PART II: STUDY DESIGN AND METHODS

5. CHALLENGES AND APPROACHES

5.1 Design Challenges and Approaches

A major challenge in designing the National Children's Study is to balance the power of the large sample size, enrollment of women early in (or prior to) pregnancy, longitudinal follow-up, and breadth of exposure and outcome measurements with the real life considerations of participant burden and cost. Because the Study is observational, respondent burden must be commensurate with the motivations and limited benefits of participation. Using other longitudinal observational studies (Golding, 2004) as a guideline, the NCS will try to limit any single face-to-face data collection to no more than half a day (four hours). Similarly, procedures must pose no more than minimal risk, and biospecimens will be limited in quantity. Thus, only some of the many possible clinical assessments are appropriate, and only a finite number of tests can be run on each specimen. Funds are also limited, thus the planned tests or procedures implemented in the entire cohort must be carefully selected. A core set of contacts and data collections with Study participants has been proposed, and forms the framework for the Study. It is expected that sub-studies and adjunct studies will supplement the full Study, utilizing additional, more in-depth data collections on targeted areas of interest and involving subsets of the full Study population (see Chapter 16).

5.2 Measurement Challenges and Approaches

A number of approaches will address the measurement challenges of this large, longitudinal, epidemiological study. The best measures possible will be employed in the full Study, but they may not always mirror more in-depth assessments used in more circumscribed research studies because of the cost, time, and burden involved. Again, it is expected that these issues can be addressed in sub-studies or adjunct studies. For some measures, for example certain of the unstable and expensive environmental chemical assays that are important to assess in the entire population, a validation subsampling methodology will be considered to reduce costs while still including critical exposure measures (Strauss, Lehman, Morara, & Ryan, 2003). It is likely that more extensive measures focused on specific areas will be utilized in anticipated sub-studies or adjunct studies.

To limit respondent burden, questionnaires developed for use in the core protocol incorporate short versions of scales or selected targeted subscales, when possible and appropriate. Moreover, a number of the questions are viewed as "screens" and will be followed by a lengthier set of questions for those with a positive screen. Face-to-face data collections are supplemented with mail-in or computer-based self-administered data questionnaires. These additional remote data collections not only provide valuable data for the Study, but also serve as a means to maintain meaningful, frequent contacts with Study participants.

5.3 Processes for Continuing Protocol Development

As a longitudinal study of more than 20 years, the NCS will face demands of continually changing and advancing science, technology, and methods. Wherever possible, the Study must anticipate and accommodate evolving science and technologies. For example, a large National Institutes of Health (NIH) program to develop efficient, inexpensive, and accurate exposure assessments is underway. It is

likely that some of the methods from this initiative would increase the power of environmental assessments for the NCS (http://www.gei.nih.gov/exposurebiology/index.asp). Development of technologies and methodologies for genomic measurement and analyses will continue to evolve rapidly during the Study. It is expected that as this field advances and expands, so too will the opportunities for understanding gene-environment relations and mechanisms of disease. Information management systems (IMS) can be expected to be outdated at least every 5 years, and the IMS for the NCS is being built to allow incorporation of changes as they occur.

Accordingly, the Study's protocol will require continual planning for each successive phase of the cohort as the participants advance through life. The initial research plan and protocol focus on the first phase of pregnancy and on infancy. Subsequent plans and phases will address preschool, elementary school, early adolescence, and late adolescence. Planning the specific methods for these respective protocols will be undertaken as the cohort approaches each phase with enough time for careful planning and implementation but close enough to the needed protocol so methods can be as current as possible.

As in the planning of the Study thus far, future protocol planning will seek to include the best scientific input possible. To seek input and guidance on specific issues, The Study will continue to utilize the Federal Advisory Committee, ad hoc workshops, and literature reviews and white papers. When needed, methods development and pilot studies will be conducted to resolve issues and to refine measures for each respective phase. In contrast to the first several years of Study planning, the Study will not have numerous expert working groups under the Advisory Committee. Instead, investigators from the 30-40 Study Centers and Coordinating Center will provide ample depth and breadth of expertise in the form of subject matter expert teams for input into planning the respective protocols. These working teams will propose methods and measures for the respective protocols to the staff of the Program Office and Coordinating Center. The Steering Committee of Principal Investigators will consider and propose decisions regarding Study priorities and similar issues, and the Interagency Coordination Committee will continue to provide review and oversight with regard to the Study's ability to address the goals and missions of the respective federal agencies. Though committed to input from broad scientific expertise, ultimate decision-making authority rests with the Director of the National Institute of Child Health and Human Development and, on his behalf, the Director of the NCS.