National Children's Study
Federal Advisory Committee 11th Meeting
April 27–28, 2005
Crystal Gateway Marriott
Arlington, VA

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

Day One

Welcome and Introductions

Alan R. Fleischman, M.D., NCSAC Chair, Senior Advisor, The New York Academy of Medicine

Dr. Fleischman welcomed National Children's Study Federal Advisory Committee (NCSAC) members and other participants to the 11th meeting of the NCSAC. He briefly reviewed the history of the NCSAC and described key elements of the Federal Advisory Committee Act of 1972:

- The federal government may obtain advice for long-range planning and development of programs from groups of outside experts through the formation of advisory committees.
- The Federal Advisory Committee Act (FACA; Public Law 92-463; passed on October 6, 1972) creates standard and uniform procedures governing the operation of all advisory committees.
- The function of a federal advisory committee is to advise.
- Advisory committee meetings are generally open to the public with specific limited exceptions.

To better serve the National Children's Study (Study), the NCSAC charter was amended in December 2004 to include the following:

- The NCSAC shall advise, consult with, and make recommendations to the Director, NICHD; the Study Director; and the Study's Interagency Coordinating Committee (ICC).
- The NCSAC shall consist of no more than 40 members from multiple disciplines.
- The NCSAC will include four nonvoting ex officio members:
  - Director, NICHD
  - Director, NIEHS
  - Director, CDC
  - Administrator, EPA.
- The NCSAC will be composed of:
  - Members
  - Ad hoc members
  - Ex officio members.

Dr. Fleischman presented a slide that depicted the relationships among the governance and management entities of the Study in order to help the NCSAC members understand the complexity of the management of the Study and the relationship of the NCSAC to the other individuals and entities involved in the National Children's Study.

Dr. Fleischman introduced the following meeting participants present at the table:

- Marion Balsam, M.D., NCSAC Executive Secretary
- Jessica Sapienza, M.H.S., NCSAC Committee Liaison Officer
- Peter Scheidt, M.D., M.P.H., Study Director
- Sarah Keim, M.A., Study Coordinator.

Dr. Fleischman described the role of the ex officio members who will represent the agency directors at the NCSAC. He read excerpts from a letter from Julie L. Gerberding, M.D., M.P.H., Director, CDC, to Duane F. Alexander, M.D., Director, NICHD:

> "As the nation's lead public health agency, CDC protects the health and safety of people at home and abroad, provides credible information to enhance health decisions, and promotes health through strong partnerships. As such, CDC has a strong interest in this study's potential to (1) provide data that will help define the nature and extent of health problems facing infants, children, and adolescents, including health disparities and determinants of such disparities; (2) address knowledge gaps regarding the impact of environmental and genetic factors on child health and development; and (3) evaluate exposure-outcome relationships using the life stages approach. . . .
>
> "I am delighted that our agencies are now expanding our partnership through a formal memorandum of understanding to establish CDC's environmental health lab as the lead on biological specimens. I look forward to CDC's continued role in the NCS and to future collaborations with the National Institute of Child Health and Human Development."

Dr. Fleischman reviewed the agenda for the 2-day meeting.

NCSAC members, ad hoc members, and ex officio members introduced themselves and briefly described their educational background, professional experience, and current affiliation.

Welcome and Overview of the National Children's Study

Peter C. Scheidt, M.D., M.P.H., Study Director, NICHD, NIH, DHHS

Dr. Scheidt welcomed NCSAC members—both new and continuing members. He explained that the rationale for the Study evolved from the following findings from the President's Task Force on Environmental Health and Safety Risks to Children, 2000 (reappointed in 2001 and 2003):

- Compared with adults, children are especially vulnerable to environmental exposures—for example, because of their metabolism and behavior.
- Exposures to some agents demonstrate potential for serious developmental effects—for example, lead and prenatal alcohol.
- Current known exposures of high frequency include pesticides, violence, and the media.

- There are numerous high-burden conditions with suspected environmental contribution—such as learning disabilities, autism, diabetes, asthma, birth defects, and premature birth.
- Existing research is too limited in size and scope to answer the questions concerning exposure-outcome relationships.
- A life-course (that is, longitudinal) study design is needed to correctly link multiple exposures with multiple outcomes.

Dr. Scheidt outlined a very brief history of the Study:
- Spring 2000—ICC established
- October 2000—Children's Health Act authorized the Study
- December 2000—First Study Assembly meeting
- October 2001—NCSAC established under FACA
- 2001–2004—Working Groups (22) focused on hypotheses and measures development
- 2002–2004+—Pilot studies reported annually
- 2002–2004—Sample considerations; probability sample announced June 2004
- Fall 2003—Expansion of Program Office staff
- June 2004–April 2005—Advisory Committee pause for procurement
- November 16, 2004—Release of hypotheses, Study Plan, Study sites, Coordinating Center request for proposals (RFP), and Vanguard Centers RFP.

Study concepts include:
- Aims
  - Identify potential environmental effects: harmful, harmless, helpful
  - For important conditions and diseases of children, identify potential preventable causes
  - National resource for future studies
- Hypothesis driven
- Exposure begins with pregnancy
- Power to study high-priority conditions (~100,000 children to be studied)
- Environment and genetic expression
- State-of-the-art technology
- Consortium of multiple agencies
- Public-private partnerships.

Regarding research questions and hypotheses, Dr. Scheidt listed the following:
- No single research question
- Assures answers about "big issues"
- Importance of child health and development (prevalence, morbidity, mortality, cost, public health significance)
- Cannot be reasonably studied with fewer children or another study design
- Measurable with study of this size
- Long-term follow-up required
- Evolving as Study progresses
- Posted on the World Wide Web at nationalchildrensstudy.gov.

Regarding the Study's scope, Dr. Scheidt listed some of the priority exposures:
- Physical environment

  - Housing, neighborhoods/communities, climate, radiation
- Chemical exposures
  - Air, water, soil, food, dust, industrial products, pharmaceuticals
  - Complex ubiquitous low-level exposures; unique exposures (special substudies)
- Biological environment
  - Intrauterine environment, infection, nutrition; inflammatory and metabolic responses
- Genetics
  - Genetic components of disease; effects of environmental exposures on gene expression
- Psychosocial milieu
  - Influence of family, socioeconomics, community, stress.

Regarding priority outcomes for the Study, Dr. Scheidt listed the following:
- Pregnancy outcomes (which will produce early Study results)
  - Preterm birth, birth defects, fetal influences on adult health
- Neurodevelopment and behavior
  - Cognitive development (IQ), autism, learning disabilities, schizophrenia, depression, adjustment, normal variation, resilience
- Injury
  - Intentional and unintentional, violence
- Asthma
  - Environmental, genetic, infectious, and immune factors
- Obesity and physical development
  - Diabetes, pubertal/reproductive development, growth, obesity "epidemic."

Regarding sampling and center strategies, Dr. Scheidt noted the following:
- National probability sample is important:
  - Exposure-outcome relationship representative of the U.S. population
  - Important exposures with varied and unknown distributions are not missed
  - Clustered for community attributes and logistics.
- Centers of excellence are important:
  - Broad scientific input
  - Measures require center based expertise and facilities.

The Coordinating Center and Vanguard Center contracts will be announced in September 2005. RFPs for the Repository, Laboratory(ies), and the remaining Centers will be forthcoming at the end of the 2005–2006.

Funding status was discussed, including the need for substantial new federal dollars for the 2006 budget.

Dr. Scheidt presented a map of the United States that depicted the Study's sites. The map identified the eight potential Vanguard Center locations by name:
- Duplin County, NC
- Lincoln, Pipestone, and Yellow Medicine counties, MN, and Brookings County, SD
- Montgomery County, PA
- New York City (Queens), NY

- Orange County, CA
- Orange County, FL
- Salt Lake County, UT
- Waukesha County, WI.

Dr. Scheidt characterized Study locations and centers:
- Sites—geographic locations (counties) from which participants will be recruited
  - Selected by stratified probability sample of primary sampling units
  - 101 sites
- Centers—entities or institutions that will carry out the Study at the sites
  - Selected via a competitive process
  - Each will cover more than one site
  - 30–50 centers.

The rationale for using a contract mechanism for the Study is:
- To ensure that a consistent rigorous core protocol is carried out at all sites
- To ensure that the Study addresses the goals of the funding agencies
- To allow flexibility for leadership and capacity building.

Regarding Study procurements, Dr. Scheidt noted the following:
- Ongoing
  - Logistics
  - Scientific support—reviews and analyses
  - Information technology development
- In process
  - Clinical and data Coordinating Center (1)—announcement by September 2005
  - Vanguard Centers (3–8)—announcements by September 2005
- Ahead
  - Repository
  - Laboratory(ies)
  - Remaining centers.

Dr. Scheidt explained that prior to November 16, 2004, media coverage of the Study was limited. Since that day, media coverage has expanded. Study media attention includes:
- Media placements since November 2004 RFP announcement: 40
- Estimated print audience to date: 29 million
- National highlights: *U.S. News & World Report, USA Weekend*, *Science*, Associated Press, *Newsday*, and Reuters
- Local highlights: *Chicago Sun-Times*, NPR-affiliate radio station in Los Angeles, *The Oklahoman*, *The Philadelphia Inquirer*, and the Southern Urban Radio Network
- Recent satellite media tour included 14 interviews with television stations across the county; a radio tour is scheduled for May 2005.

To date, sources of scientific input for the Study include:
- Chartered NCSAC
- Working Groups (22)—hypotheses and measures

- Subcommittees
- Assembly meetings (December 2000, October 2001, April 2002, December 2003, December 2004)
- Workshops (28)
- Reviews and white papers (15)
- Pilot studies (22)
- More than 2,425 individuals.

The roles and responsibilities of the NCSAC have been evolving into a major role that now focuses on:

- Issues, policies, and ethical dilemmas
- Concerns of communities
- Consideration of outside proposals
- Concept reviews of pilot and adjunct studies.

Regarding the Study's organization, the key federal stakeholders include:

- Unprecedented collaboration among DHHS (NICHD, NIEHS, and CDC) and EPA, involving more than 40 federal agencies and departments
- ICC
  - NICHD—Peter Scheidt, M.D., M.P.H.; Mark Klebanoff, M.D., M.P.H.; and Ms. Keim
  - NIEHS—Sheila A. Newton, Ph.D.
  - CDC—Amy Branum, M.S.P.H.; Kenneth Schoendorf, M.D., M.P.H.; Marshalyn Yeargin-Allsopp, M.D.; and Adolfo Correa, M.D., Ph.D.
  - EPA—Pauline Mendola, Ph.D.; Sherry G. Selevan, Ph.D.; and James J. Quackenboss, M.S.
- NCSAC
- Program Office at NICHD.

Dr. Scheidt listed the Study's Program Office staff scientists and their roles:

- Full-time staff members
  - Ruth Brenner, M.D., M.P.H.—protocol development leader, project officer for the Vanguard Centers
  - Sarah S. Knox, Ph.D.—behavioral scientist, project officer for the Coordinating Center
  - Warren Galke, M.S.P.H., Ph.D.—repository and laboratory
  - Dr. Balsam—partnerships, project officer
- Part-time staff members and "detailees"
  - Dr. Fleischman, ethics, human subjects issues
  - Dr. Schoendorf—National Center for Health Statistics (NCHS), CDC, pediatric epidemiology
  - Carole A. Kimmel, Ph.D.—contractor (formerly EPA), developmental toxicology
  - Mr. Quackenboss—exposure lab
  - Rebecca Brown, M.P.H., M.E.M.—EPA
  - Randy Curtin, Ph.D.—NCHS, CDC, sampling statistics
  - Lew Berman—NCHS, CDC, information technology
  - Cynthia Moore, M.D., Ph.D.—CDC, genomics

- Denise Dougherty, Ph.D.—Agency for Healthcare Research and Quality, DHHS; health services.

