

**National Children's Study
Federal Advisory Committee 30th Meeting
October 19, 2011
5635 Fishers Lane Conference Center
Rockville, MD**

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

Welcome and Introductions

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

Dr. Henry welcomed the meeting participants, who introduced themselves. She thanked Benjamin S. Wilfond, M.D., for chairing the July 20, 2011, NCSAC meeting. Dr. Henry reviewed the highlights of the July meeting:

- Summary of meeting and presentations posted to Study Web site
- Study Update: Increased Sample Size
- Presentations
 - Practice-Based Recruiting Opportunities and Challenges—Daniel Hale, M.D., University of Texas Health Science Center at San Antonio
 - Provider-Based Sampling for the National Children's Study: Some Thoughts—Michael Elliott, Ph.D., University of Michigan School of Public Health and Michigan Alliance for the National Children's Study
 - Draft Concept of the National Children's Main Study—Ruth Brenner, M.D., M.P.H., Associate Director for Science and Protocol Development (Study Visit Measures), Program Office, National Children's Study
 - Final Report of the NCSAC Data Presentation Working Group—Jonas H. Ellenberg, Ph.D., University of Pennsylvania School of Medicine
 - Table Shells for Presenting Vanguard Study Data from the Alternate Recruitment Substudy—Brian Haugen, Ph.D., Senior Scientist (Analysis and Evaluation), Program Office, National Children's Study
- Meeting Summary—Ana V. Diez-Roux, M.D., Ph.D., M.P.H., University of Michigan

Dr. Henry reviewed the agenda for the October 19, 2011, NCSAC meeting.

National Children's Study Update

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

The Study was congressionally mandated by the Children's Health Act of 2000. It is an integrated system of activities to examine the effects of environmental exposures and genetics on

children's growth, development, and health. Environment is broadly defined to include factors such as air, water, soil, dust, noise, diet, social and cultural settings, access to health care, socioeconomic status (SES), and learning. The Study is required to

- Incorporate behavioral, emotional, educational, and contextual consequences to enable a complete assessment of the physical, chemical, biological, and psychosocial environmental influences on children's well-being
- Gather data on environmental influences and outcomes on diverse populations of children, which may include the consideration of prenatal exposures
- Consider health disparities among children, which may include the consideration of prenatal exposures.

Dr. Hirschfeld briefly reviewed the following:

- Study principles
- Examples of exposure areas of interest
- Examples of outcome areas of interest
- Study structure
- Study activities
- Vanguard Study goals
- Current sampling frame
- Alternate Recruitment Substudy.

Dr. Hirschfeld explained that the Vanguard Study will precede the Main Study by about 3 years and run parallel to it. Because the Study is data-driven and not calendar-driven, there is no commitment to begin the Main Study at a particular date. The Study is still gathering and analyzing data and, based on data, will re-evaluate the approach and time for initiating the Main Study.

The Alternate Recruitment Substudy is gathering data on recruitment and retention to inform the Main Study. The three alternate recruitment strategies are provider-based, enhanced household, and direct to the public recruitment (also known as Hi/Lo). The Alternate Recruitment Substudy will use both direct data analyses and predictive modeling. The goal of the substudy is to compare strategies to assemble a toolkit for cost-effective directed recruitment for the Main Study launch. A newly initiated recruitment strategy will use a variation on the current sampling frame based on the address of health care providers within a geographic sampling unit instead of the address of the potential study participant. Thus all women served by a particular provider are eligible in contrast to the prior model where only women with a home address in a preselected geographic segment who were served by a provider were eligible. The goal is to test the efficiency and dynamics of the variant sampling frame.

Prevalence of Conditions of Potential Interest. It is estimated that, of 100,000 children, the prevalence of conditions of potential interest are:

- 30,000 overweight, 17,000 with obesity
- 5,000 with learning disorders
- 5,000 with asthma
- 1,000 with autism spectrum disorders
- 1,000 with high risk of schizophrenic disorders

- 750 with congenital heart disease
- 320 with childhood cancers
- 125 with Down syndrome
- 50 with Fragile X syndrome.

The Study is not proposing a threshold for rare disease. The U.S. legal definition (from the Orphan Drug Act) of a rare disease is a prevalence rate of about 0.06 percent or 64 per 100,000 births. Conditions of interest such as congenital heart disease, childhood cancer, and autism spectrum disorders have prevalence rates between 0.5 percent and 1 percent. Because they are topics of separate NIH initiatives and congressional mandates and are supported by advocacy groups, they are expected to be addressed by the Study. The Study has implied or, in some cases, stated commitment to acquire data about these conditions.

Study Recruitment Status. As of October 6, 2011, 37 Vanguard Centers, including 30 Centers implementing the alternate recruitment strategies plus the initial 7 Vanguard Centers, have contacted about 75,000 women and screened about 60,000. A total of about 9,000 women have been identified as pregnant or trying to become pregnant. In 18 months of active recruitment and 12 months of monitoring, the initial household-based recruitment strategy in 7 locations enrolled 2,000 women and 1,000 babies. In 10 months, the alternate recruitment strategy Centers in 30 locations have enrolled about 4,000 women and 800 babies. All Vanguard Centers have enrolled about 6,000 women and 1,800 babies. Vanguard Study recruitment will end in the next month as all Vanguard Centers enter a retention phase.

Alternate Recruitment Substudy Recruitment Summary. As of October 6, 2011, the provider-based recruitment strategy enrolled 1,150 women, the enhanced household strategy enrolled 1,300 women, and the direct to the public recruitment strategy enrolled 1,500 women. The provider-based strategy was the most efficient at enrolling pregnancy-screened women (91 percent). The efficiencies of the other two strategies were about 57 percent. However, the mean number of women enrolled per week was 3.7 for provider-based, 3.5 for enhanced household, and 4.2 for direct outreach. The mean number of women identified per woman enrolled was 2.0 for provider-based, 17.3 for enhanced household, and 8.4 for direct outreach. All three strategies will be able to provide a preconception cohort. However, experience to date shows that less than 20 percent of the preconception women in the cohort deliver within a year of enrollment.

Pregnancy Screening Completion by Recruitment Strategy. As of October 6, 2011, the pregnancy screening completion rate was 74 percent for provider-based recruitment, 67 percent for enhanced household, and 86 percent for direct to the public recruitment. Dr. Hirschfeld noted that the current screening questionnaire could probably be improved. However, the overall screening completion rates were 74 percent to 88 percent, which is comparable to other published results and can be considered successful. The screening questionnaire will be evolving as the Study moves forward.

Consent Rates by Recruitment Strategy. As of October 6, 2011, the consent rate was 81 percent for provider-based, 62 percent for enhanced household, and 82 percent for direct to the public recruitment. These are highly respectable rates compared with other published studies.

