United States Environmental Protection Agency

Office of Research and Development

The Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) Study

QUALITY SYSTEMS AND IMPLEMENTATION PLAN

Battelle
Columbus, OH 43201
Contract No. 68-D-99-011

Source: Battelle

U.S. Environmental Protection Agency
Office of Research and Development
Human Exposure & Atmospheric Sciences Division
Exposure Measurements & Analysis Branch

QUALITY SYSTEMS AND IMPLEMENTATION PLAN

A STUDY OF CHILDREN'S TOTAL EXPOSURE TO PERSISTENT PESTICIDES AND OTHER PERSISTENT ORGANIC POLLUTANTS "CTEPP"

Approvals:

_____	_____
Battelle Task Order Leader	Date
_____	_____
EPA Task Order Project Officer	Date
_____	_____
Battelle Quality Assurance Officer	Date
_____	_____
EPA Quality Assurance Officer	Date

TABLE OF CONTENTS

Page

1.0 PROJECT PLANNING AND ORGANIZATION 5

1.1 Introduction 5
1.2 Background 7
1.3 Project Scope and Work Objectives 8
1.4 Project Description 14
1.5 Experimental Design 16
1.6 Personnel Qualifications 36
1.7 Training Required 39
1.8 Communication Plan 42

2.0 MANAGEMENT ASSESSMENT 43

2.1 Assessment Responsibility 43
2.2 Assessment Type(s) 44
2.3 Assessment Usage 44
2.4 Assessment Criteria 45
2.5 Assessment Documentation 45

3.0 PROJECT IMPLEMENTATION 46

3.1 Project Responsibilities 46
3.2 Project Design Criteria 49
3.3 Data Quality Indicators 56

4.0 DATA ACQUISITION 58

4.1 Data Recording 58
4.2 Identification of Data 61
4.3 Control of Erroneous Data 64
4.4 Data Evaluation 65
4.5 Data Validation 66

5.0 DATA MANAGEMENT 67

6.0 RECORDS MANAGEMENT 69

6.1 Records Management System 69
6.2 Records Identification, Authentication, and Indexing 70
6.3 Records Distribution and Storage 70

6.4 Records Retrieval 70
6.5 Records Retention 71

7.0 ROUTINE CONTROLS AND PROCEDURES 72

7.1 Control and Calibration of Measurement and Test Equipment 72
7.2 Procedures 72
7.3 Establishing the Adequacy of Technical Practices 93
7.4 Maintenance of Equipment 94
7.5 Quality of Consumables 94
7.6 Labeling 94
7.7 Acceptance of Equipment and Materials 94
7.8 Storage of Equipment and Materials 95

8.0 TECHNICAL ASSESSMENT AND RESPONSE 96

8.1 Assessment Procedures 96
8.2 Assessment Evaluation 97
8.3 Assessment Response and Follow-up 99

9.0 REFERENCES 99

DOCUMENT DISTRIBUTION LIST

Individual	Organization	Document Version	Receipt Confirmation Date
Roy Fortmann	U.S. Environmental Protection Agency		
Nancy K. Wilson	U.S. Environmental Protection Agency (retired)		
Marsha Morgan	U.S. Environmental Protection Agency		
Gary Evans	U.S. Environmental Protection Agency (retired)		
Elizabeth A. Betz	U.S. Environmental Protection Agency		
Carvin D. Stevens	U.S. Environmental Protection Agency		
Sydney M. Gordon	Battelle		
Jane C. Chuang	Battelle		
Christopher Lyu	Battelle		
Marielle Brinkman	Battelle		
Sandra M. Anderson	Battelle		

QUALITY SYSTEM IMPLEMENTATION PLAN FOR A STUDY OF CHILDREN'S TOTAL EXPOSURE TO PERSISTENT PESTICIDES AND OTHER PERSISTENT ORGANIC POLLUTANTS "CTEPP"

1.0 PROJECT PLANNING AND ORGANIZATION

1.1 Introduction

The research study, "Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants," (CTEPP) is a pilot-scale project involving about 260 children, which investigates the possible exposures that young children may have to common contaminants in their everyday surroundings. These contaminants include several pesticides, phenols, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, some of which are suspected of being endocrine disrupters. The targeted compounds are persistent in the indoor and sometimes the outdoor environments, so that very low levels may exist in the children's surrounding microenvironments and provide a source of chronic, non-acute exposure. The primary purposes of the research are to increase our understanding of children's exposures to persistent pollutants, to gain information on the various activities, environmental media, and pollutant characteristics that may influence children's exposures, and to generate further questions and hypotheses for future research.

Young children, especially those of preschool ages 1-5, are hypothesized to have greater exposures than do older children or adults to persistent pesticides and other persistent organic pollutants (POPs), including some compounds that may have endocrine-disrupting effects or developmental toxicity. These greater exposures may result from what children eat and drink, where they spend their time, and what they do there. The impact of the exposures may be greater on young children because of their smaller body masses, immature body systems, and rapid physical development. Very young children learn about their environment by exploring not only the appearance and texture of objects, but also their taste and smell. Thus nondietary ingestion can play an important role in their exposures.

The Food Quality and Protection Act of 1996 (FQPA) sets new, more stringent standards for pesticide residues in foods, and provides increased emphasis on health protection for infants and children. The exposure component of the risk assessment for pesticides is now required to consider the susceptibility of children to increased exposure, and account for aggregate exposures to the pesticides from all sources, including food, drinking water, and non-occupational applications of the pesticides in homes, schools, day care centers, and other microenvironments. Essentially, the FQPA states that exposure assessments must be conducted for infants and children, and that these exposure assessments must include and be reliable for all sources of

pesticide exposure. However, very little information on children's aggregate exposures is available at the present time, the methods for obtaining this information need improvement, and the pathways and media through which such exposures may take place are known uncertainly.

Thus, the CTEPP study has direct practical utility to FQPA. It will provide data on aggregate chronic, sub-acute pesticide exposures and pathways for approximately 260 children in several microenvironments, improve the methods for determining their exposures and pathways, and allow generation of hypotheses for further research . The objectives of CTEPP are thus twofold: (1) To measure the total exposures at sub-acute levels of a small set of preschool children in several NC and OH counties to a suite of persistent pesticides and other persistent organic pollutants that they may encounter in their everyday environments, and (2) To apportion the exposure pathways and to identify and formulate the important hypotheses to be tested in future research. Therefore, CTEPP investigates the total exposures to persistent organic compounds in the environment of a group of pre-elementary school children through the ingestion, inhalation, and dermal absorption pathways, in several non-occupational settings, through multiple environmental media. Targeted organic chemical pollutants include polycyclic aromatic hydrocarbons; chlorinated, carbamate, triazine, pyrethroid, and organophosphate pesticides; phthalate esters; phenols; and polychlorinated biphenyls. The specific compounds were selected because they may be carcinogenic, mutagenic, acutely or chronically toxic, or possibly disruptive to the human endocrine system; and because they are widespread and often persistent in the indoor or outdoor environment.

Children who stay at home with an adult caregiver and children who attend preschool or day care are included in the study. Emphasis is on the younger children aged 18 months to 4 years. Exposures of the children and their primary adult caregivers living in the same household are estimated through the collection and analysis of samples of food, beverages, and drinking water; indoor and outdoor air; hand wipes; house dust, classroom dust, and play area soil; and smooth floor and food preparation surface wipes. Urine samples are also collected for analysis for biomarkers of exposure. Children who are not able to provide one or more spot urine samples during the day (who are not at least partially toilet-trained) and children who are still being breast-fed are excluded. Information about the children's activities during the sampling period is collected via activity diaries and food diaries. Approximately 10% of the children are videotaped for about 2 hr periods during the sampling to supplement and validate the activity diaries and observations. The range of exposures through multiple environmental pathways and media is estimated. Potential external doses are determined through a combination of micro-environmental measurements and time-activity diaries; and insofar as is possible, effective doses are estimated through the analysis of urinary biomarkers. Sample collection in the targeted NC and OH counties will extend over a two-to-three year period.

The CTEPP study will provide generic data for many exposure factors, such as time spent in microenvironments, time spent in activities, hand-to-mouth contact, and contact area. This type of data is not tied to the registration of a single pesticide and hence will be useful in refining many of the assessments required by FQPA. In addition, much of the data that are chemical-

specific (transfer and distribution coefficients) can be applied more generally to pesticides and other POPs that have the same physical and chemical properties.

Clients for the results of this research include the EPA Office of Children's Health Protection, and the EPA Office of Prevention, Pesticides, and Toxic Substances. Additionally, the results will complement related research funded by the EPA Office of Research and Development under its Science to Achieve Results (STAR) grants program, the National Institute of Environmental Health Sciences, the EPA National Health and Ecological Effects Research Laboratory (NHEERL), and the Consumer Product Safety Commission (CPSC), the scientific community, and the public, particularly parents and caregivers of young children. Some of the specific ongoing projects to which CTEPP is complementary are, for example, at NIEHS, Dr. Matt Longnecker is looking at persistent organochlorine pesticides and phthalate esters in mothers' blood and the relationship with children's health outcomes; Dr. Jane Hoppin is also examining phthalate esters and their potential effects on the health of young children. The Environmental and Occupational Health Institute at Rutgers University is conducting a nine-subject study of exposures of children to chlorpyrifos after crack and crevice application, "Children's Post-Application Pesticide Pilot Study." Current STAR grants include, among others, "Assessing levels of organophosphate insecticides, which could expose children from pets treated with flea control insecticides," Dr. Janice Chambers et al.; "Exposure of children to pesticide in Yuma County, Arizona," Dr. Mary Kay O'Rourke et al.; and "A study of pesticide exposures in Minnesota children," Dr. Edo Pellizari et al. (Organophosphates only) [U1].

The expected benefits include a greater understanding of children's total exposures to persistent pesticides, possible endocrine disrupters, and similar pollutants; improved knowledge of the environmental pathways that are most important in young children's exposures; and generation of hypotheses for further research on children's exposures. Most importantly, the enhanced knowledge of children's total exposures and the improved exposure models afforded by CTEPP will benefit many young children in addition to the study population.

1.2 Background

Exposures of young children of preschool age to persistent pesticides and other POPs may be greater than those of older children or adults. These greater exposures may result from what children eat and drink, where they spend their time, and what they do there. The impact of the exposures on children's health may be greater than that on adults' health, as a result of children's smaller body masses, immature body systems, and rapid physical development [P1, V1]. Very young children learn about their environment by exploring not only the appearance and texture of objects, but also their taste and smell. Thus, non-dietary ingestion can play an important role in their exposures.

