MOVING FORWARD: MEETING THE CHALLENGES OF THE NATIONAL CHILDREN'S STUDY

Laying the Groundwork: Pilot Studies and Discussion Groups

The research questions reflect the ambitious scope of the National Children's Study. Its research plan has tremendous range and significance. Study designers are fully aware of the extent of the challenge and the dimensions of the work to come.

The National Children's Study has already initiated a number of preliminary research efforts that will allow investigators to understand where challenges lie and what obstacles might be encountered. Already producing useful data, these efforts ensure that the Study identifies the best and most cost-efficient methods and practices for meeting complex scientific goals.

For more than three years, scientists from many disciplines, including medicine, environmental science, chemistry, biostatistics, social and behavioral sciences, and human growth and development, have worked to build a foundation for the National Children's Study. These efforts, collectively known as "pilot studies," range from evaluating the possibility of recruiting primary care physicians as local Study researchers, to finding inexpensive and unobtrusive techniques for measuring various exposures in homes and schools, to identifying the best ways for collecting and storing specimens, to ensuring accuracy in the data from numerous Study sites within the United States.

These pilot studies, which will be conducted throughout the life of the Study as new issues and challenges arise, encompass the questions that must be addressed to enable a functional and cost-effective National Children's Study. As results from the pilot studies become available, they will be incorporated into the research design.

Among the pilot efforts are *exposure studies*, which seek to predict the where, when, and why of environmental exposures, along with the different pathways of those exposures. For example, because infants interact with their environment differently than older children and adults, it is essential to understand what exposures they encounter and how these exposures can be accurately measured.

Health-related studies evaluate and recommend testing and measurement techniques. Efforts are under way to develop simple, reliable, and inexpensive "field-ready tests" to assess and measure child development.

Study design pilot studies explore different ways to conduct a study, such as optimal approaches to involving communities and recruiting participants.

Cross-cutting studies combine the insights of scientists working in different disciplines. A geneticist may partner with an environmental chemist, a pediatrician, and an ethicist, for example, in an effort to identify the ways in which genes interact with a specific chemical exposure to influence child behavior in different locations in the United States. Cross-cutting studies capitalize on multidisciplinary collaborations in many of the Study theme areas simultaneously, and, along the way, offer exceptional potential to identify new and emerging technologies of use to the National Children's Study. Such studies also lay the groundwork for a children's environmental health research database of substantial utility and range.

This is a once-in-a-lifetime opportunity. It will shape the research agenda for the next generation.

Robert Chapin, Ph.D., head, Investigative Developmental Toxicology Lab, Pfizer Pharmaceuticals

In the context of these strategies and techniques, experts from various disciplines relevant to the Study have assembled as working groups to discuss the scientific, medical, and ethical issues pertinent to a study of this magnitude. Numerous analytical papers have been or are now being prepared, looking at the "state of the art" in the interconnecting scientific arenas that comprise the Study's research themes.

Administrators and investigators remain aware that, as the Study unfolds, new challenges will arise. Participants will age, society will evolve, new technologies will emerge, and scientific and health priorities will respond to shifting needs and capacities. The National Children's Study pilot studies are preparing for the road ahead, laying critical groundwork to ensure that the Study reaches its goals and offers a substantive return on investment in terms of health, knowledge, and new capabilities.

Planned Approaches to Study Challenges

CHILDREN AS RESEARCH PARTICIPANTS

It has become increasingly clear over the last 30 years that toxic exposures have different—and sometimes more serious—effects on children than adults. For a long time, children were excluded from clinical research because the risks were considered too great. But now the nation realizes that not including children in research poses even greater risks to public health and safety. If children are at the highest risk, they need and deserve our best research efforts.

The National Children's Study is a response to the need for new knowledge in the area of environmental exposures in children. But what are the issues surrounding recruitment of children before birth, long before they can express an opinion about their participation?

There are established precedents for the safe and responsible recruitment of children, and institutional regulations govern ethical conduct of research involving children. National Children's Study planners are committed to making every effort to ensure participants' safety.

The recruitment of children is generally achieved with at least one parent's or guardian's permission. As part of this informed consent process, the National Children's Study will discuss important aspects of the Study's structure, intent, and methods with every mother, father, or guardian involved.

The Study will adopt a policy of open communication that emphasizes clarity and accessibility. Informational materials, Web sites, informed consent forms, and possibly interactive consent computer programs will be made available at appropriate reading levels and in the languages spoken by the families involved.

The families of participating children (and, eventually, the children themselves) are the pivotal Study partners. They will be encouraged to provide ongoing feedback on their experiences in the Study. Their questions, problems, and issues will be critical to creating the balance that will guide the conduct of the National Children's Study, ensure responsible and responsive Study management, and make this a truly unprecedented national research effort.

PARTICIPANT CONFIDENTIALITY

In discussion groups conducted during the Study's planning stage, expectant and current parents and other stakeholders consistently raised privacy as a key issue. Community leaders and health care providers echoed these concerns. All believe that participants must clearly understand the Study's benefits, promise, and process for protecting the privacy of personal data.

