National Children's Study Workshop
Cancer and the National Children's Study: Opportunities and Challenges
May 20, 2004
Holiday Inn Select
Bethesda, MD

This meeting was held in conjunction with the National Children's Study, which is led by a consortium of federal agency partners: the U.S. Department of Health and Human Services (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).

Welcome and Review of Meeting Purpose and Objectives

Peter C. Scheidt, M.D., M.P.H., NICHD, NIH, DHHS, and Rebecca Brown, M.P.H., M.E.M., ORD, EPA

Ms. Brown opened the meeting, welcomed the participants, and thanked them for participating. She explained that the purpose of the workshop was to advise National Children's Study (Study) planners and the Program Office about the potential role of childhood cancer in the Study. The participants introduced themselves by describing their backgrounds and, in some cases, their involvement with the Study thus far.

Dr. Scheidt thanked the workshop participants for attending, saying the Study was privileged to obtain input from some of the top researchers, primarily epidemiologists, in the field of childhood cancer. He asked that they use their experience and expertise to help guide a discussion that might clarify what changes should be made to the developing protocol on behalf of their specialty.

Introduction to the National Children's Study

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

Dr. Scheidt named the federal agencies that are partnering in the Study and briefly explained how these agencies have funded the Study to date. Dr. Scheidt then described the history of the Study and answered workshop participants' questions about the Study.

Cancer—like autism, diabetes, and babies that do not survive or have defects at birth—is defined as a "big issue" low frequency outcome. While incidence alone is not the major criterion for inclusion in the Study, even the planned cohort of 100,000 may be too small for cancer to be used as a single incident primary outcome. The agenda for the day's presentations made clear that while childhood cancer had not thus far been driving many Study decisions, the Program Office was very open to suggestions; it is important that no significant opportunity is overlooked.

Cancer Outcomes in the National Children's Study

Barry A. Finette, M.D., Ph.D., University of Vermont College of Medicine

Dr. Finette, a pediatrician who also trained as a microbiologist, has been looking at multifactoral diseases in children; he framed cancer as a genetic susceptibility to environmental exposures, which manifests itself in subpopulations of human cells. These events involve metabolic pathways and lead to somatic mutational events. He advocated that cancer be included in the Study, notwithstanding its low relative risk; as a physician-scientist in a roomful of epidemiologists, he made the case not in terms of statistics, but rather of an opportunity presented by such a broad and large cohort.

The issue at hand: Is it possible to measure cancer in the Study? If so, what sorts of measurements might be useful? Dr. Finette maintained that genetic samples of a representative population like the Study cohort could provide insight into some of the genetic and cellular events well upstream of actual cancer proliferation, and might one day lead to age-specific curves of susceptibility and a new approach to risk factor analysis for specific diseases.

In discussing the question of how the Study might provide valid and useful outcome data, the participants raised a number of possibilities. Each was subjected to skeptical inquiry and very few survived a two-pronged challenge:

- Could a search for this particular disease outcome in patients be better framed and pursued in another study targeted directly at the research question? That is, how would any specific suggestion(s) about using the Study improve upon approaches currently taken by the childhood cancer research community to that same issue?
- If the Study instead targets intermediate markers or indirect associations, can meaningful links be demonstrated?

Martha S. Linet, M.D., NCI, NIH, DHHS, cited the experience of radiation as an example. After 50 years' evaluation of the impact of radiation on cancer, scientists have demonstrated only a weak association. Studies on the survivors in Japan and the events at Chernobyl provide the kind of focused population where research questions can be meaningfully framed. Yet one result of that research indicates that cells near those directly altered by the radiation may experience profound if indirect impacts (the bystander effect) that confound unambiguous conclusions about a causal impact on the cells known to be damaged. In the Study, she suggested, you would not even know what organs to look at. One could frame very intensive studies and still miss the actual mechanisms at play. Current research is at the cellular level and is barely ready for animal studies.

