The following is a summary of comments the National Children's Study received during a public request for commentary on the Research Plan. To protect the identity of individuals commenting on the Research Plan, all identifying information, such as names and contact information, have been removed from these comments. In a few cases, the names of those offering comments were not removed, at the request and permission of the original sender.

E-mail

I wish that these two things were included as outcome measures:

- 1) Obesity and insulin resistance from formula feeding
- 2) Breastfeeding and asthma; breastfeeding and celiac disease; breastfeeding and diabetes.

With the CDC predicting that 1 child in 3 born in 2000 will develop diabetes, and with 1 child in 5 being overweight/obese, and with much strong evidence that what the infant is fed is a contributory factor to these condition, it would be easy to ask a question or two about infant feeding as part of the data collection.

Using Labbok and Krasovec's definitions, participating mothers could be asked:

- 1) Was the child breastfed?
- 2) Exclusively, partially, or not at all?
- 3) If breastfed, how old was the child when other food or drink was introduced?

E-mail

Dear NCSinfo:

I apologize for missing "breastfeeding associated with lower rates of obesity and insulin resistance."

Asking the questions about type of breastfeeding (exclusive, partial, or none) and the age of the child when other food or drink was introduced is significant.

Again, my apologies for reading too fast.

E-mail

Please review, print out and include Ventilation Inspection in the NCS research program as described in the URL at:

http://groups.msn.com/IAQ

Select "IAQ" and print out for advised Health Department Residential Ventilation Inspections as to how to inspect same.

The book "Ventilation Inspection Advisory" is available for interlibrary loan at selected libraries, including EPA Libraries.

E-mail

I briefly read the plan and I applaud this endeavor! I would only make one comment as you move forward - actually a plea - for some other measure of a child's behavior (sleep problem or whatever) than what is typically obtained from the mother.

If a mother is anxious or depressed, it is likely that she'll report problems with the infant/child sleep or other behavior. The mother's self-report measure should be validated either by also having a father or other family member measure, or by a teacher or staff person in day care.

E-mail

Dear Sir:

I have read your study and would like to comment that I hope you will study the effects of stillbirth and the link to environmental effects. I am currently on the Board of Angel Names Association, along with other bereaved parents, and we are looking into funding research along these lines. I would like to commend you and your staff on the breadth and scope of your study. I would like to hear from you or your staff regarding your efforts to study stillbirth and the possibility of being effected by environmental, including chronic stress, and its relationship to stillbirth, if there is any relationship.

E-mail

Dear National Children's Study,

Congratulations on a good beginning!

A study about children's health MUST include breastfeeding and the use of human milk and their role in infant health outcomes.

E-mail

I would like to add that pediatric sleep medicine is an emerging field as more people recognize the value of appropriate sleep habits. For children, few studies on sleep provide data-based guidelines for appropriate sleep schedules, particularly in the area of napping. At the same time, educational systems have made decisions for full-day kindergartens which may not incorporate a napping period into the curriculum. Some of the data indicate that as many as 25% of 5 year olds still need a nap. There are also limited studies in the sleep medications for children which are used in clinical practice, despite the lack of FDA approval.

E-mail

Dear Coordinator,

Please let me know if this Study will include participants from outside USA.

E-mail

I trust breastfeeding status will be included in the National Children's Study

E-mail

You should consider inclusion of suicidal and self-injurious thoughts and behaviors. It would be very important and powerful to identify any potential pathways for the emergence of these behaviors from the very earliest years of life, across adolescence, and into early adulthood.

E-mail

Witnessing intimate partner violence is consistently associated with poor behavioral outcomes for children. However, it did not appear in any of your hypotheses or measures as an important family process. The impact of prenatal exposure on perinatal outcomes and infant temperament should also be examined.

It would also be important to include observations of brain function (e.g., fMRIs) to establish the impact of differing levels of exposure to nurturing-abusive parent/nonparent caregiver-infant interactions on the developing brain in order to establish how much and what types of care is "good enough" care.

E-mail

To Whom it May Concern,

I am worried about your acceptance of existing documents for classifying learning disabilities, developmental disorders and the nature of environments.

As regards the classifications of learning disabilities and developmental disorders, I fail to see any concern for the ubiquitous problem of concordance of symptoms. Put differently, it is clear that classifications have a far way to go before we can claim that we have anything like a Linnean or other valid classification scheme.

As regards the matter of the environment: I strongly recommend a paper that Richard Solomon wrote many years ago on the question of what counts as control conditions for assumed deprivation or hurtful environment. There is no question that asbestos is bad. The same is true for other chemicals in the environment. But counts as a good environment for children who first do a lot of learning on the fly about the world, social relations also suffers from the absence of a theory of how to cut the environment into its psychological joints. The latter applies to families whose home language is not English and are at or just above the poverty line as much as it does to all families.

E-mail

The way children learn healthy relationality (love) and psychological, emotional and spiritual resiliancy is by example but, unfortunately, the health of American marriages (and/or long-term committed love relationships) and families has been plummeting, especially among African Americans. Because of this, and other related factors (e.g. racism, sexism and the media),

America has an epidemic of LOVELESSNESS, which then contributes to MANY other problems (obesity, depression, suicide, anger, behavior problems, divorce, substance abuse, poor school performance, poor contraceptive use, hypertension, and PTD).

So please collect as much psychosocial info as you can, over the entire life course, so that correlations with later outcomes (especially very preterm birthrates, or birthweights) can be found over the next 60 years. American doctors may be using pills and technology to their maximum effect; I believe improvements in many of our public health problems will only come with decreases in our LOVELESSNESS.

Please have one of your researchers call or contact me if they are interested in MANY scientific references supporting these ideas.

E-mail

Dear NCS Team,

Very admirable study, but I think that most of the jury is already in on what you are trying to accomplish. Besides, by 2034 it will be too late. Also, can we, as a nation, morally afford to let children continue to suffer?

As you point out, the children are experiencing increasing difficulties in realizing a healthy life in our country.

E-mail

Dear Sirs

I have been following with interest, your information about the study

I would suggest that having the infrastructure of the study, you may begin to go deeply into those fields where you begin to find a high incidence or prevalence rate.

For example, it is known that children's discapacities are, I think, a Public Health problem. So, my suggestion is to study this more deeply. And so, I would suggest the same, for at least the first 5 to 10 causes of mortality and/or morbidity.

