7. SELECTION OF OUTCOME AND EXPOSURE MEASURES

To guide the selection and prioritization of exposure and outcome measures, 28 hypotheses were developed based on the input from multiple federal agencies and scientific experts. The criteria for these core hypotheses were that they be scientifically compelling, have important public health implications, be feasible to test, and clearly justify the need for a prospective birth cohort study of 100,000. These hypotheses can be found in Appendix A. Although it is expected that many other scientific questions will be investigated, the core hypotheses have served as guidelines for prioritization of measures.

Due to the breadth of the National Children's Study, each contact between the participant and NCS personnel must capture information pertinent to multiple exposure and outcome domains. Thus, the length of time a measure takes to administer is an important issue with respect to overall participant burden and retention. Also for these reasons, measures that are generally perceived as invasive or uncomfortable are less likely to be included in the full protocol. Each of the procedures, measurements, and assessments associated with the NCS must meet the criteria for "minimal risk" as defined in the Code of Federal Regulations [§45 CFR 46.102(i)]. In addition, the NCS is committed to minimizing even minimal risks.

7.1 Exposures, Outcomes, Mediators, and Confounders

To some degree, the categorization of certain measurements as an outcome, an exposure, a potential mediator, or a confounder is arbitrary because a factor that is an exposure in one hypothesis may be a mediator, confounder, or outcome for another. For example, childhood obesity can be considered an outcome related to fetal growth and maternal glucose tolerance and also a risk factor for subsequent development of diabetes or cardiovascular disease. For consistency, this document categorizes outcomes and exposures as they are presented in the NCS hypotheses while acknowledging the fluidity inherent in many of the areas. For a more in-depth discussion of mediators and confounders see the Statistical Analysis Plan (Chapter 10).

7.2 Overview of Measures

As described previously, the NCS will engage in a continual process of planning the protocol measures to ensure they reflect the best science and technology available. Protocol development will continue as the children age and new scientific data become available. Specific measurements for each new wave of data collection will begin approximately two years before the measures are needed in the field.

Assessment of exposures and outcomes will utilize tools suitable for a large-scale, longitudinal, multi-site, geographically dispersed epidemiologic study. In general, measurements used successfully in other large studies of child health are most likely to be included in the NCS because they have a record of past performance and will facilitate the comparison of NCS results to those from other studies. However, some novel or less frequently used tools may provide important high-quality data and are included where appropriate for the entire cohort, while others may be more suitable for focused adjunct studies.

7.2.1   Organization of Rationale for Measures Chapters and Appendices

The rationale for outcome and exposure measurement strategies is presented in Chapters 8 and 9. The domains of exposures and outcomes described in these chapters extend from birth to age 21. There is more specificity, however, relating to assessments through infancy since protocol development is still ongoing. These chapters are supported by Appendices E through I, which contain detailed information about the domains of measurement at each participant contact through child age 24 months.

Chapter 8 describes the rationale for measurement strategies with regard to each of the seven priority outcome areas: pregnancy; neurodevelopment and behavior; child health and development; asthma; obesity and growth; injury; and reproductive development.

Chapter 9 describes the rationale for measurement strategies with regard to chemical exposures, physical exposures and environment, psychosocial environment, biological exposures, and genetics.

7.2.2   Overview of Measures Related to Specific Hypotheses

As mentioned previously, the NCS core hypotheses served as guidelines for the selection of outcome and exposure measurement domains. Consequently, in conceptualizing the relation between the outcome and the exposure measurement domains, it is helpful to think about their connections within these core hypotheses. Table 7-1 presents the 28 core hypotheses across the top of the table organized by priority outcome area. Domains of exposures and covariates are listed down the side. For each hypothesis, the exposures and covariates central to that hypothesis are indicated in the table.