Julie A. Ross, Ph.D., University of Minnesota, concurred that the target of such hypothetical research in the Study would be very hard to discern and isolate, because research in the field of childhood cancers suggests the disease presents with a very heterogeneous set of indicators and associations. The Study's broad brush necessarily would miss the intensely timed sequence of events and exposures that researchers in the field are trying to identify. The relative risk in such a longitudinal prospective study provides too few cases to sufficiently power sharp research

questions. She advised that Study planners look carefully at the landscape of current research:

- The Children's Oncology Group (COG), a project designed to coordinate the surveillance of all childhood cancers in North America, is now involved in the treatment of more than 90 percent of known cases at more than 200 centers in the U.S. and Canada. Their effort is creating a de facto national pediatric cancer registry. Using that predefined population allows them to frame most childhood cancer in a much more fruitful context.
- The National Collaborative Perinatal Project followed 58,000 pregnant women and their children from 1959–1974, collecting data from children up to 8 years of age. This NIH project (while smaller in scope and about half the size of the Study) also identified cancers at a rate that would reaffirm the misgivings of workshop participants as a targeted outcome of the Study.

Shalom Wacholder, Ph.D., NCI, NIH, DHHS, summarized that the incidence of childhood cancer precludes the kind of longitudinal studies where one takes serial measures in a large population and correlates them with cancer cases as they are diagnosed. Rather, he suggested, the legitimate goal it is to collect biological specimens and take serial measures prospectively in order to develop data to look at intermediate end-points, what geneticists call endo-phenotypes. While such data is not likely to produce a causal link between mutations and cancer, it is data that could one day be useful when the context for analysis will have changed because of advances in the science.

It comes back to what the research questions are, said Andrew F. Olshan, Ph.D., University of North Carolina. Studies focused on mechanism probably can be framed in identified populations, for example, those at high risk of exposure to certain pesticides, said Catherine Metayer, M.D., Ph.D., University of California, Berkeley. Dr. Scheidt said the Program Office anticipates RO1s to do precisely that. Ellen Velie, Ph.D., M.P.H., Michigan State University, added that the Study's size could be leveraged by combining data with similar large cohort studies underway in Norway and Sweden for the purposes of meta-analysis.

National Children's Study Participants as Control Subjects

Shalom Wacholder, Ph.D., NCI, NIH, DHHS

Dr. Wacholder provided a framework in which the Study data could be used as a set of case controls for other unaffiliated research studies. The standardized diagnostic criteria used in cancer make it a reliable endpoint (compared to other possible outcomes, where the diagnostic criteria may exist, but for which reproducible results across centers and diagnosticians are more problematic). The COG's registry also provides comprehensive case ascertainment above 90 percent, so that using the Study for control group purposes fits into a ready-made universe. The reason the Study itself is not adequate for effective childhood cancer endpoint studies is the low relative risk: the data suggest that only 36 leukemias of all kinds, for example, would be expected in 100,000 children followed for five years.

Sound experimental science suggests that controls must be "representative" of the population from which the cases themselves arise. Because the COG case ascertainment is so high, it can be

fairly described as a national population, so that the Study population would provide a representative match only if it were random. If the Study is to be a population sample, the National Health and Examination Survey (NHANES) example suggests that with certain types of cluster sampling, distributions could be derived and the cohort might also serve as an effective control. The challenge—which is relevant because of the very high participation rate in COG—is to determine and control for selection bias by looking at factors influencing who participates in each group.

Other issues arise from the type of Study being considered:

- Gene studies would be comparatively straightforward. The Study provides a better context for controls for childhood cancer studies because, for example, NHANES IV has no children at all, and NHANES III has only several thousand, all over 12 years of age.
- Environmental studies such as those COG has been thinking about would probably require richer and more densely collected information and greater detail than the Study questionnaire is likely to yield. Further, COG obtains information from patients after diagnosis of disease, and is thus affected by rumination and other sociological effects of the disease experience not present in the Study because of its prospective, survey approach. Further, if the Study is strictly center based, regional differences in environmental factors and selection effects would require extra measures be taken to ensure a random sample. COG is also exploring drawing controls based on birth certificates supplied by local health departments around the country.
- Studies of biomarkers are possible but have one major confounder: because the biological specimens collected from the COG cases are taken after diagnosis, the challenge is to tease out those that are likely an effect of disease—and which would not have been present had specimens been taken prospectively—as compared to those biomarkers that may have changed and be implicated in causing the disease.

Thus, a nested case-control study—termed a case-cohort study when the sample is random—is feasible and appropriate, and could also be used for other outcomes. Moreover, this structure would permit researchers to partially overcome the problem of not-so-rich information by identifying a representative sub cohort for more intensive biological monitoring. For that sub cohort, a new questionnaire could be devised and additional specimens could be collected. To pave the way for this option, most of these details would have to be included in the original consent for the entire Study, and those participants chosen for the sub cohort would be revisited, asked more and more probing questions, and asked to provide more biological specimens. On balance, Dr. Wacholder does not believe the value of such data should trump other considerations and drive the Study to do a random sample.