Although studies of young children's exposures to various environmental pollutants have been done in the past, these have been confined largely to studies involving one specific pollutant, for example lead, one environmental source, for example, environmental tobacco smoke (ETS), or to

studies involving one pathway or route of exposure, for example, inhalation [O1, O2, R1, W9]. A few small studies have evaluated methods for sampling and analysis to be used in exposure studies, for example, the Household Infant Pesticide Exposure Study (HIPES) [L1]. To allow management and reduction of the possible risk from a given pollutant or pollutant class, however, it is necessary to know the total exposure to individuals from all environmental media with which they come in contact, through all pathways. This total exposure estimate can then be used to derive an estimate of the potential intake or applied dose of the pollutant, which can in turn be used to estimate the potential health impact on the individual. The pioneering research in the application of such Total Exposure Assessment Methodology (TEAM) was done by Wallace and coworkers in the late 1980s [W9]. The first major TEAM study, of volatile organic compound (VOC) exposures, was completed in 1985. A large prospective study of the exposures of farmers and farm families to agricultural pesticides – the Agricultural Health Study (AHS) – is ongoing, but its focus is not primarily on children, nor does it include families of non-farmers [A1]. However, there are many questionnaire and epidemiologically based studies of children's exposures reported in the literature. Several recent studies have implicated pesticide exposures and exposures to other xenobiotics, for example potential endocrine disrupters, as possible causes of children's health problems [B2, D1, D2, D3, D4, H2, K1, K2, K3, L2, L3, M2, M3, O7, P2, P3, R2, R4, R6, S7, T1, W10, Z1, Z2], and several have estimated the exposures of small numbers of children to specific pesticides [B1, B6, E1, H1, L4, L5, N4, S2, W8].

In recent years, Wilson and Chuang, in a series of small methodology studies, have used the TEAM approach to examine the total exposures of preschool children in low-income families to polycyclic aromatic hydrocarbons [C7, C10, C12, W5]. On the basis of their findings, these investigators extended the research to a small study of total exposures of preschool children who attend day care centers to an extended list of target persistent chemicals [W1, W2, W6, W7]. The results of these studies are provocative in that they suggest that young children's exposures to some persistent pollutants may be greater than those of adults who inhabit the same microenvironments, especially when the potential dose, which takes into account a child's body mass, is considered. Furthermore, for these sensitive young persons, both dietary and nondietary ingestion appear to be significant pathways for exposure to some compounds. Because of the small size of these studies, however, a larger study is needed to confirm these findings with a greater degree of statistical confidence.

1.3 Project Scope and Work Objectives

1.3.1 Primary Study Objectives

The general objective of this research is to support the mission of the National Exposure Research Laboratory (NERL) to characterize, predict, and diagnose human exposure [N2].

Within this framework, the CTEPP study has two major objectives:

(1) To measure the total exposures of a small set of preschool children, approximately 260 children total, in several NC and OH counties, to sub-acute levels of a suite of

persistent pesticides and other persistent organic pollutants that they may encounter in their everyday environments, and

(2) To apportion the exposure pathways and identify the important hypotheses to be tested in future research.

The long-range objectives of this research are thus responsive directly to FQPA requirements, to EPA goals as expressed in the NERL research strategy [N6], which defines several long-term goals related to the ORD Strategic Plan [O3] and those defined in the EPA Children's Risk Strategy [O4]. Those related to this study include development of approaches to characterize, predict, and diagnose human exposures and to provide improved exposure information, especially for sensitive subpopulations.

This research also supports directly the Government Performance and Results Act (GPRA) goals for EPA under Goal 8 in the following ways:

- ORD Science Sub-Objective #2.2: The research will provide improved tools and data for more quantitative human health risk assessments. It will enhance the scientific basis for identification, characterization, and assessment of exposures that pose the greatest health risks. It will provide information on the exposures of a group of individuals chosen from a susceptible population, preschool children, to persistent organic pollutants in the environment.
- ORD Science Sub-Objective #2.3: The research will develop and improve methods to assess the susceptibilities of populations to environmental agents. It will improve human exposure methods and measurements.

Annual performance goals to which this research is relevant include Goal 194, Provide Exposure and Effects Methodologies; and Goal 837, Initiate Field Exposure Study of Children to Two EDCs.

1.3.2 Specific Study Objectives

The main objectives of the CTEPP study, as discussed above, are: (1) To measure the total exposures of a small set of preschool children in several NC and OH counties to chronic, sub-acute levels of a suite of persistent pesticides and other persistent organic pollutants that they may encounter in their everyday environments, and (2) To apportion the exposure pathways and identify the important hypotheses to be tested in future research. There are several hypotheses that can be tested within this group of children using the CTEPP data.

Under main objective (1), total exposure measurement, it is possible to ask the questions:

- Are the targeted children's exposures at home and at day care/preschool equally important?

- Are exposures approximately the same or significantly different for the targeted children in low-income households compared with the targeted children in middle/upper-income households?
- Are exposures approximately the same or significantly different for the targeted urban and rural children?

Under main objective (2), apportionment of exposure pathways, it is possible to ask:

- Are the exposure pathways and their relative importance different for the different chemical classes of persistent pesticides and other persistent organic pollutants?
- Is the ingestion pathway a major pathway for exposure of the targeted adults and preschool children living in the same household?
- Is diet the major contributing factor to the ingestion exposure of this group of children and
- In the sample population, are children's exposures to the targeted pollutants approximately the same or significantly greater than those of the adults living in the same household?

As mentioned previously, these hypotheses can be tested for the subpopulation of approximately 260 children, who reside in the selected counties, and who are the focus of the CTEPP study. The results will not be generalizable to larger populations of children, for example, they will not be generalizable to "all children in NC or in OH (or in the US, for that matter)," or to "all children in low-income and middle-income families," or to "all day care centers," and so on. Neither can they be used to test such hypotheses as "are exposures of NC children the same as or different from those of OH children?" The great value of CTEPP lies in its generation of information on the total exposures of a subpopulation of preschool children, in its provision of real, physical data that can be used to test existing exposure models and improve their accuracy and predictive ability, and in its expansion of knowledge of the routes and pathways through which these children may be exposed.

The specific objectives of this study are thus as follows:

- Estimate the total exposures of a group of young, pre-school children to selected persistent organic pesticides and other persistent organic pollutants via all three environmental pathways: ingestion, inhalation, and dermal absorption. Include all environmental media that are likely to provide the opportunity for significant exposures. Through the use of collected data on activity patterns, environmental and biological measurements, and appropriate exposure models, estimate the exposure and potential dose of each of the target chemicals. Compare the potential doses with actual, biological doses estimated from urinary biomarkers of exposure.
- Obtain comparisons, by stratification of the sampling, between children who stay at home and who attend pre-school or day care, of children in low-income and in middle/upper-income families, and of children in urban and in rural environments. Compare actual dose estimates, obtained from urinary biomarkers measurements,

for adults and children in the same households, with potential dose estimates obtained from exposure measurements. Include children in six counties in each of two states: North Carolina and Ohio.

- Apportion the pathways of exposure for the various target chemicals included in this study, using actual, CTEPP-measured, multimedia concentration data and observational and questionnaire data. Identify those microenvironmental media and activities that contribute most to the total exposures.

1.3.3 Data Analysis Objectives

Children's Total Exposure to POPs. A major objective of the CTEPP study is to measure the total exposures of the study subjects to a suite of persistent pesticides and other POPs. We will characterize children's total exposures to POPs and their urinary biomarker concentrations within the individual strata and compare exposures and biomarker concentrations across strata. One-factor-at-a-time comparisons, averaged across all other factors, will be carried out. No comparison between the two states will be performed. These comparisons can include, for example:

- Urban versus rural
- Day care versus no day care
- Low income versus middle/upper income
- Children versus adults in the same household.

Exposure Pathways Components Analyses. Another major objective of the CTEPP study is to apportion exposure pathways and identify the important media where exposure can occur. The major component exposure pathways are inhalation, dietary ingestion, non-dietary ingestion, and dermal absorption. We will compare the components of exposure across the major pathways, averaging across all the stratification factors. Examples of such comparisons include:

- Ingestion - Dietary versus all others. We will determine the proportion of total exposure attributable to diet (food, beverage, and drinking water).
- Dietary ingestion versus non-dietary ingestion.
- Comparisons of percentage distribution of exposure by pathway across the target compounds to be monitored.

We will also study how the various exposure pathway components differ across the key subpopulations. Examples of such analyses include:

- Percentage of exposure by pathway between low income and middle/upper income children
- Percentages of exposure by pathway between
  – Urban and rural regions
  – Day care and home care
  – Children and adults residing in the same household.

1.3.4 Quality Objectives

This document, a Quality Systems and Implementation Plan (QSIP), which combines the work plan and the quality assurance plan, has been developed for the CTEPP study. The requirements for the quality assurance program are stated in EPA Order 5360.1, "Policy and Requirements to Implement the Quality Assurance Program." This order requires that quality assurance become an integral part of all data collection activities and be totally integrated into the program to assure the reliability of environmental measurements and data. Guidance is available in EPA documents EPA QA/R-2 and EPA QA/R-5.

The QSIP will include Project Quality Objectives (PQOs) and, for individual target analytes, Data Quality Objectives (DQOs). These will be set before field sampling begins. Preliminary PQOs include the following:

Recruiting

- Eligibility: The initial recruitment activities will screen the eligibility of the study participants. Children who stay at home with an adult caregiver and children who attend preschool or day care are included in the study. Emphasis is on the younger children aged 18 months to 4 years. Children who are not able to provide one or more spot urine samples during the day (who are not at least partially toilet-trained) and children who are still being breast-fed are excluded.
- Response: With the intensive recruiting efforts and guaranteed confidentiality, we expect to achieve response rates of about 85% in each of these two stages for the day care sample component. For the telephone sample component, we anticipate that about 75% of eligible households will participate in the study. A variety of non-monetary and monetary incentives will be used [K4]; we will seek advice on non-monetary incentives from faculty in developmental psychology at the North Carolina State University.

Statistical Power

- Sample Size: Sufficient to detect a 50% difference in POP exposures with a

standard deviation of 1.0 at 90% power

Sampling and Analysis

- Standard Operating Procedures (SOPs) will be prepared
- Data Quality Indicators will be established (see section 3.3)
- Consistent application of study methodology.

1.3.5 Study Milestones

The CTEPP study is expected to span a period of four to five years, beginning in FY98, and will occur in three phases. Key milestones are listed below.

Phase I Milestones – initiated in FY98

- Design a pilot study of children's total exposure to persistent organic pesticides and other persistent organic pollutants that considers all three environmental pathways: ingestion, inhalation, and dermal absorption, and all environmental media that are likely to provide the opportunity for significant exposures.