Dr. Scheidt presented a slide that depicted the interrelationships among the governance and management groups and entities of the Study. The slide included the ethics advisory subcommittee under the NCSAC. Dr. Scheidt noted that this depiction was an attempt to describe the functions of the various entities, as envisioned by the ICC and Program Office.

Upcoming Study activities include:
- Establishing the Coordinating Center and Vanguard Centers
- Implementing pilot studies
  - North Carolina Herald Study
  - Information management system informed consent
  - Electronic capture of medical data
  - Quality assurance/quality control plan
- Presenting a workshop at the international cancer cohort consortium
- Providing an update to the Pediatric Academic Societies Annual Meeting, May 16, 2005
- Holding the Study assembly meeting November 29–30, 2005
- Acquiring funding.

Dr. Scheidt described the Study's funding status:
- Planning (fiscal year 2000–2003)
  - $20.7 million (from existing DHHS and EPA budgets)
- Start-up (fiscal year 2004–2005)
  - $12 million available each year (from existing budgets)
- Implementation (fiscal year 2006–2029)
  - $2.7 billion total cost spread over 25 years (approximately $100 million/year).

National Children's Study, Study Plan

Ruth Brenner, M.D., M.P.H., Director, Study Protocol Development, NICHD, NIH

Dr. Brenner noted that the Study Plan is now available online (www.nationalchildrensstudy.gov), and she listed the topics of her presentation:
- Background
- Sampling strategy
- Schedule of visits
- Proposed specimen/data collections
- Exposure and outcome domains.

The guidelines used to develop the Study Plan included:
- Study of environmental influences on children's health and development
- Environment broadly defined (physical, chemical, biological, and psychosocial)
- National in scope
- Longitudinal cohort study, beginning prior to birth continuing through age 21 years
- Sample size of approximately 100,000 live births
- Enrollment during or before pregnancy.

Dr. Brenner described the Study Plan as follows:

- The Study Plan is the document that outlines the general study design of the Study.
- Its purpose is to guide offerers so that they are better able to develop their proposals.
- The plan is less detailed than a full Study protocol or operational manual, yet more detailed than many RFPs.
- It is the first public documentation of many aspects of the Study.
- The Study Plan will evolve in greater detail with input from investigators from the Vanguard Centers and from initial Study experience.

Dr. Brenner said that with the publication of the Study Plan, the Program Office received a number of questions about whether a particular exposure or a specific outcome would be included in the Study. She explained that just because an exposure was not mentioned by name in the Study Plan does not mean that it will not be measured in the Study. Other Study documents include:

- Study protocol
  - A document that specifies data collections for the Study
  - Currently being developed by the Study Program Office, to be further developed with input from the Study Steering Committee
- Manual of operating procedures
  - A document that details all procedures to be used in the conduct of the Study
  - Prepared by the Study Coordinating Center, in collaboration with investigators from the Vanguard Centers and staff from the Program Office.

Dr. Brenner presented the following outline of the Study Plan:

- Background
- Study design and methods:
  - Who we will be enrolling (sampling)
  - When and where contacts will occur (schedule of visits)
  - Types of specimens
  - Exposure and outcome domains
- Ethical considerations.

Dr. Brenner provided an overview of sampling goals:

- A national probability sample has been selected as the sampling strategy that best fits the goals and needs of the Study.
- The target population is 100,000 live births delivered in the United States between 2008 and 2011:
  - Vanguard locations 2007–2011
  - Additional locations 2008–2011.
- Women will be enrolled as early in pregnancy as possible, with a target of 25 percent enrolled before conception.

Dr. Brenner characterized the sampling approach:

- Multi-stage, clustered household sampling approach
- Three stages of sampling

  - Selection of Study locations
  - Selection of segments
  - Selection of households
- CDC/National Center for Health Statistics conducting this aspect of Study design
- The goal is to have a sample that is representative of the demographic characteristics of births in the United States in geographic areas with varying population densities.

Most Study locations correspond to a single county. However, six locations include more than one county due to the small number of anticipated births in these areas. The Study sample can be characterized as follows:

▪ All births in the nation	Approximately 4 million births in 3,141 counties
▪ Sample of Study locations	More than 100 locations
▪ Sample of Study segments	Selection of neighborhoods
▪ Sample of Study households	All or a sample of households within neighborhoods
▪ Sample of Study women	All women eligible in the household

First stage of sample selection:
- The 101 Study locations were drawn from the full list of all counties in the United States.
- There were 13 self-representing counties (that is, counties that would be included in any probability sample of 100 counties).
- Remaining counties were placed into strata based on:
  - Metropolitan status
  - Geography
  - Average number of births per year
  - Race, ethnicity, percentage low birth weight.
- The counties were then selected based on factors such as
  - Probabilities proportional to the number of births
  - Characteristics such as the racial and ethnic composition of the county
  - Percentage of infants who are of low birth weight.
- From these strata, 26 nonmetropolitan and 62 metropolitan areas were selected.

Dr. Brenner presented a map of the United States depicting Study locations color-coded by:
- Certainty Metropolitan Statistical Area (MSA)
- Metropolitan
- Nonmetropolitan.

Dr. Brenner explained selection of Vanguard Center locations:
- From the list of Study locations, eight locations were selected to potentially serve as Vanguard Center locations
- All locations were placed into strata
  - Geography
  - Metropolitan status
  - Average number of births per year.
- Locations were randomly selected from these strata

- Two certainty MSAs; four metropolitan, noncertainty; and two nonmetropolitan
- Two locations in each of the four U.S. Census regions.

Dr. Brenner presented a map of the United States depicting the Study's sites and identifying the eight potential Vanguard Center locations by name. She said that the second stage of sampling includes selection of segments:

- Several options for defining boundaries of segments
  - Census boundaries
  - Neighborhood boundaries
  - School catchment areas
- Will be testing some of these options in the North Carolina Herald Study
- Solicit input from the successful offerers to help define the segments
- To maintain the integrity of the sample, offerers will not be involved in the actual selection of segments.

The third stage of sampling includes selection of households:

- Highly clustered sample
  - Facilitates community input and engagement
  - Facilitates collection of community measures
- May include all households or a sample of households within the segment.

The enrollment process will include:

- Community outreach and engagement
- Initial enumeration of households
- Face-to-face screening to identify eligible participants
- Enrollment of all eligible women and their partners.

The goal of recruitment is to enroll 25 percent of participants before conception, with 90 percent within the first trimester. There should be a sufficient number of women such that there are 250 live births per year. The Study hopes to recruit a statistically representative sample of the targeted area. Recruitment of Study participants will include:

- Household recruitment approach
- Supplemented with recruitment through other mechanisms such as prenatal care providers
  - Anticipate that some groups of women (for example, women not planning pregnancy) might be underrepresented in the household screening approach
- Offerers were asked to suggest alternative approaches that would meet the goals of the Study.

To be eligible, women will reside within a targeted study segment and meet the following criteria at the time of the initial screening or initial contact with the Study:

- In the first trimester of pregnancy
- Eighteen years of age or older and planning pregnancy
- Eighteen to 40 years of age who are not planning pregnancy but who are at risk of pregnancy.

Exclusions of participants include the following:

- Among the group pregnant at time of screening
  - Those who intend to move out of the segment boundaries prior to delivery

- Among the preconception group
  - Those who intend to move out of the segment boundaries within a year of initial screening
  - Women at very low risk of pregnancy (for example, women who are surgically sterile or whose partners are surgically sterile)
  - Women less than18 years of age
  - Women who are cognitively impaired or mentally ill, such that they are unable to fully understand the requirements of the Study.

Characteristics of consent and incentives include:
- Written informed consent at the time of enrollment
- As children age, will obtain assent/consent
- Incentives
  - Related to burden
  - Details are being developed.

Dr. Brenner discussed the schedule of follow-up visits (preconception):
- Frequency of follow-up visits is related to the participants' probability of pregnancy.
- Women planning to become pregnant
  - Initial screening and enrollment visit
  - Home visit for the first data collection
  - Face to face contact every other month, up to a maximum of three visits
  - Monthly phone follow-up for 6 months
  - If not pregnant after 6 months of follow-up, move to follow-up schedule of the moderate probability of pregnancy group.

Dr. Brenner presented an overview of the schedule of follow-up visits:
- Moderate probability of pregnancy
  - Initial screening and enrollment visit
  - Home visit for the first data collection
  - Contacted by phone every 3 months
- Low probability of pregnancy
  - Initial screening and enrollment visit
  - Contacted annually by telephone
- More passive contacts (for example, birthday cards, newsletters) will be sent periodically.
- Participants will have16 face-to-face contacts in their homes and at the centers for data collection as well as continual interactions over the 21-year study period at:
  - Enrollment
  - 1st trimester
  - 2nd trimester
  - 3rd trimester
  - Delivery
  - 1 month
  - 6 months
  - 12 months
  - 18 months

  - 3 years
  - 5 years
  - 7 years
  - 9 years
  - 12 years
  - 16 years
  - 21 years
- Contacts more frequent early in the Study.

Other data collection includes:
- Additional home visits with each change of residence
- Environmental samples also taken from environments outside of the home (places where the child spends 30 hours or more per week)
- Additional remote data collections (mail, telephone, Internet, etc.)
- Neighborhood measures.

Types of data collection include:
- Questionnaires and interviews
  - Face to face
  - Remote (computer, telephone, mail)
  - Diaries
- Environmental samples and observations
  - Air, dust, soil, water, home observations
- Examinations
  - Clinical and behavioral assessments
- Biologic samples
  - Blood, urine, cord blood, placenta, breast milk.

Exposure domains include:
- Biological
- Chemical
- Physical environment
- Psychosocial and behavioral.

Within these exposure domains are:
- Diet and nutrition
- Medicine usage
  - Prescription and over-the-counter
  - Vaccinations
  - Herbals
  - Supplements
  - Illicit drugs
- Genetics.

The chemical exposure domain can be expanded to include:
- Inorganic chemicals

- Organic compounds
  - Persistent organic compounds
  - Nonpersistent nonvolatile organic compounds
  - Nonpersistent semi-volatile organic compounds
  - Nonpersistent volatile organic compounds
- Criteria air pollutants.

Inorganic chemical exposures can be expanded to include:
- Bioaccumulative
  - Lead
  - Mercury
  - Cadmium
- Nonbioaccumulative
  - Arsenic
  - Chromium
  - Manganese.

The psychosocial exposure domain can be expanded to include:
- Culture
  - Subjective norms, religious practices
- Neighborhood environment
  - Social cohesion, crime
- Family influences
  - Parenting, conflict
- Daycare/school
  - Student-teacher ratio, bullying
- Individual factors
  - Health behaviors, stress.

Outcome domains include:
- Pregnancy and birth
- Child development
- Medical events.