Terence Dwyer, M.D., M.P.H., NICHD, NIH, DHHS, commented that case clusters do not ipso facto rule out representativeness, and that studies can be arranged so that patients from a region provide a valid sample of the nation as a whole. Dr. Wacholder agreed that sampling fractions collected even from one center, if large enough, can yield conclusions for the entire sample, but a number of statistical techniques would be required. Dr. Ross said that referral patterns sometimes do yield characteristics that need to be accounted for. Dr. Wacholder replied that is a function of

sample size and design. Further, local Institutional Review Boards (IRB's) may impose limits on what questions may be asked. Adolfo Correa, M.D., Ph.D., M.P.H., CDC, DHHS, pointed out that some people will be re-interviewed as a function of discovered correlations with specific environmental exposures, so the opportunity is already built into the Study to some extent.

Dr. Wacholder also warned about the recall bias that he called rumination (specifically triggered by a medical event) can have; this has been the subject of much of his research. He has found that when a child is being treated for a disease, recall by parents can be biased by what he termed the "bad mom" effect. Guilt and the human drive for explanations may induce parents to misremember/exaggerate exposures to environmental hazards that are thought to be harmful. This idea fits into the larger phenomenon that is well known, of biased recall in cases as compared to controls.

Dr. Scheidt summarized the take-away message: the group was cautious about the use of the cohort as controls, but cautiously open to the possibility. In many of the COG studies, over 90 percent of those approached agree to participate; if similarly high proportions of those invited agree to participate in the Study, then some of the misgivings– about a different selection bias as between cases and controls—would be reduced. Dr. Ross continued to have major misgivings, and added that this one comparatively narrow slice in time could also limit the generalizability of results, given the inherently low number of children with childhood cancer involved.

National Children's Study Repositories of Biomarkers and Genetic Markers

Andrew F. Olshan, Ph.D., University of North Carolina

While the collection of biological specimens—for use by Study researchers and others—will benefit researchers in many fields, there are a handful of potential applications to childhood cancer:

- Determine exposure prevalence. There is always a need for more and better data on exposures. The Study's relatively high-quality data collected during pregnancy should be especially useful, in a variety of ways, some of them unanticipated but inevitably to be developed by future science.
- Validate questionnaires. The issue raised about recall bias and other problems with self-reporting can in part be overcome by clinical information from collected samples.
- Determine molecular and genetic marker prevalence and expression patterns. This category also refers to markers already known, as well as to those yet to be discovered, assuming adequate storage and preservation of the samples. Immediately appealing studies using proteomics might, for example, look at how cytokines vary throughout pregnancy; investigations will be able to track infections and inflammation pathways.
- Relate exposure to intermediate marker associations.
- Inform mechanisms. Though cancer will likely not be an endpoint in the Study, the sample repository and the serial nature of the collection open up many possibilities for study.

Dr. Olshan also listed some specimens for collection, by way of stimulating discussion as to how they might relate to mechanisms of cancer: blood, urine, hair, nails, breast milk, amniotic fluid,

semen, placenta, umbilical cord blood, buccal swabs, vaginal/cervical swabs, and stool. Such data might enable better design of questionnaires about childhood cancer, facilitate cohort studies on target exposures, and allow use of proteomics or expression data to map events during pregnancy.

Asked what markers Study planners are considering, Dr. Scheidt said one early focus was on chemical exposures (for example, pesticides, lead in the blood, and endocrine-active compounds). A range of samples is being considered, though none from the point of view of cancer researchers. Study planners need to know what biological specimens, if any, might be unique to cancer, so that adequate biological material will be collected, preserved, and made available. The search for known or yet-to-be-identified individual biomarkers can wait. But "How much?" and "How often?" are questions that also could matter to certain subsequent queries. The cost and mechanisms of storage and processing could also be an issue, notwithstanding improvements in measuring technique at the nano level. (See Claudia Holzman's unpublished proceedings from the recent workshop at Michigan State on collecting biological samples.)