- Obtain peer review of the study design and develop a Quality Systems Implementation Plan (QSIP), which follows the Quality Integrated Work Plan (QIWP) template that has been developed for the North American Research Strategy on Tropospheric Ozone. This template is available on the Internet at the following location: http://cdiac.esd.ornl.gov/programs/NARSTO/narsto/html. Use of this template ensures that the implementation plan meets the American National Standards Institute (ANSI) E-4 standard. The QIWP is equivalent to the NERL Quality Systems Implementation Plan (QSIP).

- Initiate human subjects review (Institutional Review board, IRB) and EPA human subjects approval.

- Initiate the Information Collection Request (ICR) process with the Office of Management and Budget (OMB).

- Select and modify or improve sampling and analytical methods.

- Develop a communication strategy.

Phase II Milestones – Initiated in FY99

- Obtain ICR approval.

- Obtain human subjects approval.

- Initiate and complete field sampling in six counties in each of two states: North Carolina and Ohio. (No recruiting or field sampling will be conducted during the U.S. Census 2000 period, specifically, March 1, 2000 to June 30, 2000.)

Phase III Milestones – Initiated in FY00

- Analyze samples.

- Interpret the results in the light of the CTEPP objectives.

- Publish the results in one or more peer-reviewed scientific journals.

1.4 Project Description

The CTEPP study is a probability-based, stratified study of the exposures of approximately 260 preschool children to POPs that may persist in their daily surroundings. The study is intended to apply the methods already developed as much as is possible to field measurements of exposures. However, because of the high unit cost of measuring the total exposures of a large number of children, it is possible to include only about 260 children. To improve the response rates and to ensure representativeness of the study, a two-frame sampling plan has been developed, which will allow probability-based stratified sampling of preschool children who attend day care centers and who stay at home from two states, NC and OH. However, it is important to note that the results of this pilot study will apply only to the study population, and no inferences to larger populations can be made.

A target sample of 128 children (and associated caregivers) per state will be obtained. This sample will be balanced evenly between the day care and no day care components. The sampling design will over-sample the low-income strata, but sample sizes will still be smaller for the low-income than for the middle/upper-income group overall. Sample sizes will also be smaller in the rural than in the urban stratum. The sampling design provides a compromise in sensitivity between analytical inferences and population-based inferences. On one hand, a more representative sample provides more nearly proportional representation of these groups rather than equal representation. Proportional representation would be more appropriate if the analytic goals were restricted to population-based inferences. On the other hand, equal group sample sizes maximize the power of group comparisons, an important element of analytical inferences. The study design is discussed in detail in Section 1.5, Experimental Design.

The survey, recruitment, sampling, and analysis methods, and the associated activity logs and questionnaires that were developed or refined in the previous pilot studies of preschool children's exposures; and the findings of those studies are the initial basis for the CTEPP study [C1, C2,

C3, C8, C9, C11, C14, G1, H3, M1, N1, N5, N7, S1, T2, W12]. The methods and associated documents are being modified and refined as necessary to meet the study objectives.

The field study is an investigation of the total exposures to persistent organic compounds in the environment of pre-elementary school children through the ingestion, inhalation, and dermal absorption pathways. Targeted organic chemical classes include polycyclic aromatic hydrocarbons; chlorinated, carbamate, triazine, pyrethroid, and organophosphate pesticides; phthalate esters; phenols; and polychlorinated biphenyls. The specific compounds were selected because they are carcinogenic, mutagenic, acutely or chronically toxic, or potentially disruptive to the human endocrine system [C15, C16]; and because they are persistent and often ubiquitous in the environment. Although some of the pesticides, for example the organophosphates, are not generally thought to be persistent, in the absence of sunlight and moisture – in the indoor environment – they degrade slowly if at all, and hence may pose an exposure risk for many years.

Children who stay at home with an adult caregiver and children who attend preschool or day care are included in the study. Emphasis is on the younger children aged 18 months to 5 years. Exposures of the children and their primary adult caregivers living in the same household are estimated through the collection and analysis of samples of food, beverages, and drinking water; indoor and outdoor air; hand and forearm wipes; house dust, classroom dust, and play area soil; and smooth floor and food preparation surface wipes. Urine samples are also collected for analysis for biomarkers of exposure. Children who are not able to provide one or more spot urine samples during the day (who are not at least partially toilet-trained) and children who are still being breast-fed are excluded. Information about the children's activities during the sampling period is collected via activity diaries and food diaries. The range of exposures through multiple environmental pathways and media is estimated. Potential external doses are determined through a combination of microenvironmental measurements and time-activity diaries; and, insofar as is possible, effective doses are estimated through the analysis of urinary biomarkers. Sample collection in the targeted NC and OH counties will extend over a two-to-three year period.

The data that result from this study will be formatted in such a way as to be compatible, insofar as possible, with other EPA/ORD exposure data bases. It is anticipated that most of the study data can be formatted to be compatible with current EPA exposure data bases, such as TherdBase. The CTEPP study is not intended to be a comprehensive study of activity patterns *per se,* to avoid the extreme burden that maintaining comprehensive activity observations places on participants. It therefore will not include the complete detailed descriptions and codes of activities that would allow its full incorporation in the Children's Health and Activity Data (CHAD) data base. However, approximately 10% of the children will be videotaped for 3-4 hr each during the sampling period, to supplement the activity logs and confirm the levels of reported activities.

The recruitment, field sampling and analysis, and data analysis procedures for the CTEPP study are described in section 7.2, Procedures. A summary of CTEPP Standard Operating Procedures (SOPs) is given in Table 1.1.

1.5 Experimental Design

1.5.1 Primary Objectives and Specific Hypotheses to be Tested

The main objectives of the CTEPP study, as discussed above, are: (1) To measure the total exposures of a small set of preschool children in several NC and OH counties to chronic, sub-acute levels of a suite of persistent pesticides and other persistent organic pollutants that they may encounter in their everyday environments, and (2) To apportion the exposure pathways and identify the important hypotheses to be tested in future research. There are several hypotheses that can be tested within this group of children using the CTEPP data.

Under main objective (1), total exposure measurement, it is possible to ask the questions:

- Are the targeted children's exposures at home and at day care/preschool equally important?
- Are exposures approximately the same or significantly different for the targeted children in low-income households compared with the targeted children in middle/upper-income households?
- Are exposures approximately the same or significantly different for the targeted urban and rural children?

Under main objective (2), apportionment of exposure pathways, it is possible to ask:

- Are the exposure pathways and their relative importance different for the different chemical classes of persistent pesticides and other persistent organic pollutants?
- Is the ingestion pathway a major pathway for exposure of the targeted adults and preschool children living in the same household?
- Is diet the major contributing factor to the ingestion exposure of this group of children and
- In the sample population, are children's exposures to the targeted pollutants approximately the same or significantly greater than those of the adults living in the same household?

As mentioned previously, these hypotheses can be tested for the subpopulation of approximately 260 children, who reside in the selected counties, and who are the focus of the CTEPP study. The results will not be generalizable to larger populations of children, for example, they will not be generalizable to "all children in NC or in OH (or in the US, for that matter)," or to "all children in low-income and middle-income families," or to "all day care centers," and so on. Neither can they be used to test such hypotheses as "are exposures of NC children the same as or different from those of OH children?"

The specific objectives of this study are thus as follows:

- Estimate the total exposures of a group of young, pre-school children to selected persistent organic pesticides and other persistent organic pollutants via all three environmental pathways: ingestion, inhalation, and dermal absorption. Include all environmental media that are likely to provide the opportunity for significant exposures. Through the use of collected data on activity patterns, environmental and biological measurements, and appropriate exposure models, estimate the exposure and potential dose of each of the target chemicals. Compare the potential doses with actual, biological doses estimated from urinary biomarkers of exposure.
- Obtain comparisons, by stratification of the sampling, between children who stay at home and who attend pre-school or day care, of children in low-income and in middle/upper-income families, and of children in urban and in rural environments. Compare actual dose estimates, obtained from urinary biomarkers measurements, for adults and children in the same households, with potential dose estimates obtained from exposure measurements. Include children in six counties in each of two states: North Carolina and Ohio.
- Apportion the pathways of exposure for the various target chemicals included in this study, using actual, CTEPP-measured, multimedia concentration data and observational and questionnaire data. Identify those microenvironmental media and activities that contribute most to the total exposures.

Table 1.1. Summary of CTEPP SOPs

CTEPP SOP Number	CTEPP SOPs
	1. Subject Recruitment
CTEPP-SOP-1.10	Sample Selection Procedures
CTEPP-SOP-1.11	Day care Centers Recruitment Procedures
CTEPP-SOP-1.12	Telephone Sample Households Recruitment Procedures
CTEPP-SOP-1.13	Informed Consent Procedures
CTEPP-SOP-1.14	Assigning ID Numbers Procedures
	2. Field Sampling
CTEPP-SOP-2.10	Household Sampling Schedule Procedures
CTEPP-SOP-2.11	Field Operations Procedures
CTEPP-SOP-2.12	Collection of Fixed Site Indoor and Outdoor Air Samples for Persistent Organic Pollutants Procedures
CTEPP-SOP-2.13	Collection of Food Samples Procedures
CTEPP-SOP-2.14	Collection of Urine Samples Procedures
CTEPP-SOP-2.15	Collection of Dermal Wipe Samples for Persistent Organic Pollutants Procedures

CTEPP SOP Number	CTEPP SOPs
CTEPP-SOP-2.16	Collection of Hard Floor Surface Wipe Samples for Persistent Organic Pollutants Procedures
CTEPP-SOP-2.17	Collection of Food Preparation Surface Wipe Samples for Persistent Organic Pollutants Procedures
CTEPP-SOP-2.18	Collection of Dislodgeable Residues - PUF Roller Samples for Persistent Organic Pollutants Procedures
CTEPP-SOP-2.19	Collection of Floor Dust Samples for Persistent Organic Pollutants Procedures
CTEPP-SOP-2.20	Collection of Soil Samples for Persistent Organic Pollutants Procedures
CTEPP-SOP-2.21	Collection of Personal Interview Data Procedures
CTEPP-SOP-2.22	Recording Data Collection Forms Procedures
CTEPP-SOP-2.23	Video Taping Child Activities Procedures
CTEPP-SOP-2.24	Handling Missing Samples/Data Procedures
CTEPP-SOP-2.25	Conducting Internal Field Audit/Quality Control Procedures
CTEPP-SOP-2.26	Handling Sample/Data Custody Procedures
CTEPP-SOP-2.27	Conducting Staff and Participant Training Procedures
	3. Storing and Shipping Samples & Data Collection Forms
CTEPP-SOP-3.10	Storing Study Samples Procedures
CTEPP-SOP-3.11	Packing and Shipping Study Samples Procedures
CTEPP-SOP-3.12	Shipping and Storing Data Collection Forms Procedures
	4. Data Processing
CTEPP-SOP-4.10	Processing Completed Data Forms Procedures
CTEPP-SOP-4.11	Maintaining/Recording Electronic Chain of Custody Procedures
CTEPP-SOP-4.12	Entering or Importing Electronic Data Into CTEPP Data bases Procedures
CTEPP-SOP-4.13	Translating Videotapes of Child Activities Procedures
	5. Laboratory Procedures
CTEPP-SOP-5.10	Pre-cleaning Filter and XAD-2 Procedures
CTEPP-SOP-5.11	Pre-cleaning Filter and PUF Procedures
CTEPP-SOP-5.12	Extracting and Preparing Air Samples for Analysis of Neutral Organic Pollutants Pre-cleaning Procedures
CTEPP-SOP-5.13	Extracting and Preparing Air Samples for Analysis of Polar Organic Pollutants Procedures
CTEPP-SOP-5.14	Extracting and Preparing Dust and Soil Samples for Analysis of Neutral Organic Pollutants Procedures
CTEPP-SOP-5.15	Extracting and Preparing Dust and Soil Samples for Analysis of Polar Organic Pollutants Procedures