An expanded child development outcome domain includes:
- Functional
- Physical growth, motor and sensory development
- Physiologic
- Cognitive
- Social, emotional, and psychiatric.

An expanded cognitive outcome domain includes:
- General intelligence
- Learning and memory
- Executive function

- Attention
- Language/verbal skills
- Achievement.

Dr. Brenner provided the following projected Study timeline:

▪ Fall 2004	Initial posting of RFPs for Coordinating Center and Vanguard Centers
▪ 2005	Initial contracts awarded (Coordinating Center and Vanguard Centers)
▪ 2005–2006	Start-up phase for Vanguard Centers
▪ 2006	Posting of RFP for additional sites
▪ 2007	Begin full Study with Vanguard Centers
	Contracts for additional centers awarded
	Start-up phase for additional centers
▪ 2008	Begin full Study with additional centers
▪ 2009–2010	First preliminary results available from pregnancy

Panel and General Discussion

Dr. Scheidt, moderator
Panel members:
Dr. Brenner
Warren Galke, M.S.P.H., Ph.D. Environmental Epidemiologist, National Children's Study Program Office, NICHD, NIH, DHHS
Sarah S. Knox, Ph.D., Behavioral Scientist, National Children's Study Program Office, NICHD, NIH, DHHS

The public was invited to ask questions and give brief comments toward the conclusion of all general discussion sessions.

During this session, the panel responded to questions and comments. They answered, addressed, and discussed the following issues and concerns:

- **Quality assurance/quality control (QA/QC).** Results from the North Carolina Herald Study will be available to the Vanguard Centers and will be made public. These results will help to address QA/QC issues for the Study.
- **Quality management plan (QMP).** The North Carolina Herald Study will be used to develop the Study's overall QMP, which defines QA/QC for all entities. Dr. Galke noted that EPA contractors are familiar with QMP approaches for study design, data collection, and data analysis.
- **Study measures.** An NCSAC member commented that, based on the presentations, there appeared to be some glaring absences with regard to exposure and outcomes measures. This person asked whether the final measures will evolve from the Steering Committee process. Dr. Brenner said that final measures will be specified in the Study protocol, which is still being developed. After initial contract awards, the draft protocol will be reviewed by the Steering Committee, the Coordinating Center, and the Vanguard Centers. These latter groups will help to fine tune the protocol.
- **Recruitment.** An NCSAC member asked how the Study will recruit across ethnic groups and socioeconomic strata. Dr. Brenner replied that diversity can be selected during the

second and third stages of recruitment when the segments, neighborhoods, and households are selected. Ethnicity, socioeconomics, immigrant status, and geography will be important to the success of the probability sample and a great challenge. Substantial thought and resources will be required to accomplish this goal.

- **Migration and attrition.** In response to a question about the magnitude of missing data and follow-up, Dr. Scheidt explained that issues of migration and attrition are being carefully studied. It is estimated that 5 percent of the Study participants will migrate each year, but mostly short distances. Tracking of participants is a critical element of the Study and will be the Coordinating Center's responsibility. Funding will be provided for tracking. Ways to handle migration within the United States is being planned; however, migration out of the country may be problematic.
- **Maternal oral health.** This important determinant of pregnancy outcomes will be addressed in the Study. Maternal oral health is considered under the maternal inflammation hypothesis.
- **Exclusion criteria.** Although there is no clear definition of mental illness (versus mental health) for recruitment purposes, the intent is to exclude in the preconception group women who are cognitively impaired or mentally ill such that they are unable to fully understand the requirements of the Study and provide a voluntary informed consent. In regard to other exclusion criteria, Dr. Scheidt noted that women who are less than 18 years of age will be included in the Study if they become pregnant and are part of a household selected for recruitment. However, women less than 18 years of age will not be included in the preconception group.
- **Surrogate mothers and assisted reproductive techniques (ART).** Children born to surrogate mothers and children conceived through ART will be included in the Study. There will be intentional oversampling of these exposure groups. This group of individuals may be considered for an adjunct study in the future.
- **Women in the military.** Because some of the Study sites are located near military bases (e.g.in Fayetteville, NC, and San Diego, CA), recruitment should draw in some women who are in the military, as well as their children. Dr. Balsam said that the military has expressed interest in the Study and that discussions to involve women in the military have begun.
- **Social and cultural environments.** An NCSAC member asked how the Study was going to measure exposures to social and cultural environments. Sampling social and institutional environments can be time-consuming and expensive and may require strategic subsampling. Dr. Knox noted that capturing such exposures in an epidemiological issue. The Study is considering multiple options for gathering data in ways other than face-to-face interviews. There are alternatives to in-depth data capture and many resources and entities to help gather data on these important exposures. There are numerous instruments and questionnaires for collecting data in the psychosocial and behavior domains.
- **Merged datasets.** Dr. Scheidt noted that the analysis of the Study could benefit by merging Study data with data from other sources. He suggested that there might be a database with different data sets, some of which would be on an individual-level and some of which would be on a non-individual or community level.
- **Safety of Study participants.** An NCSAC member expressed concern that simply collecting data from Study participants (for example, mothers) could have social implications to the individual, family and/or community. There may be risks for participants to honestly answer questionnaires or in-person inquiries, such as domestic violence.

- **Number of births for Vanguard Centers.** It is estimated that there will be approximately 1,250 births per Vanguard Center. There are eight potential vanguard sites, but it is anticipated that between three and eight contracts will be awarded. Therefore, the total number of births for Vanguard Centers alone could range from 3,750 to 10,000.
- **Oversampling.** An NCSAC member commented that oversampling of any particular subgroup (for example, ART pregnancies) would lead to the loss of the probability sample. Dr. Scheidt acknowledged this possible consequence but said that oversampling can be accomplished with additional births greater than 100,000 through adjunct studies
- **Data collection and tracking.** An NCSAC member commented that given the number of Study locations, there will be many schools involved in data collection. There will be challenges to measuring an enormous number of environmental variables with consistent sensitivity across the many schools. Dr. Knox said that secondary sampling may occur on the level of school districts, not at the level of individual schools. Children will have to be tracked across school districts and across counties. It was noted that school districts and school systems are not necessarily stable units or systems. There will be many challenges to achieving adequate power to discern social influences and factors as exposure variables.
- **Languages other than English.** An NCSAC member expressed concern regarding recruitment and assessment for non-English speaking Study participants. Dr. Scheidt noted that Spanish is most common second language across the United States. However, third most common language varies from region to region, and even from locale to locale. The Study intends to address language issues at the regional and local levels.
- **Manual of operating procedures.** This document will be reviewed at multiple levels of deliberation and at different stages of development, including by the Program Office, the Steering Committee, and ICC.
- **Nomenclature.** Edna Ranck, Ed.D., Westover Consultants, Inc., suggested that the Study reconsider the use of the terms *daycare* and *childcare*. Dr. Ranck said that the phrase *early childhood education and care* (ECEC) was more appropriate in this context.
- **Obstetric interventions.** Doris B. Haire, American Foundation for Maternal and Child Health, commented that the Study had the potential to change obstetric care practices and management. She noted that the exposure measures had not included obstetric interventions such as drug-induced contractions, induced labor, or off-label use of certain drugs. Drs. Brenner and Scheidt responded that the Study will assess obstetric practices and obstetric medications and treatments will be considered in assessments of expanded exposures.

In sum, the NCSAC raised the following important issues for consideration:

- A Quality Management Plan for all aspects of the Study is essential.
- The Steering Committee will need to assist in the finalization of the protocol and address specificity of measures.
- Substantial thought and resources will be required to successfully recruit diverse participants; of particular concern is the ability of the Study to recruit immigrants, minority, and rural participants.
- Substantial resources will need to be provided to address the problems of migration and attrition of the sample.
- While it is important to share information with participants and families, the safety of those individuals is important and protocols need to be developed to address concerns such as the potential for domestic violence when information is revealed.

- The integrity of the full probability sample needs to be maintained while oversampling and adjunct studies are considered.

Federal Advisory Committee Act (FACA) Overview

Mary Plummer, Director, Office of Committee Management, NICHD, NIH, DHHS

Ms. Plummer provided an overview of FACA during a working lunch/closed session.

NCSAC Ethics Training

Gretchen Weaver, J.D., Ethics Counsel, Office of General Counsel, Office of the Director, NIH, DHHS

Ms. Weaver provided ethics training during a working lunch/closed session.

Concept Evaluation: North Carolina Herald Pilot Study

Pauline Mendola, Ph.D., Interagency Coordinating Committee (ICC) Member, National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency

Dr. Mendola described the background of the North Carolina Herald Pilot Study:

- It is a response to a recognized need to test potential Study methods to be applied to the Study protocol in order to diminish uncertainties associated with methods and procedures for recruitment and retention

Study features include:

- Longitudinal cohort of prospective parents, pregnancies, and children to precede Study vanguard sites
  - Pilot test potential procedures, particularly population-based sampling and recruitment
  - Field test potential protocol items
  - Use expanded eligibility to include all pregnancies
  - Have short household enrollment time of approximately 4 months
- Goal is to improve the efficiency and likelihood of success of the vanguard and main Study sites.

Dr. Mendola provided a basic outline of the Herald Study plan including the proposed timeline:

Pilot sampling strategies include:

- Location
  - North Carolina
  - Two non-Study counties—one "urban" and the other "rural"
  - Two segments per county
- Size
  - Screen approximately 10,000 households
  - Evenly divided among segments (approximately 2,500 each)
  - Resulting in an estimated 250–400 births (approximately 80 births in each segment)
- Strategies to test

- Define study sites by Census boundaries versus school catchment areas
- Two enumeration plans—counting/listing and commercial lists.

Uncertainties regarding recruitment include:

- Test screening process (five home visits or two maximum?)
  - Assume face-to-face contact is the best to maximize recruitment
  - Mix locations—one each in urban and rural settings
  - Each segment has a consistent strategy
  - All get advance letter with telephone option
  - All get incentive to call (magnet, hang tag)
- Evaluate optimal number of visits, cost per enrollee, potential cost savings of call center
- Community, medical care system, development of optimal contact strategies.

Details of logistics and subject burden include:

- Vary measures, not visits
  - Same schedule/timing of visits as the Study
  - Visits are "home" or "clinic," same as for the Study
- Observe retention over time to estimate response in the full Study.

The Herald Study will collect the following types of data:

- Questionnaires and interviews
  - Face to face
  - Remote (computer, telephone, mail)
  - Diaries
- Environmental samples and observations
  - Air
  - Dust
  - Soil
  - Water
  - Home observations
- Examinations
  - Clinical assessments
  - Behavioral assessments
- Biologic samples
  - Blood
  - Urine
  - Cord blood
  - Placenta
  - Breast milk.

The timeline for the Herald Study is as follows:

- Enrollment begins in early 2006.
- Because women at all stages of pregnancy are eligible, the cohort is accelerated.
- Testing methods, procedures and measures are 1–2 years ahead of vanguard sites.

Details of Herald Study cohort implementation include:

- Builds on the Study plan
  - Field testing feasibility
  - Policies
  - Complex data collection protocols
- Key differences from the Study's national probability sample and vanguard sites
  - Earlier timeframe (fiscal year 2006)
  - Expanded enrollment criteria to produce early results
  - No teenage mothers
  - Scope is less comprehensive than the Study
- Conduct more validation substudies
  - Exposure measures
  - Recruitment strategies
  - Incentives
  - Alternative measures.