Cumulative Enrollment of Women Since Work Began. Cumulative enrollment for all three alternate recruitment strategies had a steep increase in the first 20 weeks and began to plateau at about 30 weeks.

Race/Ethnicity Distribution among Study-eligible and Enrolled Women Compared with County Population. The number of women enrolled reflected, for the most part, the race and ethnicity distributions of the 10 county populations for each strategy. Bias of race or ethnicity is not being introduced by these strategies. Data on socioeconomic status is still under analysis.

Sample Size Considerations. The following are considerations for the Study's sample size:

- The attrition rate from enrollment to birth is currently about 20 percent. This rate is most likely a reflection of the protocol rules that the mother at the time of enrollment and the time of birth must reside in a preselected secondary sampling unit (segment). Approaches to follow women from enrollment to birth remain under study. Changes of protocol eligibility criteria may address some of the observed attrition. Once enrolled, the Study will continue to follow the children and their families for 21 years. Other studies indicate differential attrition rates for various subpopulations and the Study anticipates similar patterns. Re-examination of the initial assumptions about recruitment and attrition with 70 percent of the sample remaining after 21 years showed that these assumptions were probably over optimistic.
- Modeling using three different methods indicated potential attrition over 21 years to yield a population of about 40 percent of initial enrolled population.
- Given these factors, the options for the Study are to increase sample size or improve retention. However, no decision has been made; many options are being explored. Because more data and analyses are need, the Vanguard Study will transition to focusing exclusively on retention and capturing metrics to understand why women leave the Study and why they stay.
- The Study's two major cost drivers are recruitment and data acquisition.

NCSAC Discussion and Recommendations

- Jeffrey Krischer, Ph.D., asked how the Vanguard Centers will be used to gather data on retention and how the Study will seek input from other studies that have addressed retention issues and strategies. Dr. Hirschfeld explained that because the visit schedule is "front loaded," meaning that more visits are scheduled during the early years of the Study than in later years, there will be opportunities to interact with participants. Measures have been developed to analyze item and visit completion—also known as adherence and compliance—early in the Study. The oldest babies in the Study are now about 2 years old, and some data on engagement and maintaining interest have been collected on the 2,000 families enrolled by the initial 7 Vanguard Centers. The Study now has multiple liaisons working with other studies. Investigators from these studies meet with Study investigators to share their experiences and insights. A panel of these other investigators has critiqued the Study's retention approaches and efforts. In addition, the Study reviews retention data every 2 weeks to identify trends. Several models are being used to analyze the data and guide questions.
- Dr. Wilfond asked how many Vanguard Centers are implementing a sampling frame based on the providers' location. Dr. Hirschfeld said 3 Centers are implementing this strategy:

Baylor College of Medicine (Harris County, TX), the University of Louisville (Jefferson County, KY), and the University of Massachusetts (Worcester County, MA). Currently, the geographic definition of the sampling frame is being completed. The target date to begin fieldwork and enrollment is March 2012. Although adequate data may be collected in the first 6 months, enrollment will probably continue for about 12 months. Retention analyses will be periodic but will be continuous for the length of the Study.

- José F. Cordero, M.D., M.P.H., asked whether prematurity is an area of interest and whether information on risk factors for preterm births will be collected. He also asked for clarification on the Study's intention to follow participants who move out of the geographic sampling units. Dr. Hirschfeld replied that prematurity is an area of interest and that the Study will definitely follow participants who move after the child's birth. Once a mother and child are enrolled, the Study's intent is to follow them for the length of the Study.
- Bruce D. Gelb, M.D., noted that in previous NCSAC meetings, the Program Office provided questions to help focus on the issues and guide the NCSAC's input. He asked what questions and issues the NCSAC will address at this meeting. Dr. Hirschfeld said the purpose of this meeting is to present data from the formative research studies, seek the impressions about the directions of the future studies, and identify gaps in activities outside the Study's core activities. The NCSAC's input will help the Study make strategic decisions.
- Dr. Ellenberg proposed that a working group be formed to explore how the NCSAC can optimally advise the Program Office. Such a working group can be created under the Federal Advisory Committee Act (FACA) rules. The working group would develop ground rules to ensure that the NCSAC is providing needed advice and input to the Program Office. NCSAC members who are interested in serving on the working group should contact Dr. Henry.
- Joan Y. Reede, M.D., M.P.H., M.B.A., asked how the Study is addressing immigrant status of Study participants. Dr. Hirschfeld said the Study is exploring how immigrant status can be addressed systematically. However, currently the Study does not ask about immigrant status. He said the Study is hosting a conference on immigrant health disparities on December 15–16, 2011.
- Edward J. Sondik, Ph.D., M.S.Hyg., noted that asking about immigrant status could dissuade people from participating in the Study. He asked Dr. Hirschfeld to define retention. There may be different levels of compliance and therefore different levels of retention. He also asked whether there is information about why people are not retained in the Study. Dr. Hirschfeld said the Study is now systematically examining information from people who leave and as well as why people stay in the Study. Operationally, retention is defined as continuing contact and participants voluntarily providing data. However, the parameters for item/unit completion and adherence/compliance have not been formally defined. Some preliminary modeling is being used to examine thresholds and triggers for acceptability. Retention thresholds have not yet been formally statistically defined.

Comments from Alan E. Guttmacher, M.D.

Dr. Guttmacher said the Study values the NCSAC's input on a range of questions and issues. The NCSAC will continue to be an integral part of the Study through its duration, and the NCSAC's best use will always be considered and evaluated. Formative research is an important element of the Study. The breadth and depth of the kinds of formative research can distinctly serve as a platform for informing and guiding the Study's direction.

Review of Presentations from NCS Research Day, August 24, 2011

Genetics

James M. Swanson, Ph.D., Co-Principal Investigator, Southern and Central California (SCCA) Study Center, University of California, Irvine

Dr. Swanson reviewed three presentations:

- The Human Genome Project—Dr. Guttmacher
- Genetic Approaches and the NCS: Transition from Genetic to Genomic Medicine—Jeffrey C. Murray, M.D.
- Whole Genome Sequencing in the NCS: “100 Trios”—Michael J. Bamshad, M.D.

The Human Genome Project. The Human Genome Project (HGP) showed how centrally coordinated “big science” contributes to biological sciences. It proved that nonhypothesis driven science can be of great value. It demonstrated the value of public release, rather than hoarding, of data. In addition, the HGP (1) earmarked funds for consideration of its ethical, legal, and social implications and (2) generated new technology and sequenced the human genome. The project discovered that there are about 20,500 human genes. Dr. Guttmacher concluded that, like the HGP, the Study will change the basic ways that people think about biology, behavior, health, and development. The Study will help determine the complex interactions between environmental and genetic factors that make people who they are.