CTEPP SOP Number	CTEPP SOPs
CTEPP-SOP-5.16	Extracting and Preparing Dermal Wipe Samples for Analysis of Neutral Organic Pollutants Procedures
CTEPP-SOP-5.17	Extracting and Preparing Surface Wipe Samples for Analysis of Neutral Organic Pollutants Procedures
CTEPP-SOP-5.18	Extracting and Preparing PUF Roller Samples for Analysis of Neutral Organic Pollutants Procedures
CTEPP-SOP-5.19	Extracting and Preparing Liquid Food Samples for Analysis of Persistent Organic Pollutants Procedures
CTEPP-SOP-5.20	Extracting and Preparing Solid Food Samples for Analysis of Persistent Organic Pollutants Procedures
CTEPP-SOP-5.21	Extracting and Preparing Urine Samples for Analysis of Hydroxy-PAH, Pentachlorophenol, and 2,4-D Procedures
CTEPP-SOP-5.22	Extracting and Preparing Urine Samples for Analysis of 3,5,6-Trichloro-2-pyridinol Procedures
CTEPP-SOP-5.23	Extracting and Preparing Drinking Water Samples for Analysis of Persistent Organic Pollutants Procedures
CTEPP-SOP-5.24	Detection and Quantification of Target Analytes by Gas Chromatography/Mass Spectrometry (GC/MS) Procedures
CTEPP-SOP-5.25	Preparation of Surrogate Recovery Standard and Internal Standard Solutions for Neutral Target Analytes
CTEPP-SOP-5.26	Preparation of Surrogate Recovery Standard and Internal Standard Solutions for Polar Target Analytes
CTEPP-SOP-5.27	Extracting and Preparing Dermal Wipe and Surface Wipe Samples for Analysis of Polar Organic Pollutants Procedures
CTEPP-SOP-5.28	Extracting and Preparing Solid Food Samples for Analysis of Polar Organic Pollutants Procedures
CTEPP-SOP-5.29	Extracting and Preparing Liquid Food Samples for Analysis of Polar Organic Pollutants Procedures

1.5.2 Sample Size

A preliminary estimate of the number of children and households to be sampled was derived from the results of the PAH studies described earlier [W5, W7, C7, C10, C12]. For children in 24 homes, the mean potential dose of B2 PAH (PAH that are probable human carcinogens) was 34 ng/kg-day, with a standard deviation of 24 ng/kg-day. To test whether the potential dose is the same for children in low- and middle/upper income families, a two-sample t test was used, at the 5% significance level. The minimum sample sizes necessary to detect differences in various potential doses of B2 PAH at two statistical powers are shown in Table 1.2. At 80% power, with a mean difference in the potential dose of 25%, approximately 126 participants are needed in each of the two groups being compared. An improved estimate of the sample size necessary, based on the results of the day care study [W2, W6, W7, W1], which includes most of the target

chemicals in this study led to the results shown in Table 1.3, described in the following paragraphs.

Table 1.2. Minimum Sample Size to Detect Various Percent Differences

	Percent Difference in Mean Potential Dose				
	15	25	30	40	50
80% Power	350	126	88	50	32
90% Power	470	170	120	66	43

Table 1.3. Minimal Sample Sizes (Children/Group) Required to Detect a Difference in Persistent Organic Pollutant Exposures Between Two Groups of Children Based on a Two Sample t-Test Conducted at the 5% Significance Level

Power	Estimated Standard Deviation[a]	Percent Difference Between Geometric Mean POPs Exposures for Two Groups of Children[b]					
		10%	25%	50%	100%	150%	200%
80%	0.5	433	80	25	11	<10	<10
	1	1729	316	97	34	20	15
	1.5	3889	710	216	75	43	30
	2	6913	1262	383	132	76	53
90%	0.5	579	107	33	12	<10	<10
	1	2314	423	129	45	26	19
	1.5	5206	951	289	99	57	40
	2	9255	1689	512	176	101	71

(a) Standard deviation of ln-transformed POPs concentrations.
(b) Two groups of children could be low- and middle-income children, at-center and at-home children, inner city and rural, or children from smokers and nonsmokers homes.

To support the sample size calculations, data on children's exposures to POPs from the PAH studies [C7,C10,C12,W5,W7] and the two day care studies [W1, W2, W6, W7, C13] were reviewed. The review assessed the distribution and variability of POPs concentrations in house dust, indoor and outdoor air, solid and liquid food, and soil for seven target POPs, namely: B2 PAH, organophosphates, phthalate esters, phenols, diazinon, chlorpyrifos, and bisphenol-A. In addition, the distribution of hydroxy-PAH in urine was reviewed. It was found that

(a) POPs concentrations tend to be lognormally distributed.

(b) Although there are differences in the variability of POPs concentrations among the six media and in urine, the standard deviations of log-transformed (ln) POPs concentrations generally range from 0.50 to 2.0.

(c) Differences in geometric mean POPs concentrations between low-income and higher-income families as well as between day care centers and homes generally range from 0 to 500%, between city and rural areas, they range from 0 to 150%, and between smokers' and non-smokers' homes, they range from 0 to 250% (B2-PAH only), depending on the compound and medium.

Based on the analysis of the historical and current data, the calculations were performed as follows:

1. A two-sample t-test was conducted at the 5% significance level on ln-transformed POPs to compare the POPs exposures in the following groups of children:
   - low-income families versus middle/upper income families,
   - at day care centers versus at home,
   - inner city versus rural areas,
   - smokers' homes versus nonsmoker's homes. The comparison of POPs exposures in smokers' versus non-smokers' homes was performed on B2 PAH only, because only these two groups have data from the PAH exposure studies.
2. Sample sizes were computed that provide 80 or 90 percent power for detecting a significant difference between the two groups when the actual percent difference ranges from 10 to 200 percent. (The power represents the level of confidence desired to detect a specified difference between the two groups. An experiment designed to have 90 percent power for detecting a specified difference will be more sensitive than one designed to have 80 percent.)
3. Sample sizes were computed assuming that the standard deviation of ln-transformed POPs concentrations is either 0.5, 1, 1.5, or 2.

Table 1.3 summarizes the estimated sample sizes required to detect specific differences between any two groups of children, i.e., low- and middle/upper income children, at-center and at-home children, or inner-city and rural children. For example, to detect a difference between two groups of children if the standard deviation of ln-transformed POPs is 1.0 and the actual percent difference between the two groups is 100 percent, roughly 34 children are needed in each group to give 80% power. If the standard deviation of ln-transformed POPs is 1.5, the number of children increases to approximately 75 per group.

For all seven target POPs concentrations and all six media (floor dust, indoor and outdoor air, solid and liquid food, and soil), the median percent difference in POPs concentrations between

the two groups of children was 60 percent, and the median standard deviation in ln-transformed POPs concentrations was 1.0. As shown in Table 1.3, if the standard deviation in ln-transformed POPs concentrations is 1.0 and the actual percent difference between the two groups of children is 50 percent, then a sample size of approximately 100 children per group will provide 80 percent power for detecting a statistical difference in POPs exposures between any two groups of children. Under the same conditions, a sample size of approximately 130 children per group provides 90 percent confidence that a statistical difference will be detected between the two groups. To allow for missing samples and other data issues, a sample size of 120 to 160 children per group is recommended.

To test the above hypotheses with maximum power, at least 120 children each from low-income and middle/upper income families (targeted at 80 % power), who will be in the age range 18 months to 5 years at the time of sampling, would participate. Those under age 4 are preferred. Children must be able to provide spot urine samples during the day, and those who are still being breast-fed will be excluded. Children who attend day care centers and children who stay at home will be included. They will be monitored at their homes and at the centers. Ideally, the 120+ children in each group (low-and middle/upper income) would be evenly distributed in each subgroup, for example, inner city versus rural, to provide the same power. U.S. Census Bureau definitions of urban and rural will be used. Low-income families are defined as those who meet the qualification criteria for the Women, Infants, and Children program (WIC), i.e., household income not exceeding 185% of the federal poverty level.

If equal numbers of children were selected in each stratification, there would be 128 households in each category in each state. The total number of households would be 256. Overall there would be 128 households in each category: rural, urban, low-income, middle/upper income, at home during the day, at pre-school or day care during the day. Based on the sample size requirements in Table 1.3 and an estimated standard deviation of 1.0, 128 children per group would allow detection of a difference of 50% between groups at 90% power, or with a standard deviation of 2.0, detection of a difference of 100% at 80% power.

However, to increase the representativeness of the study and obtain a probability-based stratified sample, the sample group of low-income subjects would be smaller than the sample group of middle/upper income subjects; and the rural group would be smaller than the urban group. Extreme over-sampling of the low-income or rural groups would result in an imbalance in sampling rates and weights and inefficient sampling design. Alternatively, balancing the sizes of the two groups leads to better statistical power for group comparisons. To increase the representativeness of the study, improve response rates, allow intergroup comparisons, and meet the study objectives, yet stay within the confines of reasonable expenditures of resources, a sampling plan has been developed that takes into account the necessary compromises between the conflicting statistical goals.

1.5.3 Survey Sampling Design

The survey sampling design that is presented here seeks to accomplish the following:

- Acquire the data necessary to meet the major objectives of the CTEPP study regarding total exposure measurement, evaluation and refinement of models, and apportionment of exposure pathways for young children
- Increase the representativeness of the CTEPP study by using two sample frames for recruiting subjects
- Achieve response rates of at least 75% for participation
- Maximize the amount of useful information that can be obtained while, at the same time, balancing the conflicting demands of representativeness and hypothesis testing, and
- Minimize the total cost of the study, recognizing that the per-child unit costs to measure total exposures are high.