Table 7-1.   Measures by Hypotheses

Measure	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Questionnaire - Mother																												
HH Composition and Demographics		C	C		C		C	C	N	C	C	C		C	C		C	C	N	C	C	C	C		C		N	C
Parental Stress		C				C	N		N	N			N	N												N	N	
Maternal Exhaustion *Prop							C							C												C		
Social Support							N		C				N	C			C											
Family Process							N		N	C			N					N						C		N	N	C
Health Behaviors	C	C					C				C		N	C	C					C	C	C	C			C		C
Diet and Toxicants through food					N													N		C	C	N	N	N				C
Media Use									C		N	C																
Maternal Mental Health & Cognition					C		N		N		C	C	N													N	N	
Parenting Style							N		N		C		N													N	N	
Maternal / Paternal Attachment					N		N		N			N	N															
Child Care									N	N	N	N	N															
Neighborhood									C	N		C																N
Public Policy													N															N
Housing Characteristics				C	C	C	C	C		C					N	C	C	C	C			C	C		C			C
Occupation / Hobbies				N	N	C	C	C						N	N	C	N	N	N			C	C	N	C			N
Appliance and Product Use				N	N	C	C	C							N	C	N	N	N			C	C		C			N
Use of medicines	C				N	C	N								C		C					C	C		C			
Time and Activity (mother / resident father)				N	N	C	C	C				C			N	C	N		N	C	C	C	C		C			N
Family Environment (observation only)						N		N	N				N													N	C	
Brief Medical History	N	N	N		C	N		N	N	N	N	C		N	N	N	N	N	N	N	N	N	N	N	N	N	N	C
Child Language Development					N		N		N			N	N															
Child Temperament / Emotional Regulation							N		N				N													N	C	
Socio-Emotional Functioning					N				N	N	N	N	N															
Social Competence / Behavior Problems													N														C	
Child Autism Screening					N		N		N																	N		
Adaptive Behavior							N		C																	N		
Questionnaire - Child																												
Neonatal Neuro-behavior	N		N		N	N				N			N													N		
General Cognitive Ability					N				N	N	N	N	N															
General Motor Development					N				N	N	N	N	N														N	
Cognitive Processes					N	N			N	N	N	N													N	N	N	
Language Development					N				N	N	N	N	N														N	
Infant Emotion					N		N		N																	N	N	
Parent-Child Interaction							N		N				N													N	N	
Attachment Status					N				N	N	N	N															N	
Sensory Function					N				N	N	N	N																
Questionnaire - Father																												
Demographics									N	C		C																N
Paternal Mental Health and Cognition					C		N		N		C	C	N													N	N	
Social Support							N		C				N	C			C									C		
Experiences with Target Child																												

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

Measure	Pregnancy Outcomes: Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Neurodevelopment and Behavior: Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Child Health and Development: Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Asthma: Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Growth: Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Injury: Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Reproductive Development: Hormonally Active Environmental Agents and Reproductive Development
Questionnaire - Father continued																												
Parenting Style							N		N		C		N													N	N	
Paternal Attachment					N		N		N			N	N															
Child Care									N	N	N	N																
Tobacco Product Use, Alcohol Use, Illicit Drug Use and Prescription Drug Abuse (5.10)																												
Use of Medicines and Alternative Medicines																												
Brief Medical History																											N	
Occupation / Hobbies					N	N									N		N	N	N					N				N
Family Process							N		N	C		C	N				N							C	N	N		
**Subdomains are shown if they are a confounder/covariate only.																												
Environmental																												
Indoor air																												
PM2.5 - ETS, Pb, Cd, Mn	C	C	C		C	C									N	C	N		N									N
PM10 - PAHs, pesticides	C	C	C	N	N	C	N,C	C							N		N		N									C
VOCs					C	C		C							N				N									C
Aldehydes & Ketones								C							N	C	C		N									
NO2															N	C	N		N									
Hg					N	C	C	C	C															C				C
O3															N	C	N		N									
CO					C										N	C	N		N									
House dust																												
Allergens, endotoxin															N	C	N		N									
Mold															N	C	N		N									
Metals - Pb, Cd, Mn, As					C	C	C																					N
Pesticides: OPs, Carbamates, Pyrethroids					N	N	C	C	C																			C
Pesticides: OCs					N		C	C	C																			C
Drinking water																												
Disinfection Byproducts (DBPs) - HAA9	C	C	C	C				C																				
VOCs	C	C	C		N,C	N,C	N,C	C							N													C
Metals - Pb, Cd, As			C	C	C	C	C	C																				N
Nitrate	N,C	N,C	N,C	N,C																								
Perchlorate					N																							N
Pesticides: OPs, Carbamates, Pyrethroids					N	N	C	C	C																			C
Pesticides: Atrazine																												N
Pesticides: OCs					N																							
Soil																												
Metals - Pb, Cd, Mn, As							C	C																				N
Pesticides - OPs, Carbamates, Pyrethroids					N	N	C	C	C																			C
Near CCA treated wood - Cr+6 (as total), As						N	C	C	C																			C
Visual assessment		C			N	N,C	C		C						N,C	C	N,C				C	C				C		N
Noise survey														C														
Indoor/Outdoor measurements																												