Genetic Approaches and the NCS: Transition from Genetic to Genomic Medicine. Dr. Murray's presentation reviewed two formative research projects: (1) Expanding Capacity for NCS Genomics, Epigenomics, and Informatics (Project #44) and (2) Applications in Genomics, Epigenomics, and Ancestral Informative Markers (AIMs) (Project #38). The approaches to gene finding for pediatric complex diseases include:

- Candidate genes (animals/expression)
- Location (chromosomal/linkage)
- Single gene models
- Environmental/maternal issues
- Genome-wide association studies (GWAS; common diseases, common variants)
- Genome-wide sequencing (rare variants, common diseases)
- Maternal effects/imprinting
- Epigenetics
- Microbiome.

The presentation described how GWAS works, the 2011 successes of GWAS, and the use of massively parallel (next generation) sequencing for detecting rare variants and defining structural variants. It compared two approaches for gene discovery using common variants and rare variants. Ethical considerations of genomic medicine include impact on children of “adult” disease findings, insurance, early lifestyle changes, incidental findings, and re-consent.

Whole Genome Sequencing in the NCS: “100 Trios.” Dr. Bamshad’s presentation reviewed the following:

- Next generation sequencing (NGS)—importance, genome basics, Mendelian disorders, disease gene discovery, and *de novo* changes
- Whole genome sequencing (WGS) pilot study—preliminary results
- Return of results—impact, challenges, and a customizable Web-based tool for study of results return.

The goals of the WGS pilot study are to engage experts, build an infrastructure, and determine WGS variation in Study trios (mother, father, and child). The preliminary results determined the number of single nucleotide substitutions, novel variants, small indels, and variants in coding (exome) in three trios. With regard to *de novo* mutations, the study found about 50 putative events per exome and about 2,000 putative events per genome. The challenges of the return of results include lots of data, unanticipated results, varied utility of results, meaning of results that change over time, and challenges to communicating results. Dr. Bamshad concluded that, in order to develop policies and guidelines for return of results from genome-wide sequencing, a framework and tool to deliver and study return of results are needed.

Discussion Championed by NCSAC Member

Dr. Wilfond, Director, Treuman Katz Center for Pediatric Bioethics, Professor and Head, Division of Bioethics, Department of Pediatrics, University of Washington School of Medicine and Seattle Children’s

- Dr. Wilfond asked whether there have been barriers or problems in moving the WGS feasibility study forward. Dr. Swanson replied that one of the purposes of feasibility studies is to identify barriers and problems. The consent form was analyzed to conform to new NIH regulations for WGS of an individual. Investigators want their genomic data to be put into a public data repository for data sharing. The data repository has not yet been determined, but additional consent and information will likely be required. In addition, there are Office of Management and Budget (OMB) issues for using genomic data. An OMB application has been submitted but has not yet been approved. Other studies have received OMB approval to sequence in autism trios. Although there are concerns about budget cuts, the costs of sequencing are decreasing and funding is available to continue sequencing of Study trios.
- Dr. Gelb commented that, most likely, the genome of every Study participant will be sequenced. He asked how, in the shorter term, the Study can uniquely contribute to WGS knowledge. Dr. Swanson explained that the current goal of the WGS pilot study is to eventually collect data on mutation rates in 100 trios. The ultimate goal is to develop the capacity for genomic medicine (examination of the entire genome including known genes and additional sequences, modifications, and structures) rather than genetic medicine

(examination of specific parts of the genome characterized as genes). A feasibility study will help discover the potential of genomic medicine and how it can be incorporated into the Study in the coming years.

- Dr. Hirschfeld commented that feasibility studies can inform about the types of real-time analyses that can be done, the types of information that can be collected, the application of the information, and the type of infrastructure needed for real-time analyses.
- Dr. Reede asked whether there are ongoing discussions of legal, insurance, and ethical implications with regard to genetic and genomic findings in Study participants. Dr. Swanson noted that part of Project #38 involved informed consent and return of results. There are ongoing discussions about the future of informed consent and the issues of returning results. Another part of Project #38 involving AIMS is exploring ethnicity issues. The projects are evaluating why potential participants decide not to agree to consent.
- Ellen Silbergeld, Ph.D., commented on the strategies of genomic medicine in the context of the Study's mandate to collect data on a variety of exposures, outcomes, and genetic variability. The strategies of the genomic projects enhance the ability to identify variance that has real meaning in terms of biomedical risk. She asked how the Study will combine the information into a larger package relating to influences related to developmental trajectories and health status at particular developmental stages, which involve a mixture of risk factors. An integrated understanding is needed. Dr. Swanson explained that other projects are addressing these concerns. For example, the exposome project is sequencing RNA for samples that have exposures already measured. Carol H. Kasten, M.D., has been asking that the WGS project be linked to other genetic feasibility projects, such as epigenomics studies.
- Dr. Wilfond asked Dr. Hirschfeld to describe some of the challenges with OMB approvals for formative research projects. Dr. Hirschfeld said the OMB has to oversee research because the Study is collecting data on behalf of the federal government. The Study is governed by the Paper Reduction Act and the Privacy Act. The Study needs approval for collecting data from more than nine people. The paradigm for the OMB is submission of a single protocol, OMB review and comments, approval, and periodic subsequent reviews. The Study first submitted an application for the Vanguard Study protocol and then submitted applications for many formative research projects. The OMB had to develop mechanisms and build capacity for the portfolio of Study applications and now has a separate review team just for the Study. Current estimates are that the OMB will complete reviews of the remaining formative research projects in the next calendar quarter.

Community Engagement

Nancy Dole, Ph.D., North Carolina Study Center, University of North Carolina, Chapel Hill

Dr. Dole provided a consolidated summary of the highlights of four presentations:

- Fundamentals of Community Engagement—Dana Sampson, M.S., M.B.A.
- Community Retention in Duplin County, NC—North Carolina Study Center
- Outreach and Engagement Strategies in Douglas County, CO—Colorado Study Center

- NCS Community Outreach: Successful Recruitment of Latina Participants—Arkansas Study Center.

What Is Community Engagement? The presentation by Ms. Sampson (from the NIH Office of Behavioral and Social Sciences Research) outlined a few of the key elements of community engagement. The presentation addressed community engagement in a more general way and talked about getting the community involved and having community partner organizations. This approach can focus on small short-term projects or long-term partnerships. It often involves partnerships and coalitions that are mobilizing resources to change situations by being a catalyst. The presentation discussed community-based participatory research, which the Study is not engaged in.