Figure 1.1 presents an overview of the CTEPP survey sampling design. A target sample of 128 children (and associated caregivers) per state will be obtained. This sample will be balanced evenly between the day care and no day care components. The sampling design will over-sample the low-income strata, but sample sizes will still be smaller for the low-income than for the middle/upper income group overall. Sample sizes will also be smaller in the rural than in the urban stratum.

Although every attempt will be made to obtain samples that are truly representative of the populations from which the samples are drawn, there are potential confounders that may limit this representativeness. For example, the no day care component will be drawn from those households that have telephones; this will exclude families that have no phone, which means that the most indigent families, families who have recently moved, migrant workers' families, and others may not be represented. By inclusion of day care centers that serve primarily low-income clients, this limitation will be partially ameliorated. A small degree of self-selection into the day care sample is also possible, if families who receive public assistance are more likely to apply for day care. Because of the difficulty of obtaining physical and biological samples from children who are still breast-fed or who are not toilet-trained, these children will also be underrepresented. Through analysis of the pre-monitoring questionnaire data and related Census data, it should be possible to obtain rough estimates of the fraction of the targeted population who are underrepresented; these estimates can then be used to control for the confounders. Nevertheless, the information that CTEPP will generate will be tremendously useful in meeting the objectives of the study and in testing the study hypotheses, as discussed earlier.

The sample design provides a compromise in sensitivity between analytical inferences and population-based inferences. In other words, a more representative sample provides more nearly

proportional representation of these groups than does equal representation. The target population is children between ages 1½ and 5 in NC and OH. We expect to select a total of 256 children for the study, 128 in each state, of which about 64 will attend day care facilities and 64 will stay at home.

The primary, county-level stratification will be by region within the state and urbanicity. Six sample counties in each of the two states will be selected using stratified random sampling and will reflect three distinct geographical areas in each state. Within each of the two states, the samples will be further stratified according to urbanicity and family income. The urbanicity stratification will be imposed at the first stage of selection by classifying counties as predominantly urban or predominantly rural. Income stratification will be performed at subsequent stages of selection for the two sample components and will distinguish between low-income and mid- to high-income households/day care centers.

In the day care sample component, we will identify all the day care centers in the six selected counties. This list, the second-stage sampling frame, will be then divided into two income strata. From these strata, we will take a random sample of 16 centers and a random sample of eligible children within each participating center. In the telephone sample component, we will take a random sample of eligible children who do not attend day care centers using list-assisted telephone sampling techniques in the six counties in each state. The anticipated sample size will be 128 children in each state, with half (64) from the day care center sample (children who attend day care) and the other half (64) from the telephone sample (children who do not attend day care). This dual frame approach will provide maximum coverage for the target population.

The design simplifies the sampling frame construction and sample selection process. At the same time, by concentrating our efforts in a few selected counties (and frames) we can make the recruitment effort more intensive and effective, thus maximizing response rates to 75% or higher, as well as keeping costs within reasonable limits.

The stratification dimensions, coupled with disproportional sampling, are important to ensure good statistical precision and power for the comparisons of priority interest in the study. In particular, to ensure sample representation of low-income households, both sample components will over-sample children in low-income strata. A low-income group is defined following WIC guidelines, i.e., 185% of the federal poverty level.

1.5.4 Sample Areas

The sample will be representative of the selected counties in the two states (NC and OH), and includes the following sampling design features:

- Stratification of the sample of counties in each state
- Selecting counties with probability sampling (or random sampling) methods
- Selecting counties with probabilities proportional to size (PPS).

The target counties will be chosen to represent different geographic regions of the state, as well as variations in socioeconomic, demographic, geologic, and climatic characteristics within the state.

Defining the target area as a discrete set of counties has the following advantages:

- It facilitates the construction of sampling frames of telephone exchanges and day care centers in the area
- It facilitates pre-survey contacts, endorsements, and information campaigns
- It facilitates the use of U. S. Census Bureau statistics for weight adjustments for each sample component, and for the combined sample.

1.5.5 Sample Representativeness

The CTEPP study requires a large number of study measurements, generally costly and complex in nature. It will estimate the total exposure to persistent organic pollutants of a large group of preschool-age children via inhalation, dietary and non-dietary ingestion, and dermal pathways. The measurements will involve parents and day care centers for each subset of participating children. The study also requires a battery of measurement devices and monitors that are not only expensive, but also costly to transport to more than a few selected sites. The CTEPP study thus has unusually high costs per child.

These features of the study dictate essentially that the sample be both highly clustered and confined to a few sites. They also limit the total sample size that may be measured within a reasonable budget. Given the complexity of the study measurements, obtaining a national sample is secondary to obtaining a cross-section of children in the selected counties of the targeted states.

A variety of errors can affect sample representativeness. There can be discrepancies between the survey population and the target population, that is, there can be coverage errors. There can be non-sampling errors and biases, such as non-response. Additionally, there can be deviations from probability sampling.

Our sampling design will minimize these potential errors. First, coverage errors are minimized with the dual frame design. Second, non-response errors will be minimized by our efforts to maximize response rates, and to have all population subgroups represented in the respondent pool. Third, the sampling design will use probability sampling methods at every stage and for every component.

General Coverage Errors. Our sampling design ensures coverage of non-telephone households via the day care component, and coverage of children not attending day care via the telephone

sample. Two additional measures will be used for minimizing both under-coverage errors and their potential biasing effects:

- The stratification of the telephone sample by income levels, and the targeting (over-sampling) of low-income households in this sample component
- Post-stratification weight adjustments that force the sample distribution (participating households) to reflect the population distribution by income levels.

One example of non-coverage would be the failure to include population segments such as non-telephone households. With the proposed dual frame approach, however, non-telephone households are included in the day care component. It is worth noting that only about 5% of U.S. households do not have telephones.

It is also important to ensure that the selected counties include poorer counties, i.e., counties where the prevalence of lower-income households is greater than most counties in the state. This requirement will not only help make the sample counties more diverse, but also facilitate the selection of low-income households into both sample components.

Coverage of Low-Income Households. A related issue concerns providing sufficient representation of low-income households. Ideally, for statistical power in data analysis, we need an equal distribution between low- and mid- to high-income households/day care centers. In the general population, however, the low-income households represent only a small percentage of the whole.

By over-sampling low-income groups in both the day care and telephone samples, the sampling design will yield sample sizes that permit inferences about these groups (e.g., comparisons of low- and mid- to high-income households). For example, the allocation of the sample 64 children (per state) participating in the telephone household component may include 24 children in the low stratum and 40 children in the mid- to high-income stratum. With this allocation, the low-income group will constitute 37.5% of the sample, although it represents a much smaller proportion of the population.

More extreme over-sampling would induce extreme imbalance in sampling rates (and weights), and hence, inefficient sampling designs. However, balancing the sizes of the two groups (low and non-low income households) leads to better statistical power for comparisons between these income groups. Similar compromises between conflicting statistical objectives were considered in the allocation of the sample to urban and rural strata.

Non-Response Errors. We accumulated considerable experience in enhancing response rates in the earlier pilot studies. The following measures will be used in the CTEPP study to enhance the response rates:

- Provide participants with a certificate of confidentiality

- Obtain endorsements from state licensing agencies and day care organizations at the national, state, and local levels
- Obtain endorsements from past pilot study participants
- Design promotional brochures/flyers
- Conduct community-wide campaigns that target families with children, especially low-income families
- Send out press releases to local newspapers and TV/radio stations
- Conduct focus group meetings with directors and teachers of day care centers, and with parents, before recruiting
- Establish good rapport with center directors by personal involvement
- Provide non-monetary and monetary incentives to day care centers and parents, and non-monetary incentives to children
- Facilitate access to children through day care personnel
- Send out advance mailing of survey information materials including EPA logo (for recruiting households), endorsements/letters of support, and provide toll-free telephone number for inquiries
- Use experienced staff for recruiting.

We will consult faculty in the field of development psychology at the North Carolina State University to advise us on the selection and presentation of non-monetary incentives to day care centers, parents, and children in an effort to increase response rates.

Sampling Errors. The sampling design includes a number of features that will minimize sampling errors and enhance the statistical validity and accuracy of the study results. These features include:

- The use of probability sampling methods at every stage
- Stratification by region, urbanicity, and income levels
- Selection of sampling units with probability proportional to size (PPS) methods at the first two stages (counties and day care centers)
- Selection of lower-income children with disproportionate sampling.

These methods will also ensure that the study objectives are met with the greatest statistical efficiency and cost effectiveness.

1.5.6 Selection of Counties

Within each state, six counties will be selected for the study using stratified random sampling. Because of stratification, the sample will represent different regions, urban and rural areas, and low-income and high-income areas of the state.

We expect to target counties with larger population sizes, and in particular larger populations in the low-income groups, by selecting counties using probabilities proportional to size (PPS) within each stratum. We will use the county population in the low-income segment as a measure of size. An alternative measure of size is the total county population.

The PPS sampling methods can be combined with an implicit stratification of the sampling frame, that is, the list of counties in the state, by size. The sample design will use systematic PPS sampling from the sorted frame to ensure that the sample counties vary across the range of income levels. In addition, with PPS methods we can select with certainty very large counties within a given stratum.

Regional Stratification. North Carolina will be divided into three geographic regions: Piedmont, Mountain, and Coastal. We will select three counties from the Piedmont, two counties from the Eastern (Coastal) region, and one county from the Western (Mountain) region. Ohio will also be divided into three geographic regions: South, Central, and North. We will select two counties from the North, three from the Central, and one from the South region.

Urbanicity Stratification. To determine urbanicity, counties will be classified as predominantly rural or urban based on whether or not the county contains part of a Metropolitan Statistical Area (MSA), as defined by the Office of Management and Budget (OMB Bulletin No. 99-04). We will select four predominantly urban counties and two predominantly rural counties in NC. Similarly in OH, we will select four urban and two rural counties.

Selection Using PPS. Within each stratum, counties will be selected using PPS, with the size measure incorporating the size of the low-income group in the county. Thus, the sample will more likely include in each stratum those counties of largest population, in total population and in the low-income group. The number of low-income households is available from Census county-level data. For example, the file http://www.census.gov/hhes/www/saipe/estimate/cty/cty37135.htm in the Census Web site contains relevant county-level poverty data. In the PPS selection of the counties within primary strata (regions and urban/rural) in each state, counties will be sorted by size. The county size measure is the number of low-income households in the county.

Initial steps in the sampling design work will be based on U.S. Census county-level statistics available for each state:

- Classify counties into the strata listed above

- Derive the number of counties to be selected in each stratum cell based on the cross-classification
- Select target counties in each stratum cell (using PPS).

Table 1.4 shows the distribution of the six sample counties across the three NC regions and three OH regions, substratified by urban versus rural.