I want to thank you again for having me in your list. Although I am in another country, very different; at least your information gives me some idea of thing happening here.

E-mail

National Children's Study

Dear participants:

As you know, the National Children's Study is an outstanding opportunity to study congenital factors that may be involved in various forms of intellectual disability and autism. When we look back in the future at this study, undoubtedly one of the questions to be asked will be – did it help

us understand the increasing number of children diagnosed with autism spectrum disorders (ASD)?

I might get involved in the National Children's Study, undoubtedly because I am a specialist in autism. I have reviewed the study and would like to give you my thoughts on it.

One) The timing of the samples. There is good evidence that the disease process in children with autistic features starts in the first or second trimester at the latest. In Chapter One (pages 5-10) of The Neurology of Autism (1), there is a section on the timing of autism, which explains that it is primarily a first and second trimester phenomenon (2). Children with autism that have been documented with third trimester insults appear to be mostly affected by infections, such as symptomatic congenital cytomegalovirus infection (3). That autism is a prenatal syndrome was further supported by the Nelson study (4) that showed that 99% of the children who later developed autism or intellectual disability had abnormal levels of neurotrophins and neuropeptides already present in their blood at birth, levels not present in controls. Therefore any sampling of toxins during pregnancy might turn out to be invaluable, as early as possible.

Two) Type of samples to be collected. In the case of ASD, it is likely that the majority of children have a genetic or epigenetic mutation underlying their disease process. However, as in the case of the intellectual disability population, we could not anticipate based on current techniques that more than 10% to at most 20% of the children will be found to have a classic monogenetic disorder. The genetic material might reveal results in the future based on methodology yet to be available. The two-hit hypothesis suggests that other background or toxic environmental insult might also be crucial, so these kinds of samples could be equally important.

Three) Include the fathers in the sampling. So much time and money is going to be spent on this project, it would be ideal to include at least one sample from the fathers in this project. I know in a practical sense it is more difficult than to include the mothers. The reason to include the fathers is that there are subgroups of autism that have a familial pattern on the male side. Autism is a male disease 4:1. In addition, there is a hypothesis that the parents could be affected in the preconception period by whatever is causing this increase in cases of autism.

Thank you for your consideration.

With best regards,

Mary Coleman, MD

References:

- 1). Coleman M (2005) The Neurology of Autism. Oxford University Press.
- 2). Coleman M. (1994) Second trimester of gestation: a time of risk for classical autism. Developmental Brain Dysfunction 7:104-109.
- 3). Yamashita Y, Fujimoto C, Nakajima E, Isagai T, Matsuishi T (2003) Possible association between congenital cytomegalovirus infection and autistic disorder. Journal of Autism and Developmental Disorder 33;455-459.

4). Nelson KB, Grether JK, Croen LA, Dambrosia JM, Dickens BF, Jelliffe LL, Hansen RI, Phillips TM (2001) Neuropeptides and neurotrophins in neonatal blood of children with autism or mental retardation. Annals of Neurology 49:597-606.

E-mail

This project is an amazing undertaking and has incredible potential to improve child health. I have a son with autism. I have been wondering for many years why so many more children have mental and developmental disabilities (esp autism, ADHD, bipolar, depression) now when compared to the 1950s when I grew up. I don't buy the diagnostic substitution or better detection/healthcare arguments. Everyone has genetic predispositions to disease and environmental exposures. Historically, infectious diseases have been the most significant environmental exposures. I would like you to assess every pre and postnatal infection (no matter how mild) in the cohort to see if kids with ADHD (for example) have had more respiratory infections than controls. Have kids with autism had more Strep than controls? One Arizona study found that kids with autism had been given more antibiotics than controls (presumably for bacterial infections).

E-mail

Dear Sir or Madam,

The American Society for Bone and Mineral Research (ASBMR) is pleased to submit the following comments on the first phase of the National Children's Study Research Plan. A study of bone health would complement and broaden the current specific aims outlined within the NCS proposal. If you have any additional questions, please do not hesitate to contact me.

Comments related to Bone Health Outcomes

Given recent reports that childhood fracture rates have increased over the last 30 years (Khosla S, et al. JAMA 290:1479-85, 2003), impaired bone health should be considered among the list of chronic childhood diseases and development conditions on the rise.

The NCS provides a unique opportunity to answer questions regarding the effects of environmental exposures on bone mineral accrual trajectories, and life-long bone health. Specifically, the study could examine how maternal exposures (vitamin D levels, alcohol consumption, smoking), and childhood exposures (vitamin D levels, calcium intake, physical activity) at particular points in development impact bone accrual, and how these exposures interact with genetic influences.

Other primary study outcomes of the NCS (e.g. obesity and insulin resistance) may be associated with outcomes of relevance to bone health in children. For example, the relationship between obesity and fracture is not well-understood. Obesity also predisposes to vitamin D deficiency (Am J Clin Nutr. 2000;72(3):690-3), with this deficiency having associated with a variety of adverse sequalae on bone and other tissues. The current NCS document focuses primarily on prenatal outcomes and those within the first 2 years of life. However, bone density measures by dual-energy x-ray absorptiometry would be informative, especially later in the study (i.e., during the school-age years) when positioning for DXA scans becomes much easier and precision is

improved, and normative data for DXA are more available and reliable (compared to infants and young children).

The study of bone health is in alignment with the NCS Specific Aims (Research Plan page 53) to determine the effects related to the timing, frequency, magnitude and duration of specific chemical, physical, biologic, and psychosocial exposures in children's environment; determine possible environmental contributions to specific diseases; determine how genotypic variation and mechanisms, and the interaction of genes with environmental factors, influence disease risk and developmental trajectories in children.

The Research Plan states "Many experts believe that fundamental changes in children's environments appear to be a common pathway for these increases," alluding to the increase in many chronic diseases and health conditions among youth. There are increasing reviews and reports in the medical literature providing strong evidence that the childhood and adolescent years are critical ones for the development of peak bone mass and adult bone health (Endocrinol Metab Clin North Am. 2005;34(3):521-35; Arch Pediatr Adolesc Med. 2006;160(10):1026-32; J Bone Miner Res. 2005;20(12):2075-81; among others). Poor diet and the link to obesity are currently discussed in the NCS proposal's Background, but there is no mention of the critical link noted between dietary influences and bone health. Vitamin D and calcium could be discussed among other important dietary components that are of relevance to bone health. Therefore, bone health and osteoporosis prevention should be considered among the list of health outcomes that are being considered by the planned study, and would be a natural extension to the issues currently discussed. Even the long-term health effects of prematurity and obesity, issues that are currently mentioned in the proposal's Background, could have significant effects on bone health that are not currently discussed within.