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1. Measures by Hypotheses (continued)

Measure	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Environmental - Continued																												
Community air																												
PM2.5								C							N	C	N		N									N
PM10 - PAHs			N		N	C	C	C							C											C		
O₃															N	C	N		N									
NOₓ, SO₂															N	C	N		N									
Pollen (non-NCS data collection)										C				C	N		N		N									
Outdoor water samples at homes	C	C	C	N	N	C		C							C				N					C	C			N
Community water systems (non-NCS data collection)																												
Hg				N	C	C	C	C																	C	C		
Perchlorate				N																								N
Pesticides				N	N	C	C	C																		C		N
Nitrate	C	C	C																									
Physical Exam - Mother																												
Anthropometric									C	C	C									C	C	C	C					C
Ultrasound				N																N	N							
Physical Exam - Father																												
Anthropometric									C	C	C									C	C	C	C					C
Blood Pressure									C	C																		
Physical Exam - Child																												
Anthropometric									N	N	N									N	N	N						
Blood Pressure									N	N																		
Dysmorphology/Physical Exam	N				N						N																	
Physical Activity									C		C									C	C		C					
Biospecimen Collection - Mother																												
Blood																												
Endocrine Panel																												
Cortisol	C						C	N						N												C		
Cortisone	C						C	N						N												C		
Corticotropin releasing hormone (check volume)	C						C	N						N												C		
Cortisol binding globulin	C						C	N						N												C		
CRH binding protein	C						C	N						N												C		
Reproductive																												
Estriol	C						C	N						N												C		
Estradiol	C						C	N						N												C		
Progesterone	C						C	N						N												C		
Infection/Inflammation/Biological																												
CBC (WBC, RBC, Hgb, Hct, MCV,MCH, MCHc, RDW, Plt, MPV, (NE, LY, MO, EO, BA % and #))		N			N	N		N										N				N	N					
cytokines/interleukins		N				N		N														N	N					
Ig types and subtypes and org specific		N				N		N															N					
Rubella (IgM antibody)		N			C	N		N											N									

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

Biospecimen Collection - Mother (continued)

Measure	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Syphilis (Ig)		N			C	N		N										N										
Varicella (Ig)		N			C	N		N										N										
Herpes Simplex 1&2 (Ig)		N			C	N		N										N										
Hepatitis Profile (a and b) *Medical Records* (Ig)		N			C	N		N										N										
Toxoplasmosis (toxoplasma gondii) (Ig)		N			C	N		N										N										
IgE (cat, dog, cockroach, dust mite, fungi, mouse/rat urine)		N				N		N							N			N	N									
CRP		N			C	N		N										N										
Heat Shock proteins		N			C	N		N										N										
Homocysteine and folate (fasting?) serum or red cells (prenatal vitamin influence)		N			C	N		N								N		N										
Cells T-cell subsets for Th-type *Prop		N			C	N		N										N										
thyroid (TSH and free t4)				N																								
Fasting N3-N6 Fatty Acids *Prop																N												
Antioxidant (vit A/E/Carotenoids)																N												
Vitamin C																N												
%carb deficient transferrin (alcohol)	C	C																								C		C
Glucose Metabolism																												
Fasting C-peptide *Prop	N																			N								
Fasting Glucose	N																			N								
HgbA1C	N																			N								
Insulin like Growth Factor *Prop	N																			N								
Fasting Insulin	N																			N								
Fasting lipids (included in chemical volume)	N																			N								
Genetic Tests																												
DNA, DNA & protein adducts for Exposure Assessment (Chemical Changes)					N														N									
Gene Expression (RNA)					N														N								N	
Epigenetic changes (genomic DNA)					N														N									
Genetic Variation: Paraoxonase Gene, glucokinase, vntr insulin, etc. (DNA)	N				N	C		C											N	N	N	C	C	C		N		
Cryopreserved PBMCs	N				N	C		C											N	N	N	C	C	C		N		
Cell lines *Prop	N				N	C		C												N	N	C	C	C		N		
mitochondrial DNA *Prop	N				N	C		C												N	N	C	C	C		N		
Chemical Exposures																												
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds(PFOA,PFOS) (4 mL Serum)				N	C																							N
Lead, Mercury, Cadmium (3 mL bld)				N	C																					C		N
Combination of dioxins/furans and all other chemicals (excluding metals)				N	C																							N
Stored Samples																												