Table 1.5 presents the primary strata defined for NC in terms of regions and urbanicity. Table 1.6 presents the region-by-urbanicity strata for OH.

1.5.7 Sampling Design for the Two Sample Components

The two sample components consist of the day care center sample and the telephone sample. The day care center sample will be selected in two stages, as illustrated in Figure 1.1.

Day Care Center Sample – Stage 1. Our aim in the first stage is to produce a sample consisting of 16 day care centers. We will start by examining the lists of licensed day care centers. The state licensing agencies are the key sources of comprehensive lists of licensed day care centers in North Carolina and Ohio. We expect the lists to be complete because every eligible day care center must be licensed in its state. We have contacted both state licensing agencies and have confirmed that the day care center contact information is public information which can be purchased via formal request. To further ensure the completeness of the lists in the target counties, we will search a national telephone data base for the target counties and generate a list of day care centers using the standard industrial classification (SIC) codes assigned to these centers (Pro-CD, 1999-2000, infoUSA Inc.).

Day care centers listed in the six counties in each state will be assigned to one of two income strata based mainly on tuition and location (census tract statistics). To increase the representation of low-income children, we will oversample licensed regular day care centers serving primarily low-income children (including Head Start centers). (Oversampling means that greater numbers of children from low-income rather than mid- to high-income families will be selected in the centers.) A sufficiently large sample size of low-income children also ensures that non-telephone households are adequately represented.

The stratified sample of day care centers in each state (total of 16) will be selected, using PPS, from the sorted list of eligible centers compiled over the six counties selected in the state. Within each state and income, the list will be further sorted by county to help ensure that the sample day care centers are evenly distributed across the target counties. Even with this implicit stratification by county, it is still possible that some of the smaller counties may be assigned 1 or 0 sample day care centers. This possibility, which would not jeopardize the representativeness of the sample, would be stronger in counties with fewer children attending day care centers, perhaps by a combination of fewer and smaller day care centers.

Day Care Center Sample – Stage 2. We will next select a random sample of age-eligible children from each participating center. The aim of our sampling approach is to yield at least 64 participating children and 14 participating day care centers in each of the two study states. (We assume that 14 out of 16 day care centers will agree to participate.)

Table 1.4 Selected Counties by Region and Urbanicity Class

		Region			
State	**Urbanicity**	**Piedmont**	**Eastern**	**Mountain**	**TOTAL**
NC	Urban	2	1	1	4
	Rural	1	1		2
		3	2	1	6
		North	**Central**	**South**	
OH	Urban	1	2	1	4
	Rural	1	1		2
		2	3	1	6

Table 1.5. Primary Strata for North Carolina Counties by Region and Urbanicity Class

	1	Coastal Plain	1	Urban
	2	Piedmont	2	Rural
	3	Mountain		
Region	Urban or Rural	County NAME	ST	HOUSEHOLDS
2	1	ALAMANCE	NC	46,900
2	1	ALEXANDER	NC	11,800
3	2	ALLEGHANY	NC	4,100
2	2	ANSON	NC	8,900
3	2	ASHE	NC	9,800
3	2	AVERY	NC	6,000
1	2	BEAUFORT	NC	17,500
1	2	BERTIE	NC	7,600
1	2	BLADEN	NC	11,700
1	1	BRUNSWICK	NC	26,300
3	1	BUNCOMBE	NC	80,300
3	1	BURKE	NC	32,000
2	1	CABARRUS	NC	44,800
3	1	CALDWELL	NC	29,300
1	2	CAMDEN	NC	2,200
1	2	CARTERET	NC	24,600
2	2	CASWELL	NC	8,100
2	1	CATAWBA	NC	51,500
2	1	CHATHAM	NC	17,900
3	2	CHEROKEE	NC	9,200
1	2	CHOWAN	NC	5,600
3	2	CLAY	NC	3,600
2	2	CLEVELAND	NC	34,900
1	2	COLUMBUS	NC	20,000
1	2	CRAVEN	NC	31,500
1	1	CUMBERLAND	NC	95,200
1	1	CURRITUCK	NC	6,400
1	2	DARE	NC	11,400
2	1	DAVIDSON	NC	54,900
2	1	DAVIE	NC	12,400
1	2	DUPLIN	NC	16,300
2	1	DURHAM	NC	80,200
1	1	EDGECOMBE	NC	20,400
2	1	FORSYTH	NC	117,400
2	1	FRANKLIN	NC	16,900
2	1	GASTON	NC	68,800
1	2	GATES	NC	3,700
3	2	GRAHAM	NC	3,000
2	2	GRANVILLE	NC	14,400
1	2	GREENE	NC	6,300
2	1	GUILFORD	NC	154,200
1	2	HALIFAX	NC	21,700
1	2	HARNETT	NC	30,600
3	2	HAYWOOD	NC	21,000
3	2	HENDERSON	NC	33,600
1	2	HERTFORD	NC	8,600
1	2	HOKE	NC	10,000
1	2	HYDE	NC	2,100
2	2	IREDELL	NC	42,400
3	2	JACKSON	NC	10,900
1	1	JOHNSTON	NC	40,100
1	2	JONES	NC	3,500
2	2	LEE	NC	18,700
1	2	LENOIR	NC	23,200
2	1	LINCOLN	NC	21,900
3	2	MCDOWELL	NC	14,900

	1	Coastal Plain	1	Urban
	2	Piedmont	2	Rural
	3	Mountain		
Region	Urban or Rural	County NAME	ST	HOUSEHOLDS
3	2	MACON	NC	11,800
3	1	MADISON	NC	7,300
1	2	MARTIN	NC	10,300
2	1	MECKLENBURG	NC	245,200
3	2	MITCHELL	NC	6,000
2	2	MONTGOMERY	NC	8,400
2	2	MOORE	NC	28,800
1	1	NASH	NC	33,700
1	1	NEW HANOVER	NC	60,300
1	2	NORTHAMPTON	NC	7,900
1	1	ONSLOW	NC	38,500
2	1	ORANGE	NC	44,600
1	2	PAMLICO	NC	5,100
1	2	PASQUOTANK	NC	12,700
1	2	PENDER	NC	14,800
1	2	PERQUIMANS	NC	4,200
2	2	PERSON	NC	12,800
1	1	PITT	NC	45,400
3	2	POLK	NC	7,100
2	1	RANDOLPH	NC	46,900
2	2	RICHMOND	NC	17,400
1	2	ROBESON	NC	40,100
2	2	ROCKINGHAM	NC	35,200
2	1	ROWAN	NC	48,500
3	2	RUTHERFORD	NC	23,800
1	2	SAMPSON	NC	19,500
1	2	SCOTLAND	NC	12,800
2	2	STANLY	NC	21,500
2	1	STOKES	NC	16,500
3	2	SURRY	NC	26,600
3	2	SWAIN	NC	4,700
3	2	TRANSYLVANIA	NC	11,200
1	2	TYRRELL	NC	1,500
2	1	UNION	NC	37,600
2	2	VANCE	NC	15,200
2	1	WAKE	NC	222,500
2	2	WARREN	NC	6,800
1	2	WASHINGTON	NC	5,300
3	2	WATAUGA	NC	15,300
1	1	WAYNE	NC	41,700
3	2	WILKES	NC	24,500
1	2	WILSON	NC	26,300
3	1	YADKIN	NC	14,000
3	2	YANCEY	NC	6,800
				2,878,300

Table 1.6. Primary Strata for Ohio Counties by Region and Urbanicity Class

1	North	1	Urban
2	Central	2	Rural
3	South		

Region	Urban or Rural	County NAME	ST	Total HOUSEHOLDS
3	2	ADAMS	OH	10,700
1	1	ALLEN	OH	38,400
2	2	ASHLAND	OH	18,900
1	1	ASHTABULA	OH	38,500
3	2	ATHENS	OH	21,200
2	1	AUGLAIZE	OH	17,400
3	1	BELMONT	OH	28,100
3	1	BROWN	OH	14,600
3	1	BUTLER	OH	119,500
2	1	CARROLL	OH	10,600
2	2	CHAMPAIGN	OH	14,300
2	1	CLARK	OH	55,700
3	1	CLERMONT	OH	61,700
3	2	CLINTON	OH	14,800
2	1	COLUMBIANA	OH	43,000
2	2	COSHOCTON	OH	14,000
1	1	CRAWFORD	OH	18,400
1	1	CUYAHOGA	OH	561,600
2	2	DARKE	OH	20,000
1	2	DEFIANCE	OH	14,500
2	1	DELAWARE	OH	30,500
1	2	ERIE	OH	30,100
2	1	FAIRFIELD	OH	43,800
2	2	FAYETTE	OH	10,800
2	1	FRANKLIN	OH	404,000
1	1	FULTON	OH	14,800
3	2	GALLIA	OH	12,400
1	1	GEAUGA	OH	28,900
3	1	GREENE	OH	49,600
3	2	GUERNSEY	OH	15,800
3	1	HAMILTON	OH	337,300
1	2	HANCOCK	OH	26,200
2	2	HARDIN	OH	11,500
2	2	HARRISON	OH	6,200
1	2	HENRY	OH	10,800
3	2	HIGHLAND	OH	15,000
3	2	HOCKING	OH	10,700
2	2	HOLMES	OH	10,900
1	2	HURON	OH	21,600
3	2	JACKSON	OH	12,200
2	1	JEFFERSON	OH	30,400
2	2	KNOX	OH	19,400
1	1	LAKE	OH	84,900
3	1	LAWRENCE	OH	24,400
2	1	LICKING	OH	52,000
2	2	LOGAN	OH	17,500
1	1	LORAIN	OH	101,100
1	1	LUCAS	OH	173,600
2	1	MADISON	OH	13,400
2	1	MAHONING	OH	100,400
2	2	MARION	OH	24,000
1	1	MEDINA	OH	49,300
3	2	MEIGS	OH	9,400
2	2	MERCER	OH	14,200
2	1	MIAMI	OH	36,800
3	2	MONROE	OH	5,700

1	North	1	Urban
2	Central	2	Rural
3	South		

Region	Urban or Rural	County NAME	ST	Total HOUSEHOLDS
3	1	MONTGOMERY	OH	222,600
3	2	MORGAN	OH	5,400
2	2	MORROW	OH	11,000
3	2	MUSKINGUM	OH	32,200
3	2	NOBLE	OH	4,400
1	2	OTTAWA	OH	15,600
1	2	PAULDING	OH	7,300
3	2	PERRY	OH	12,500
2	1	PICKAWAY	OH	16,800
3	2	PIKE	OH	10,300
1	1	PORTAGE	OH	53,600
3	2	PREBLE	OH	15,400
1	2	PUTNAM	OH	11,700
2	1	RICHLAND	OH	49,300
3	2	ROSS	OH	26,100
1	2	SANDUSKY	OH	23,100
3	2	SCIOTO	OH	31,400
1	2	SENECA	OH	21,900
2	2	SHELBY	OH	16,800
2	1	STARK	OH	144,000
1	1	SUMMIT	OH	210,900
1	1	TRUMBULL	OH	86,500
2	2	TUSCARAWAS	OH	34,200
2	2	UNION	OH	13,600
1	2	VAN WERT	OH	11,300
3	2	VINTON	OH	4,700
3	1	WARREN	OH	48,400
3	2	WASHINGTON	OH	24,800
2	2	WAYNE	OH	39,200
1	2	WILLIAMS	OH	14,500
1	1	WOOD	OH	42,800
1	2	WYANDOT	OH	8,500

4266300

We plan to select more eligible children from the low-income centers than from the mid- to high-income centers; that is, higher sampling rates will be used within each center in the low-income stratum. For example, if a sample of 24 low-income children and 40 mid- to high-income children is desired in each state, the allocation of participants might look as follows:

- 4 low-income centers: 6 children per center
- 10 regular day care centers: 4 children per center.