It is mentioned that two endocrine exposure measures of specific interest to the NCS are maternal thyroid hormone, and cortisol status in both the mother and child. Vitamin D status of both the mother and child be also considered as another endocrine exposure given this vitamin's effects on multiple tissues and its potential role in conferring protection against many forms of disease (N Engl J Med. 2007;357(3):266-81). Serum 25-hydroxyvitamin D levels would be informative, collected at the same intervals as those proposed for thyroid function and cortisol studies. Data on vitamin D intake, in addition to calcium intake, would also be informative in both the mother and child.

E-mail

This is a comment about the National Children's Study.

I believe that a child sleep measure should be added. Poor sleep in children has been related to neurodevelopmental functioning, socioemotional functioning, asthma and obesity. A substantial literature exists to support these relationships.

E-mail

I am writing to share my comments on the National Children's study.

I find this study plan to be very exciting. As a developmental psychologist and psychopathologist I see great benefit in this large proposed project. I would encourage the investigators to consider adding four types of assessments:

- 1) A measure of relational aggression (Crick & Grotpeter, 1995, Child Development) as part of psychosocial risk. Teacher, parent, peer, friend, self and observational measures are all readily available for various developmental periods and I would be glad to provide you with further details if needed. Measures are easy to administer and have good psychometrics.
- 2) A measure of hostile attribution biases for relational and instrumental provocation situations (Crick, 1995, Development & Psychopathology). Relational aggression is associated with hostile attribution biases (inferring hostile intent in ambigous situations) for relational but not instrumental situations. Self-report measures are easy to administer and have good psychometric properties.
- 3) A measure of both media violence and educational media exposure. It has been found that educational media exposure predicts relational aggression over time (Ostrov et al., 2006, Social Development). Parent measures are easy and efficient.
- 4) A measure of deceptive ability. Deception has been found to be uniquely associated with relational and physical aggression in short-term longitudinal studies. A teacher report or parent report measure is available, easy to use and has good psychometric properties (Ostrov, 2006, Journal of Experimental Child Psychology).

Thank you for the opportunity to comment and good luck with the project.

E-mail

Good Morning—

I would like to recommend a pediatric sleep component to this study. We know very little about sleep patterns in children with chronic illnesses & the extent to which disturbed sleep impact child well being. In addition, longitudinal studies addressing sleep are scarce. This would be an excellent opportunity to examine infant and child sleep patterns across early child development as well as examining environmental variables.

Some suggestions: The Children's Sleep Habits Questionnaire -- a parent report of their child's sleep by Judy Owens.

Additional questions:

- ➤ Does you child nap (at home & at childcare)? (frequency, duration)—very few studies address nap patterns in children.
- ➤ Does your child frequently wake up during the night? Frequency? Duration? What awakens your child?
- > Does your child/infant fall asleep on their own?

➤ Does your child snore?

Hope this information is helpful.

Good luck with your study. And thank you for allowing us to comment—great idea!

E-mail

Dear Duane Alexander,

I am responding for the request for comments on the National Children's Study 2007 Research Plan. I am writing as a researcher of cultural aspects of human development, and a former member of the HUD-1 study section of NICHD.

This ambitious study seems to overlook the role of cultural processes in the health practices and childrearing practices of the varied communities of our nation. Many aspects of health care and of childrearing are conceptualized and carried out differently according to varied cultural practices (see The Cultural Nature of Human Development, Oxford, 2003, and other works dealing with cultural practices). Cultural practices are not the same as race or identity, nor the same as poverty or neighborhood.

The design of a large-scale study such as this tends to rely on 'variables' that are measured independently of each other and to focus on individuals as the unit of analysis, overlooking the coherent constellations of practices that characterize cultural communities. With such approaches there is not much information to help avoid a deficit model, based on the idea that the dominant population's ways are the best, when the researchers attempt to interpret differences between individuals differing in ethnicity or racial identity.

To address this issue more effectively would require including cultural expertise and research on cultural practices in varying US communities, relevant to many of the research questions to be asked. Although a few parts of the design show that some cultural experts have been consulted, the major design seems to be at risk for deficit interpretations due to little or no attention to cultural practices of varying communities.

E-mail

The National Children's Study is obviously an extremely important and impressive project. One of the most commendable aims is to achieve a better understanding of the development of aggression. Two notable additions to Susanne Denham's review in this area are:

1) It is extremely important to determine what aggressive behaviors children actually do as well as the frequency and severity with which they do them. This information may be most usefully embedded in the longitudinal study of aggression using group trajectory analysis. Consultation with major investigators in this area like Rowell Huesmann and Richard Tremblay is highly recommended, if this has not already been done.

2) There is a burgeoning interest in children's tantrums which should be strongly encouraged and supported. Firstly, tantrums are among the most common of early childhood behavior problems with 60-90% of two year olds having them. Tantrums are largely why the terrible two's are terrible (the three's sometimes, also.) Correspondingly, tantrums can be major challenge to the parents of young children. When tantrums are frequent, prolonged, or involve serious destruction or aggression, parents can become angry at their child's behavior and than anxious about their own feelings. Secondly, there is some emerging evidence that various tantrum characteristics may be early markers of psychopathology. It has become clear that children's tantrums at age 3 can predict future antisocial behavior and aggression in later childhood (Stoolmiller 2001) through adulthood (Caspi et al 1987, Stevenson & Goodman 2001.) As always, early detection is perquisite to early intervention. However, there is nothing even remotely close to age- and sexrelated "norms" which would allow researchers and practitioners to determine with any confidence what is developmentally appropriate and what may deserve clinical attention. Finally, the study of tantrums can provide tremendous new insights into children's emotions; they are a window onto anger and sadness, some of it so intense as to be otherwise inaccessible to scientific observation. Despite all of this, very little is actually known about this important phenomenon of early emotional life. What is needed is a long-term research program to develop a general theory of tantrums encompassing their neural bases, ontogeny and development, dynamics, physiology, and relationships to child temperament and parental intervention.

