the definition of adjunct studies. An adjunct study is a focused modular study of a portion of the entire cohort or their biospecimens or environmental samples. A request for data only is not an adjunct study. Adjunct studies are additions to the core protocol. They are initiated and planned outside the Study planning process and are funded from outside the Study. They may be initiated by a Study Center, federal agency, industry, or research advocacy organization. There is a formal review process for adjunct study requests. There are two review groups: the Adjunct Studies Review Group and the Sample Oversight Group. There is an electronic application process with two tiers of review. Review of applications will begin in fall 2009. Requests for data are reviewed by the DACC.
- Dr. Curie said it is important to anticipate linkages of Study data with other databases and seek consent/permission as early as possible. Dr. Scheidt said the Study has anticipated linkage with other databases, and a list of potential databases has been developed. The Informatics Working Team is addressing issues related to linkage with administrative databases. Analyses of linkages are included in the consent form.

## **Report from the Director’s Office, NICHD**

*Duane F. Alexander, M.D., Director, NICHD*

Over the past 6 months, the Program Office has been very busy, beginning with its consideration of a request to include Study funding in the President’s budget. The Program Office decided to request funds, which led to a dialogue with NIH leadership about the size and scope of the Study, cost estimates, and processes for protocol development. There was particular interest in cost analyses and the accuracy of cost projections. The Program Office indicated that costs provided to Congress were old estimates that were developed in the Study’s early planning phase.

Although it was anticipated that the cost estimates would increase, the Study was not allowed to change the estimates for fiscal purposes.

The Program Office provided an analysis of what the costs would be if the Study did everything requested in the current protocol. Many proposals have augmented the pilot study protocol, and the Program Office understood that the Study was piloting more things than could be included in the original budget projections of \$3.1 billion. The Program Office projected separate costs for both the pilot study and a core Study (that is, only the essential components of the full Study that are necessary to address the hypotheses). These cost projections have been submitted to NIH leadership and are being analyzed by contractors. The Program Office has indicated that the costs are rough estimates. The actual costs will not be known until the pilot study is completed. The pilot study should help determine what approaches and components are feasible; whether the Study will be acceptable to parents and families; what the actual costs of the Study in the field are, compared with the hypothetical cost estimates; and how many of the proposed tasks can actually be accomplished within the available time, the protocol, and the participant burden approved by the OMB.

During this period of uncertainty, Congress has inquired about the amount of funding that will be needed in fiscal year 2009, how much will be needed in fiscal year 2010, what the Study's ultimate cost will be, and whether the Study will be affordable. The Program Office professional judgment cost estimates for fiscal year 2009 and fiscal year 2010 were based on the Study's original cost estimates. When the appropriation was passed in March 2009, the funding was included but with the wording of "up to \$192 million." For fiscal year 2010, the requested funding of \$194 million was included in the President's budget (again with the wording "up to \$194"). The funding is allocated to the NIH Office of the Director.

Recruiting for an intense year-long pilot study has begun, and all seven Vanguard Centers are now in the field. The pilot study will continue until the end of May 2010, when a data lock will be imposed. The Study will continue to follow participants who have already been recruited and enrolled. Some recruiting of new participants may occur. The Study will evaluate pilot study data to determine actual costs, how well participants accepted requests for data collection, actual time needed, and alternative approaches, from sample acquisition to data collection. Alternative approaches will be assessed for effectiveness and cost savings, as recommended by the National Academy of Sciences (NAS) expert panel.

Outcomes from the evaluations and assessments will be used to determine the Study's final protocol, what the costs will be, how well the protocol addresses the hypotheses, and how the Study can be scientifically sound and fiscally responsible. The final protocol and cost estimates, which should be completed by July 2010, will be reviewed by the NCSAC. The NCSAC will provide advice and recommendations on issues such as whether the protocol adequately addresses the hypotheses and whether the costs are reasonable. An NAS expert panel will also review the final protocol. Reviews will be submitted to NIH leadership, lead federal agencies, congressional appropriations committees, and the OMB.

The Study's survival may depend on how well the pilot study is conducted, the quality of information derived from the pilot study, how well the Study's scientific community develops a

final protocol and the rationales for it, the cost estimates, and the reviews of the NSCAC and NAS expert panel. There are reasons to be optimistic about the Study's survival: Congress has been responsive to funding requests, the Program Office continues to hire new staff members, and there is continuing support from advocacy groups and the scientific community. Despite the optimism, challenges remain. The Program Office, lead agencies, the ICC, and the NCSAC will continue to meet the challenges and the Study will continue to move forward.

## **NCSAC Questions and Comments**

- Dr. Clayton reiterated the importance of addressing consent issues for access to administrative databases.
- Dr. Rhoades noted the concerns about the costs of the Study and asked Dr. Alexander for some comparative costs. Dr. Alexander said the Human Genome Project cost about \$3.2 billion over 12 years and the Women's Health Initiative cost about \$1 billion over 10 years. The original cost estimates for the Study were \$3.1 billion over 25 years.

## **Day 2**

### **The National Children's Study in Urban America: Queens, NY**

*Leo Trasande, M.D., M.P.P., Co-Principal Investigator (Co-PI), Mount Sinai School of Medicine Vanguard Center; Assistant Professor of Community and Preventive Medicine, Assistant Professor of Pediatrics, Mount Sinai School of Medicine*

The Queens Vanguard Center is a consortium of five distinguished institutions and key community partnerships. The consortium includes the Mount Sinai School of Medicine, Columbia University's College of Physicians and Surgeons, Columbia University's Mailman School of Public Health, University of Medicine and Dentistry of New Jersey's Environmental and Occupational Health Sciences Institute, and the New York City Department of Health and Mental Hygiene. The Queens Vanguard Center has three field offices (in Long Island City, Elmhurst, and Jamaica), with additional facilities at the Long Island Jewish Hospital and the Addabbo Family Health Center.