To explain why the pilot study chose the term *herald*, Dr. Mendola presented the following:

- Herald (noun)
  - Sign or indication of something to come; forerunner; harbinger
  - One who actively promotes or advocates
- Herald (transitive verb)
  - To give notice of
  - To proclaim, announce, greet with enthusiasm
- A new public name is likely with input from our community liaisons.

The study team for the North Carolina Herald Study includes:

- Members of the ICC, Program Office, other federal partners
  - Dr. Mendola, Primary Investigator
  - Dr. Schoendorf
  - Debra Walsh, M.S., U.S. Environmental Protection Agency
  - Dr. Brenner
  - Dr. Galke
  - Ms. Keim
- Contract support from RTI International
  - Jerry Rench, Ph.D., Project Manager
  - Sharon Myers, M.P.H., Work Assignment Leader.

Report of the Concept Review Working Group

Lucina Suarez, Ph.D., NCSAC and Senior Scientist, Texas Department of State Health Services

A Concept Review Working Group was established to evaluate the concept underlying the North Carolina Herald Study. The group was composed of three NCSAC members: Dr. Suarez, Judith A. Graham, Ph.D., American Chemistry Council, and Willa M. Doswell, Ph.D., R.N., F.A.A.N., University of Pittsburgh. The concept review was not a scientific evaluation but rather an assessment of whether the Herald Study makes sense with regard to the overall mission of the Study and whether the results of such an endeavor are worth the time, effort, and expense for this pilot study. The working group was asked to specifically address the following issues:

- The significance of the proposed research project goals from a scientific or technical perspective
- The availability of technology and other resources necessary to achieve the goals of the project
- The extent to which are identified the practical, scientific, or clinical uses for the anticipated results of the proposed study
- Attention to ensure the adequacy of inclusion of women and minorities in clinical research.

In beginning the working group's report, Dr. Suarez noted that the investigators for the Herald Study would be a collaboration of federal and nonfederal researchers. The cost of the study will be approximately $2 million. Dr. Suarez emphasized that it is important that the Herald Study results be available in time to guide the Vanguard Centers. Therefore, it is important that the study adhere to its timeline. The working group was not too concerned with the sampling protocol, which will include women at all stages of pregnancy; but it urged the inclusion of minorities and special populations. The Herald Study should address recruitment and community partnership issues.

The Concept Review Working Group unanimously approved the concept of the Herald Study.

General Discussion

Dr. Fleischman, moderator

During this session, the meeting participants addressed and discussed the following issues and concerns about the North Carolina Herald Study:

- **Exclusion criteria.** Dr. Mendola explained that the decision to exclude teenagers from the Herald study was primarily a matter of logistics. North Carolina state laws make it difficult to enroll adolescents in studies such as this one. Individuals under the age of 18 cannot provide consent for themselves; consent is required from either parents or legal guardians.
- **Data collection staffing.** Given the pace, density, and variability of data collection for the Herald Study, an NCSAC member asked what model was used for the data collection staff (that is, generalist versus specialized) and what special training, if any, the staff would require. Dr. Mendola said that the data collection team would be optimally staffed and trained and that quality assurance mechanisms would be built in. However, for the validation substudies, the requirements for specialized technicians are still being assessed.
- **Childcare environments.** The Herald Study provides an opportunity to systematically vary the childcare environments to relate these exposures to later outcomes. Dr. Schoendorf said that the Herald Study intends to include ECEC as an exposure measure.
- **Diversity and recruitment.** Ruby Takanishi, Ph.D., NCSAC ad hoc member, Foundation for Child Development, commented that North Carolina is a good state for a pilot study because of the diversity of its population. However, there must be specific recruitment strategies for immigrants, ethnic groups, and minorities. Recruitment strategies must be flexible in order to reach vulnerable subpopulations. These subgroups have particular issues with consent, migration, and mobility. Dr. Mendola explained that the household-based recruitment strategy will provide a cross-section of race, ethnicity, and socioeconomic strata. The study

will include urban and rural populations, which should capture Hispanic groups and communities.

- **Relevance to the Study.** One of the goals of the Herald Study is to inform the Study protocol regarding visit schedule, screening, recruitment, and enrollment. Dr. Schoendorf noted that because the protocol for the Vanguard Centers is not yet final, data collection processes and procedures are not set. The Herald Study can inform the Study, but the developing Study protocol may also be able to inform the Herald Study.
- **Timeliness.** Because the Herald Study schedule is about 1–2 years ahead of that for the Vanguard Centers, there will be adequate time to identify any early problems as well as areas of special interest. The early identification of problems could lead to cost savings for the Study. Dr. Scheidt commented that the Herald Study results will be available in time to inform the Vanguard Centers, that the costs of the Herald Study will be supported from existing budgets, and that the sampling panel recommended testing the feasibility of Study's recruitment and retention approaches.
- **Demographics.** The demographics of the Herald Study segments is not yet known, but the intent is to select sites that reflect the general characteristics of the U.S. population as a whole. Dr. Schoendorf said that the study team is examining data on demographics, hospital systems, and health care systems for several potential Herald Study sites. Diversity within the counties will be considered.
- **Community outreach.** The Herald Study team is exploring strategies for community outreach and involvement. The pilot study should also involve community partnerships. Evaluating previous or existing NICHD-community partnerships may inform the Study. Dr. Mendola said that there would be a suite of strategies. The pilot study will involve school systems and will contact numerous community groups, local governments, and a variety of community-based organizations.
- **Retention.** The Herald Study team plans to maximize the lessons learned regarding retention by soliciting feedback from study participants. An NCSAC member suggested that the study team examine previous or existing NICHD-community partnerships to evaluate incentives that have worked, as well as those that have not worked. Another NCSAC member asked whether the findings would be translatable to a broader arena and whether there were contingency plans for alternative recruiting strategies. Dr. Mendola said that 10,000 urban and rural households would provide an adequate test of recruitment strategies. She acknowledged that the Herald Study population probably would not be comparable to the U.S. population at large but that it would be a fair representation to inform the Study about effective recruitment strategies. Dr. Mendola noted that there is flexibility within the Study's contracting mechanism to address ineffective strategies and approaches.
- **Coverage of sampling.** An NCSAC member suggested that the Herald Study include an assessment of the coverage of sampling. Such an assessment would focus on births that are missed by the study team and evaluate models of undercoverage. The study can assess recruitment efforts and efficiencies and determine the effects of incentives on retention. However, issues of instruments, methodologies, and test names remain.
- **Measuring techniques.** An NCSAC member noted that exposure measuring techniques is rapidly evolving field, and that Herald Study has the opportunity to experiment with different data collection techniques. Qualitative techniques should also be assessed. Information can be gathered from exit interviews and other feedback from study participants. Early childhood

education and care status should be recorded as an exposure measure. Dr. Mendola said that the Study is conducting 30 focus groups to gain insight on use of technologies.

In sum, the NCSAC raised the following important issues for consideration:

- Minorities and special populations must be included in the pilot study and special attention given to strategies that will enhance recruitment and retention.
- Community partnership issues should be considered, and examining previous and existing NICHD funded community partnerships would be important.
- The relationship between the Herald Study and the National Children's Study can and should be bi-directional.
- The Herald Study has the opportunity to explore the rapidly evolving techniques for environmental exposure assessment/measurement.
- Early childhood education and care status should be measured as an exposure.
- The Herald Pilot Study appears to be consistent with the overall mission of the National Children's Study, and the results obtained appear worth the time, effort, and expense.

NCSAC Roles, Responsibilities, Processes, and Procedures

Dr. Fleischman

The purpose of this presentation was to describe the roles, responsibilities, and procedures of the NCSAC. The roles of the NCSAC are to:

- Advise, consult with, and make recommendations to the Director, NICHD; the Study Director; and the ICC
- Respond to specific requests for advice
- Serve as "ambassadors" for the Study
- Provide a forum for discussion and be available for consideration of concerns of the public, the scientific community, industry, and advocacy groups.

NCSAC members must appropriately represent the Study, support the efforts of the Study, and adhere to the rules and regulations set forth for Special Government Employees (SGEs). They may express their personal views about the Study in a public forum but may not present their views as representing those of the Committee or of the Study;

The NCSAC may have meetings and conference calls and may create subcommittees to facilitate the work effort. The NCSAC may also create Working Groups as needed.

The creation of three subcommittees was suggested for consideration by the NCSAC:

- Concept Review—provide advice and recommendations concerning pilot studies, adjunct studies, scientific questions, and aspects of the protocol as requested by the Study Director
- Ethics—provide advice and recommendations concerning various ethical issues and concerns
- Community Involvement—provide advice and recommendations concerning community involvement/engagement.

After this presentation, the meeting participants addressed and discussed the following issues and concerns about the roles and responsibilities of the NCSAC:

- **Communications.** Because the many different audiences and vehicles to disseminate information, an NCSAC member suggested a fourth subcommittee for communications. Another NCSAC member commented that strategic communications require more than community involvement; communications need to include dissemination of research findings. As the Study results are disseminated, they can become tools for change, to ultimately close the gap between evidence and policy. Dr. Fleischman noted that the Study's communication strategies are outlined in a document included in the materials that were distributed prior to the meeting. Ms. Keim commented that different communication tools should be used for different audiences.
- **Subcommittee membership/composition.** Because the next NCSAC meeting will occur in fall 2005, an NCSAC member asked whether specific subject-area experts could join the NCSAC subcommittees. Dr. Fleischman responded that the NCSAC members were selected because of their expertise in Study-related areas. Subcommittees can use the expertise of all NCSAC members and can gather information and opinions from outside experts, if necessary. However, all NCSAC members have gone through a vetting process for potential or perceived conflicts of interest and have been reviewed and approved by the directors of NICHD and NIH. Outside experts can be called on as ad hoc members.
- **Cultural competency.** An NCSAC member noted that cultural competency in an important issue for the Study. Because it will be a major issue as the Study evolves, this member suggested a subcommittee for cultural competency. Dr. Scheidt welcomed this idea but said that the identified areas of immediate need for advice were concept review, ethics, and community involvement. Subcommittees can be formed as the needs of the Study change.
- **New technologies.** Another NCSAC member suggested a subcommittee to address issues of emerging or evolving technologies. It was noted that technological issues, as well as cultural competency issued, are entwined with and cut across the areas of the three current subcommittees.

In sum, the NCSAC raised the following important issues for consideration:

- Communication is a critical aspect of the Study, and it should be addressed within the Community Involvement Subcommittee.
- Cultural competency is a critical aspect of all parts of the Study. It should be an overarching theme of all subcommittee and advisory committee deliberations.
- Emerging and evolving technology is an important theme of the Study and would benefit from its own subcommittee.
- The NCSAC should create four subcommittees: ethics, community involvement, concept review, and technology.

Public-Private Partnerships

Dr. Balsam

Dr. Balsam described the public-private partnerships in the Study as providing unique opportunities and interesting challenges. She described the formation of public-private partnerships for the Study as "a work in progress," and outlined the topics of her presentation:

- Definition
- Types/purposes and sources of public-private partnerships
- Benefits of public-private partnerships

- Challenges
- Foundation for the NIH (FNIH)
- Adjunct studies

In the context of the Study, public-private partnerships are defined as partnerships between government and non-government entities, which have been established to

- Enhance the Study's effort
- Support the biomedical research itself or the infrastructure necessary for successful implementation of the Study.