References

Caspi, A., Elder, GH, Jr, & Bem, DJ. (1987) Moving against the world: Life course patterns of explosive children. Dev. Psychology, 23, 308-313

Stevenson, J., & Goodman, R. (2001). Association between behaviour at age 3 years and adult criminality. British Journal of Psychiatry, 179, 197-202

Stoolmiller, M. (2001) Synergistic interaction of child manageability problems and parent-discipline tactics in predicting future growth in externalizing behavior for boys. Developmental Psychology 37, 814-825.

E-mail

To Whom It May Concern

I looked at the measures of socioemotional development in the proposal. I am concerned that so much of the data are primarily mother reported. I realize there are some observed behaviors/interactions, but they are limited. Given the sample size and high cost of observed variables, I would make several suggestions. First, it would be useful to get father and nonparental caregiver ratings on many of the measures as often as possible and from a young age. The proposal says teacher data will be added at older ages, but many children have babysitters, etc, who could fill out some measures. In addition, I was unclear if there would be behavioral measures of simple self-regulatory/executive functioning skills (I may have missed this), but some are easy to administer and to score on site. In addition, the experimenters working with the parents and children could provide some valuable ratings after interacting with members of the families (again, I am unsure if those are included). There is a need for rich data on individual differences in children's self-regulation, emotionality, etc., and questionnaires to mother provide

only limited data. Similarly, for parent-child interactions, it is important to be sure the observations and reports are appropriate and that multiple sources of data are used. I realize that this is in the plan, but I hope that experts from the developmental sciences are involved in the decision making. They likely are, but I have not really heard much in this regard.

E-mail

September 27, 2007

Duane Alexander, MD Director, NICHD The National Children's Study 6100 Executive Boulevard, Room 5C01 Rockville, MD 20892-7510

Dear Dr. Alexander:

On behalf of the American Speech-Language-Hearing Association's more than 127,000 members and affiliates, I am submitting comments on the proposed Research Plan for The National Children's Study. First, ASHA has been and will continue to be a strong supporter of this historical and monumental study. ASHA members and staff have been closely following the development of this study from concept, to federal legislation, to annual funding, and now, to implementation.

ASHA's has five specific comments on the Research Plan. They are as follows:

We strongly support the collection of data regarding language(s) spoken by the caregiver and the child. Language(s) spoken may change over time. It is an important variable to consider as the outcomes are being examined.

We encourage the training of data collectors so that they will be aware of the influences of culture and linguistic factors and will take them into consideration when working with translators and/or culturally appropriate procedures and measures to gather information. It was not clear from the research plan how information would be collected from linguistically diverse populations.

We strongly recommend that hearing status should continue to be monitored as the child ages, as some congenital hearing loss may not become evident until later in childhood.

We encourage researchers to make it clear to the study participants that participation in the project means that the child will be monitored and does not mean the child will receive treatment or care through the study.

We appreciate and support that the data collected from the study can be used for adjunct studies and will encourage our members to take advantage of this opportunity.

As you know, ASHA is the professional, scientific, and credentialing association for more than 127,000 members and affiliates who are speech-language pathologists, audiologists, and speech,

language, and hearing scientists in the United States and internationally. ASHA's mission is to promote the interests of and provide the highest quality services for professionals in audiology, speech-language pathology, and speech and hearing science, and to advocate for people with communication disabilities. We convey our excitement and support of this study and look forward to working with study designers, clinicians, and participants over the course of the study.

E-mail

National Children's Study Comments on Study Plan

Sampling

- 1. Sampling women who are not currently pregnant. The study design calls for inclusion of women who are currently pregnant and women who are not currently pregnant but have a high probability of becoming pregnant (are actively trying to become pregnant). The problem with this design is that a high percentage of pregnancies and births are unintended, and unintended pregnancies/births are not randomly distributed throughout the population. For example, in 2001 49% of pregnancies in the United States were unintended. About 5% of women aged 15–44 had an unintended pregnancy. The rate of unintended pregnancy was substantially above average among women aged 18–24, unmarried (particularly cohabiting) women, low-income women, women who had not completed high school and minority women. The proportion of unintended pregnancies ending in abortion among all women has declined, while the unintended birth rate has increased. Thus, the current design of the National Children's Study will produce a biased sample of mothers who are not currently pregnant but will give birth soon.
- 2. Focus on fathers. Biases could be introduced if unmarried or other women do not wish to identify the biological father for enrollment in the study.
- 3. Biases based on incentives (including social desirability pressures) for participation. What will women be told about the study goals, their participation, and incentives for participation? Community based efforts to promote participating may become problematic if women try to become pregnant in order to participate?

Psychosocial Constructs and Measures

These measures (from preconception onward) are very important to the ability to test study hypotheses. In general, these are not as well described as the biological and physical environment measures. Indeed, a look at the measures appendix shows that some items have not yet been chosen. Other key constructs that should be considered for the psychosocial assessment are outlined below.

1. Possible "silver bullet" measures of developmental processes. The child measures are focused on outcomes or diagnoses rather than on the developmental processes that may give rise to problem outcomes. There are a handful of constructs that, recent literature suggests, appear to underlie a wide range of problematic child outcomes, including those that are the focus of the NCS hypotheses.

- **a.** <u>Attention</u>: Attention is tied to a number of the primary outcomes or interest in the NCS (e.g., neurodevelopment, injury). Therefore, thorough-going assessment of attention should be a priority. One way to assess attention development would be to videotape the administration of the Bayley and the BAIT for researchers to code such constructs as effortful control, joint attention with parent and other such indicators. Although these videos would raise assessment costs, they would provide a rich source of data. Peter Mundy at University of Miami of Florida and Cynthia Huang-Pollock at Penn State are potential resources. Some measurement of attention would be appropriate at each data collection point since it develops quickly in the first two years of life.
- **b.** Emotion Regulation: Like attention, emotion regulation abilities are have been tied to a range of child outcomes. One way to learn about emotion regulation in the context of the planned assessment would be to collect short videotapes of the planned physical exams and procedures (e.g., blood draws, heel pricks) so that researchers could assess child emotional reactivity and regulation as well as parental responses that support or hinder return to equilibrium.
- **c.** Resiliency: The proposed work seems largely based on a deficit model. A body of research on "hardiness" (Kobasa, 1979) and positive psychology (Seligman & Csikszentmihalyi, 2001) has garnered increasing attention in the prevention science and treatment of mental health problems. Relevant constructs would seem an important focus of data collection. The Connor-Davidson Resilience Scale (CD-RISC: Connor & Davidson, 2003) or the Resilience Scale (RS: Wagnild & Young, 1993) may be appropriate measures.
- **2. Measures of parenting and family processes**. The proposed measures of parenting seem static and miss important components of parenting and family process. Key constructs to consider include the following.
- **a.** <u>Assessment of Neglect</u>: Child neglect relates to all kinds of child injuries, and, despite reductions in rates of child abuse over the last ten years, child neglect rates have remained relatively stable. Although there may be ways to piece together a picture of neglectful parenting with the proposed measures, this construct could be measured directly (see Dubowitz, Pitts, & Black, 2004; John Lutzker [John.Lutzker@Marcus.org] is an expert in this area). Lack of supervision and home safety are two constructs that relate to neglect. Potential measures are:

Supervision Attributes Profile Questionnaire (PSAPQ) measures aspects of supervision related to child injury risk (Morrongiello &House, 2004). It has 4 subscales: protectiveness, worry about safety, vigilance, and confidence in the ability to keep your child safe. It has been shown to relate to child injury levels and observed supervision level on the playground.

Home Accident Prevention Inventory (HAPI-R) assesses home safety (Mandel, Bigelow, & Lutzker, 1998; Tertinger, Greene, Lutkzer, 1984) using 26 home hazards (fire, electrical, firearms, solid and liquid poisons). Home visitors examine areas of the home accessible to the target child and rate various risks.

b. <u>Sleep</u>: This could be considered a child outcome variable but also relates to parenting and family processes; amount and quality of sleep in children and parents does not appear to be a

focus of the proposed data collection protocol. Importantly, however, sleep and disturbances in sleep are implicated in many health outcomes for youth and parents, as well as many important process variables implicated in health outcomes, such as maternal/paternal napping while ambulating children are awake (injury), abusive and neglectful behavior, and quality of parenting. Further, the physical environment, a focus of interest in the NCS, would seem relevant to quality and quantity of sleep (e.g., noise in house or community, temperature of the house), and sleep patterns may be mediators of the effects of these contextual factors on health outcomes. Hormonal correlates of sleep could also be examined if diurnal cortisol patterns are being assessed. Possible measures of sleep quantity and quality are the Infant Sleep Questionnaire (ISQ: Morrell, 1999) or the Maternal Cognitions about Infant Sleep Questionnaire (MCISQ: Morrell, 1999). Parental sleep could be assessed using the Pittsburgh Sleep Quality Index (PSQI: Buysse, et al., 1989).

E-mail

September 25, 2007 Duane Alexander, MD Director National Institute of Child Health and Human Development National Children's Study 6100 Executive Boulevard, Room 5C01 Bethesda, MD 20892

Dear Dr. Alexander:

On behalf of the American Psychological Association (APA), I am writing to provide comments on the National Children's Study (NCS) 2007 Research Plan. I would like to commend you and the NCS Program Office for the tremendous effort in developing the study protocol over the past seven years and for providing us with multiple opportunities to speak with you and to the NCS Advisory Committee about our concerns and priorities for this important study. APA is the largest scientific and professional organization representing psychology in the United States and is the world's largest association of psychologists. APA's membership includes 148,000 researchers, educators, clinicians, consultants, and students. Through its divisions in 53 subfields of psychology and affiliations with 59 state, territorial, and Canadian provincial associations, APA works to advance psychology as a science, as a profession, and as a means of promoting health, education, and human welfare. As APA represents a broad range of psychological scientists and practitioners, we are interested in many of the exposures and outcomes that will be examined by the NCS, including: cognitive, emotional, and social development; parent and child mental health; high risk behaviors; health disparities; healthy behaviors; child maltreatment; childhood obesity; learning disabilities and educational attainment.

We believe this groundbreaking study offers unique opportunities to examine the complex interactions of genetic and environmental influences on child health and development, including the critical role of the social and family environments. The NCS will also provide a rich resource of information for future scientists to utilize in studying their own hypotheses, so it is vital that the following issues are considered as the hypotheses continue to evolve and the cohort approaches adolescence and emerging adulthood.

Mental Health Outcomes

Mental health is a key component of overall health and plays a significant role in the prevention or exacerbation of chronic diseases. Given the prevalence of mental, behavioral and emotional disorders in childhood, we support the NCS's inclusion of learning, sensory and motor disorders; attention and other conduct disorders; autism spectrum disorders; depression and anxiety disorders; and schizophrenia. Given the prevalence of eating disorders in adolescent and college-aged populations, we would recommend these also be included.

Mental health is also more than the absence of mental illness. Positive mental health outcomes should also be measured, including resilience, optimism, and emotional regulation. Resilience in children in the face of adversity, including poverty, trauma, bullying, stress or family violence, may prevent the onset of some mental and physical disorders. Measures such as the Children's Attributional Style Interview or the Children's Attributional Style Questionnaire would provide important information on a child's resiliency and risk for depression.

Positive Child Health and Development Outcomes

As the overall goal of the study is to improve the health and well-being of children, it is important to reiterate that a child's optimal health and development are more than the absence of disease. We are disappointed that the NCS continues to reflect a strong focus on the antecedents and consequences of pathology and disease, while providing insufficient measures of protective factors that promote positive developmental and health outcomes.

The NCS offers a tremendous opportunity to provide scientists with information about positive cognitive, social, emotional and behavioral developmental outcomes. Unfortunately, it appears that direct behavioral assessments of the children are extremely limited, with the remaining core measures being assessed from reports by parents or other adults. It is especially disconcerting that temperament and emotional/social indicators come from parent report when other well-validated behavioral assessments are available, such as the Laboratory Temperament Assessment Battery (LAB-TAB) for temperament. Furthermore, it appears that parent-child attachment quality is not assessed. The Brief Infant-Toddler Social Emotional Assessment-Parent Version (BITSEA) being proposed in the study does not measure attachment. Failure to address the attachment domain of development seems short-sighted, given the consequences of early relationship quality to future relationship development and mental health. While there are legitimate concerns about overburdening the participants, it would be unfortunate not to collect data on these critical developmental outcomes.