**Community and Hospital Engagement.** The goal of community engagement is to ensure that the communities of Queens are aware of and familiar with the Study and that their perspectives, interests, and needs are represented and incorporated in the planning and implementation of the Study. There are seven community partners and engaged organizations. The goal of hospital engagement is to ensure that all delivery hospitals are identified, engaged, and prepared to have Study staff perform data collection activities during birth events. The Queens Vanguard Center identified 43 delivery hospitals used by women living in Queens segments.

**Enumeration and Pregnancy Screening Segment Rollout.** Segment rollout will occur in two phases. Phase 1 will begin in January 2009 (eight segments). Phase 2 will begin in April 2009 (10 segments). Targeted media and community outreach strategies, including ethnic media, will continue throughout the recruitment period. Demographics of field staff and segment populations will be matched. Queens is the most ethnically diverse county in the United States, with more

than 140 languages spoken throughout its households. Consent and promotional materials will be translated into the 10 most common languages.

**Early Challenges in the Field.** Even with the best of media and community outreach, many households still have not heard about the Study beforehand. However, once a door is opened, enumeration and pregnancy screening proceed quickly. Obtaining consent for a 21-year study will take patience and persistence. Appropriate participant concerns require special attention by the staff, including a reminder that each component of the Study is optional.

**Upcoming Challenges.** These include the following:

- Length and coordination of home visits
- Retention of participants in a highly mobile population
- Maintaining community enthusiasm in a long-term study
- Coordination of birth visits given that there are 43 birth hospitals in New York City and Nassau County where Queens residents typically deliver.

### **The National Children's Study in Salt Lake County, UT**

*Sean D. Firth, Ph.D., M.P.H., Project Director, University of Utah Vanguard Center;  
Department of Pediatrics, Primary Children's Medical Center, University of Utah Health Sciences Center*

**Vanguard Location Overview.** Salt Lake County is a mostly urban region that is economically above average. As of July 1, 2008, the population was estimated at 1,022,651. All births in the county are linked to the Utah Population Database, which includes more than 10 million records and genealogy of more than 4 million individuals. The county has a high birth rate, and families are generally large. The population is relatively young: 10 percent are younger than 5 years old, and 23 percent are younger than 18 years old. The racial makeup of the county is about 86 percent White, about 1 percent Black or African American, about 1 percent Native American, about 3 percent Asian, about 1 percent Pacific Islander, about 5 percent from other races, and about 3 percent from two or more races. About 12 percent of the population is Hispanic or Latino. The county's environmental challenges include 13 sites on EPA's National Priority List, air quality compromised by a "stagnant bowl" effect, and a critical water supply.

**Operations.** The Salt Lake County Vanguard Center offices are located at the University of Utah Research Park. The Vanguard Center includes investigators, staff, and field offices; training facilities; conference rooms; specimen processing and shipping center (biospecimens); specimen receiving and shipping center (environmental samples); precollection workroom; warehouse facility; and call center. There are two ultrasound locations: the University of Utah Health Sciences Center and the Intermountain Riverton Obstetrics Clinic. There are two clinical locations: the University of Utah Health Sciences Center Diabetes Center Pediatric Clinic and the Intermountain Riverton Obstetrics Clinic.

**Hospital and Practitioner Engagement.** At eight hospitals, staff have met with administrators, delivering practitioners, nurse managers (labor and delivery, postpartum, nursery, neonatal intensive care unit, and so on). Obstetric and gynecology research nurses will meet with nursing staff and will conduct birth visits.

**Marketing and Media.** The goals of marketing are to create Study brand recognition, ensure that the knock on a door at enumeration is not a “cold call,” and build “buzz” to create a sense of the “Golden Ticket.” A Salt Lake City–based advertising agency schedules television and radio interviews, as well as meetings with new editors (television and print). Communications include print advertising (countywide and in community newspapers), billboards, banners (schoolyards, recreation centers and so on), posters (schools, churches, and doctors’ offices), pass-along cards, radio ads (production and ad-lib), and television ads (15-, 30-, and 60-second spots).

**Staffing and Training.** Study managers must recruit, interview, hire, and train 30 enumerators, five field data collectors and supervisors; five environmental monitoring sample collectors and supervisors, specimen handling and processing personnel, an environmental monitoring equipment technician, and other staff, while obtaining the same training themselves, conducting quality assurance/quality control activities, and managing differing personalities and interpersonal communication styles.

**Recruitment and Enrollment.** Although there have been some barriers to recruitment at enumeration (for example, men answering doors who act as gatekeepers), women have enthusiastically received enumerators, with a high proportion completing the screener consenting. There are anticipated challenges to sample collection among special populations.

### **NCSAC Questions, Comments, and Discussion**

- Dr. Lebowitz asked about the interactions between investigators and field staff assessing social and physical environments. Dr. Trasande said there are monthly investigator meetings and frequent interactions among consortium institutions and Study staff. There is feedback from field staff to investigators. At the Salt Lake County Vanguard Center, there are monthly co-PI meetings. The co-PIs lead different teams, including environmental monitoring and social assessment teams. Several investigators are involved with Study working teams.
- Dr. O’Campo asked whether the Vanguard Centers have established community advisory boards (CABs) and developed plans to evaluate effectiveness of community engagement and benefit to local communities. Dr. Firth explained that the community relations director for Salt Lake County has established ties with some of the more challenging communities, including a number of community liaisons, especially in special and minority populations. Dr. Trasande noted that, for the Queens Vanguard Center, there is an overall Queens CAB and a Rockaway CAB. He said the Study must be careful about making promises to share findings, particularly at the segment level. Extant databases may serve as examples of the type of data the Study can share.
- Dr. Rhoades asked whether data will be aggregated in a way such that the communities can be compared. Dr. Trasande said the DACC has been discussing the levels at which data analyses are permitted while still protecting participants’ confidentiality. This issue (that is, the level of identifiable data that will be made available) is well recognized and has been questioned by IRBs.