Telephone Sample. The telephone sample will be selected using list-assisted techniques, which have several advantages over strict Random Digit Dial (RDD) sampling: lower costs due to more productive calls, and smaller variances due to less sample clustering.

By using information available on exchanges that are likely to have working residential numbers, list-assisted techniques show higher production and hit rates, and hence lower costs. Eligibility rates are also improved by using commercially available information on households likely to have young children and on income groups to target the stratified random sample of telephone numbers. This information will be used in the telephone household sample selection by our sampling vendors (Survey Sampling Inc. or Genesys Inc.) following our specifications, a process that we have successfully employed in dozens of other targeted telephone surveys. Note that the telephone screening will preclude the selection of households with children in day care, and thus prevent any duplication.

The telephone sample design will also incorporate stratification by urban versus rural areas and by income levels. Urban versus rural stratification will be performed at the county level. Stratification into two income groups will be implemented by classifying each household in the telephone sampling frame as either low income or non-low income. Such sample targeting will lead to improved eligibility and response rates.

As with the day care sample, the low-income stratum will be sampled at higher rates than the mid- to high-income stratum in the telephone sample. The allocation of the sample 64 children (per state) participating in the telephone household may include 24 children in the low-income stratum and 40 children in the mid- to high-income stratum. With this allocation, the low-income group will constitute 37.5% of the sample, although it represents a much smaller proportion of the population.

The CTEPP telephone sampling design capitalizes on information available on telephone number exchanges to stratify the sampling frame of possible telephone numbers. This information is used in the construction of (1) blocks or clusters of telephone numbers known to contain higher concentrations of working residential numbers (WRNs), and (2) strata consisting of blocks with high and low densities of WRNs. Then, high-density strata can be oversampled (i.e., selected with greater probabilities of selection than lower-density strata) to yield more effective stratified sampling designs.

Specifically, telephone numbers are grouped into 100-blocks with the same area code, prefix (3 digits), and first two digits of the suffix, and all possible combinations of the last two digits of the suffix. One example 100-block would include all numbers starting with the eight digits (410) 377-28 _ _, where the last two digits range from 00 to 99 (100 possible combinations).

These list-assisted samples permit the exclusion of all telephone numbers that are non-working or non-residential (business numbers). This exclusion increases the efficiency of the telephone survey operations. Typically, however, the elimination of these ineligible numbers is made at the cost of some loss in coverage because, as described below, it is made by deleting blocks of telephone numbers that are very likely to contain no WRNs but may still contain a few eligible numbers.

Hundred blocks with one or more listed household numbers are put into a high-density stratum, which is expected to contain a large proportion of households. This classification is aided by directory listings (telephone books); the stratification is even more effective to the extent that exchanges (6 digits) and blocks (8 digits) with some listed telephone numbers are also more likely to contain unlisted numbers. Hundred blocks with no listed household numbers are put into a low-density stratum, which is expected to contain a small proportion of households. Both strata are sampled to obtain a probability sample of all households with telephones, but the high-density stratum is oversampled, i.e., the high-density stratum is sampled at a higher rate than the low-density stratum. Variations of this basic design may consider: (1) more than two density strata; (2) different thresholds for classifying telephone numbers into high- and low-density strata, e.g., they require at least two or three listed household numbers to classify a 100-block into the high-density stratum; or (3) truncating the frame rather than sampling low-density blocks at a lower rate than high-density blocks.

List-assisted stratified sampling methods are also easily coupled with additional stratification by household characteristics available from commercial sampling vendors (SSI or Genesys Inc., for example). The telephone sampling design will include stratification by income levels and by the likely presence of children in the target age range. The telephone sample in each state will then oversample low-income households and households more likely to contain eligible children.

1.6 Personnel Qualifications

All of the EPA/NERL and Battelle project team members who are involved in the CTEPP study are highly qualified and experienced in different aspects of human exposure research.

The EPA/ NERL team includes:

Dr. Nancy K. Wilson was the Principal Investigator (PI) and Task Order Project Officer (TOPO) on the CTEPP study until she retired in September 2000. She was a research chemist with extensive experience in the human exposure field, including study design, sampling and analysis, and interpretation of results. She has a B.S. in chemistry from the University of Rochester and an

M.S. and Ph.D. in physical chemistry from Carnegie-Mellon University. *After Dr. Wilson retired, Dr. Marsha Morgan became the PI and TOPO for the CTEPP study.*

Dr. Marsha Morgan was a NERL postdoctoral fellow on the study and became the EPA PI and TOPO for the CTEPP study in September 2000. She has experience in analytical laboratory and field work, as well as in toxicology. She has a B.S. in pre-medicine zoology from Ohio University, a MS in environmental health from East Tennessee State University, and a Ph.D. in environmental toxicology and animal science from Michigan State University.

Mr. Gary Evans is a chemical engineer with extensive experience in exposure measurements and modeling. He retired from the EPA in 2001.

Dr. Robert G. Lewis is a research chemist with extensive experience in the human exposure field, especially in the methods development and application areas. He has a significant and extensive background in the measurement of pesticides exposure in environmental and human media, including that of young children. Dr. Lewis has a B.S. in chemistry from the University of North Carolina, Chapel Hill, and a Ph.D. in organic chemistry from the University of Wisconsin, Madison. He retired from the EPA in 2002.

Mr. Thomas R. McCurdy is a physical scientist with extensive experience in atmospheric measurement and exposure, project management, and the statistical handling of research data. He has over 15 years of exposure modeling and assessment experience.

Dr. Shaibal Mukerjee is a research physical scientist. He has experience in exposure monitoring and atmospheric modeling efforts in the Lower Rio Grande Valley of Texas, and was guest editor for a special issue of *Environmental International* on the exposure assessment results from the Lower Rio Grande Valley Environmental Scoping Study.

Dr. Elaine Cohen-Hubal is a research chemical engineer with a background in mathematical modeling of environmental and biological systems. She has a B.S. in chemical engineering from MIT, and an M.S. and Ph.D. in chemical engineering from North Carolina State University.

Mr. Carvin Stevens is a chemist with wide experience in a variety of areas, including field measurements, chemical analysis, and quality assurance. He is the EPA QA Overseer for the Human Exposure Analysis Branch at NERL.

Dr. Maurice Berry is the NERL Program Manager for dietary exposure research. He has a background in dietary exposure measurement, modeling, and methods development. He also has experience in numerous multimedia measurements programs, and will serve as an advisor and consultant to the project.

Dr. James Quackenboss is a research scientist with an extensive background in environmental chemistry, mechanisms of exposure, and field measurements of exposure. He will serve as an adviser and consultant to the project.

Because of the extensive field work that this research will entail, most of the field work and chemical analysis will be done by Battelle through the Human and Ecological Exposure Monitoring Research (HEEMR) contract (68-D-99-011).
The key Battelle team members include:

Ms. Jane C. Chuang, Task Order Leader (TOL), is a senior research scientist at Battelle. She has a B.S. in chemistry from Tunghai University and an M.S. in organic chemistry from Ohio State University. For the past five years, she has been the Principal Investigator for a series of small methodology studies for EPA/NERL, using the TEAM approach to examine children's total exposure to POPs. Ms. Chuang's areas of expertise include project management, study design, human exposure field studies, sampling and analysis methods development for various sample media, QA/QC, and reporting. Ms. Chuang has served as Principal Investigator on many EPA work assignments and cooperative agreement studies dealing with the development, evaluation, validation, and application of field methods for monitoring human exposure to POPs, including PAH, PCB, organochlorine and organophosphate pesticides, herbicides, and phenols. Ms. Chuang serves as the Task Order Leader for the CTEPP Study.

Dr. Sydney Gordon, HEEMR contract Project Manager, has extensive experience in the areas of project management, exposure study design, human exposure measurements, and methods development. Dr. Gordon has served as Principal Investigator on many level-of-effort work assignments and on large cooperative agreements to develop, evaluate and implement methods and instrumentation for monitoring human exposure to multimedia, multipathway pollutants. Dr. Gordon provides project management support to the TOL.

Mr. Christopher Lyu has an M.P.A. in public policy research and public administration. Mr. Lyu has over 12 years of experience in conducting survey research, health, and environmental studies. Mr. Lyu played a key role in the development of subject recruitment strategies, data collection forms, field data collection procedures, and field sampling methods in several pilot-scale exposure field studies. He also provided technical support to EPA/NERL in the development of the Information Collection Request (ICR) for the CTEPP study. Mr. Lyu serves as the Task Leader for subject recruitment in both NC and OH; he leads the field sampling effort in NC.

Mr. Jan Satola has a B.S. in physics. Mr. Satola has more than 10 years of field sampling experience in collecting multimedia samples in residential homes and day care centers. Mr. Satola serves as a field team leader for field sampling in OH and oversees all field sampling activities conducted in OH.

Ms. Marielle Brinkman has a B.S. in chemistry. Ms. Brinkman has considerable experience designing and implementing networked electronic data base systems. She developed an effective sample "cradle to grave" tracking and chain-of-custody database system for the NHEXAS Arizona project. For NHEXAS, she also programmed Visual Basic Application (VBA) macros that save time and minimize transcription errors by electronically transferring data with a minimum of human intervention from each analytical instrument into the NHEXAS data base.

Ms. Brinkman is responsible for the development and maintenance of the data base for all CTEPP measurements.

Dr. Nadia Junod has a Ph.D. in analytical chemistry. Dr. Junod has more than 5 years' research experience in sample preparation and analytical chemistry. She has worked extensively with a variety of matrices, including soil, plant and animal tissue. She is responsible for GC/MS analysis of all CTEPP samples. She serves as a laboratory coordinator to assist the TOL in planning and coordinating laboratory activities.