Child Neglect, Maltreatment and Trauma

Measuring levels of maternal stress, depression and other psychosocial factors during pregnancy, post-partum, and throughout the study will provide critical information about the family environment. The influence of maternal or paternal mental illness or substance abuse on child development, child maltreatment and the development of mental disorders in children is also an important issue for this study.

Exposure to trauma in childhood, whether in the home, school or community, is a critical area of importance, as research indicates that childhood trauma contributes to many health problems later in life. Child maltreatment, particularly neglect, can have a major impact on development. As the participants will be referred to social services under conditions of child maltreatment, it would be important to retain those families in the study, particularly if the children are removed from the home. Information on child maltreatment could be obtained through parent report, child welfare records, and retrospective report from the child at 21 years of age.

Health Disparities

We commend the NCS for including attention to health disparities across multiple hypotheses and for attempting to oversample racial and ethnic minority populations in the study. Behavioral and social scientists have a history of studying the influence of environmental, physical and social factors on health outcomes for diverse populations. The strong association of low socioeconomic status (SES) and race with a multitude of health and education outcomes requires further in-depth evaluation.

Minority populations face higher rates of asthma, obesity, diabetes, sexually transmitted diseases, severe mental disorders, and unintended pregnancies. Access to high quality health care, childcare, and education resources are also affected by circumstances related to SES. Likewise, parental educational attainment also plays a role in a child's health and educational achievement. Measuring cultural and environmental factors related to these outcomes will provide a clearer picture of what leads to such disparities.

As the NCS moves into the recruitment and implementation phase, it will be important that research staff are aware of potential cultural and language differences in both assessments and outcomes. To accommodate populations with limited English proficiency, the NCS Program Office should consider having bilingual interviewers or translators involved with the project from the initial stages to assist with appropriate translations of the materials and the measures being utilized. For those measures that have not been validated in ethnically and socioeconomically diverse samples, researchers should also be prepared to address potential cultural differences. While the NCS has planned to measure acculturation, which is an important factor in determining health outcomes, there is no indication of which definition of acculturation is being used or which measure of acculturation, among the several available, is going to be utilized in the study. Further discussion of these critical factors should be undertaken before recruitment begins and should be addressed in the community outreach process.

Underserved Populations

Much more work is needed to analyze the differences among minority populations as well, including Hispanic, African-American, Asian Pacific Islanders and Native Americans. By oversampling from these groups, from low and high SES backgrounds, critical information can be learned about the effect of SES and distinct cultural, racial, and ethnic factors.

The NCS research plan unfortunately does not mention the inclusion of same-sex families, a chronically understudied population that is rarely included in population-based studies, despite the significant presence of households headed by lesbian or gay parents in U.S. society. Given the increasing rates of non-traditional family structures, it is important that information regarding

non-marital domestic partnerships, including same-sex families, be collected to provide a more complete picture of American families.

The NCS also provides an unprecedented opportunity to prospectively explore the development of gender identity and sexual orientation. We recommend that the NCS include developmentally appropriate assessment of gender identity and sexual orientation. There is no evidence across several major surveys of the general population (including the National Longitudinal Study of Adolescent Health, the Nurses Health Study, the Women's Health Initiative, the National Survey of Family Growth, the National Health and Nutrition Examination Survey) that assessment of sexual orientation markers limit survey quality. Although there is less experience with the assessment of gender identity in research populations, developmental psychologists have developed methods for assessing gender identity in children and adolescents.

Understanding linkages of sexual orientation and gender identity with other biological and environmental factors and processes will shed light on both basic mechanisms of biobehavioral development and on mechanisms through which sexual orientation and gender identity affect health disparities. Both variables are crucial to two of the major areas of hypotheses in the NCS: family influences on child health and development and reproductive development.

Furthermore, minority sexual orientation and gender identity represent social challenges profoundly affecting parenting behaviors, relationship formation and maintenance, and child and adolescent development. Understanding how a subpopulation regularly exposed to high rates of social discrimination maintains healthy, happy, and productive lives, both as individuals and in families, offers a rare scientific opportunity to study human resiliency.

Adolescent Behaviors

As the NCS is focused on child health and development, it is important to maintain a longitudinal framework when developing hypotheses. A child's environmental exposures will change over time as children progress from elementary school to secondary school and college, and the influence of their peer groups will have an additional impact on their health behaviors. Adolescent sexual behavior can have serious implications for physical and emotional health that last into adulthood.

Other high risk behaviors common in adolescents and young adults include substance abuse, binge drinking and high risk sexual behaviors and should be examined as outcomes associated with early exposures to parental substance abuse, domestic violence, child maltreatment or neglect.

Thank you for considering our comments on the NCS 2007 Research Plan. Though we have mentioned several alternative measures for your consideration, APA does not endorse any specific measure or instrument.

Sincerely,

Norman B. Anderson, PhD Chief Executive Officer

E-mail

We strongly support the concept of a well designed National Children's Study (NCS) that fully assesses children's exposures at school and in day care centers. To do anything less will seriously compromise the Study's outcomes, the health agencies' ability to promote the development of healthy children, and EPA's ability to properly develop policies, programs and/or regulations to reduce environmental threats to children throughout their developing years.

While the current NCS Study Plan covers only the first 24 months, it is crucial at this juncture to have well-developed plans for assessing exposures in day care and in schools. Today there are 54 million children in our nation's 120,000 schools. Repeated federal studies have shown that schools are in poor condition and present an array of toxic exposures that can exceed exposures at home. Further, children age 0-3 years with special education needs may be placed in 'early intervention' educational programs supported by or housed in local facilities. Also, increasing numbers of families rely on early-age, full-time day care as more women and more single mothers work outside the home.

Thus, our <u>primary recommendation</u> is that given the complexity of school environments and the lack of current data, as well as the knowledge that spending 30 hours/week in schools is what 54 million children are doing this week and for most of their developing years (ages 5-18 years):

• we urge the NCS to convene a Work Group on day care and school environments to assist with the development of study features that will tackle these environments and their impacts on children's health and development.