Why Is Community Engagement a Cornerstone of the Study? The focus of the Vanguard phase is moving from recruitment to retention, which is a multi-level process. Much of recruitment and retention is focused on individual Study participants, but the recruitment and retention must be in the context of households, families, and communities. Community engagement branches into all of these areas.

What Does Community Engagement Mean in a Study with a Standard Protocol? One of the Study's challenges is implementing a standard protocol across all of the Study locations, which are quite diverse. The Study Centers are involved in a lot of different community groups, for example, the Duplin County, NC, Community Advisory Group. Diversity among community advisory groups is essential. It is possible to engage many of the key community leaders in dialogue and get their advice. In Duplin County, community members provided advice on defining their neighborhoods, beyond census boundaries. Maps were shown to community members to help determine how to approach communities and who needs to be informed. According to the county manager (one of the Community Advisory Group members), it is essential to reach out to local politicians to inform them of the Study's challenges in engaging the communities and seek their input on appropriate incentives. The community members suggested that, although the Study is national, its outreach needs to be localized to send a message that the Study is part of the community. Community members helped the Study emphasize the bilingual aspects of Duplin County (about 40 percent of the births are to Hispanic women). Community members also emphasized the importance that introductory materials such as brochures be brief.

What Are the Communities the Study Needs to Reach? The Study is composed of communities of scientists who care about children's health. The Study must build links to local geographic communities, explain the Study to many communities, and champion the potential benefits of the Study. Study recruitment involves identifying eligible women in defined communities and enrolling them as Study participants. The enrollment process should be put in the context of family members. Outreach and engagement should include family members to help them understand the importance of the Study and what it means to them for the long term. Neighbors, friends, community leaders, politicians, faith leaders, health care and social service providers, and teachers all need to be included in the multi-level process of community engagement, recruitment, and retention.

What Are the Study’s Community Engagement Challenges? In rural counties such as Duplin County, the Study is engaging and recruiting the entire county. Engagement and recruiting are not limited to specific communities. In a metropolitan area such as Los Angeles, “community” takes on a different context, where community outreach is focused on specific neighborhoods. Another challenge is gated communities, where outreach needs to focus on gatekeepers. Rural areas have “gated communities,” where trespassing is an issue. Locked apartments are another challenge, as are the many cultures, languages, and diversity of communities. Engaging military communities is also challenging. Community engagement is key to understanding how to reach out to these communities and retain the participants.

How Is Community Engagement Implemented Across the Study Centers and Study Population? Community engagement activities and their focus are building awareness, having families consider participation, establishing intent to participate, and then moving into recruitment, participation, retention, and continuation in the Study. Strategies for outreach involve TV ads, publicity, mailings, events, providers, faith-based organizations, and social media. The results of a Colorado Study Center survey found that women who completed a pregnancy screener learned about the Study primarily through advance letters and print media. Potential participants need to see something about the Study six or seven times before it resonates. Using different outreach methods helps with understanding the Study and engaging potential participants. The Arkansas Study Center uses several approaches for reaching out to hard-to-reach populations: 50 percent of staff are bilingual, 20 percent of staff are Latina and native Spanish speakers, bilingual community leaders serve on Community Action Boards, and how Hispanic families receive information has been identified.

Approaches to Maintain Community Awareness of and Support for Study. Study Centers use a variety of approaches to maintain community awareness of and support for Study, including advertising (for example, billboards and newspaper ads), presentations to community and care providers, and partnerships with local organizations (for example, fire departments). Study Centers have engaged schools and local social events (for example, festivals). It is important to maintain contact at all levels with the state, including health care and social services and environmental departments. Statewide newsletters report on activities at Study locations and provide an educational component. Study Centers have provided information and fun activities for children in elementary school newspapers.

Resource Sharing. The Study Centers are giving back to the community while promoting the Study by sponsoring events, employing people, and participating in community activities.

Discussion Championed by NCSAC Member

Wilma Brakefield-Caldwell, R.N.

- Ms. Brakefield-Caldwell commented that when working with communities, the Study should not assume participants’ technological knowledge and ability to use the Internet.
- Maria Cancian, Ph.D., asked how the Study will address changing family constellations and same-sex families. She noted that the Study’s images show mother-father families. Dr. Dole replied that the Study will address children who move to other caregivers. The Study will

track children whose mothers change locations and family arrangements. Dr. Dole concurred that the Study should have diverse family images and more images of fathers—not just mothers and children.

- Dr. Reede commented that the Study images show healthy people. Many children have disabilities, and images of these children should be included. Dr. Dole said the Study is developing a photo repository with diverse images.
- Dr. Wilfond noted that the Study encourages women not to disclose their participation in the Study. He asked whether communities are enthusiastic about keeping their participation secret and whether they would be more interested if their participation was more publicly known. Dr. Dole said it is important that the Study not encourage women to reveal their participation due to potential disclosure risk about their address and the precise geographic location of recruitment. Women may make a personal decision to reveal their participation. Many women take pride in their participation, and the Study encourages this but remains cautious about revealing certain types of information. Because the Study is cautious about revealing a participant, it has taken a conservative approach to using social media.
- Dr. Ellenberg asked whether data have been collected to evaluate the effectiveness of different community engagement approaches used by the Study Centers. Dr. Dole said data are being collected on what approaches are being used within each Study location. Cost data are also being collected and analyzed. All Study Centers are evaluating the effectiveness of their community outreach and engagement activities in reaching target populations. Dr. Dole noted that it is important for the Study to gather information from communities and from women who participate and those who do not.
- Dr. Sondik said communities are concerned when programs such as the National Health and Nutrition Examination Survey (NHANES) engage for a short time and then leave. He asked whether the Study might be doing the same thing, that is, front-loading community outreach and engagement but then reducing activities as the Study proceeds. He asked whether communities expect something in return longitudinally and whether the Study owes communities for their participation. Developing and maintaining trust and reporting back to the community are important and help with retention. Dr. Dole said these concerns have been expressed in Duplin County. The Study Center is examining the types of things that can be given back to families and the types of information that can be shared with communities. Issues of revealing results are still being discussed.
- Dr. Reede said the systematic approach to community engagement has a broader context for Study sustainability and maintaining interest and involvement. Because the Study is national in scope, it is important to inform the nation as a whole.
- Ms. Brakefield-Caldwell explained that Community Action Against Asthma met separately with study participants, people in the community, and residents of Detroit. Community members and researchers collaborated to identify the types of information and findings that would be shared.