Some issues and ideas discussed by participants were:

- Serial collection may add value to many future studies and expand the scope of potential hypotheses.
- The value of most biomarkers will be directly affected by the frequency of the environmental exposure assessments, facilitating possible correlations without the passage of time as a confounder.
- Chromosome aberrations are probably the best candidates to demonstrate links to cancer.
- DNA should be collected on as many occasions as feasible, to account for age-variant gene expression during development. Such samples will be more likely to yield meaningful data in children younger than 8, and especially so in utero and shortly after birth. Sequencing these samples will permit researchers to track the natural progression of how and when chromosomal locations appear and disappear.
- DNA should be collected from both parents if possible.
- Snap-freezing of placental samples for DNA adducts, which serve as transfer pathways to chemical mutagens. Adducts that are not repaired before replication can cause rearrangements in the chromosomes by deleting and substituting various nucleotide sequences.
- Folate levels during pregnancy vary and can be related to the genotype.
- How cytokines and immune response may fluctuate with certain exposures.
- Hurdles that could be posed by IRBs in the collection of samples from healthy children should be anticipated.
- IGF-1 has proven to be a useful marker for adult malignancies; it has been associated with high birthweight, which in turn has been associated with some childhood cancers.
- Issues about uniform procedures for collecting and storing samples across all centers and sites should not be underestimated.
- For some biomarkers, complex analysis is required and would be more feasible only in a sub cohort.

- Since the Children's Health Act specifies "From birth to adulthood," associations that are known or suspected should inform the collection process (for example, growth factors, early childhood adipose tissue in the breast—because age at menarche and height have been linked to breast cancer).
- To the childhood cancer community, the primary value of such a repository of samples and the potential data to be derived from it is largely indirect (for example, mechanisms, genotype/phenotype correlations, exposure prevalence).

Validating Retrospective Exposure Assessment

Nancy Potischman, Ph.D., NCI, NIH, DHHS, said that dietary intake was a good example of the type of variable for which multiple measures were useful. Dr. Olshan saw the value as two-fold: getting better prevalence data on some of the less studied effects, as well as validating and perhaps improving the instruments/questionnaires commonly used in childhood cancers. Dr. Ross said that diet and other factors may be associated with cancer risk. Participants listed potentially useful targets for retrospective assessment:

- Possible links between the genotype and levels of folate. Greta Bunin, Ph.D., Children's Hospital of Philadelphia, pointed out that biomarkers are rarely available or sought in case control studies because of the time lag between when the sample is available and the time of interest; nonetheless, it might be worth trying to explore the retroactive significance of current folate levels. Folate aflatoxins might also be considered because they impede folate metabolism and may be a risk factor for neural tube defects.
- Flavenoid metabolism, and other indicia to confirm diet self-reporting of pregnant women.
- Vitamin supplementation.
- Alcohol and smoking, primarily from conception through nursing.
- Breastfeeding.
- Use of pesticides in the home, which can differ dramatically in reports from mothers and fathers. This effect applies to other issues as well, and it was noted that fathers are sometimes less cooperative and harder to locate. Parental interviews should be conducted separately and in private.
- Paternal exposures, which are not often aggressively pursued or collected (for example, smoking, drinking, occupation, general environmental exposures, and family history of cancers).

Dr. Correa described the Study plans for the use of questionnaires, which will explore a wide range of exposures (occupational and at home), including diet. Validation studies using biomarkers could be fairly easily done. If the Study begins to produce reliable data on bias recall, said Dr. Potischman, the childhood cancer research community would certainly benefit. Dr. Wacholder pointed out that focus groups at Children's Hospital in Washington, DC indicate that it is especially tricky to determine when (and to some extent how) to approach mothers whose children are in treatment for cancer. He aspires to one day be able to calibrate the rumination/recall bias as related to different kinds, stages, and severity of disease. Nonetheless, said Dr. Dwyer, the Study's large cohort size presents the first opportunity to systematically look at recall bias in case controls for childhood cancer measures. Dr. Ross stated that those types of

effects are not tightly confined to cancer and may be fairly consistent across a number of childhood diseases.

Summary Statements

Ms. Brown asked the workshop participants to provide recommendations about how the Study could contribute to cancer research for children. They were asked to summarize their final reactions to the issues raised throughout the meeting, suggest any specific strategies that should be woven into the protocol, and recommend additional issues that Study planners should explore further.