Types/purposes of public-private partnerships include:

- Adjunct studies
- Partnering assistance integral to conducting the Study
- Recruitment/retention
- Media support.

According to Dr. Balsam, partnerships can help with incentives for recruitment and retention. The incentives can be gifts of appreciation.

Public-private partnerships can provide ideas, funds, and support from:

- Industry
- Academia
- Research advocacy groups
- Associations
- Foundations.

There are three contexts in which public-private partnerships provide benefits:

- Benefit to the Study
- Benefit to the donor
- Benefit to society.

The challenges to public-private partnerships include:

- Real or perceived conflicts if interest
- The creation of undue inducements to participants
- The potential for undue influence on the Study impacting Study integrity or the appearance thereof
- Government liability
- Appearance of government endorsement of a product or company.

These are among the challenges being considered in the ongoing development of the review process for partnerships and adjunct studies.

Dr. Balsam discussed the association between the Study and the FNIH, with which there is a Memorandum of Understanding. The Foundation is authorized to raise private funds for the purpose of support of NIH scientific projects.

According to Dr. Balsam, adjunct studies are modular, focused studies that:

- Complement the core protocol
- Use the Study structure
- Involve part or all of the cohort at one or more centers, but not the entire Study cohort
- Have various initiators and funding possibilities
- Focus on research interests or community issues.

A review process is being developed for adjunct studies.

Criteria for adjunct studies include but are not limited to:

- The science is of significant public health importance
- The science and logistics are a good "fit" with the Study
- Leveraging on the Study benefits both the adjunct study and the Study as a whole
- No excessive Study/participant burden
- Appropriate for number of participants
- No problematic ethical issues
- Funding can be made available.

In summary, public-private partnerships:

- Are a natural fit for the Study
- Provide unique opportunities for
  - Collaboration
  - Funding
  - Creative thinking.

General Discussion

During this session, the meeting participants addressed and discussed the following issues concerning public-private partnerships:

- **Consent.** An NCSAC member asked whether the initial consent for the Study will also provide consent for additional studies in the future. Dr. Fleischman replied that the initial Study consent will inform the participants that they may anticipate requests for participation in additional adjunct or special studies in the future, but these will be voluntary and additional consent will be obtained.
- **Data sharing.** In response to a question, Dr. Balsam explained that the procedure for sharing data related to public-private partnerships and adjunct studies is in the process of being developed.
- **Data dissemination.** The NCSAC can play a role regarding data dissemination through its ability to advise, consult with, and make recommendations to the NICHD Director, the Study Director, and the ICC.
- **Restricted versus unrestricted funding.** An NCSAC member expressed concern about issues of restricted versus unrestricted funding. Dr Balsam explained that the process for review of public-private partnerships and adjunct studies will ensure that private (industry) funding not allow for or be viewed as "tainting" the Study.

In sum, the NCSAC raised the following important issues for consideration:

- Public-private partnerships provide excellent opportunities to enhance the Study.

- Data-sharing issues need to be discussed and policies adopted.
- The initial informed consent for the Study must inform participants that they may anticipate requests to be involved in additional adjunct and special studies. Participation in such studies should be voluntary and require additional consent.
- There is a need for a procedure to review public-private partnerships to ensure that such relationships do not create conflicts of interest, impact on the integrity of the Study, or create the impression of inappropriate influence on the Study from a partner.

Report From the Director, NICHD

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

Dr. Alexander began his report by thanking NCSAC members, both new and continuing. He explained that some of the former members left the committee to take on new roles in the Study; others left to avoid conflicts of interest as they chose to help prepare proposals for the Coordinating Center and Vanguard Centers. Those members that have stayed on continue to support the Study through their involvement with the NCSAC.

Dr. Alexander is actively engaged in soliciting funding for the Study centers so they can begin recruitment efforts. He acknowledged that it is a difficult time to obtain funding and that there are challenges in acquiring funding for full implementation of the Study. For example, Congress reduced the 2005 budgets of both NIH and NICHD. Despite these budget cuts, NICHD will contribute $7.5 million per year for the Study, as well as an additional $1.5 million year for staffing and managerial support. Other federal agencies continue to share Study costs. However, because funding from these federal agencies does not fully cover the costs, the Study will rely on other sources of support, including advocacy groups and other private organizations, to help lobby Congress for appropriate funding for the Study. Dr. Alexander emphasized the importance of funding and implementing the Study on the present timeline.

Regardless of funding difficulties, NICHD continues to lead new research initiatives, including those for:

- Obesity prevention and interventions
- Preterm labor
- Newborn screening to apply the newest genetic technologies
- The National Children's Study.

Dr. Alexander recognized the accomplishments in planning the Study over the past 4–5 years, much of which have occurred with the active support of the NCSAC, the staff recruited by NICHD (for example, for the Program Office), and staff "donated" by other federal agencies (for example, ICC members). During this period, approximately 40 federal agencies have contributed to the Study. Dr. Alexander cited the particular support of the following individuals:

- Ed Sondick, NCHS, CDC, for his contributions in developing sampling approaches
- Henry Falk, CDC, for his contributions to arranging the laboratories for measurement of biologic samples
- William Farland, EPA, for his contributions to information technology and QA/QC.

The planning phase of the Study is one of the largest federal collaborations for a research endeavor. This phase has been led by four major federal agencies (NICHD, NIEHS, CDC, and EPA), and a fifth agency (U.S. Department of Education) will be added at the specific request of Congress, which continues to support the Study in terms of language providing guidance and direction for planning and eventual implementation. However, funding for full implementation of the Study is still not assured.

Dr. Alexander stated that the Study has enormous potential to improve health care and health outcomes. He cited several examples of areas in which information developed from the Study could improve health care and health outcomes, and provide long-term benefit to America's children, including:

- Prenatal screening
- Treatment of preeclampsia
- Care of premature infants
- Autism
- Asthma
- Vaccinations (and combinations of vaccines)
- Use and safety of household products.

The Study could ultimately provide many practical applications across the whole of American society, from cost savings to improved health. The Study has the potential to have a tremendous impact in many areas of health research. Dr. Alexander urged the NCSAC to keep the goals of the Study in mind. The time spent to help plan and implement the Study will prove to be an important investment and will help reduce adverse health outcomes, saving both lives and money. Dr. Alexander again thanked the NCSAC for their participation in and support of the Study.

Recognition of Service

Dr. Alexander

Dr. Alexander recognized the outstanding service of Donald R. Mattison, M.D., former NCSAC Chair (2002–2004), NICHD, NIH, DHHS, and Jan L. Leahey, former Executive Secretary (2002–2004), NCSAC, NICHD, NIH, DHHS.

Dr. Alexander reviewed Dr. Mattison's educational background, professional experience, areas of expertise, and accomplishments. Dr. Mattison joined NICHD in July 2002 as a special assistant and senior advisor to the Director, NICHD (Dr. Alexander). His primary role was to help implement the initiatives of the Best Pharmaceuticals for Children Act (BCPA), to implement a new program for obstetric testing and pharmacology, and to assist with ongoing pediatric research. Dr. Mattison had the ideal background and experience for this role, but he also had the ideal background and training to serve as the first NCSAC Chair. Dr. Mattison agreed to serve in this capacity at the request of Dr. Alexander. In recognition of his outstanding service to the Study, Dr. Alexander presented Dr. Mattison with the Achievement Medal of the U.S. Public Health Service (PHS). Dr. Alexander described the details of Dr. Mattison's accomplishments as NCSAC Chair and read the citation of the PHS Achievement Medal.

Dr. Alexander reviewed Ms. Leahey's background, citing her superior performance as NCSAC Executive Secretary. Ms. Leahey joined NICHD not to help with the Study but to work in the Institute's contract program. She previously worked for the Health Resources and Service Administration, where she played a major role in implementing initiatives of the Ryan White AIDS legislation. Ms. Leahey's efforts were instrumental in establishing NCSAC operations. Ms. Leahey agreed to serve as the first NCSAC Executive Secretary at Dr. Mattison's request. Dr. Alexander described Ms. Leahey's roles, responsibilities, and accomplishments as executive secretary. Ms. Leahey's work allowed the NCSAC to make major contributions to the Study. She currently collaborates with Dr. Mattison on projects such as BPCA, the Pediatric Pharmacology Research Network, and the Obstetric and Pediatric Pharmacology Research Branch of NICHD. In recognition of her service to the Study, Dr. Alexander presented Ms. Leahey with an award from her colleagues as a symbol of their appreciation and affection. Ms. Leahey previously received awards from NICHD and NIH for her role as NCSAC Executive Secretary.

Day Two

Community Involvement

Community Involvement in Environmental Health Research

Giselle Corbie-Smith, M.D., M.S., NCSAC ad hoc member, University of North Carolina, Chapel Hill

Dr. Corbie-Smith presented a brief overview of the general issues of community involvement in environmental health research. She explained that her material was derived from the experiences of a National Academy of Sciences, Institute of Medicine (IOM), committee that examined some of the ethical issues in housing-related research, particularly as it pertains to children and families. One of this committee's primary areas of concern was the disparate perceptions of the community members and those of a research team that conducted a lead-abatement study in Baltimore. The perceptions involved risks to and benefits from the study for participants. Community involvement became a salient theme during the IOM committee's deliberations. Dr. Corbie-Smith did not discuss the committee's specific recommendations because the results were not public at this time.

Dr. Corbie-Smith provided the following reasons why it is important to involve communities in environment health research:

- Investigators bring technical knowledge about topics and expertise in research methodology.
- Community members bring in-depth knowledge of community concerns, needs, values, and priorities.
  - Providing the framework for study questions
  - Identifying ethical concerns about the project
  - Suggesting how to modify the study to increase acceptance of the research in the community
  - Assuring that data collection instruments are culturally appropriate
  - Promoting enrollment and retention in the study.
- Input from community members can be important for understanding the risks that research poses and identifying the most acceptable methods of ameliorating them.

- Community involvement enhances the ability of community groups to use research results in advocating for social change.

Due to social, historical, and economic contexts, classic ethical principles need to be examined in the context of application in underserved communities. Dr. Corbie-Smith cited the following reasons for this examination:

- Respect for persons—Informed consent may need to be examined if participants are vulnerable in many ways and live in communities that lack economic and political power.
- Beneficence—Participants and community representatives may have a markedly different assessment of benefits and risks of research than do researchers or institutional review boards (IRBs).
- Justice—This aspect focuses on the equitable selection of subjects. In communities where there may be multiple vulnerabilities, additional issues of power, responsibility, trust, context, and history must be considered.

Dr. Corbie-Smith listed the following concepts of community:

- The community is not the same as the target population. The distinction highlights differences between the community as self-defined compared with researcher-defined target population.
- Communities can be defined by geography, shared history, cultural identity, and other social bonds.
- Individuals can be part of multiple and overlapping communities; membership can be voluntary or through innate characteristics.
- Communities are complex associations of individuals, organizations, sectors, and social and political networks.
- Researchers should have a well-grounded understanding of the history, culture, traditions, demographics, leadership, and the institutions that are important in communities.
- A challenge is to determine who represents the community and how the community is defined.
- Research often involves participants from communities that are geographically bounded, but they may also be from overlapping cultural, social, economic and racial/ethnic communities.
- The range of stakeholders that should be considered for involvement may extend beyond the study participants.