<u>In addition</u>, recognizing that there is a balance between science and budgets, and recognizing that there are as yet insufficient data on schools and health, and recognizing that NCS has the potential to gather a solid basis for improving our understanding of school environments, we support full funding of NCS that includes:

- study-wide uniform protocols for the collection and onsite assessment of exposures in day care centers and schools for all enrollees;
- school and day care-specific Study Hypotheses that will help drive NCS to a more complete understanding of the factors impacting child health and development, such as researching if there are more toxic and more varied chemical exposures in schools than in homes, or linking school exposures to increases in asthma or other diseases and disabilities;
- assessing a full array of exposures in schools, including but not limited to CO, CO2, PCBs, radon, asbestos, mercury and other heavy metals, lead in paint and in drinking water, molds and other microbials, dusts/silica, carcinogens, VOCs, dampness and mold infestations, as well as *characterizing the facility in some detail* (to help identify what hazards or features to monitor, we suggest that NCS review the recent National Research Council/NAS report "Green Schools" and the many other expert, peer-reviewed published studies on school Indoor Air/Environmental Quality);
- the ability for researchers to conduct both scheduled and unscheduled site visits to day care centers and schools;
- a method for tracking children in the special needs community who are newly identified during their school years or who develop secondary disabilities during that period; and,
- a common NCS methodology for intervening when children are in harm's way in school since schools are mandated reporting sources for abuse and neglect, but can refuse

an onsite public health investigation. To that end, NCS may wish to review a recent white paper developed by CDC on if/how/when it can order school closures, or the NIOSH/HHE on a school in lower Manhattan in 2002 that found new onset illnesses among the 300 school personnel, but had no authority to assess the impacts of the 9/11 dusts and fumes on the 3,000 children in the same facility.

Thank you for your work thus far. We look forward to working with you and to supporting NCS.

E-mail

Hello from Norway.

The ongoing Norwegian Mother and Child Cohort Study (MoBa) conducted by the National Institute of Public Health is one of the largest pregnancy/birth cohorts ever. In this study we have possibilities to test very many hypotheses about child development and health.

Do you know about it?

It is aiming at including 100,000 pregnant women in 2008. The majority of all pregnant women in Norway are invited to participate in the study. The women are recruited through a postal invitation when they present themselves for an ultrasound scan about 17th week of pregnancy. Nearly all women in Norway go through an ultrasound scan at their nearest hospital (www.fhi.no.morogbarn).

The women receive 3 questionnaires during pregnancy, two about week 17-18, and one about week 30. The father will also fill out a questionnaire. The study is also linked to the Norwegian Medical Birth Register. Further on, questionnaires are sent when the child is 6 months, 18 months, three year and 7 year.

The MoBa Biobank is containing blood from the mother, father and baby, urine etc. It is very modern and expensive, a future gold mine.

Questions to you:

- 1) have you consulted our experiences with this study?
- 2) have you seriously discusses how many cm of space you allow for questions about the child's health and development which compete with questions about the parents?
- 3) have you tried to deal with the attrition and
- 4) do you think you can allow many subsamples to be drawn from the main sample in order not to tire out the participants?
- 5) do you know that there are NIH interests in this study, and how would you likewise allow Norwegians to be part of your study?

I am sure, after having scrolled through all the written material, you have been thinking about it all. But do you really known how we struggled to get this study on going?

I have been affiliated with the NHIP for many years and I was the one suggesting including questions about infant temperament in the 6 months questionnaire - the majority concerned questions to the mother. Now, there is a huge staff in charge of this great study.

I am now analyzing extremely interesting research issues from the data files that are made available to the researchers involved in the study- and it costs a lot to buy this data - at least a considerate sum - but we only have to rely on one informant- which is a problem. I am planning to submit a paper to the special issue on the programming hypothesis of the journal Child Development, and it will about the association between caffeine in pregnancy and ADHD symptoms in the 18 months old. I am also part of a paper submitted titled "Mother's antenatal anxiety and behavior difficulties in the child at 6 months of age" - just to give you an indication of the possibilities here. In the present file, I have more than 70,000 births, but the sample is reduced to 34,000 when using longitudinal data from wave 1 to wave 4.

I am impressed by your efforts to start this study. The US of America is the place with the best researchers in our world, and we do read your results all the time and you have so many to ask advice from. You have, though, no identification person number as we have, and the possibility to trace people is not as good as in Scandinavia, but again, I think you must have been discussing all this things and I do not know how I can contribute. Other than to say, this work is indeed important and I do wish you all the best and I am glad you inform us.

E-mail

September 21, 2007

The National Children's Study National Institutes of Child Health and Human Development National Institutes of Health 6100 Executive Blvd., Room 5C01 Bethesda, Maryland 20892

Dear Sir/Madam:

The American Association for Clinical Chemistry (AACC) appreciates the opportunity to provide comments on the National Institutes of Health's National Children's Study 2007 Research Plan. As a strong supporter of this initiative, we are very pleased with the agency's efforts in advancing this study. In general, we believe the research plan is well crafted, clearly delineating the purpose of the study, its design, and the measures that will be employed. We urge the study planners, however, to consider a number of minor refinements to the study.

Chapter 7: Selection of Outcome and Exposure Measures

The research plan lists carbohydrate-deficient transferrin as the test that will be utilized to detect alcohol use. The use of carbohydrate-deficient transferrin is known to lack sensitivity in detecting mild to moderate alcohol use. This is a serious limitation given that many mothers may not be willing to admit to alcohol use. We urge that the plan be modified to include additional measurements of biomarkers that are sensitive to milder alcohol intake, such as fatty acid ethyl esters or phoshatidylethanol, which would more accurately assess alcohol use in the study population.

Also, there are a number of potential confounding issues that might impact outcomes. For example, the study may end up including up to 40 subjects who will have inborn errors of

metabolism that will be detected by newborn screening and an undefined number of other metabolic diseases in addition to those cases with impact from maternal metabolic abnormalities (pregnancy associated diabetes etc). These cases could potentially skew such areas as neurodevelopment and mortality. The numbers are relatively small but the effects huge. The research plan should address how it will deal with this issue in the final document.

Chapter 8: Rationale for Outcome Measures

In 8.5.3, the research plan states that "Potentially relevant laboratory analyses can include assessment of ghrelin, leptin, adiponectin, and other adipocytokines" to determine if those compounds are causally related to increased weight and adiposity or are an intermediate phenotype." These analytes are not on the list of specimens in Appendix G: Detailed Overview of Biospecimens. Will the list of analytes be continually updated as the study moves forward? Will there be opportunity for additional public comment if new tests are added?