For Dr. Linet, the Study's most obvious value would be to provide background information (expected rates, prevalence) on the common environmental exposures experienced by the children in the cohort. While this information would be valid and useful, it also could be developed in other ways and contexts. The use of the Study subjects as case controls in a joint study with COG is not viable; they would not truly match the study group (in having been chosen all at once, and covering only a short, young age span). The use of planned specimen repositories as biomarkers, while valid in the types of exploratory studies they are suited for, does not reflect the types of focused studies that are compelling to researchers in the field.

Dr. Wacholder recommended that Study designers not be constrained in making decisions about the basic protocol by trying to perfect the cohort as a group of controls. He does not believe it will qualify as a compelling substitute for the next generation of cancer case control studies. Once the optimal Study design based upon other considerations is reached, then it may be possible—but not a matter of great urgency or economy—to work within that framework to use some or all of the cohort as controls for certain specific studies. He rated the collection of serial biological specimens for retrospective exposure assessment much more highly, and stated that such information would not be needed from the entire cohort, even though the incidence of childhood cancer was so much smaller than that of other diseases and conditions under study (asthma, ADHD, and others). Validation studies relating biomarkers to questionnaire responses could produce some powerful and fairly novel results, though he warned that design issues were especially tricky in such protocols. He had high hopes that the data, when combined with the NHANES, for example, could help improve researchers' odds ratios in case-only studies by at least an order of magnitude.

Dr. Velie emphasized a point that was not much discussed: using Study data and especially the biomarker specimens as intermediary markers for adult cancer. Very little longitudinal data exists for the age range from in utero to puberty, though it is believed many events in that time frame will eventually be confirmed as links to subsequent cancer in adulthood. She does not think the use of longitudinal data to validate diet or physical activity will bring much new power to conclusions that have already been established in those areas.

Dr. Dwyer concurred about the adult cancer opportunity and said that some of the prospective exposure data the Study plans to collect would be relevant in the context of other case controlled

data on childhood cancer. For example, recall bias as framed by Dr. Wacholder will almost certainly be superior to other large cohort studies, if not due to the Study's design, then for its sheer size. He also believes the idea of using the Study's cohort as controls for another national study has only a limited and conditional value. He was more optimistic about the prospect of pooling data with some other large (tens of thousands and greater), standardized, global cohort studies that are looking at exposure measures and outcomes. Though methodological differences will frame and limit such correlations, joint data analysis should raise the number (*n*) of children diagnosed with childhood cancer to several hundred and thereby enhance the power of that kind of analysis.

Dr. Metayer specified the Study might obtain valuable results by targeting specific groups in rural areas at risk for high pesticide exposure and deriving data on the relationship of sequential exposures to different agents to underlying cancer mechanisms. Like others, she also hedged her enthusiasm because of the problem of how well the cohort may or may not represent the population base. That factor, for her as for most of the group, threatens the value of the Study as a large set of case controls. She agrees that the Study can provide relevant data on self-reporting and recall bias, at least in the context of pesticide and other environemntal exposures, and possibly in the wider context of human subject studies. The strategy she favored was to put more detailed and specific questions to a defined subgroup—a scope that would not be feasible for the entire cohort.

Lynn Ries, M.S., NCI, NIH, DHHS, described the paradox that was discussed earlier: the incidence of childhood cancer is low overall, and even lower for specific diseases and types of cancers; however, the Study subjects' parents can be expected to experience cancer at rates much more conducive to study. Thus, the Study's biomarker specimens could be of great interest to researchers outside the NICHD universe. She recommended that recruiters make use of state cancer registries to locate known cancer cases for specific Study centers—as a strategy to characterize the cancer patients being missed in that area/region/specific environmental context––and thus derive measures of the Study's possible bias. The NCI Cancer Statistics Branch's experience in collecting biological specimens (or accepting into their repository samples collected by others) suggests that Study designers try to be as forward-looking as possible, so that the means of collection and storage do not preclude future studies which, in the context of present technology and research issues, can hardly be imagined.

Dr. Potischman agreed that the Study's proposed use of prospective data to probe recall bias could provide potentially valuable results. As a biomarker surveillance epidemiologist for the Applied Research Program of NCI's Division of Cancer Control and Population Studies, she referred to an upcoming large epidemiological study to assess dietary methods. Preliminary results could perhaps guide designers in framing Study questions about not only what and how people eat, but also the bias involved in subject recall. She advised contacting designers of similarly large (more than 100,000 subjects) studies underway in Norway and Sweden on pregnant women and their children; future studies of cancer mechanism might be possible across these populations—thus tripling the sample size—if the methods and targets of biological specimen collection and even some questionnaire data were systematized across the studies.