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

Measure	Pregnancy Outcomes				Neurodevelopment and Behavior				Child Health and Development					Asthma						Obesity and Growth					Injury			Reproductive Development
	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Mother (continued)																												
Serum	N	N		N	N	N		N						N	N	N		N	N	N								N
Plasma	N	N		N	N	N		N						N	N	N		N	N	N								N
RBCs (folate and fatty acids)	N	N		N	N	N		N						N	N	N		N	N	N								N
Lavender Top	N	N		N	N	N		N						N	N	N		N	N	N								N
Buccal Cells *Prop																												
Nails																												
Organic Hg (ethyl, methyl)					N	C																						N
Hg inorganic					N	C																						N
Hair																												
Cd					N	C																						N
cotinine	C	C			N	N		C						C	N	C										C		C
Hg inorganic					N	C																						N
Organic Hg (ethyl, methyl)					N	C																						N
nicotine	C	C			N	N		C						C	N	C										C	C	C
Saliva																												
Cortisol	C						C	N						N												C		
storage	C						C	N						N												C		
Breast Milk																												
Antioxidants: Vit C/E/ Beta Carotene																N						N						
Component: lipid, proteins, carbohydrates, enzymes, immunoglobulins, minerals, vitamins, cytokines, hormones																N						N						
Chemical Exposures																												
Dioxins/furans; Organochlorine Pesticides; PCBs					C																			N				N
Pesticides					N																			N				N
PBDE (frozen) flame retardant					C																			N				N
Perchlorate					C																			N				N
Metals: Manganese and others					C																			N				N
phytoestrogens					N																			N				N
MTBE methyl tertiary butyl ether (fuel additive)					N																			N				N
Bisphenol A					N																			N				N
Urine																												
Illicit Drug Panel	C	C																								C		C
alcohol marker *Prop	C	C																								C		C
Antioxidants																N												
Catecholamine	C						C							N												C		
Cortisol	C						C	N						N												C		
Asymptomatic bacteriuria		N				N		N													N							
Fertility Monitor																												
Pregnancy Test Kit																												
PCR for identification of specific organisms *Prop		N				N		N													N							
Chemical Exposures																												

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

Measure	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Mother continued																												
PFBS, Creatinine, alkyl phenols (Bisphenol A, nonylphenol), Hg(inorganic), As(speciated), perchlorate, halogenated phenols(PCP), phthalates, atrazine, OPs, carbamates, pyrethroids, EBDC/ETU, Cadmium				N	N																							N
PAH (may be storage issues); requires separate analysis (3-4 ml)				N	N										N													N
ICP/MS urine screen *Prop				N	C																							N
cotinine	C	C			N	N		C						C	N	C												C
Phytoestrogens					N	N										C												N
Storage	C	N			N	N	N	C	N					N	N	N		N								C		N
Vaginal Swabs																												
Chlamydia		N				N		N											N									
Bacterial Vaginosis		N				N		N											N									
Cultures antibodies		N				N		N											N									
Cultures cytokines		N				N		N											N									
Cultures metalloproteinase		N				N		N											N									
Group B Strep		N				N		N											N									
Gonorrhea		N				N		N											N									
Placenta																												
Cultures antibodies and cytokines		N				N		N											N									
Pathology		N				N		N																				
Chemical Contaminants				N	N										N													N
Umbilical Cord																												
Cultures antibodies and cytokines		N				N		N											N									
Pathology		N				N		N																				
Chemical Contaminants				N	N										N													N
Biospecimen Collection - Child																												
Blood (NOTE: Because of the limited blood draw volume for the child, samples will be stored for future analysis. Final protocol for analytes will be decided in the future.)																												
Infection/Inflammation/Biological																												
CBC (WBC, RBC, Hgb, Hct, MCV,MCH, MCHc, RDW, Plt, MPV, (NE, LY, MO, EO, BA % and #))		N			N	N		N		N				N	N		N	N	N					N				N
Chemical Exposures																												
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds(PFOA,PFOS) (4 mL Serum)				N	C																			N				N
Stored Samples																												
Serum	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Lavender Top	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Guthrie Card at birth	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Buccal Cells *Prop																												
Hair																												
Cd				N	C																					N		N
cotinine	C	C			N	N		N						C	N	C										N	C	C