- Dr. Diez-Roux said the issue of what information will be shared with communities is critical. It is probably not realistic to expect that the data collected as part of the Study will be useful to communities and can be shared in a timely and useful manner. The Study should consider extant data that can be packaged and shared with communities (for example, county-level child health data).
- Dr. Clayton asked whether participants understand that their data may be combined with information from public databases. The distinction between research and immediate personal benefit is unresolved. Participants may not understand that personal data will be combined with other data as part of the Study analysis. Dr. Trasande said the Queens Vanguard Center has added detailed information to its consent form about this issue, but it may not be enough—at least not in the initial consent. Reconsenting may be necessary. Dr. Firth commented that the University of Utah School of Medicine’s IRB questioned the Vanguard Center about possible linkages between Study data and the Utah Population Data Base. The IRB said that amendments would need to be filed if linkages are planned. In addition, the informed consent must be amended and the participants reconsented.
- Dr. DuPlessis said the Study should recognize the importance of developing long-term community relationships in order to optimize recruitment and retention. She said the idea of giving back to communities has been discussed. She asked Drs. Trasande and Firth whether they have considered what the Study can contribute to communities other than Study data. Dr. Trasande explained that if an exposure–outcome relationship is identified, and something can be done about it, the Study will inform the New York City Department of Health and Mental Hygiene, which is obligated to intervene.
- Wilma Brakefield-Caldwell, R.N., asked how the Study will engage and recruit women who do not seek prenatal care until the second trimester. Dr. Firth replied that recruiting first-trimester pregnancies is more of a problem in a clinical setting than in the Study’s household approach. Dr. Trasande noted that the general lack of available prenatal care across the country is a factor. The Queens Vanguard Center is making outreach efforts to recruit women who are in their first trimester.
- Dr. Currie said the issue of data linkage needs to be addressed by the DACC, the National Children’s Study policy could then be communicated to the NCSAC.
- Dr. Fleischman noted the level of staffing, both office personnel and field staff, that is necessary for the household recruiting approach. He asked whether efforts will be made to decrease costs and increase economic efficiencies as the pilot study proceeds. Dr. Scheidt explained that the Study is just beginning the geographically based household screening and recruitment, and the Study is just beginning to learn what it takes to implement this approach. Alternative recruitment approaches are being considered. At this time, Vanguard Centers are not being asked to reduce staffing to reduce costs. The pilot study must proceed as planned in order to understand the actual costs of the household approach.
- Dr. Fleischman asked Drs. Trasande and Firth how their Vanguard Centers would respond if given fewer resources or asked to reduce staffing. Dr. Trasande said Centers would adapt but

most likely productivity and yield would suffer (that is, there would be downstream consequences). Dr. Firth explained that the Centers will expend a lot of resources, both time and money, to hire and train staff in the early phase of the Study. Work over the first 2 years will be intense. The work load will eventually level off, and there will be some staff attrition. Dr. Fleischman commented that data from the pilot study evaluation may demonstrate the benefits of the costs based on productivity.

- Benjamin S. Wilfond, M.D., noted that hospitals focus on continuous process improvement as a mechanism to increase efficiencies, and continuous process improvement has been increasingly applied to research. The Study could benefit from input from expertise in this area. Dr. Wilfond proposed determining the level of concern about data linkages as part of community engagement and outreach. The best way to disclose data linkages may not be through a single line in the consent form but by openly acknowledging, explaining, and addressing concerns about data linkages in Study materials.

### **Formative Research**

*Ken Schoendorf, M.D., M.P.H., Director of Protocol Development and Study Center Project Officer, National Children's Study*

The Study's formative research falls under the domain of an OMB "generic clearance." Generic clearance provides expedited OMB review of small studies designed to improve federal data collections. Approval of formative research allows Study Centers to design individual products to address local needs or interests and engage the creativity and expertise of Center personnel.

The purpose of formative research studies is to maximize the efficiency of procedures, materials, and methods. They are designed to improve recruitment and retention of participants, engage communities including both the local and medical communities, and improve the efficiency and validity of data collection tools.

Proposals for formative research studies are submitted to a Project Officer and, if approved, are forwarded for local IRB approval. If approved, the proposal is sent to the Program Office via the Data and Clinical Coordinating Center and then to the OMB via NIH Project Clearance. With final approval, the study begins its field work.

Vanguard Centers have submitted several proposals for formative research. Two have been approved, and one is pending. The Data and Clinical Coordinating Center proposal is currently being reviewed by the Program Office and will then be submitted to the OMB. (The OMB reviews only one proposal at a time under the Study's generic clearance.) Wave 1 Study Centers have also submitted a number of proposals to the Program Office, which are also awaiting submission to the OMB. Because the OMB generic clearance is for the pilot study, formative research can be conducted only by Vanguard Centers. Formative research to be conducted by Wave 1 Study Centers will require separate OMB review and approval.

Four Vanguard Centers have been approved to convene focus groups:

- University of North Carolina at Chapel Hill (Duplin County, NC)—to encourage participation of Latina/o and undocumented workers

- University of California, Irvine (Orange County, CA)—to evaluate socioeconomic, cultural, and political facilitators and barriers to participation
- Children’s Hospital of Philadelphia (Montgomery County, PA)—to encourage participation of nonresidential fathers
- Data and Clinical Coordinating Center—to evaluate automatic self-response methods for pregnancy follow-up.