Dr. Olshan added his misgivings about using the Study cohort as a control group. He did believe value would be added by looking for patterns in the exposure data, which could help fill out the picture during pregnancy and early childhood. He also concurred that the Study experience should help the field evaluate questionnaire approaches to environmental exposures. He believes the Study design also lends itself to correlation studies looking at genotype/phenotype, but would have to delve into complexities and change during the course of pregnancy in order to plow fresh territory. The fact that the Study was consulting the childhood cancer epidemiology community should enhance any future nexus, even though there seems no urgent priority at present.

Dr. Ross concurred that genetic data to be collected by the Study promised interesting opportunities to probe connections between genes and the environment. Studies measuring diet, folate levels, and metabolism could provide solid prospective serial data on the susceptibility to childhood leukemia, an approach she believes more promising than looking at specific polymorphisms and retrospective disease incidence.

Dr. Bunin described the Study's contributions as primarily methodologic. She expects useful data might emerge on the recall bias issue. She also viewed the Study as an excelelnt opportunity to evaluate the reliability of survey information from the questionnaires because measured exposure levels (through biological specimens) will be available.

Dr. Finette was optimistic about the value of the Study as a lens on the biological, genetic, and socio-economic status mechanisms that occur—and change—during human development, which he said were completely unknown. He also emphasized that the Study need not be massively recast to probe cancer; smaller mechanistic studies, as yet undesigned, could be extremely well staged in the context of the project. Sampling issues have clouded such efforts in the past, so the sheer size of this cohort of (randomly) healthy children from whom (along with their families) a range of biomarker specimens will be collected, should not be undervalued as a lens on normal biological, genetic, and mutalogical processes—not just cancer—that change with age and over time. This framework also facilitates looking at how cancer develops, not just its occurrence as an endpoint. He recommended that these opportunities not be wasted.

Dr. Correa believes the Study will be of value, as long as its data collection falls in line with standard measures in the field of childhood cancer. He pointed to an international interest group meeting in Washington, DC this August that hopes to develop a multi-national cohort study of children, and suggested the Study planners explore a possible link. He was not so quick to dismiss the value of the Study cohort as controls because—while representativeness is often sought—it is much less successfully attained. Thus as "another control group for controls," the Study cohort or subgroups could be invaluable because of the linkage with exposure data. In the context of childhood cancer, this may be the first and only study of its size that could be used to evaluate both the validity and the reliability of exposure measures.

Russell D. Owen, Ph.D., ORD, EPA, stated that the link between childhood exposures and cancers that develop later in life is an important scientific goal, for which the Study is uniquely

positioned to provide a basis. That same view reinforces the value of the specimen repository to provide intermediate biomarkers for subsequent disease; he said there were a number of exploratory studies that could go forward as soon as the data becomes available. He pointed to some already-completed pilot studies that could be tested and possibly confirmed in the much larger Study. Strictly from the cancer viewpoint, he would recommend that more elaborate and intensive staging of samples in a sub-population be done at the expense of broader, more superficial collection. As areas of likely interest, he mentioned hypothetically important exposures such as pesticides in the home and occupational exposures. He echoed earlier remarks about trying to anticipate the needs of future studies in collecting and storing current samples, especially as to possible proteomics applications. As to validating retrospective exposure assessments and questionnaire information, he advised Study planners to use currently developed techniques and do more on a subsample rather than less on the entire population.

Dr. Scheidt said that he was most intrigued by the positive and thoughtful comments participants had made about using the data for near-term and far-future studies of cancer in adults. The National Human Genome Research Institute is exploring the feasibility of a large study from the genetic viewpoint. There may be linkages with that project that would inform the selection and collection of samples to look for biomarkers.

Dr. Scheidt thanked the group, saying the comments and discussions had been very helpful, especially in pointing out the limitations the Study and its potential for some methodological contributions to the field of childhood cancer. He restated the consensus message of the day's work: While there may be a few opportunities not to be missed, the Study does not represent a significant tool to study childhood cancers. Nonetheless, as the Study proceeds towards a more definitive form, he wants to be sure that any opportunities for the study of childhood cancer not be overlooked. He invited those who are interested to stay available for ongoing consultation.

Participants

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