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

Measure	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Child continued																												
Hg inorganic				N	C																			N				N
Organic Hg (ethyl, methyl)				N	C																			N				N
nicotine	C	C		N	N		C							C	N	C			N					N		C	C	C
Saliva																												
Cortisol	C						N							N						C	C	C	C	N		N		C
storage	C						N							N						C	C	C	C	N		N		C
Urine																												
Chemical Exposures																												
PFBS, Creatinine, alkyl phenols (Bisphenol A, nonylphenol), Hg(inorganic), As(speciated), perchlorate, halogenated phenols(PCP), phthalates, atrazine, OPs, carbamates, pyrethroids, EBDC/ETU, Cadmium				N	N								C		N				N					N				N
PAH (may be storage issues); requires separate analysis (3-4 ml)				N	N										N				N					N				N
ICP/MS urine screen *Prop				N	C										N									N				N
cotinine	C	C		N	N		C							C	N	C								N		C		C
Phytoestrogens				N	N											N						C	C	N				N
Storage	C	C		N	N	N	C							C	N	N	N	N		N	N	C	C	N				N
Meconium																												
Cotinine	C	C		N	N		C							C	N	C								N		C		C
Organophosphate Metabolites				N	N																			N				N
Cord Blood																												
Cortisol	C						N							N						C	C	C	C	N		N		C
Cortisone	C						N							N						C	C	C	C	N		N		C
Corticotropin releasing hormone	C						N							N						C	C	C	C	N		N		C
Cortisol binding globulin	C						N							N						C	C	C	C	N		N		C
CRH binding protein	C						N							N						C	C	C	C	N		N		C
Reproductive																												
Estriol	C						N							N						C	C	C	C	N		N		C
Estradiol	C						N							N						C	C	C	C	N		N		C
Progesterone	C						N							N						C	C	C	C	N		N		C
Infection/Inflammation/Biological																												
CBC (WBC, RBC, Hgb, Hct, MCV,MCH, MCHc, RDW, Plt, MPV, (NE, LY, MO, EO, BA % and #))		N			N	N	N		N	N				N	N			N	N					N				N
cytokines/interleukins		N				N	N		N	N				N	N			N	N					N				
IgE (cat, dog, cockroach, dust mite, fungi, mouse/rat urine)		N				N	N	N	N	N				N	N	N		N	N									
Ig types and subtypes		N				N	N	N	N	N				N	N	N		N	N									
N3-N6 Fatty Acids							C									N				C	C	C	C					
Antioxidant (vit A/E/Carotenoids)							C									N				C	C	C	C					
Vitamin C							C									N				C	C	C	C					
Lymphocyte Subsets Th status (processing difficult)																												
Glucose Metabolism																												
Glucose	N								N	N										N	N	N	N	N				
HgbA1C	N								N	N										N	N	N	N	N				
Insulin like Growth Factor	N								N	N										N	N	N	N	N				