Currently, there is a moratorium on additional submissions to the Program Office. Next steps include encouraging clearance of the Vanguard Center proposal that is under OMB review, submitting the Data and Clinical Coordinating Center proposal, revisiting the submission and review process, and developing projects directly related to the pilot study.

### **NCSAC Questions, Comments, and Discussion**

- Dr. Lengua asked about plans to translate data collection instruments and whether the translated instruments have been validated. Dr. Schoendorf said the instruments are in English and Spanish; not all of the Spanish-language instruments have been validated. Dr. Scheidt said there are cost issues for translating and validating instruments. The Study will analyze costs of using translators versus using translated printed materials. Cost-effectiveness may depend on the size of the subpopulation.
- Dr. O’Campo asked about the length of the focus group studies. Dr. Schoendorf said focus groups may take 4–6 months from approval to completion, not including analysis of outcomes. Findings will be disseminated among Vanguard and Wave 1 Centers via established meetings and communication mechanisms (for example, the Web Portal, the Study newsletter, conference calls, and Steering Committee meetings). Dr. Schoendorf said there may be more central input and coordination of formative research activities.
- Dr. DuPlessis asked whether only one study could be reviewed at a time by the OMB or whether only one study could be in the field at a time. Dr. Schoendorf said the OMB would review only one study proposal at a time. Multiple studies can be conducted at one time. The advantage of having the Program Office submit proposals to the OMB—instead of directly from Vanguard or Wave 1 Study Centers—is that, once approved, the Program Office can delegate the work to the Center it wants through the existing and legitimate contract mechanisms.

### **Community Outreach and Engagement Subcommittee Report**

*Helen DuPlessis, M.D., M.P.H., Community Outreach and Engagement Subcommittee Chair;  
University of California, Los Angeles*

During a breakout session on May 26, 2009, the subcommittee was updated on recent community outreach and engagement (CO&E) activities. The subcommittee discussed the findings of a review of 26 Study Center CO&E plans. The review provided important information on promising practices as well as an expected variance in approaches to CO&E across the Study Centers. The findings provided useful feedback for Study Centers as well as the

Program Office and project officers, and it motivated the development of a CO&E guidance document.

The NCSAC subcommittee reviewed and discussed the guidance document, which was created to provide national-level guidance to Study Centers in developing and implementing CO&E plans. The subcommittee made the following recommendations:

- Refine the definition of “community” with exemplars at the Study Center level
- Include a definition of “collaboration” and “partnership” within the context of CO&E
- Include a set of core principles of CO&E
- Clearly state the purpose of CO&E, which is to
  - Optimize recruitment and retention
  - Commit to establishing long-term relationships with mutual benefit (and work with CABs to define what the benefit to the community is)
  - Become knowledgeable about key communities within a Study location
  - Mobilize assets and develop capacities of the community (and clearly state them).

Additional guidance document recommendations are as follows:

- Include recommended timeline for CO&E milestones (not just for communication strategy)
- Describe responsibility for and approach to disseminating data/information to the community (coordinated with the DACC and the iSMOC)
- Broaden discussion/guidance about use of new media (for example, include text messaging and online social networking and blogging services)
- Include guidance about how CO&E activities of the Study Center can be leveraged to stimulate the parent institutions (that is, universities) to reconsider the value of and innovative approaches to CO&E
- Encourage development of “toolkits” and promising practices
- Encourage NCSAC members to offer additional feedback on the guidance document.

The subcommittee recommended the following:

- The Program Office and Study Centers should view the development and evaluation of CO&E strategies as an opportunity for significant innovation and contribution to research in community settings.
- The Study should create an interim approach to optimizing communications among all Study groups involved in CO&E.
- The Study should identify a menu of CO&E activities Study Centers could engage in during the pause.

## **NCSAC Discussion**

- Dr. O’Campo asked about the type of guidance that each Study Center will get in order to work with communities and establish relationships that yield mutual benefit. She also asked about the guidance document’s level of detail. Dr. DuPlessis said the guidance document’s specificity depends on what the Program Office determines to be appropriate and what the NCSAC recommends. Dr. Fleischman commented that the NCSAC does not need to be too “granular” with its recommendations, but it should comment on the direction of CO&E activities and make recommendations accordingly.

- Dr. O’Campo commented that there needs to be clear guidance—perhaps from the DACC—about revealing findings to communities, and there needs to be clear communication to the communities about the limits and possibilities of revealing findings.
- Dr. Lebowitz said “engagement” should be defined within the context of the type of study. The Study is not community-based participatory research. “Collaboration” and “partnership” would then be defined within that framework. It may be beneficial for Study Centers to focus on statements of the purpose of CO&E. It is critical for Study Centers to know the required scope of CO&E. Dr. Lebowitz supported the subcommittee’s recommendations.
- Dr. Fleischman said the primary principle of CO&E is respect for a community and the individuals who comprise that community. The primary purpose of CO&E is to show affection for a community because the community is allowing itself to be studied. This affection is shown through respect. There is a potential for institutions, catalyzed by their Study CO&E activities, to develop and maintain strong, long-term, and meaningful community engagements. A possible future recommendation is for the Study to consider how CO&E efforts at Study locations can result in institutionalized community engagement relationships between institutions and their communities.
- Dr. Tassinari emphasized the importance of capitalizing on pilot study findings, which should be able to show value to the community and demonstrate the Study’s value as a whole. It will be important to coordinate with the DACC to ensure that pilot study findings are disseminated as quickly as possible.
- Dr. Gelb questioned whether it is the NCSAC’s purview to propose items for a menu of CO&E activities during the pause. It may be more appropriate for the NCSAC to simply recommend that the Study develop a menu that the NCSAC will then comment on.
- Dr. Tassinari said it may be appropriate for the Study to assess how it will disseminate data during the pause period—in particular, how Study Centers will disseminate pilot study findings to their communities.
- Dr. Diez-Roux noted focus groups could be convened during the pause to (1) identify barriers to recruitment and enrollment, (2) discuss acceptability of different procedures, and (3) describe participants’ expectations after enrolling.
- Dr. Lebowitz described his experience with convening focus groups within CABs and their respective organization to identify and discuss lessons learned. A pause period can provide an opportunity to “catch up” and educate participating entities.
- Dr. Clayton commented that there is an array of issues regarding the sharing of findings, both aggregate and individual. The Study has an opportunity to work with community groups to identify the types of findings they are interested in and how they want to be informed. She cited the results of a survey conducted by the Genetics and Public Policy Center that