- Aubrey K. Miller, M.D., noted the community-based participatory research (CPR) model can be adapted to different communities. He said the NIEHS-sponsored GuLF Study of the Deepwater Horizon Oil Spill has been active in determining the types of information to give back to communities in ways that make sense and keep people involved in the study. The study seeks to find out what the participants want to hear. The use of appropriate CPR models is being explored. Dr. Miller said potential outreach targets include occupational cohorts, large employers, and unions. Dr. Dole agreed and said there are different approaches to engaging the business community.
- Dr. Ellenberg asked about the scientific community's view on the responsibility for long-term retention, that is, once women are recruited into the Study should community outreach and engagement be a major focus. Dr. Dole replied that community outreach and engagement is a multi-level process that is important not only to recruitment but to retention. Part of the process is to keep the community informed about the Study. One vehicle for disseminating Study information would be a national newsletter.

Recruitment and Retention

Dean Baker, M.D., M.P.H., Co-Principal Investigator, SCCA Study Center, University of California, Irvine

Dr. Baker reviewed four presentations:

- Success of Provider-Based Recruitment in the National Children's Study in Wayne County, Michigan—Nigel Paneth, M.D., M.P.H.
- Implementing Provider-Based Sampling for the National Children's Study: Opportunities and Challenges—Stephen Buka, Sc.D., on behalf of the provider-based Study sites
- National Children's Study: Recruitment Experiences in Orange County, CA—Dr. Baker
- Comparison of Completion Rates between Post-Natal Telephone and In-Person Data Collection Events, Salt Lake County, UT—Salt Lake County Vanguard Center.

Success of Provider-Based Recruitment in the National Children's Study in Wayne County, Michigan.

This presentation described the challenges of the household-sampled, provider-based recruitment model, the prioritization and selection of practices, and the steps in provider recruitment. Major problems included a low yield of eligible women per practice and difficulty in first-trimester enrollment because of address-matching from existing records before approaching women. In addition, some women did not show up for prenatal appointments, making for fruitless trips to practices. The key strengths included community engagement operations that support the Study; a three-step recruitment procedure, which allows the potential participant woman to gradually consider joining the Study; and division of responsibilities of Study tasks, with expertise applied to each task. Dr. Paneth concluded that provider-based recruitment in this design is expensive. Study Centers must work with all practices and hospitals in a region and invest major resources to negotiating with and developing strong partnerships with providers and hospitals. Community engagement must span segments distributed widely across a large county.

Implementing Provider-Based Sampling for the National Children's Study: Opportunities and Challenges.

The central challenges with the provider-based recruitment approach include:

- There is considerable variability by Study Center in numbers of practices and proportion of births that are segment-eligible.
- In large counties, there may be up to 150 prenatal care practices and 20–30 hospitals providing care to geographically dispersed, segment-eligible women. Only 1–2 percent of patients may be eligible.
- In small counties, there are a small number of providers to recruit a large proportion of segment-eligible women. But small counties have a considerable proportion of women receiving prenatal care outside of the county.

Issues and other challenges of the approach include:

- Type of providers to include in the sampling frame
- Optimization of key parameters of sampling design
- Operational challenges to sampling provider groups
- Stratification factors for sampling providers
- Sampling pregnant women within provider groups
- Potential bias from enrolling women from provider practices (exclusion of women who receive late or no prenatal care)
- Challenges in obtaining a preconception cohort.

National Children’s Study: Recruitment Experiences in Orange County, CA. Orange County, CA, was selected as one of 7 initial Vanguard locations to pilot test a draft Study protocol, including community household-based recruitment. Dr. Baker described the recruitment yield in the 2-year pilot phase, possible factors affecting low enrollment and birth yield, the sampling frame, community outreach and engagement efforts, the household-based enumeration and pregnancy screening process, and ongoing recruitment and enrollment activities. From April 2009 to June 2011, the Orange County Vanguard Center listed a total of 10,500 households and completed 9,550 household enumerations. Of the households enumerated, 5,850 age-eligible women were identified. Of these women, 5,400 pregnancy screens were completed and 250 eligible pregnant women were identified. Of these women, 150 pregnant women consented. With regard to factors affecting low enrollment and birth yield in the pilot study, Dr. Baker noted that low numbers of actual births in segments and lower than anticipated participation rates were not factors. However, low follow-up of nonpregnant eligible women was a factor. Methods to improve follow-up of nonpregnant eligible women include:

- Improved messaging about prospective enrollment component of Study design
- Formal enrollment of all age-eligible women
- Obtaining more information for follow-up contact
- More intense and multi-method follow-up (for example, texting, e-mail, social media, and the Web)
- Continuous segment tracking to monitor dwelling unit turnover.

Comparison of Completion Rates between Post-Natal Telephone and In-Person Data Collection Events, Salt Lake County, UT. The Study’s data collection modes are telephone-administered questionnaires, hospital/clinic data collection, and in-person home visits. From April 2009 to September 2010, the “legacy” protocol included longer interviews, anthropometric measures, and biological and environmental sample collections. From October 2010 to July

2011, a “light touch” protocol was implemented using shorter interviews and no sample collection. The light touch protocol collected data at four postnatal time points. The completion rates were as follows:

- 3-month telephone event, 88.2 percent
- 6-month in-person event, 98.6 percent
- 9-month telephone event, 84.7 percent
- 12-month in-person event, 98.7 percent.

In conclusion, despite greater respondent burden, the in-person visits had higher completion rates. Face-to-face contact may enhance Study bonding and influence retention. Therefore, it is important to monitor factors influencing completion rates. It is vital to identify operational elements that promote successful data collection and participant retention.

Discussion Championed by NCSAC Member

Maria Cancian, Ph.D., Professor of Public Affairs and Social Work, Institute for Research on Poverty, University of Wisconsin-Madison

- Dr. Cancian commented that in order to judge which recruitment and retention strategy worked better, the Study needs to be explicit about the trade-offs across a set of goals. Issues are (1) the strategy that is the most efficient versus the strategy that recruits the largest numbers, (2) which strategy will allow probability sampling, and (3) which populations are not being recruited in each strategy. SES is a concern, and mobility is often related to SES status. Different strategies may have different biases. In processing data, it will be important to focus attention on and be clear about the Study’s goals and priorities.
- Dr. Baker explained that a fundamental decision needs to be made about using a geographic-based sampling frame, a provider-based sampling frame, or a mixture of sampling frames. Each Study location (that is, primary sampling unit) would probably have to use a single, not blended, sampling frame. For a geographic sampling frame, every type of community outreach and engagement approach should be used to identify and recruit all populations. In the Alternate Recruitment Substudy, the provider-based strategy was reaching out to engage communities, and the enhanced household-based strategy was reaching out to engage providers. Each strategy used media for outreach and engagement. Mobility is a specific issue the Study will address. The cohort should be defined at a particular time, which is at birth. Once a child is born into the Study, he or she will be followed. Two other issues are whether families that move are different than families that do not and whether it is worthwhile to follow and continue studying movers.
- Dr. Silbergeld commented that it should be understood exactly what the Study is about in terms of the sampling frame and how much control and predictability is possible. The Study needs to know whom it is studying and what the children represent. She noted that there is a powerful effect of incentives.
- Dr. Baker said the in-person visits did have incentives, but the telephone visits did not. There are several types of incentives: monetary, nonmonetary, and simply being part of the Study community. With regard to revealing results to communities, there has been a shift from a

rigid stance to a less rigid stance. Over time, as people move in or out of Study segments, the nature of the communities will gradually transform. One of the best incentives is having people feel involved with the Study. There needs to be a community of stakeholders that support the Study.