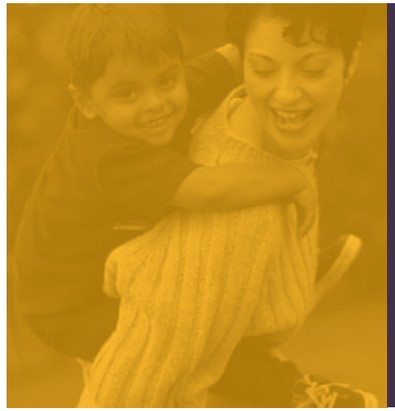
Prospective participants may wonder about the ability of any large-scale study to protect their family's private information over the long term. They might fear that employers, health insurers, and other third parties will gain access to their information. To address these concerns, the National Children's Study will devote careful attention to personal privacy. Among other protections, DHHS recently released new guidelines under the Health Insurance Portability and Accountability Act of 1996 to protect the confidentiality of individuals' medical records, which the National Children's Study program staff will follow. Study coordinators will also construct the Study's databases to ensure the protection of privacy (e.g., encrypted sites and secure data entry forms) and will proactively address security issues (e.g., protecting data from outside attack).

The National Children's Study also will rely on institutional review boards to review ethics safeguards and participant protections. The Study may assemble an independent panel to provide an extra level of review in managing issues related to confidentiality.

PROTECTING PARTICIPANTS (INFORMED CONSENT)

A critical factor in mounting such a broad-based research effort hinges on how individuals will give permission for their children's participation in the National Children's Study.

The National Children's Study is a national response to the need for new knowledge in the area of environmental exposures. If children are our most at-risk population in this arena, they need and deserve our best research efforts.



Every American citizen is a stakeholder in the nation's future, and, as such, shares the rights and responsibilities inherent in well-informed decision making. Informed consent affirms and actualizes the national commitment that scientific research must never take precedence over the safety and well being of individuals participating in that research.

Informed consent is the mechanism by which any individual choosing to participate in research does so independently and on the basis of open communication about a study's aims, goals, and potential risks and benefits. Informed consent also provides a potential participant with adequate time to reflect before making a decision. It is fully embraced by the National Children's Study and supported by rigorous federal guidelines for investigators and individuals that govern the ethical conduct of research, especially efforts involving pregnant women and children.

Within this context, the following series of related concepts drive the Study's approach to informed consent:

- Informed consent is fundamental to the Study.
- The risk posed by participation in the Study is expected to be minimal.
- Additional safeguards will be in place to protect the rights and interests of child participants.
- Because participants will reflect the diverse nature of the United States, every effort will be made to provide useful Study information in understandable terms and appropriate languages.
- When Study participants reach a predetermined age, they will have the opportunity to actively affirm their parents' endorsement of their participation in the Study.

PARTICIPANT RECRUITMENT

Recruiting and retaining 100,000 participants is unquestionably the greatest challenge for the National Children's Study. Because the Study will begin by following fetal health, Study coordinators must enroll pregnant women early enough to monitor their fetuses as well as their diets and other factors. Enrolling such a large number of participants—from every corner of the country and virtually every racial, ethnic, and socioeconomic group—will require a coordinated effort of research staff, health care providers, and intermediaries who can reach and inform families about the Study. Recruitment is slated to begin around 2006, after the National Children's Study is launched, and will last through 2011.

Study information materials must emphasize benefits while allaying potential concerns. Study coordinators are designing a strategy that meets these needs,

including a major information campaign that will educate the public about the Study and promote recruitment. The campaign will commence at the Study launch and will run at least through the recruitment phase. In addition, recruitment teams will carry out local campaigns within communities hosting the Study. Every participating clinic and hospital will also receive assistance with setting recruitment goals and providing information for the population(s) they serve.

Study planners anticipate that intense, local grassroots campaigns will yield the greatest recruitment for each site. Local campaigns will promote the formation of community partnerships; build relationships with area obstetricians and other health care providers; and direct outreach to parenting groups, religious and community institutions, and other organizations offering health information and support to families. Previous studies have demonstrated that endorsement and referral from trusted community leaders is a significant factor in encouraging study participation.

PARTICIPANT RETENTION

The task of keeping track of 100,000 families, through changes in family structure, new residences, and departures for college or work, is formidable. The National Children's Study is developing a retention strategy that builds on its recruitment efforts and draws from past study successes. Because it is such a crucial aspect of the Study, retention is being considered at virtually every step of the planning process, from protocol design and ethical considerations to data monitoring and recruitment. Study planners will not take for granted anything that might compromise a family's ability or willingness to stay the course of the Study.

Building trusting relationships with community leaders will be critical to the success of the recruitment efforts.

According to published reports on previous longitudinal studies, a critical factor in keeping participants "on board" is the bond they develop with Study staff and fellow participants. That Study investigators and support staff, in particular, personally care about the children and families involved is a powerful motivator toward continued participation. Building on the relationships between participants and Study staff, the National Children's Study will seek to create a community of "National Children's Study Families" in which each site—as well as the entire community—recognizes and celebrates the role of participants. Some tools and activities to promote connection and cohesion among participants may include newsletters (both electronic and print), interactive Web sites for the children, periodic get-togethers, public presentations, and birthday greetings. As in most studies of this kind, participants will receive incentives for their continued participation.

Study coordinators will need to be creative and flexible in developing ways to keep 100,000 families engaged in the Study through its completion.

COMMUNITIES OF THE NATIONAL CHILDREN'S STUDY

NATIONAL CHILDREN'S STUDY SPONSORS

- U.S. Department of Health and Human Services
  - — National Institutes of Health
  - — Centers for Disease Control and Prevention
- U.S. Environmental Protection Agency