concluded that people are more likely to participate in genetic studies if they are given their individual research results.

- Dr. O'Campo said the Vanguard Centers should begin to consider ways in which pilot data from their Study locations can be used in adjunct studies.
- Dr. DuPlessis said the Vanguard Centers could characterize segments and create profiles to share with CABs and other community groups. These groups will then be able to provide feedback on the accuracy of the segment profiles.

## **NCSAC Recommendations**

The NCSAC accepted the Community Outreach and Engagement Subcommittee's recommendations.

### **Scientific Review Subcommittee Report**

*Liliana Lengua, Ph.D., Scientific Review Subcommittee Chair; Associate Professor; Department of Psychology, University of Washington*

In a breakout session on May 26, 2009, the subcommittee addressed two topics: obesity and review of Study protocol changes. The subcommittee agreed that the Study is in a unique position to (1) inform science on the etiology and sequelae of childhood obesity and (2) make protocol decisions based on what the Study can uniquely contribute to the scientific knowledge of obesity.

**Obesity.** The subcommittee acknowledged that the study of obesity requires a complex bioecological approach. To sufficiently study obesity, the Program Office needs to:

- Ensure that the Study has adequate measurements of the potential mechanisms and mediators of the effects of broader sociocultural factors
- Ensure adequate assessments to address gene–environment interactions.

The subcommittee discussed whether there are critical biospecimens to obtain at critical periods of the Study and/or development. The subcommittee agreed that the Study should take full advantage of standard/common tests (for example, glucose screen and oral glucose tolerance test) and have the best samples/volumes ready for the appropriate analysis when the time comes.

The subcommittee also discussed whether BMI will be collected frequently enough and at the right times to address critical developmental questions. Although some developmental questions will not be addressable because of the infrequency of assessments, data obtained from medical records or well-child visits may supplement Study data.

Dr. Ludwig identified prenatal programming as a key scientific issue that the Study is particularly poised to uniquely address by assessing variations in maternal weight and other factors across multiple pregnancies.

**NCSAC Comments.** NCSAC comments included the following:

- Dr. Lebowitz commented on the disease mechanisms and outcomes related to obesity.
- Dr. Fleischman noted that the Institute of Medicine is releasing a report on the impact of weight gain on pregnancy. (Note: *Weight Gain During Pregnancy: Reexamining the Guidelines* was published May 28, 2009.)
- Dr. Reede said one of the ways of determining key economic and sociocultural factors is to look at disparities in obesity, including geographic variation and markers across factors.
- Dr. O'Campo said prioritizing questions about obesity could be based on critical periods of exposure. Defining the critical periods of development would help determine when measurements should be made.
- Dr. DuPlessis said schools are collecting anthropomorphic and other types of information that could be linked to Study data.
- Dr. Currie commented that the Study could develop a list of types of things that could be well addressed in adjunct studies. The list would provide some guidance for investigators who are interested in adjunct studies.
- Dr. Diez-Roux said the Study is uniquely poised to address natural experiments; therefore, linkages to school and neighborhood data are crucial. The Study is also uniquely poised to address gene–environment interactions, and key environmental factors should be included in the core protocol.
- Dr. Gelb encouraged the Study to convene outside groups of experts, such as Autism Speaks, for all outcome domains, including obesity. This expertise would help ensure that the right questions are identified prospectively and that the right data are collected to answer the questions. Dr. Fleischman explained that the working teams are responsible for bringing this type of expertise into the Study.
- Dr. Tassinari said that many of the key issues relating to obesity are currently being debated. The guiding understanding for the proper clinical biomarkers is coming from the groups that are conducting industry-sponsored clinical studies. Because of such work, the Study may not need to convene groups of experts in certain scientific areas.
- Dr. Lebowitz noted the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducted a long-term longitudinal study of obesity, diabetes, and heart disease and could provide expertise to the Study. The NIDDK study extensively assessed biomarkers and genetic materials.
- Dr. Lengua observed that the subcommittee's discussion might have been more fruitful if there were specific obesity-related questions to address or a protocol that could have been reviewed and commented on.

- Dr. Williams commented on the importance of using the most broadly applicable, valid, and low-burden methods for assessing body composition in population-based settings. Skinfold measurement is one approach, but previous studies have shown that this is a challenging method. In its protocol review, the NCSAC might be able to determine the key measures that have to be held at the highest standards (for example, measures for body composition and obesity). Dr. Scheidt said skinfold measurement is one of the measures being used in the Study. Dr. Williams noted that skinfold measures were not used in the National Health and Nutrition Examination Survey because they could not be standardized. Skinfold measures may not be the best method for the Study.