- Dr. Hirschfeld said the Study is still exploring how to define communities. An individual can be part of multiple communities at the same time. He explained that the Study's focus is the children of America and the health of children in America. However, the definition of health has not been resolved, including the objective and quantitative parameters of health. A Study task force is exploring this topic.
- James J. Quackenboss, M.S., commented that there is an opportunity to further study the loss of women during the follow-up over the recruitment period and find ways to improve follow-up of age-eligible women and increase retention.
- Dr. Baker said attrition during the follow-up period is not gradual. Loss to follow-up is greater during the initial phase but then becomes gradual. The Study needs to get more contact information up front and inform women that they are going to be followed for a certain number of years. Because there is a waiver of written consent, less information can be collected at initial contact. With a written consent, more information could be gathered to help improve follow-up. Different size counties may have to have different enrollment periods. Smaller counties may need longer enrollment periods, for example, up to 4 years, or additional counties may need to be added. Larger counties may need only 2 years, particularly if there are more or larger segments. The Study could use different sampling approaches to increase efficiency of enrollment.
- Dr. Ellenberg asked how the provider-based sampling strategy compares with the other strategies. Dr. Baker replied that provider-based sampling could be an adjunct to the household-based strategy and should be included. It is possible for one county to use provider-based sampling while another county uses geographic-based sampling, but they should not be mixed in a single county. However, there needs to be a nonbiased sampling frame for eligible women. The Study also needs clear ideas for recruitment and retention strategies; comparing strategies will be challenging.

Informatics/Technology

Michael G. Kahn, M.D., Ph.D., Associate Professor, Colorado Study Center, University of Colorado, Denver

Dr. Kahn summarized three presentations:

- Neonatal Research Networks Terminology (NRNT) Project—Dr. Kahn
- Open Source Software: Laying the Foundation—Warren A. Kibbe, Ph.D.
- Meeting the Informatics Challenges of the National Children's Study—William R. Hogan, M.D., M.S.

Neonatal Research Networks Terminology (NRNT) Project. The objectives of this project were to create a harmonized neonatal terminology that builds upon accepted neonatal research

data collection needs, harmonizes across the stakeholders to provide a common data view, aligns with an accepted international clinical care terminology standard, but does not require participating networks to change current data collection and analysis practices. Another objective was to develop a set of terminology harmonization procedures, methods, and tools that can be reused in other areas of pediatrics research. This project harmonized the data collection terms across three existing national neonatal research networks and linked the harmonized terms to SNOMED, a license-free terminology identified by the federal government as a national standard for electronic medical records (EMRs).

Open Source Software: Laying the Foundation. In his presentation, Dr. Kibbe described Northwestern University's effort to create a comprehensive clinical research management system using an open-source multi-institutional consortium development model. Seven Study Centers formed a consortium to design NCS Navigator—an open source set of tools for managing the Study informatics that uses modern software development practices. A key component of the NCS Navigator is the NCS Navigator Master Data Element Specification (MDES) Warehouse. It is a computable representation of the data definitions, rules, and collection instruments available in the MDES. The MDES Warehouse versions and accessions submissions are based on the then current version of the MDES and migrate existing data to newer MDES schemas with as little human intervention as possible.

Meeting the Informatics Challenges of the National Children's Study. In this presentation, Dr. Hogan described the Arkansas Study Center's experience with implementing and integrating multiple open-source software applications developed by other organizations to support the Study's data collection needs. The informatics challenges are to capture numerous and diverse types of data in a comparable way across dozens of Study Centers over two decades, for which there are minimal standards for the types of data for planning the Study. The Arkansas experience demonstrates that (1) the use of open-source software has indeed enabled more rapid progress, (2) modifications of software to meet Study requirements have benefited other research, and (3) the Arkansas Study Center has benefited from development done by other Study Centers.

Discussion Championed by NCSAC Member

Jeffrey Krischer, Ph.D., Professor, Department of Pediatrics, University of South Florida

- Dr. Krischer said the presentations outline some critical elements that underpin the success of the Study. The Study will collect large amounts of data from many sources. Issues for Study informatics involve standards and terminologies that are available to apply to the data. Many of the Study's data elements have no standards, and terminologies are lacking to describe, for example, social structures and communities. In addition, there are competing standards. The Study's informatics must consider data sources such as the role of EMRs.
- Dr. Kahn explained that the informatics challenges include determining whether standards exist, identifying standards that do exist, leveraging on existing standards, and building collaboratively with other communities. If there are no standards, then the Study needs to be the leader in developing them, in an open, collaborative manner. Dr. Kahn's view is that

EMRs will eventually go away. In their place, there will be a lifelong unified data store for each person.

- Dr. Wilfond asked whether the “old” way of collecting data, such as case report forms (CRFs), will also go away. Dr. Kahn replied that CFRs would work well for just the Study, but by relying on them, the Study will lose cross-linkages between that data and other data sets. Linkages between data sets are still being discovered, and the Study needs to take advantage of these linkages. A new focus of data collection is comparative effectiveness research.
- Dr. Ellenberg asked Dr. Kahn to explain the differences between the open-source model and the vendor model. Dr. Kahn said they differ with regard to who is driving the development. The open-source model is driven by a community of users and developers based on their needs. The vendor-driven model relies on specific customer needs and the costs of the product. The open-source model is better in dealing with future changes. Open-source systems are transparent and have no barriers to system migration.
- Rick Chestek of Booz Allen Hamilton commented that, in addition to CFR data, there are many other data sources that can be leveraged in the future, for example, genetic/genomic data. Health data can be collected in many ways and with a variety of technologies. Extant data from many sources can be acquired and integrated with Study data.

Environmental Analysis

Howard Andrews, Ph.D., New York-Northern New Jersey (NY-NNJ) NCS Center, Columbia University Mailman School of Public Health

Dr. Andrews reviewed five presentations:

- An Integrated Approach to Health System Analysis and Response—Timothy J. Downs, D.Env.
- Remote Sensing Technology for Indoor Air Quality Monitoring—Dorr G. Dearborn, Ph.D., M.D., and Ellen M. Wells, Ph.D.
- Blood Metals in Pregnant Women Enrolled in the Vanguard Study: Comparison with NHANES—Mary Ellen Mortensen M.D., M.S.
- Comparison of Wipe Materials and Wetting Agents for Pesticide Residue Collection—David E. Camann
- Using Community-Level Indicators in the National Children’s Study—Dr. Andrews.