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

	Pregnancy Outcomes				Neurodevelopment and Behavior				Child Health and Development					Asthma						Obesity and Growth					Injury			Reproductive Development
	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Child continued																												
Insulin	N								N	N										N	N	N	N	N				
lipids (included in chemical volume)	N								N	N										N	N	N	N	N				
Genetic Tests																												
DNA, DNA & protein adducts for Exposure Assessment (Chemical Changes)					N								N											N				
Gene Expression (RNA)					N		N						N									C	C	N	N	N		
Epigenetic changes (genomic DNA)					N		N															C	C	N	N			
Genetic Variation: Paraoxonase Gene, glucokinase, vntr insulin, etc. (DNA)	N				N	C	N	C												N	N	C	C	N	N			
mitochondrial DNA *Prop	N				N	C	N	C												N	N	C	C	N	N			
Chemical Exposures																												
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds (4 mL Serum)				N	C								C											N				N
Lead, Mercury, Cadmium (3 mL bld)				N	C								C											N		C		N
Stored Samples																												
Serum	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Plasma	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
RBCs	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Guthrie Card	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Lavender Top	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Whole blood storage PCR	N	N		N	N	N	N	N	N	N				N	N	N	N	N	N	N	N	N	N	N		N		N
Biospecimen Collection - Father																												
Blood																												
Genetic Tests																			N									
DNA, DNA & protein adducts for Exposure Assessment (Chemical Changes)												N/C							N									
Gene Expression (RNA)												N/C							N								N	
Epigenetic changes (genomic DNA)																			N									
Genetic Variation: Paraoxonase Gene, glucokinase, vntr insulin, etc. (DNA)	N				N	C		C											N	N	N	C	C	C		N		
Cryopreserved PBMCs	N				N	C		C											N	N	N	C	C	C		N		
Cell lines *Prop	N				N	C		C												N	N	C	C	C		N		
mitochondrial DNA *Prop	N				N	C		C												N	N	C	C	C		N		
Chemical Exposures																												
lipids, PCBs, organochlorine pesiticides, PBDE, Perfluorinated cmpds(PFOA,PFOS) (4 mL Serum)					C																							
Lead, Mercury, Cadmium (3 mL bld)					C																							
Combination of dioxins/furans and all other chemicals (excluding metals)					C																							
Stored Samples																												
Serum					N	N		N																		N		
Plasma					N	N		N																		N		

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure

Table 7-1.   Measures by Hypotheses (continued)

Measure	Birth Defects from Impaired Glucose Metabolism	Increased Risk of Preterm Birth from Intrauterine Exposure to Mediators of Inflammation	Increased risk of fetal growth restriction, birth defects, and disabilities in children born through assisted reproductive technologies	Maternal Subclinical Hypothyroidism and adverse pregnancy outcomes	Nonpersistent Pesticides and Poor Neurobehavioral and Cognitive Skills	Prenatal Infection and Neurodevelopmental Disabilities	Gene Environment Interactions and Behavior	Prenatal and Perinatal Infection and Schizophrenia	Family Influences on Child Health and Development	Impact of Neighborhood and Communities on Child Health	Impact of Media Exposure on Child Health and Development	Social Institutions and Child Health and Development	Influences on Healthy Development	Prenatal Maternal Stress and Genetics in Childhood Asthma	Indoor, Outdoor Air Pollution, Aeroallergens and Asthma Risk	Dietary Antioxidants and Asthma Risk	Social Environmental Influences on asthma disparities	Early Exposure to Components and Products of Microorganisms Decreases the Risk of Asthma	Environmental Exposure and Gene Interaction and Asthma and Wheezing in Children	Obesity and Insulin Resistance from Impaired Maternal Glucose Metabolism	Obesity and Insulin Resistance form Intrauterine Growth Restriction	Breastfeeding Associated with Lower Rates of Obesity and Lower Risk of Insulin Resistance	Fiber, Whole Grains, High Glycemic Index and Obesity, Insulin Resistance	Genetics, Environmental Exposures, and Type I Diabetes	Repeated Mild Traumatic Brain Injury and Neurocognitive Development	Behavioral Exposures, Genetics, and Childhood or Adolescent Onset Aggression	Antecedents and Resiliency to Traumatic Life Events in Childhood	Hormonally Active Environmental Agents and Reproductive Development
Biospecimen Collection - Father continued																												
RBCs (folate and fatty acids)					N	N		N																		N		
Lavender Top					N	N		N																		N		
Buccal Cells *Prop																												
Nails																												
Organic Hg (ethyl, methyl)					C																							
Hg inorganic					C																							
Hair																												
Cd					C																							
cotinine					N																							
Hg inorganic					C																							
Organic Hg (ethyl, methyl)					C																							
nicotine					N																						C	
Saliva																												
Cortisol	C						C										N									C		
storage	C						C										N									C		
Urine																												
Chemical Exposures																												
PFBS, Creatinine, alkyl phenols (Bisphenol A, nonylphenol), Hg(inorganic), As(speciated), perchlorate, halogenated phenols(PCP), phthalates, atrazine, OPs, carbamates, pyrethroids, EBDC/ETU, Cadmium					N																							
PAH (may be storage issues); requires separate analysis (3-4 ml)					N																							
ICP/MS urine screen *Prop					C																							
cotinine					N		C																					
Phytoestrogens					N																							
Storage					N		N																					
Semen																												
Quality (home collection)																												

N = Needed for Analysis   C = Confounder/Covariate   *Prop = Proposed measure