Chapter 9: Rationale for Exposure Measures

In section 9.5.6, NIH briefly discusses how information regarding illicit drug use will be obtained from the mother before and during pregnancy and after birth. We recommend that this section be expanded. Although the document mentions that "drug screening of biologic samples (blood, cord blood, and urine) can also be performed," it does not mention what methods may be employed or what detection limits will be utilized. AACC would caution against using the Substance Abuse and Mental Health Services Administration (SAMHSA) cut-off limits for screening purposes as it would fail to detect many exposures that could potentially affect child development.

Section 9.6.6 describes the rationale for collecting PBMCs and establishing future cultures to augment genomic analysis. These cultures, in our opinion, will provide an invaluable link between genotype, phenotype and mechanism that is not adequately emphasized in the current document. We recommend that NIH clarify the intent of such studies by including a few specific examples of informative experiments that might be conducted using these cell lines. We also suggest that different forms of sample collection for genomic analysis be considered, including dry DNA storage technology.

Chapter 10: Statistical Analysis Plan

The research plan states that NCS will obtain 100,000 participants from 105 geographical sites. In aggregate, the statistical power of 100,000 enrollees seems adequate. We are concerned, however, that the study design may not be sufficient to identify geographically isolated exposures. In each geographic region containing slightly fewer than 1000 participants, exposures that result in low frequency outcomes (<1%) will yield only a handful of cases. Thus, it appears that the design will not be sensitive to exposures restricted to a single geographic region. We urge that the document more clearly address this limitation.

Chapter 15: Quality Assurance and Quality Control

In 15.7, the research plan states that laboratory performance will be monitored on a continuous basis, including the use of "external QC," such as proficiency testing (PT), and through routine inspections of staff and procedures. AACC agrees with this approach. However, it is not clear from the document whether NIH is planning to perform these duties in-house or contract with a private accrediting program. We believe it would be more efficient to contract with an existing

CLIA-accredited organization, such as the College of American Pathologists, rather than to reinvent these mechanisms internally.

Appendix G: Detailed Overview of Biospecimens

In Appendix G, NIH lists the biological specimens that will be collected from the parents and the child. We are concerned that a number of analytes in the study exhibit some geographic and/or seasonal variation (e.g., hematocrit, Vitamin D). Currently, the plan does not discuss how the researchers will control for these problems when they collect the specimens or how they will address them in the statistical analyses. We recommend that these issues be addressed in the final research plan.

Also, the research plan states that 31.0 mL of blood will be collected from the child at six and twelve months. We are concerned about total volume of collection in these infants. We recommend that the NCS determine total volume of collection based on the individual infant's weight and have a contingency plan for collecting fewer samples from smaller infants. A prudent limit to adopt is 5% of the patient's total blood volume. Further, we suggest that urine specimens from babies be collected by catheterization for females and bagging for males.

AACC is the principal association of professional laboratory scientists. Our more than 9,000 members develop and use chemical concepts, procedures, techniques and instrumentation in health-related investigations and work in hospitals, independent laboratories and the diagnostics industry worldwide.

E-mail

Dear Peter,

I thought the announcement of the National Children's Study conference call was really excellent and informative, also opening the whole issue up to questions was terrific.

As a geneticist, I have been concerned from the very beginning about three things related to the National Children's Study and I keep being reassured that there is no problem, but I want to mention them to you.

The first is in a developing embryo/fetus/newborn/child there are such specific time in development windows of effect. We know that from teratology, but my guess is that the same is true at older ages and we also know that there are major changes and shifts in metabolism as a child ages that puts them at risk for specific age related diseases. Thus, I think the question of timing during development of the 100,000 children will be extremely important. It may be possible to establish the size of the windows.

The second issue has to do with genes being part of networks. As genetics has evolved and developed, it has become quite clear that each gene acts as part of a pathway and those pathways integrate and inter-relate. Thus, in terms of testing for specific genes, rather than looking at pathways, there can be major problems. However, by the time that the study is done, a lot of that will have been worked out and there will undoubtedly be microchips developed that will be able to look at pathways and their interactions.

The third issue has to do with the sibs who are "natural" controls for the children brought into the study and I have never heard anyone talk about how they plan to use the sibs. I would hope that some imagination could be used and that the sibs will be engaged in the study as well as their families and the subjects. Of course, detailed family histories going back three generations and information on mother's own pregnancy and birth weight are important.

Again, congratulations on the hard work, the determination, and the excellent conference call.

E-mail

As members of the Sleep Working Group, a task force convened by the NCS Behavior and Development Working Group to make specific recommendations on obtaining core sleep-related information as part of the National Children's Study, we wish to strongly endorse and support the continued inclusion original recommendations (attached) we submitted in August of 2003. Insofar as sleep represents a key biobehavioral variable that has enormous potential impact on health, growth, and development in children, we feel that the inclusion of a basic set of sleep-related questions is a mandatory component of a comprehensive assessment of children's health and well-being. The National Children's Study presents a unique opportunity to gather prospective longitudinal data regarding the impact of sleep on such far-ranging issues as childhood obesity, injury, asthma, attention and behavior, and cognitive development. In conjunction with many of our sleep medicine and sleep research colleagues, and as advocates for children, we are grateful for this opportunity, and look forward to providing continued assistance and advice to the NCS working groups.

E-mail

I agree that changes in the environment alters a child's health. I now have an allergy to mold. How? Long story.

I also am a survivor of suicide (sister died in '83) and am pro-art when it comes to working through times of trouble.

My question is: Will you be studying any adverse effects and offer services to help heal situations?

I would be very excited to teach children to paint in acrylics. Let's say you have 100 children, and 6 of them fall into a group that are in a position for early bereavement. You could opt to put 3 of the 6 into a painting workshop so they can heal. My "Wet Paint" workshops show children how to set up a studio space in their home and paint when they feel the need to. The right brain activity takes a person to another zone where time slips away along with other worries/stresses.

E-mail

DHS NIH - Human Development- NIH Plan For Children's Study-Attention Duane Alexander

This Collection of tons of paper will result in no help to American families with children born with autism and other maladies. This alleged "study" is simply sitting in a Washington office collecting paper and lead to nothing except paper for the wastebasket.

As I understand it, studies like this have been going on for years with no result in help for the American population and this one will join the ineffective ones that preceded it.

To concentrate on diabetes, when so few mothers in fact have it – less than one percent – and when 1 out of 66 children born in NJ have autism shows a lack of understanding of what is going on.

Why don't you concentrate on autism and find out what is going on with this disease first, which is attacking far more than one percent of American Families.