**Review of Study Protocol Revisions.** The subcommittee was asked to advise on a process for reviewing revisions to the Study protocol for the main study—that is, how the Study would obtain reviews and advice from the NCSAC and the Scientific Review Subcommittee.

The subcommittee discussed different levels or degrees of review, which may depend on the question being asked or the issue being addressed. There is sufficient expertise on the NCSAC to provide substantive input to the Study Planners. The subcommittee considered whether it could operate more as a working group, including other NCSAC members as *ad hoc* members or other subject experts. According to FACA regulations, subcommittee recommendations must be reported to the full NCSAC. The NCSAC can then refine or support the subcommittee's recommendations and formalize recommendations communicated to the PO. A framework for periodic scientific review will be required of the NCSAC over the course of the Study. The subcommittee had several questions concerning the timeline for review, the number of iterations, the frequency of reviews and meetings, and the time commitment required to achieve the needed level of preparedness to respond.

The subcommittee recommended that the review process will be most effective if:

- The NCSAC or Scientific Review Subcommittee should be presented with specific questions/issues to review
- The timeline of review should be coordinated with the timeline/needs of the Study

**NCSAC Comments.** NCSAC comments included the following:

- Dr. Gelb said the NCSAC would benefit from understanding the rationale for revisions as the NCSAC reviews the protocol.
- Dr. Fleischman asked about the stated purpose of the review of protocol revisions. Dr. Lengua said the Scientific Review Subcommittee was asked to consider how it could be involved in reviewing and advising on the changes to the protocol that would evolve from the pilot study during the pause period. Dr. Scheidt explained that the purpose of the NAS expert panel's review of the research plan was to provide an independent peer review of the Study. Subsequently, the Program Office determined that it would not be feasible or necessary to have an NAS expert panel review each phase of the protocol. The Program Office concluded that the NCSAC could conduct the necessary peer reviews of the protocol. In addition, the NCSAC would review the protocol for its scientific merit and ability to address directives in the Children's Health Act of 2000 and to meet the overall Study objectives.

- Dr. Fleischman explained that in about a year, the Program Office and other entities will analyze the present protocol and its costs, and there will be a formative evaluation of what works and what does not work. There will be recommendations about refining the protocol. Protocol review and refinement will be needed for each phase of the Study, and the Study needs to develop processes and approaches for each phase of review. Dr. Fleischman proposed that the NCSAC's Planning Subcommittee consider the timelines and most beneficial processes for review.
- Dr. Lengua commented that the protocol review should take advantage of NCSAC members' expertise in reviewing certain areas of the protocol. The review process might benefit from outside expertise.
- Dr. Butenhoff said the Scientific Review Subcommittee did not address approaches and mechanisms for protocol review (for example: Would the subcommittee review collectively or individually? Should the subcommittee address specific charge questions or critical areas such as obesity?) There needs to be more refinement and discussion about review mechanisms.
- In response to a question from Dr. Diez-Roux, Dr. Scheidt explained that the iSMOC will not review the protocol. The Steering Committee will review protocol revisions for feasibility. The ICC will review protocol revisions for adherence to the goals and missions of the lead agencies. The NCSAC will review the protocol revisions for scientific merit. An NAS expert panel will not review the protocol revisions.
- Dr. O'Campo emphasized the importance of having adequate time to review the protocol revisions. Because reviewing the revision may take months, it may be beneficial for the NCSAC to begin reviewing the existing protocol now.
- Dr. Clayton asked whether an NCSAC subcommittee can meet separately and give direct advice. Ms. Sapienza explained that according to FACA regulations, subcommittees cannot report directly to federal officials. All subcommittee recommendations must be presented to the full NCSAC for consideration. Subcommittee meetings must adhere to FACA regulations and must be announced in the *Federal Register*. The Study can consult with individual NCSAC members based on their expertise; however, an individual committee member cannot represent the NCSAC. A schedule of subcommittee meetings for the coming year could be planned and announced in the *Federal Register*.
- Dr. Lengua commented that in order for the NCSAC to review the protocol, it will need access to the information, and a process for submitting comments will be needed. Dr. Fleischman said the goals of the NCSAC's protocol review need to be clarified, and the process for meeting these goals needs to be established in accordance with FACA regulations.
- According to Dr. Clayton, the NCSAC needs to work collaboratively for the protocol review, to understand each member's area of expertise, and to establish a dialogue with the Program

Office. An advantage to such a dialogue is that the Program Office would be able to provide information, identify issues, and ask questions before the NCSAC meetings.

- Dr. Fleischman said the NCSAC Planning Subcommittee needs to work with the Program Office to determine the level of information that will be presented to the NCSAC or its subcommittees and the goals and processes for the review.

## **NCSAC Recommendations**

The NCSAC accepted the Scientific Review Subcommittee's recommendations.

## **Ethics Subcommittee Report**

*Benjamin S. Wilfond, M.D., Professor and Head, Division of Bioethics; Department of Pediatrics, University of Washington School of Medicine; Director, Treuman Katz Center for Pediatric Bioethics, Children's Hospital and Regional Medical Center*

Dr. Wilfond substituted for Ethics Subcommittee Chair Elena Gates, M.D., University of California, San Francisco.