Approaches to community involvement in research range from no involvement to passive informing to active engagement of community members and organizations as partners/collaborators. Investigators can:

- Consult with individuals "at the periphery of community cultural systems"
- Consult with influential community members for endorsement and support, but not advice or guidance
- Consult with influential community members for support, advice, and guidance, usually through a community advisory board
- Partner with the community to define the problem, identify potential solutions, and conduct research—with the community as collaborator—negotiating goals and conduct of study and analysis and use of findings

- Introduce the potential for manipulation, especially when involvement is limited and decision-making power of community members is absent.

Community-based participatory research (CBPR) involves communities as full partners in the creation of the research questions and the design and implementation of the study. It addresses issues of justice through capacity building, by directing financial and other resources back to the communities where research is being conducted, and by mobilizing the community to address issues of interest. Opportunities for community involvement in CBPR include:

- Inquiry into collaboration with those affected by the issues for purposes of education and taking action
- Stakeholders remain active partners throughout the study from formulation of research question to application of findings.
- Participants "share their knowledge and experience to identify key problems to be studied, formulate research questions, and use study results to help support relevant program and policy for social change."

In discussing its key principles, Dr. Corbie-Smith explained that CBPR:

- Recognizes the community as a unit of identity
  - Community assessment to gain knowledge about community and its economic conditions, history, norms, demographic trends and political structure
  - Recognizes the importance of relationships in "making community a reality"
- Builds on strengths and resources within the community
  - Explicitly recognizes and seeks to support or expand social structures and processes that contribute to ability of community members to work together to improve health
- Facilitates collaborative partnerships in all phases of the research
  - All participate as equal members and share control of all phases of the research
- Integrates and disseminates knowledge for mutual benefit of all partners
- Enhances collaboration that promotes co-learning and empowering that attends to social inequities
- Involves a cyclical and iterative process that acknowledges the need for commitment to the long-term nature of collaboration
- Addresses health from both positive and ecological perspectives.

One opportunity for community involvement in CBPR is through community advisory boards (CABs). CABs enhance decision making and attend to issues of justice by enhancing recruitment and advocacy for community perspectives. In addition, CABs:

- Can support informed consent by
  - Assisting in the development of materials
  - Representing participant concerns to the researchers
  - Disseminating information about the study and its risks and benefits
  - Acting as advocates for rights of participants and community perspectives
- Can refocus the research question
- Have two models
  - Study-specific
  - Institutional.

Another opportunity for community involvement is through community or participant consultation or review. Consultation engages investigators and community members in a dialogue about potential group risks, burdens, and benefits of research. Activities that might be a part of consultation include:

- Informal discussions with community members, community involvement in research planning, community participation in the evaluation of human subjects protections, and negotiations of formal community agreements
- Efforts to be "culturally sensitive, jargon free, and strictly honest," offered with "professional humility"
- Engagement before, during, and after research.

Community consultation does not replace individual informed consent but may improve and expand informed consent's function of relaying information about research-associated risks and potential benefits.

The best evidence for determining the impact of community involvement is primarily process data rather than outcome data:

- Interventions are more likely to be successful and sustained if the affected group is involved in initiation and implementation.
- Participation during program development and implementation enhances program institutionalization.
- Community involvement increases relevance, usefulness, and use of research data and improves data quality and validity.
- Demonstrating the impact of community involvement overcomes distrust of research in communities that have historically been the "subjects" of research.

Challenges to community involvement include:

- Building trust and mutual respect
- Inequitable distribution of power
  - Inequities in access to information, formal education, time, and income reflect broader social inequities structured around race, gender, and class.
  - Asks the question: Who represents the community?
  - Researchers may define "representative" differently from community members; community members may see such representation as tokenism.
- Differences in perspective, priorities, assumptions, values, beliefs, and language
- Funding conflicts
  - Conflict of principles of CBPR, with partnerships defining the issue or problem that is most relevant for them to study and the majority of funding streams that are disease- or problem-focused often narrowly defined.
- Different emphasis on tasks versus process
- Time and resources required to establish and maintain trusting relationships
- Methodological tensions—questions of scientific quality and validity; achieving balance between research and action
- Competing institutional demands—promotion and tenure, expectations of funders
- Political and social dynamics within the community.

Facilitators of effective collaboration include:

- Identification and clarification of individual and common goals; that is, community partner goals versus scientific partner goals and shared goals
- Careful attention to membership and appropriate cross-section of members
- Development of cultural sensitivity, mutual respect, understanding, and trust
- Jointly developed operating norms and procedures—encourage respect for differences and challenge processes that reinforce social inequities
- Jointly agreed upon research principles
- History of collaboration and cooperation in the community.

The role of funders in supporting community involvement is as follows:

- Funders serve as partners in collaborative effort versus only providing accountability for the project.
- The middle ground is both offering autonomy and engaging partners in conferences and other technical assistance activities.
- Funders can support organizations that promote community development.
- Funders can provide adequate and flexible funding to support the long-term need to establish academic-community partnerships and engage community members.

Community Involvement in the National Children's Study

Sarah A. Keim, M.A., National Children's Study Coordinator, NICHD, NIH, DHHS

Ms. Keim presented an historical overview of the Study's efforts in engaging and learning about communities. She outlined the topics of her presentation:

- Importance of community involvement in the Study
- Ways in which the Study is unique
- Activities to date
- Future plans.

Ms. Keim provided a long list of the numerous communities that will be involved in the Study, from researchers and clinicians to federal, state, and local governments. She said that because the Study will have 101 site locations, the Study's focus will be on local communities.

The essentials for Study success include:

- Success of participant recruitment and retention will depend on active engagement of communities.
- Not unique to this Study, but especially important
  - Length of Study, commitment
  - Localized research effort.

The Study's approach compares with CBPR as follows:

- The Study does not follow a strict CBPR model; it uses research questions that require uniform data collection from all communities in the national sample to answer its questions.
- Because the Study is not an intervention study and because there will be a nationally defined protocol, the Study does not follow a CBPR model.
- The Study will adapt CBPR principles as feasible.

- The Study intends to address big issues that often mesh with community concerns.

Community outreach activities to date include:
- Research, best practices
  - Focus groups
  - Review of literature
  - Reviews of previous studies
- Consultation
  - Community Outreach and Communications Working Group
  - Workshop on community outreach
- Outreach—national and local
- Tools development (publications, Web site)
- Requirements for Vanguard Centers and Coordinating Center.

The Study has held many focus groups to assess the distinct views of potential Study participants. Ms. Keim characterized these focus groups as follows:
- EPA led 32 focus groups in 2003–2004
  - 14 locations
  - Expectant parents, parents of children with disabilities, other parents, health care providers, community representatives
  - Couples trying to conceive, pregnant women, mothers, pregnant teenagers, teenage mothers
- Questions asked included or related to:
  - How can we get you interested?
  - Reaction to time commitment, data collection activities
  - How do we keep you engaged?
  - Incentives
  - Preferred mode of communication
  - Types of information to receive
  - Confidentiality
  - Preferred role of local physicians, community organizations
- Program Office/Ogilvy
  - Nine focus groups in 2004
  - Health care providers (physicians, nurses, pediatric and obstetric)
  - Community organizations
- What would it take to support the effort?
  - Alignment with goals, value for clients, sensitivity to special needs and potential barriers
  - Preferred role—information, recommend participation
  - Would support an effort if it improves health of community, is aligned with goals, and involves unique or high-impact research.

The Study planners examined lessons learned from previous studies such as:
- EPA/NIEHS children's environmental health centers
- Women's Health Initiative
- Framingham Heart Study

- Avon Longitudinal Study.

The Study's national outreach efforts included:
- Briefings and meetings with many national organizations
- Developing avenues of communication
- Identifying a variety of ways to assist
  - Direct connection to potential participants
  - Direct connection to clinicians, others
  - Authoritative issue representative
  - Bring ideas, concerns.

The Study's local outreach efforts included:
- Awareness-building
- Build capacity to be knowledgeable champions.

Study representatives have been invited to present the goals of the Study to two communities:
- Montgomery County, MD, in February 2005
- Orange County, CA, in March 2005.

Multiple audiences were targeted for the milestone announcement on November 16, 2004:
- Scientific and academic community
- Local governments
- Key federal partners
- State maternal and child health representatives, governors
- Participants via the media
- Reaction/response.

The Vanguard Centers' request for proposals asked for:
- Community needs assessment, including
  - Interaction with Study protocol
  - Community focused adjunct studies
- Community engagement plan
- Work with prenatal care providers for recruitment.

The Coordinating Center request for proposals asked for:
- Community outreach and communications plan
- Support for centers' efforts.

To date, the Study's tools development includes:
- Program Office role
- *Growing Up Healthy*
- *Communications Strategy*
- Brochures
- Web site—present, future.

Ms. Keim summarized the Study's future plans for community involvement:

- Program Office—ongoing outreach, work with media, tools development, promotion of concept
- Vanguard Centers—intense local work, implement proposals
- Coordinating Center—support Vanguard Centers and planning.

Response to Community Involvement Presentations

James N. Jarvis, M.D., NCSAC ad hoc member, University of Oklahoma Health Sciences Center
Peggy M. Shepard, NCSAC ad hoc member, West Harlem Environmental Action, Inc.
Bernice Pescosolido, Ph.D., NCSAC ad hoc member, Indiana University

These NCSAC ad hoc members presented their responses to the previous presentations and, within the context of the Study, offered their views on optimizing community involvement and engagement.

Dr. Jarvis began his response by noting that there are always practical challenges and risks when involving communities in research. The data are never neutral. Dr. Jarvis cited an example of study of HIV prevalence by Census tracts and the effects the study's results had on communities. Published research may actually bring harm to a community. Dr. Jarvis noted the beliefs about DNA and tissue repositories among Native Americans. There are cultural differences in the perceptions of the individual and community. Dr. Jarvis provided the following example from the Navajo nation: "We are, therefore, I am." There are different views and rules regarding an individual's autonomy. Native Americans also have different views about who is authorized to speak for the community. According to Dr. Jarvis, the notion of a single representative "speaking for the community" is a Western concept—not a Native American concept. Another important issue regarding community involvement and CBPR is the need to address risks and set policies that allow implementation of the research findings, the need to systematically address a community's issues and concerns, and the need to address a community's future needs. Dr. Jarvis recommended that organizations, individuals, and media within the greater Native American community (for example, the head of the National Indian Health Board) be included in the planning and early implementation of the Study.

Ms. Shepard began her response by commenting that significant planning for the Study has been conducted in a centralized manner. It is important that the Study has begun to survey attitudes and opinions. However, survey results and values gleaned from marketing outreach will have to be implemented strategically in different ways in different locations. Ms. Shepard identified the following issues that need to be addressed in local academic-community partnerships for the Study:

- Community involvement and partnerships need time and resources to develop.
- Research teams at each locale need to develop a solid plan to promote the Study, inform the public about the Study's goals, and emphasize the need to address concerns at both the local and national levels.
- The promotional plan should map out the key players, leaders, advocates, and community-based organizations that represent a variety of community concerns.
- Once the mapping has occurred, the research team can begin recruiting groups and constituencies for their community partnership.