An Integrated Approach to Health System Analysis and Response. An integrated health system frame includes drivers, pressures, state changes, exposures, other vulnerability factors, and health. In his presentation, Dr. Down listed examples of system indicators in the context of mortality and morbidity associated with coal-fired power plant emissions. He also listed a mixed methods approach for developing a pragmatic knowledge frame.

Remote Sensing Technology for Indoor Air Quality Monitoring. The goal of this project was to develop a new, low-cost platform technology for real-time sensing and remote monitoring of air quality. The purpose was to develop and investigate the feasibility, acceptability, and cost of

remote sensing technology to monitor residential indoor and outdoor air quality in Study homes. The approach used real-time sensors with telemetry (3G) data transfer to a central server for translation, analysis, and storage to monitor home (indoor and outdoor) air quality parameters.

Blood Metals in Pregnant Women Enrolled in the Vanguard Study: Comparison with NHANES. This pilot study included measuring a number of environmental chemicals and nutritional biomarkers in a convenience sample of about 450 participants at seven Vanguard Centers. The study's intent was to provide exposure and nutritional biomarker data to inform decisions regarding analytes for inclusion in the Main Study. A broad array of environmental chemicals and nutritional biomarkers were analyzed using blood/serum and urine (third trimester), cord blood, infant urine, and breast milk. The results from this convenience sample of pregnant women showed the following:

- Blood lead levels were about two to three times lower than reference ranges for U.S. females age 1 year and older.
- Blood total mercury and cadmium levels were generally similar to reference ranges for U.S. females age 1 year and older and also all adults age 20 years and older.
- Blood total mercury levels were about two times lower than for U.S. females age 16–49 years.

Information on manganese and selenium blood levels in pregnancy are limited, so these results serve as preliminary reference ranges until population-based data are available. NHANES data may be useful to examine the representativeness of the Study participants.

Comparison of Wipe Materials and Wetting Agents for Pesticide Residue Collection. This project studied three wipes using a 3 x 2 factorial design—three wipes at high and low pesticide concentrations. The sample size was selected to ensure 80 percent power to detect a 20 percent difference in mean collection efficiency and a two-fold difference in collection volumes between wipes. There were 26 replicates per wipe, 13 replicates at high analyte concentrations, and 13 at low analyte concentrations. Twenty-seven pesticides were tested. The results of this study demonstrated a valid methodology for comparison of wipe methods, showed clear and significant differences between collection efficiency and precision of three wipes at both concentration levels, and allows comparison of analytical results across wipe methods. The approach allows selection of a wipe appropriate to Study needs if low detection limits are required (select wipe with highest collection efficiency) and if ease of use in field is desired and participant concerns are issues.

Using Community-Level Indicators in the National Children's Study. The Queens Vanguard Center has assembled a large geographic information system (GIS) that contains key community-level indicators for census tracts containing Queens Study segments and census tracts not containing Study segments. Of the 613 populated census tracts in Queens, 44 contain portions of the identified segments in which recruitment is taking place. This study found statistically significant relationships between a number of recruitment indicators and certain community characteristics. It also found that communities in which Queens Vanguard Center segments are located are representative of Queens communities as a whole, with respect to more than 50 indicators in nine domains of interest. The NY-NNJ NCS Center consortium has established a robust GIS/informational infrastructure for using community-level information in all phases of

the Study. This infrastructure and associated statistical methods could provide a model for other Study locations and could be leveraged to operate at the national level, at relatively low cost.

Discussion Championed by NCSAC Member

Ellen Silbergeld, Ph.D., Professor, Department of Environmental Health Sciences, Johns Hopkins University, Bloomberg School of Public Health

- Dr. Silbergeld said two challenging issues for the Study are to clearly define the goals of environmental assessments and determine whether it wants to enter the debate of characterizing exposomes. Increasingly, greater weight is being given to internal measures of exposure, although such measures may not be informative about the sources of exposure. Measurements of environmental contaminants such as household pesticides need to be correlated with biomarkers of exposure. Otherwise, contaminant measures simply characterize the status of the environment. Individual-level health data should be linked to environmental status. Dr. Silbergeld noted that the Study is sampling very few children in each geographic area. Area-wide exposure assessment works well when population density is high but less well with low population density.
- Dr. Hirschfeld explained that the Study does not have enough resources and knowledge to answer many of the questions about its framework and direction. Formative research studies are gathering data to fill some of the knowledge gaps. The value of the NCSAC is in providing guidance on where the Study should direct its limited resources and help determine next steps.
- Dr. Silbergeld said that one approach for understanding exposures is to start with the person, looking at measures of exposure such as biomarkers, and then working back to the sources of exposure.
- Dr. Miller commented that the types of environmental sampling and analysis might depend on the questions the Study wants to answer. Biospecimens can be used to determine what the Study wants to understand about risks and contributions of environmental exposures. Susceptibility during critical periods is an issue with regard to when samples are collected and how analytes change over time. Analyses would then be limited to what is deemed important and what exposures need to be understood.
- Mr. Quackenboss noted that much work had been done in the Vanguard Study but the NCS Research Day presentations were on formative research projects that were designed to fill in methodological gaps in the Vanguard Study. Many of the projects involved measurement tools and analyses. Most measures are “snapshots” at a specific time and place. Community-level exposures and extant data sets can be used to supplement “snapshot” measures.

Behavioral and Social Sciences

Louise O’Donnell, Ph.D., Psychologist, Assistant Professor, University of Texas Health Science Study Center, University of Texas Health Science Center at San Antonio

Dr. O’Donnell reviewed three presentations:

- Bayley-3 Short Form for the National Children’s Study—Dr. O’Donnell
- Assessment of Executive Function for the National Children’s Study—Patricia M. McGovern, Ph.D.
- Successful Lessons Learned for Ensuring Ethnic Representation in the NCS Sample—Elaine M. Faustman, Ph.D.

Bayley-3 Short Form for the National Children’s Study. The goals of the Bayley-3 short form research project are to create a measure of children’s developmental status that will serve as an anchor measure for comparison with other outcome measures in the Study, evaluate the cognitive outcomes of at-risk children with negative exposure histories, and compare Study children’s outcomes with other studies of child development. Developing an age-specific short form would streamline administration, reduce burden to participants and data collectors, and measure children’s performance across age ranges. In her presentation, Dr. O’Donnell described the procedures for developing the short form, which involved an Item Response Theory (IRT) analysis to select an appropriate subset of items from the Bayley Scales of Infant and Toddler Development (third edition). The psychometric challenges for developing a short form were to eliminate interdependent items. Streamlined basal and ceiling rules were developed using IRT to simplify administration. Three short forms were developed: cognitive scale, language scale, and motor scale. Each short form had an IRT reliability of .80 or greater. When pilot data collection is completed, IRT analysis will be conducted to establish psychometric properties of each short form.