In a breakout session on May 26, 2009, the subcommittee addressed two issues: (1) the risk of incidental exposure of nonpaternity and (2) options for communicating the potential for discovery of nonpaternity. The subcommittee made several observations:

- The protocol does not specifically attempt to determine biological paternity status. Determining paternity is not one of the Study's objectives and is not being routinely done.
- It is possible that information about paternity status may be detected, depending on the analyses that are conducted, particularly genetic analyses. Knowing paternity status may be scientifically important in some analyses.
- The woman determines whether the man is invited to participate in the Study. If a woman is concerned about misattributed paternity, she may choose not to invite the man to participate.
- The risk of detecting and, if detected, incidentally disclosing nonpaternity is fairly low.
- During the process of cognitive testing of informed consent materials for potential fathers, two issues arose about the language on current policies on paternity. Regardless of where the language was placed in the consent materials, the men did not identify paternity as an issue of concern. In addition, the men were confused about the distinction between paternity testing not being included in the protocol and how it could be detected if it was not included in the protocol.

The subcommittee agreed that because the risk appears to be sufficiently low, it is not necessary to state information on paternity policies in the current consent materials. Such information may need to be added as the consent materials evolve. The subcommittee asked several questions:

- Should the detection of paternity be routine?
- If nonpaternity is detected, should it be disclosed?
- Should the Study's policy be stated in the informed consent form?

There is consensus among researchers that, in general, even when paternity is determined in the course of a study, such information is routinely not provided to families. There is not consensus as to whether paternity detection and disclosure policies need to be stated in consent materials. In general, however, the policies are included in consent materials for studies that involve genetic research, particularly those that involve testing multiple family members. The policies mention the possible risk of disclosing nonpaternity. Even some studies that test genetic materials in only one individual often state the policies in consent materials.

The subcommittee discussed the extent to which disclosure or lack of disclosure would affect recruitment. Risk of disclosure may deter some people from participating in the Study, and giving participants information on risk is part of informed consent. A distinction should be made between the risk of detecting nonpaternity and risk of incidental disclosure of nonpaternity.

### **NCSAC Comments and Discussion**

- Dr. Wilfond asked whether determination of the biological father is relevant to any of the Study's hypotheses and whether paternity should be routinely determined. Dr. Gates replied that because the Study will continue to develop hypotheses, knowledge of paternity could be relevant in the future. Women should be informed of this possibility when they are deciding to consent.
- Dr. Gelb noted that the Study will be collecting biospecimens (from mothers, fathers, and children) that will allow determination of paternity. At some time, paternity will inevitably be known and will be scientifically relevant. Because up to 10 percent of men labeled "father" are not in fact biological fathers, knowing paternity will be relevant in most genetic analyses. However, the issue is whether to state the Study's policy (that is, the Study will determine paternity but will not report it) in consent materials.
- Dr. Williams commented that family history may be a covariate for some of the Study's analyses. Families will report place of birth for parents and grandparents. If paternity is not determined, there may be some misclassifications and inaccuracies in paternal exposures (up to 10 percent).
- Dr. Wilfond asked whether paternity should be routinely disclosed to participants. He said the traditional approach of nondisclosure is appropriate.
- Dr. Clayton said there may be situations where a participant wants his or her biospecimens returned. The Study's policy should be that biospecimens will not be returned. Dr. Gates agreed.
- Dr. DuPlessis said that the Study's policy should recognize that disclosure of misattribution of paternity may be clinically relevant in certain circumstances (for example, in detection of inherited genetic disorders and bone marrow transplants).
- Dr. Gelb noted that the reporting of genetic test results requires tests that are approved under Clinical Laboratory Improvement Amendments (CLIA; 42 CFR 493). New York and

California have state-based CLIA processes, whereas all other states have nationally based CLIA processes.

- Dr. Wilfond asked about the content of the informed consent materials regarding plans of risk of determination and plans of nondisclosure (that is, should plans and policies be explicitly stated or simply not be included?).
- Dr. Diez-Roux asked what the consent materials currently state. Some consent materials inform participants that they will not receive any results of genetic analyses, including paternity.
- Dr. Clayton commented that that a blanket statement that the Study will not be returning genetic results may not be sufficiently nuanced to describe what may happen in the future with some results.
- Dr. Gates said if a woman is informed that nonpaternity could be discovered, it may affect her decision to invite the father to participate and may affect her decision to enroll.
- Dr. Slutsman explained that the general consent booklet is provided at the first household visit at the time of enumeration and screening. Subsequently, when the woman is deciding to enroll, she will be asked whether she wants to invite the father to participate. At this time, the woman will have already been administered the general consent.
- Dr. Fleischman described his understanding that the Study will know the genetic association between a child and putative father and that the Study will refuse to disclose any information concerning paternity. If the Study informs potential participants that paternity will be determined but that this information will be protected, there will be a nonrandom refusal to participate. If asked, field workers should tell potential participants that the Study has no intention of routinely studying paternity or informing anyone about it.
- Dr. Reede commented that telling a participant that the Study will not learn about paternity is a false statement.
- Dr. Lengua noted that the Study may not have a choice with the informed consent materials if the content is determined by local IRBs.
- Dr. Wilfond asked whether being silent about the paternity policy may help recruitment.
- Dr. Rhoades observed that if a group discusses whether information should be included in consent materials and then remains silent, informed consent is being denied. Dr. Fleischman said the Study's informed consent materials explicitly state that genetic tests—but not specifically paternity tests—will be performed but that results will not be revealed. The question is whether the Study is obligated to include the statement about not disclosing paternity in the informed consent. There are many things that the Study will not do, but that have been discussed and are not mentioned in the informed consent.