- Both the research team and the community representatives need training, which should outline study concepts and principles of collaboration. Training should address communication, decision-making processes, capacity-building, development of relationships and respect, continuity of participation, and ethical issues.
- Community partnerships need to earn and then build upon mutual trust and respect.
- These partnerships need a strong CAB mechanism. The CAB should be well trained and have defined objectives and tasks. Community initiatives should be expected from such groups of advisors.
- Resources are needed to compensate community representatives for their work and efforts.
- Community partnerships need to focus not only on the needs of the community but also on the needs of the researchers, who should be involved in a plan in which they are exposed to the community and come to understand the community's needs and concerns.
- Ethical issues need to be addressed, including informed consent, genetics, communication of findings, translational strategies, and ongoing briefings for elected officials, policymakers, and the media.
- Ongoing training and education are important to maintain community partnerships.
- Active community engagement requires a major promotional effort to galvanize the interests and communicate the common goals in an effort to recruit and retain study participants.

Dr. Pescosolido described community engagement as a "massive challenge" for the Study. Her presentation shifted from focusing on challenges of local community involvement to focusing on the link between local and national communities regarding issues of recruitment and retention. Dr. Pescosolido expressed her concern about a mismatch between community members and the researchers, with their particular set of skills and knowledge, and their lack of understanding of how, when, and where to engage communities. The Study needs strong national guidance and assistance to the local centers. Those involved in planning and implementing the Study should establish a strong national presence in the communities that participate in the Study.

According to Dr. Pescosolido, there are four reasons why individuals decide to participate in research:

- Benefit to self
- Altruism
- Curiosity
- Coercion.

Dr. Pescosolido suggested three tools, which have been used successfully in non-CBPR endeavors, to help the Study establish a national presence in participating communities

- National Mental Health Awareness Campaign—The goal of this campaign was to increase knowledge and decrease stigma of mental illness. The campaign slogan was "Change Your Mind." It applied the idea of "branding"; that is, it had its own song, brochures, public service announcements, television advertisements, a letter to Dear Abby, and links to technologies (for example, a Web site for the campaign). Dr. Pescosolido said that the Study could develop its own slogan, such as "Watch the Children Grow," and apply similar branding techniques to raise awareness. She suggested that the Study carefully choose and use its partners.

- U.S. Department of Agriculture Web site—This highly informative Web site provides what media people need and can use: ready-made news and packaged information. The USDA Web site has successfully addressed issues of translation by turning scientific findings into easily digestible news.
- New and evolving technologies—Dr. Pescosolido cited as an example "Pod casts," which are services or programs created for listening as downloads to an iPod or MP3 player. These downloads offer innovative approaches to dissemination of information. Approximately 22 million American adults own iPods; as many as 23 percent of these iPod owners have downloaded Pod casts. Ms. Pescosolido urged the Study to stay on the cutting edge of new and evolving technologies in order to engage individuals and communities and to keep them involved in the Study.

General Discussion

Dr. Fleischman, moderator

Loretta Jones, M.A., NCSAC Member, Healthy African American Families, opened the discussion with some comments on her experience with community involvement and engagement, for both the Study and her professional activities in California. Ms. Jones said that her purpose at the meeting was to represent "community." She asked: "Who is the community?" Her answer was: "We all are community." There can be no separation of "they" and "us." Ms. Jones said that language must change to be inclusive (that is, "we" and "us"). The people who help conduct the Study will need to learn to speak the language of "community." The Study's researchers must be ready to answer participating communities in language that is culturally and linguistically appropriate.

The aims of community engagement include:
- Addressing multiple levels of the social environment to bring about desired changes
- Ensuring that efforts are culturally and linguistically appropriate
- Interweaving members to provide a sense of ownership and capability
- Nurturing community mobilization and self-determination
- Building coalitions.

Successful community engagements:
- Develop meaningful partnerships
- Respect community diversity
- Identify and mobilize community assets
- Assure long-term commitment.

The community engagement model involves ongoing relationships among the following activities:
- Planning
- Evaluating
- Implementing
- Engaging community.

In concluding, Ms. Jones urged the research community to address the issues raised by their research, and to put their findings into practice and action, in order to change policies and health outcomes in communities.

During the general discussion period, meeting participants addressed and discussed the following issues and concerns about community involvement in the Study:

- **Community outreach.** In response to an NCSAC member's query about organizations contacted by the Study, Ms. Keim said that the Program Office has communicated with a variety of nursing organizations, including the American Nurses Association, the National Institute of Nursing Research, and several obstetric and neonatal nurses groups.
- **Mutual benefits.** Dr. Corbie-Smith suggested that a new emphasis, or common thread, that can be used in community outreach is to consider not what communities can do for the Study, but what the Study can do for communities. This approach shifts the focus to mutual benefits. Dr. Scheidt reminded the meeting participants that the RFP for the Vanguard Centers stipulates a needs assessment for each community, which will identify the community issues and address specific, local community needs. Dr. Corbie-Smith commented that capacity building is a common need for all communities.
- **Community recognition.** The Study needs to recognize and identify engagement strategies for specific communities, including:
  - Older, established Hispanic groups
  - New immigrant Hispanic groups
  - Teenagers, adolescents, and dropouts.
- **Open communication.** The Study needs to avoid repeating the disasters of past CBPR (such as HIV/AIDS studies). To this end, it needs transparency and openness in its communications. Communities should be involved in the design of studies and data analysis.
- **Research to practice.**
  - The Study Web site can be used as a resource for health related information.
  - The Study must find a way to convert the results from raw data to policy changes that will benefit the communities.

In sum, the NCSAC raised the following important issues for consideration:

- The Study should be cautious with what is published. Published research may actually bring harm to a community. At a minimum, communities must be informed and involved with the publication of information related to their environment and members.
- There are distinct cultural differences in the perception of the individual and the community.
- The Study must gain the trust and respect of the community as a whole, not just from the representatives of the community.
- As best possible, the Study needs to incorporate the community throughout the planning stages, during the implementation phase, and into the future.
- Research partnerships with the surrounding community take time and resources to develop.
- The Study community should be broken down into more manageable segments. Communication strategies must be geared individually to these subgroups.
- It is a challenge to correlate geographic communities and cultural communities.
- A Community Advisory Board (CAB) may provide structure for a relationship with a community.

- There are four reasons why individuals decide to participate in research: benefit to self, altruism, curiosity, and coercion. These should be taken into account in planning.
- The Study must become a brand in order to attract individuals and to develop lasting ties. Brand loyalty is a powerful relationship building tool.
- The Study Web site can be used as a resource for health related information.
- Study researchers must consider themselves as part of the community, not as a separate entity.
- Study research should be committed to being translational. The Study must find a way to convert the Study results from raw data to policy changes that will benefit communities.
- The Study must remember that it is not just what can the communities do for the Study, but what can the Study do for the communities.
- Innovative approaches aiming to build capacity in participating communities are important.
- The community is not "we" versus "them." We are all part of communities.
- Nurses are generally trusted by the community. The Study may benefit from incorporating these professionals into community outreach efforts.
- The NCSAC can play a role in assuring there is a strategy to translate Study findings into local and national "action" to enhance the health and well-being of children.
- The NCSAC can provide technical assistance to local centers and provide a forum for accountability in the area of community involvement/engagement.

Ethical Considerations: Use of Incentives to Enhance Recruitment and Retention

Dr. Fleischman

Dr. Fleischman began his presentation by noting that the NCSAC can play a vital role in ethical considerations for the Study. To this end, ethical considerations for the Study include:

- Study design/subject selection
- Recruitment/retention, including compensation and incentives
- Informed consent
- Privacy/confidentiality
- Genetic information
- Stored samples/tissue banking
- Data analysis/data ownership
- Revealing findings/informing subjects and families
- Publication/information dissemination.

Dr. Fleischman explained that the use of incentives to enhance recruitment and retention was addressed in the Study Plan (page 73 of 145):

- "Recruitment and retention will be a significant challenge in light of the observational nature of the study and the longitudinal commitment required of participants."
- "Reasonable incentives will be part of the strategy for recruitment and retention of participants."
- Compensation will include:
  - Reimbursement for expenses
  - Payment for time spent in participation
  - Small gifts of appreciation.

However, the Study will not provide undue inducements for participation. Dr. Fleischman noted that the ethical dilemma is the determination of what is "due" and what is "undue" in terms of inducements. This dilemma is not new to IRBs or researchers. Because there are not standard approaches to incentives across IRBs, the Study needs to develop its own specific approach.

After Dr. Fleischman's presentation, the meeting participants addressed and discussed the following issues and concerns about ethical considerations of incentives in the Study:

- **Vehicles of reimbursement.** There are differences for—and complications with—different vehicles of reimbursement. Checks sometimes take weeks or even months to process and mail. Study participants often need immediate reimbursement of expenses, especially for child care and transportation. Although cash is a preferable vehicle for reimbursement, some institutions and universities cannot issue cash for reimbursements. Checks may require social security numbers to cash, and not all Study participants will have a social security number. Gift cards for national chain stores may be highly valued.
- **Reimbursements to communities.** An NCSAC member suggested that community members and organizations may need to be reimbursed for their time and efforts with Study participation.
- **Transportation.** Because of difficulties with transportation in remote or rural areas, community gifts or community-specific compensation may be important.
- **Retention versus recruitment.** Over the 25 or so years of the Study, incentives for retaining participants may prove more important than incentives during recruitment. Incentives can be increased in a stepwise manner as children pass Study milestones. Incentives may be needed for both children and parents. Inducements to stay in the Study may be perceived as coercive, however. An NCSAC member expressed concern that excessive compensation may place Study participants at retaliatory risk. Another concern was that at some point incentives could transform the Study from being strictly observational to being considered an intervention study.
- **Teens.** It was suggested that later in the Study, other processes and incentives may be necessary to engage and retain teenagers in the Study.
- **Financial incentives.** Saving bonds or savings accounts, or the promise to pay future educational expenses, could place Study participants into elite or unique groups or select populations, which could conflict with the need for privacy. Class differences could create social burdens or high risk for Study participants receiving financial incentives. Different groups may need different incentives, and financial incentives may not be appropriate for all groups. There should be flexibility in and choice of incentives.
- **Health care.** Because a large percentage of the U.S. population does not have medical insurance, participation in the Study may be perceived as a means to receive health care. Dr. Fleischman explained that the Study will not provide medical or clinical care to uninsured participants. The Study will provide access to medical care through existing mechanisms (such as referral to social services and Medicaid). Access to care may include "fast tracking" to facilitate entry to care. There will be emergency contingencies and emergency protocols; there will be a threshold of action for all measures and exposures.
- **Informing communities.** If something is happening within a community, the information will be conveyed to the community. The Study will have policies for intervention, for both individuals and communities. Although the Study is obligated to provide information on

available resources and interventions, there is no mechanism to assure that participants will seek care.

In sum, the NCSAC raised the following important issues for consideration:

- The committee was impressed with the importance of engaging the trust of the participants as perhaps the greatest "incentive" to recruitment and retention. Methods to convince the participants that children and their community will ultimately benefit will be of importance.
- Incentives may differ among sites. The Study should provide general guidance about ranges of incentives and approve gifts of appreciation that are provided.