Assessment of Executive Function for the National Children’s Study. The goal of this formative research project is to develop suitable measures of executive function (EF) for use in the Study with diverse children beginning at age 36 months and their parents. Specifically the aims are to adapt and improve brief measures of a key domain of neurocognitive function by adapting the Children’s Behavior Questionnaire Very Short Form (CBQ-VSF) and lowering the floor of the NIH Toolbox measures of EF. The results showed that the new measures are low burden and could be shortened further. All EF measures worked well with respect to training and administration with disadvantaged families tested on site in a homeless shelter and a community preschool. The new measures are very promising with regard to (1) usability, time burden, and appeal; (2) continuity with Toolbox measures, and (3) inclusiveness for low-skill children. The next steps are to assess construct validity for child EF in relation to EF measures, school readiness, and traditional IQ subscales. Other next steps are to assess test-retest reliability and develop training materials.

Successful Lessons Learned for Ensuring Ethnic Representation in the NCS Sample. Grant County, WA, has a diverse population that includes a high number of Hispanics. Between 2004 and 2008, 54 percent of the county’s births were of Latino ethnicity. The goal of this project was to determine how Grant County’s Hispanic community heard about the Study. Hispanic outreach components included a culturally competent staff and advisors, targeted outreach, and personalized marketing and media campaign. Hispanics heard about the Study in a variety of ways. In addition to hearing about the Study through the advance letter (26 percent) or enumeration (12 percent), most Hispanic respondents reported hearing about the Study through media (20 percent), family or friends (12 percent), and community partners/outreach events (9 percent). A primary goal of Study outreach programs is to ensure that potential participants hear

about the Study before initial home contact for enumeration. The results for Grant County indicate that outreach activities were successful, for nearly 90 percent of Hispanic respondents heard of the Study before initial home contact.

Discussion Championed by NCSAC Member

Jose Cordero, M.D., M.P.H., Dean of the Graduate School of Public Health, University of Puerto Rico

- Dr. Cordero said that although the Bayley Scales of Infant and Toddler Development (third edition) is the gold standard for assessing development, most children receive developmental screening from their pediatricians, who are using different types of screening tools. He asked how the Study will integrate using the Bayley Scales as a standard measure with development screening through regular medical care. He also asked whether there are plans for longitudinal assessments at certain ages. Dr. O'Donnell replied that to validate the Bayley-3 short form, a child will be assessed only once. However, if the short form is validated, it can be used at multiple developmental stages in the Study.
- Dr. Cordero noted that many studies have found that the media (for example, radio and television) are the most important channels in reaching Hispanic communities. For African Americans, however, the most important channels are trusted people (for example, ministers).
- Dr. Henry asked how training will be accounted for in validating the Bayley-3 short form. Costs and time to train may be issues. Dr. O'Donnell said one of the goals is to streamline test administration. The validation study will be using testers who are not psychologists, and a specific set of training procedures will be developed. Spots checks will be used to ensure that test administrators are adhering to the procedures.
- Dr. Silbergeld asked whether the validation might be extended to a cohort of children that have already been assessed with the Bayley standard measures. She also asked whether some of the nuanced responses on the Bayley subscales will be lost in the Bayley-3 short form. Dr. O'Donnell said the effects on such responses are not known at this time. Validation studies could be conducted, but such analyses were not part of the formative research study proposal.
- Dr. Henry asked how the Bayley-3 short form will be integrated into routine developmental screening. Dr. O'Donnell explained that if there are "flags" on the Bayley assessment, Study staff will suggest referral to a pediatrician. The Study developmental assessments will not compete with other tests but will supplement other neurocognitive instruments. Dr. O'Donnell said the Bayley provides one piece of data, and conclusions and generalizations should not be based on it. She noted that an inclusion criterion for the formative research project was children with typical development. Clinical groups were not included in validity, sensitivity, and specificity testing.
- Elena Fuentes-Afflick, M.D., M.P.H., asked whether there might be potential barriers to reporting Study findings back to pediatricians. For example, the Study might have to prepare

a report to the pediatrician, which may lead to administrative issues with processes and procedures.

- Dr. Hirschfeld said the return of results and information sharing is a continuing topic of discussion in the Study. The current framework revolves around the definition of a “medically actionable finding.” The Independent Study Monitoring and Oversight Committee has been tasked with addressing this topic.

Public Comment

There were no public comments.

Meeting Summary by NCSAC Member

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

Ms. Kuby summarized the meeting as follows:

- The meeting focused largely on Study formative research projects and informative data elements.
- Dr. Henry reviewed the highlights of the July meeting.
- The NCSAC discussed its role and the use of champions in leading discussions.
- The discussions focused on the presentations at the NCS Research Day.
- The NCSAC was engaged in the presentations and discussions and responded with thoughtful questions.
- Dr. Hirschfeld provided a Study update, reviewed the Study’s purpose and history, and described the unique specificity of the Study’s congressional mandate.
- The Study is data driven, evidenced based, and community and participant informed.
- Statistics from the active 37 Vanguard locations were presented.
- The emphasis of the Vanguard Study will move from recruitment to issues of retention.
- The Study can play a unique role in genomic studies.
- Community engagement will be an essential part of alternate recruitment strategies and the recruitment strategies used in the Main Study.
- With regard to recruitment and retention, some of the central issues that were raised were methodological caveats to fully characterize the eligible populations and the subset of those that actually enroll into the Study.
- First-trimester enrollment and follow-up of nonpregnant eligible women were discussed, and these are areas requiring further study and perhaps improvement.
- Alternative recruitment strategies can enhance each other but should not necessarily be combined in a single Study location.
- The informatics/technology presentations were user friendly and informative about issues of flexibility, control, and complexity.
- The NCS Navigator and Master Data Element Specification Warehouse were described.
- Community-level versus individual-level environmental analyses was discussed.
- In the behavioral and social science area, tools to assess development (that is, the Bayley-3 short form) and executive function were described.
- Issues of reporting results were discussed and probably require further exploration.

- Other topics included optimizing the role of the NCSAC to provide advice to address the goals of the Study.
- A working group will be formed to better define how the NCSAC can provide advice to the Program Office.

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



December 2, 2011

Date

Carol J. Henry, Ph.D.

Chair

National Children's Study Federal Advisory Committee