- Dr. Slutsman said the Human Subjects Working Team discussed the issue of the burden of additional information in the informed consent materials. The working team discussed whether the risk was unique enough to warrant inclusion in the informed consent. She noted that fathers give consent only for themselves. Mothers give consent for themselves and the child. Fathers have rights to their own information but not to the information of the mother or child. Dr. Slutsman clarified that this is the working team's interpretation of the Freedom of Information Act.
- Dr. Gelb noted that typically paternity is not reported in a clinical setting, unless a person is being tested explicitly for paternity and has given consent to reveal findings. Clinicians are not obligated and typically do not reveal paternity findings.
- According to Dr. Clayton, the revelation of nonpaternity is very consequential for children because if a man is not the biological father, then within the legal system, the man has no obligations to support the child. Therefore, the Study does need to make a statement about determination and disclosure of nonpaternity. Dr. Wilfond observed that nonpaternity is consequential only if it is disclosed. Dr. Clayton said there is greater risk of not addressing the issue than of addressing it. She said the informed consent should explicitly state that the Study will not disclose paternity.
- Dr. DuPlessis noted that the consent form states that the Study will inform participants about which findings will or will not be revealed at each visit. She asked whether the Study, by specifically indicating that it will not disclose specific test result, is creating a problem by not making statements about other issues such as paternity. There may be contradictory language in the consent materials.

### **NCSAC Recommendations**

Because the NCSAC did not reach consensus, it did not make official recommendations. However, the following suggestions were made:

- The Study should inform participants that paternity will be determined.
- The Study will not disclose findings about paternity.
- Both mother and father should be informed of the Study's paternity determination and disclosure policies in the consent materials.

Because the NCSAC did not reach agreement, and discussion and decisions on the recommendations were tabled until the next NCSAC meeting. Dr. Fleischman proposed that the Ethics Subcommittee revisit the issues of revealing paternity findings and findings of medical importance (specifically, genetic importance). The subcommittee should read the informed consent materials, read past discussions of the NCSAC and the subcommittee, and reestablish its views on the issues of revealing findings. The subcommittee should then make specific recommendations about paternity to the full NCSAC. Dr. Slutsman was encouraged to continue to learn as much as possible about issues of determining and disclosing paternity.

## **Informed Consent Update**

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

Dr. Slutsman provided a status update on the current informed consent process and consent materials, described the consent video evaluation trial, and previewed the informed consent video.

The informed consent process for the pilot study is a multistage process, with ongoing dialogue with Study participants. There is a core set of consent materials that are consistent across all Study sites. Individual Study sites can expand upon the core consent process with location-specific "addenda" tailored to communities.

Pilot study consent materials include the following:

- General Consent Booklet for Women
- General Consent Booklet for Fathers
- Biological and Environmental Sample Consent Booklet for Women
- Biological Sample Collection Consent Booklet for Fathers
- Visit Information Sheets, which are provided at each Study visit for both women and fathers.

Consent forms and key Visit Information Sheets will be translated into multiple languages.

The General Consent Booklet is in plain language. It is administered at time of the enumeration and screening visit. It serves as a general introduction to the Study and agreement in principle. It describes the purpose and importance of the Study, the kinds of information to be collected, how the information will be used, the possible risks and benefits, incentives, and what information will be shared with participants.

The Biological and Environmental Sample Consent Booklet, which is also in plain language, is administered at first anticipated collection of biological and/or environmental sample data. It describes in greater detail the kinds of biological and environmental samples to be collected and mode of collection; the use, storage, and protection of information; and the voluntary nature of each sample collection. Participants are reminded that they can refuse any item at any time and still participate in the Study. The signature page, which accompanies the general and Biological and Environmental Sampling Consent Booklets, has an opt-out checkbox for genetic analyses of biological samples.

Visit Information Sheets are administered at every visit. They are tailored for each visit and are administered separately for women and fathers. They describe in detail the data to be collected, how the Study would like to collect the data, how the data will be used and protected, and which information the Study can give to participants and when. Visit Information Sheets remind the participants that they can refuse any item at any time and still participate in the Study.

The Study is planning to systematically compare an interactive video version of general informed consent to the general consent booklet used in the pilot study. Women will be randomized to either video or written administration of consent (in English or Spanish). All women will receive a written copy of the consent booklet with the signature page. The content

and organization of the video parallel the general consent booklet, and the transcript mirrors the written consent. The video will be assessed for comprehension. Viewers' impressions will be recorded immediately after administration of consent and at a later time point. The evaluation will be implemented at Vanguard Centers.

## **NCSAC Questions and Comments**

- Dr. Diez-Roux asked about the type of information that has been included in IRB addenda to consent materials. Dr. Slutsman said the addenda have provided information on local Vanguard Center contacts, procedures for Study withdrawal, additional local language on the Health Insurance Portability and Accountability Act and HIV, and elaboration on confidentiality.
- Dr. Gelb asked whether the Program Office is tracking differences among IRB practices. Dr. Slutsman said that it is tracking the IRB practices.
- Ms. Brakefield-Caldwell asked about the time needed to complete the consent form and whether any women have refused due to the length. Dr. Slutsman estimated that reading the general consent form aloud takes about 40 minutes. Because field workers and data collectors are trained to tailor the consent presentations to individuals, there will probably be variations in the amount of time to complete the consent forms. As for refusal, there is only early anecdotal information, but there are procedures for asking participants to comment on the informed consent and asking data collectors to comments on participants and nonparticipants. The informed consent process will be evaluated as part of the pilot study.
- Dr. Tassinari noted that the women will be consenting at different stages of the Study. Women consent for themselves and for their child's participation until the age of 18 years. There will be a formal assent process for the children—at age 7 years and then appropriate as the child ages. Development of informed consent materials is an ongoing process. Reconsenting may be necessary at some time.

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

07-23-09

Date

A handwritten signature in cursive script, appearing to read "Alan R. Fleischman", is written over a horizontal line.

Alan R. Fleischman, M.D.

Chair

National Children's Study Federal Advisory Committee