Support of the Study I: American Association on Mental Retardation

Michele Gagnon, M.P.H., American Association on Mental Retardation

Ms. Gagnon, Director, Environmental Health Initiative, American Association on Mental Retardation (AAMR), expressed the AAMR's strong support for the Study. She noted that:

- Research has increasingly implicated environmental toxicants as contributors to learning and developmental disabilities, including mental retardation.
- For approximately one-third of the cases of mental retardation, the cause is unknown.
- There may be connections between the environment and these cases with unknown causes.
- The Study can provide more definitive answers about the relationship between environmental toxicants and mental retardation and developmental disabilities

Ms. Gagnon reviewed research recommendations that were developed at an AAMR summit and published in a document titled *Pollution Toxic Chemicals, and Mental Retardation—Framing a National Blueprint for Health Promotion and Disability Prevention.* The specific recommendations were for research on:

- Interactive effects of chemical mixtures in "real-world" situations to better understand the link between toxic exposures and developmental disabilities
- Interactions and associations of other risk factors on disability such as pollution, health status, poverty, nutrition, and socioeconomic status
- Heightened sensitivities and impacts of toxic exposures on those currently living with mental retardation and developmental disabilities.

Ms. Gagnon expressed her opinion that, with full funding of the Study, these research areas and more would be addressed regarding the connection between environmental factors and disability. The Study holds great promise in providing answers as to how myriad toxic chemicals in the environment affect brain development and other aspects of children's health.

Support of the Study II: Society for Maternal Fetal Medicine (SMFM)

Haywood L. Brown, M.D., Duke University Medical Center, former President, SMFM

Dr. Brown expressed his strong support for the Study, noting that it is critical that a better understanding of growth and development be gained. Many diseases, conditions, and disorders have their origin in utero. Obstetrical medicine has learned much over the past century or so, but not much has changed in the natural process of conception, pregnancy, and childbirth. Advances in obstetrical medicine have lead to improved birth outcomes and higher survival rates for

mothers and children. Congenital diseases and developmental disabilities provide new challenges for this branch of medicine.

Dr. Brown briefly reviewed the history of obstetrical medicine and described its development into modern maternal-fetal medicine. He explained that maternal-fetal medicine now provides obstetrical care for women with pregnancies that are complicated by the maternal and/or fetal conditions (that is, high-risk obstetrics).

Dr. Brown provided the following information on the Society for Maternal-Fetal Medicine:

- SMFM is the membership organization for obstetricians and gynecologists who have completed an obstetrics and gynecology residency and postresidency fellowship training in maternal-fetal medicine.
- SMFM's primary mission is to promote and expand education in maternal-fetal medicine and to encourage the exchange of new ideas and research concerning the most recent approaches and treatments for obstetrical and fetal conditions and diseases.
- SMFM:
  - Currently has about 2,000 members that are dedicated to improving perinatal care
  - Hosts an annual scientific meeting for the discussion of new ideas and research in maternal-fetal medicine
  - Offers continuing medical education courses throughout the world.

Regarding medical expertise, Dr. Brown said that:

- Most women with pregnancy complications seek consultation or care with a maternal-fetal medicine subspecialist to receive treatment of complex maternal and fetal disorders.
- Maternal-fetal medicine subspecialists have expertise in genetics, prenatal diagnosis, and intrauterine conditions. They collaborate with pediatric subspecialists to outline courses of care after delivery.
- During pregnancy, patients may undergo diagnostic or therapeutic procedures such as:
  - Comprehensive ultrasound
  - Prenatal diagnostic screening and treatment
  - Chorionic villus sampling, amniocentesis, or fetal surgery or treatment.
- Maternal-fetal medicine subspecialists treat women with medical or surgical disorders such as:
  - Premature labor
  - Heart disease
  - Preeclampsia (toxemia)
  - Diabetes or other endocrine disorders
  - Kidney or gastrointestinal diseases
  - Infectious diseases.
- Other types of patients include healthy women whose pregnancies are at markedly increased risk for adverse outcomes such as:
  - Abnormal AFP (alpha fetoprotein)
  - Multi-fetal gestation
  - Recurrent preterm labor and delivery
  - Recurrent pregnancy loss
  - Suspected fetal growth restriction

- Congenital conditions or diseases.

Dr. Brown further characterized SMFM as follows:

- SMFM is an advocate for improving pubic policy and expanding research opportunities in maternal-fetal medicine through collaboration and networking with governmental and other organizations.
- SMFM's research priorities include:
  - Prematurity
  - Preeclampsia
  - Fetal diagnosis
  - *In utero* therapy and fetal surgery.
- SMFM collaborates with:
  - NIH Maternal-Fetal Medicine Network
  - March of Dimes
  - American Institute of Ultrasound in Medicine
  - Society for Obstetric Anesthesia and Perinatology
  - North American Society for Obstetric Medicine
  - CDC.

Dr. Brown concluded his presentation by sharing his excitement about implementing the Study and having an opportunity for SMFM to collaborate with the Study.

Support of the Study III: Children's Environmental Health Network

Nsedu Obot Witherspoon, M.P.H., Children's Environmental Health Network

Ms. Witherspoon thanked the NCSAC for the opportunity to participate in the meeting. She began her presentation by characterizing the Children's Environmental Health Network (CEHN):

- CEHN is a national nonprofit organization.
- Its mission is to protect fetuses and children from environmental hazards.
- CEHN's efforts focus on policy, education, and research.

CEHN's goals are to:

- Promote development of sound public health and child-focused national policy
- Elevate public awareness of environmental hazards to children
- Educate health professionals, policy makers, and community members
- Stimulate prevention-oriented research.

CEHN supports the Study in the following ways:

- CEHN board members on NCSAC
- Incorporation of Study into national presentations
- Supports of appropriation of funding
- Posts current information on Web site and listservs.

Ms. Witherspoon listed the following reasons why CEHN supports the Study:

- Goal 1: Promoting sound public health and child focused national policy
  - Opportunities for preventing disease

  - Targeted health promotion programs can address child health policies
- Goal 2: Elevating public awareness
  - Consistent messages highlighting major health challenges
  - Role environmental exposures have in health challenges
- Goal 3: Educating health professionals, policy makers, and community members in preventive strategies
  - Provide needed data
  - Data will inform needed strategies
- Goal 4: Stimulate and support prevention-oriented research
  - Opportunity to answer key scientific research questions
  - Opportunity to build data source
  - Opportunity to determine links between environment and childhood/adult diseases.

The Study needs the following support to move forward:
- True collaborative effort
- Working to address health disparities
- Effective and vital communication
- Identification of barriers and overcoming those challenges
- Unprecedented opportunity to better understand the link between children's environments and their physical, mental health, and development.

Ms. Witherspoon said that for all of the just-mentioned reasons, CEHN strongly supports the Study and stands ready to actively assist the Study in moving forward. She thanked the meeting participants and all of those involved with the Study for their wonderful work in protecting the health of children.

Friends of NICHD

Ms. Keim

Ms. Keim provided a brief overview of the Friends of NICHD. The Friends of NICHD is a very active coalition of nearly 100 organizations. It is composed of organizations representing scientists, health professionals, and advocates for the health and welfare of children, adults, families, and people with disabilities. This coalition supports the full range of NICHD projects, activities, efforts, and research and strongly supports the broad mission and goals of the Study. Several organizations have recently joined the Friends of NICHD specifically to be engaged in efforts to support the Study.

The co-chairs of the Friends of NICHD have been active supporters of the Study. The co-chairs are Marion McCabe of the Society for Research in Child Development and Mary Jo Hoeksema of the American Population Association. The immediate past chairs, who were representatives from the American Academy of Pediatrics and the March of Dimes, also actively supported the Study. Ms. Keim reported that the Study has also been supported by the American Chemistry Council, as well as some newer partners such as the National Hispanic Medical Association and the National Rural Health Association. The Friends of NICHD are always looking for new partners and are seeking speakers for briefings, meetings, and other communication efforts. Ms. Keim urged the NCSAC to contact the Friends of NICHD to see how they can help this coalition

support the Study. Ms. Keim cited a letter from the Friends of NICHD to Dr. Alexander. The letter expressed enthusiasm for and support for the Study; it was signed by more than 40 organizations.

General Discussion

Dr. Fleischman, moderator

Dr. Fleischman prefaced this discussion by explaining that the NCSAC cannot, as a group, embark on advocacy activities on behalf of the Study. However, NCSAC members can, individually, advocate on behalf of the Study. To this end, Dr. Fleischman asked the NCSAC members:

- What are their thoughts, advice, and recommendations about how to assist in getting the Study fully funded?
- What can NCSAC members do as individuals to support the Study?

In response, NCSAC members and other meeting participants answered, addressed, and discussed the following issues and concerns:

- **Communication.** Dr. Brown suggested that the NCSAC and others involved in the Study communicate with any person or organization that is willing to learn more about the Study. These communications will advance in stepwise progressions. Dr. Brown pledged to advocate for Study funding in whatever way possible.
- **Collaborators.** Dr. Scheidt said that the Study can generate support from the pediatric medical population, which should look for research opportunities within the Study. Dr. Scheidt mentioned the Pediatric Academic Societies as a potential collaborator. An NCSAC member mentioned the Society for Adolescent Medicine as another potential collaborator.
- **Congressional gate keepers.** An NCSAC member inquired about congressional members who are important or critical in unlocking the funding streams for the Study. Dr. Fleischman promised to provide this information to NCSAC members.
- **Finite funding.** There are concerns and a misperception within the academic research community that funding is finite and that funding that goes to the Study will reduce funding to other research projects. There is a need for NCSAC members and others involved in the Study to let researchers know that the Study will have its own funding stream and will not detract from others. It is well proven that such large research projects actually have a "multiplier effect." When fully funded, the Study will in turn generate other projects, activities, efforts, and research. The Study will provide "seed money" for these other activities. NCSAC members should relate this positive message. The Human Genome Project was cited as an example of the multiplier effect. This initiative broadened interest and perspectives and led to expanded human genome-related research opportunities.

NCSAC Members

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Robert E. Chapin, Ph.D., ad hoc member, Pfizer Inc.

*Frank A. Chervenak, M.D., ad hoc member, Cornell University
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*George P. Daston, Ph.D., Procter and Gamble
Allen Dearry, Ph.D., ex officio member, NIEHS, NIH, DHHS
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*Antoinette P. Eaton, M.D., ad hoc member, Ohio State University
*William H. Farland, Ph.D., ex officio member, Office of Research and Development, EPA
Myron Genel, M.D., ad hoc member, Yale University
Judith A. Graham, Ph.D., American Chemistry Council
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Loretta Jones, M.A., Healthy African American Families
Bruce Levin, Ph.D., ad hoc member, Columbia University
Jeffrey Long, Ph.D., ad hoc member, University of Michigan
Edward R. B. McCabe, M.D., Ph.D., ad hoc member, University of California, Los Angeles (participated via telephone)
Robert T. Michael, Ph.D., University of Chicago
Barbara Anne Nabrit-Stephens, M.D., M.B.A., ad hoc member, Keystone Mercy Health Plan
Bernice Pescosolido, Ph.D., ad hoc member, Indiana University
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Peggy M. Shepard, ad hoc member, West Harlem Environmental Action, Inc.
Lucina Suarez, Ph.D., Texas Department of State Health Services
Ruby Takanishi, Ph.D., ad hoc member, Foundation for Child Development
Alan M. Zaslavsky, Ph.D., ad hoc member, Harvard University

**Did not attend.*

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Program Office Scientists

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**Did not attend.*

Observers and Other Participants

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Nsedu Obot Witherspoon, M.P.H., Children's Environmental Health Network

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

8/1/2005
Date

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