Dr. Ronaldo Iachan has a Ph.D. in statistics. His areas of expertise include sample survey design and analysis. He has published on various topics in survey sampling, such as systematic and rotation sampling, multiple frames, sampling in time and space, and in health and social statistics, including measures of agreement and diversity.

Dr. Robert Lordo has a Ph.D. in statistics and 13 years' experience in experimental design, data analysis, statistical computing, and technical writing. He specializes in environmental monitoring, human exposure assessment, statistical modeling for risk assessment, and survey design. As the statistics leader for the data analysis task, he monitors the efforts of the statistics team, offer technical guidance, monitor budgets and schedules, and represent the statistics team in meetings between the Battelle project team and EPA. He provides technical review and approval of all statistical deliverables to ensure their quality and relevance to the study objectives.

Dr. Paul Feder has a Ph.D. in statistics and over 20 years' experience in mathematical statistics, risk assessment, and biostatistical applications. He provides senior-level statistical consultation on the statistical modeling efforts and will participate in technical reviews of various deliverables associated with statistical data analysis.

Ms. Sandy Anderson, Quality Assurance Officer at Battelle, oversees the overall QA/QC effort. She is responsible for review of the QSIP and has the authority to implement the QA plan in a manner necessary to ensure and maintain the highest level of data quality. She has the authority to review and assess all aspects of project performance.

1.7 Training Required

All staff members assigned to this project are experienced and have been adequately trained. However, to ensure the consistency and high quality of data collection, a comprehensive training plan will be implemented. An overview of the CTEPP training plan is displayed in Figure 1.2. As shown in Figure 1.2, the training plan consists of two components: project staff training and participant training. Before subject recruitment begins, staff who will be involved in the recruitment will undergo training in the implementation of the recruitment SOPs (See CTEPP-SOP-6.11 and -6.12.).

Standardized scripts and materials will be used. A Computer Assisted Telephone Interview (CATI) system and an Interviewer's Manual for this study will be developed. The Interviewer's Manual will document the background and the aims of this study, the standard interviewing procedures, confidentiality requirements, and question-by-question specifications for the study. Interviewers must be certified for the study before they can initiate any contact with the study subjects. In order to be certified as a CATI interviewer for the study, an interviewer must pass the following two tests:

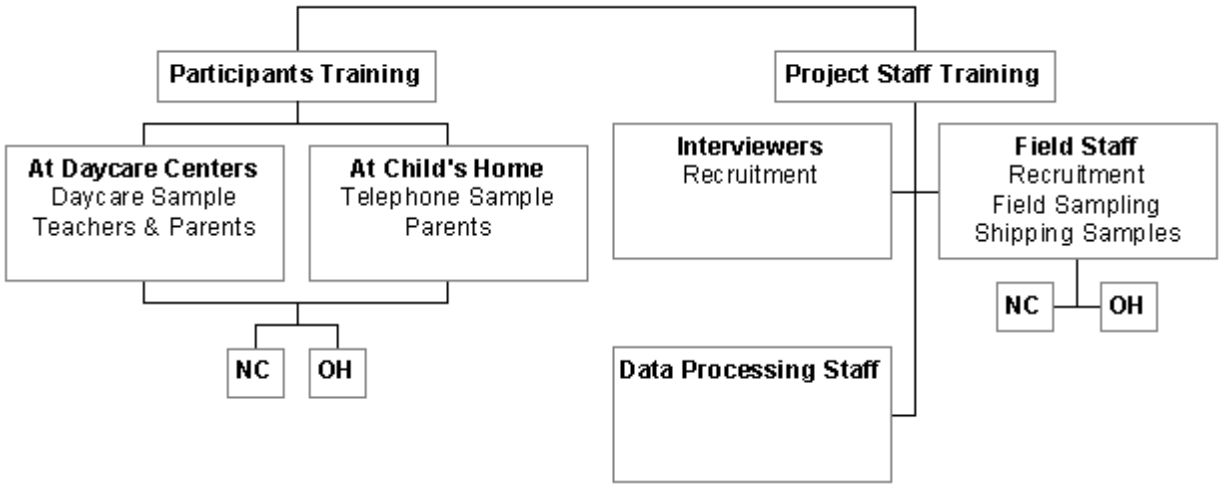

Figure 1.2. CTEPP Training Plan

1) CATI Operation Test: The interviewer must demonstrate that he/she is familiar with the CATI instrument and computer-working environment.

2) CATI Interview Test: The interviewer must conduct at least 2 mock CATI interviews and receive a satisfactory evaluation from the recruitment Task Leader, Mr. Christopher Lyu.

The field Task Leader will conduct a five-day (40-hour) training session with the field team personnel. This training session will be conducted in NC and OH. On the first day, training will cover study background, recruitment SOPs, confidentiality issues, informed consent procedures, and the interviewing protocol. On the second day, the field staff will be trained to administer all the data collection forms. On the third day, they will be instructed in the field sampling procedures, which include the use of field notebooks and the collection of air, food, urine, dermal hand wipe, hard floor wipe, food preparation surface wipe, the polyurethane foam (PUF) roller for dislodgeable residues, indoor floor dust, and soil samples. Internal field audits and QC procedures will also be discussed. A mock field sampling exercise will be conducted during the last two days of training (Days 4 and 5). The field team will visit a home and conduct actual field sampling activities. The field staff will also be certified during these two days (i.e., they will be required to pass the tests set for the field sampling procedures). Finally, training in packing and shipping procedures will be given on the final day. Training will end with a final review of all field procedures.

Before field sampling begins, the data processing staff will also undergo training. Training will cover study background, all data collection forms, data form tracking and processing procedures, coding procedures, and quality control procedures. Due to the unique features of the CTEPP study, some key information and samples will be collected by the study participants themselves. We have learned from the earlier pilot studies that keeping the participants involved and well trained are critical to the success of the study. We need to have the parents collect both the child's and the adult's samples of food, urine, and dermal hand wipes. Similar cooperation and assistance is needed from the teachers at the day care centers.

Once informed consent has been obtained from the participants, a training session will be scheduled with each participant about a week before field sampling commences. All participants (parents and teachers) will be instructed in the procedures to collect their and the child's food, urine, and dermal hand wipe samples. For the day care center participants, training sessions will be scheduled at times that are convenient to most parents and teachers, and will be conducted at the day care center. For the telephone sample participants (i.e., child does not attend a day care center), we will schedule the training session for a time that is convenient to the participant and conduct the session at the participant's home. The training and involvement in the study usually gives the participants a sense of accomplishment. This feeling is amplified by the presentation to them of a Certificate of Appreciation at the end of the study.

1.8 Communication Plan

We will follow the EPA standard clearance process before we release any study results or data to the public and interested parties. No one on the CTEPP study team will be allowed to engage in any unauthorized discussion of policy issues or premature release of study results. All reports, data base packages, manuscripts, and associated documents generated in the CTEPP study will be reviewed by the CTEPP study TOL and the EPA TOPO. The EPA TOPO will review the data and study results and submit them for peer review. The EPA TOPO will obtain approval through standard EPA procedures before submitting these documents for publication or releasing them to study participants. After EPA approval has been received, the data and study results will be made available to the general public by several different methods, including the Internet (on EPA's Home Page at www.epa.gov), EPA-sponsored hotlines, and libraries.

No data that are linked to a specific individual will be made public, without the written consent of that individual. EPA has applied for a Certificate of Confidentiality for the CTEPP study. This certificate will ensure that the researchers cannot be forced to tell people who are not connected with the study, including courts, about an individual's participation, without the individual's written consent. Additionally, information that links data with specific individuals will be kept in a secured and locked file, which will be accessible only to the Principal Investigators; this information will not be released to anyone outside the project research staff.

EPA will also review the data from the study, integrate them into a comprehensive data system, and make them available to EPA, other Federal, state, and local agencies, and the scientific community. To the extent possible, the data will be formatted in such a way as to be compatible with the EPA/ORD exposure data bases (such as THERdbaSE) and with data bases from other NERL/EPA studies, such as the National Human Exposure Assessment Survey (NHEXAS) and the Agricultural Health Study. A summary of the data will be published through the National Technical Information Service (NTIS), using recognized EPA review and publication procedures. The results obtained from the CTEPP study will be published in peer reviewed journal articles and, as such, will be in the public domain. Clients for the results include the EPA Office of Children's Health Protection, and the EPA Office of Prevention, Pesticides, and Toxic Substances. The results will also complement the research of the National Institute of Environmental Health Sciences, the EPA National Health and Environmental Effects Research Laboratory (NHEERL), and the scientific community at large. The enhanced knowledge of children's exposure will allow better understanding of children's exposure to persistent organic pollutants and thus may benefit young children in addition to the study population.

2.0 MANAGEMENT ASSESSMENT

2.1 Assessment Responsibility

Assessments and audits are management tools which will be major components of the NERL QA program for the CTEPP project. Within NERL, the TOPO will have overall responsibility for management of the project, including all contractual and external quality assurance activities. The NERL Quality Assurance Officer (QAO), working with the PI, will have responsibility for scheduling, arranging for, and overseeing the conduct of periodic external audits during the project.

At Battelle, the TOL will have overall responsibility for all aspects of the project, including project management and quality. Each project staff member who performs field, laboratory, and data processing activities will be responsible for performing the procedures in conformance with the QSIP, applicable protocols, and Battelle policies. Each staff member will also be responsible for promptly communicating to the TOL any deviation from established procedures or any issue requiring corrective action. The TOL will be responsible for ensuring that project-related documents are prepared by the project staff in a timely manner. The TOL will also be responsible for reviewing and approving all project-related documents as well as all final project deliverables to ensure their compliance with project requirements.

The TOL will be responsible for preparing or delegating responsibility for the preparation of project documents. Responsibilities include ensuring that proper quality control procedures are implemented in the project as well as in the field, laboratory, and data management offices.

The Quality Assurance (QA) Officer will assist the TOL, as necessary, in the development of the QSIP. The QA Officer will review and approve the QSIP for compliance with EPA's and Battelle's quality requirements. The completed QSIP will also be reviewed and approved by the EPA TOPO and EPA QA manager. The QA Officer is also responsible for the maintenance of the quality systems plan and for all QA/QC activities within the project. Responsibilities include verifying the proper implementation of project documents through the performance of planned and scheduled QA audits or inspections. Responsibilities also include assisting the project technical staff in the development of the required project-associated documents. The QA Officer is further responsible for developing and implementing a plan for regularly monitoring the quality aspects of project activity and providing periodic documentation of monitoring activities to the TOL. The Project Manager will assist the TOL and project staff, as required, in the resolution of quality related problems.

The QA Officer and designees are responsible for verifying that QC and QA activities are being implemented regularly by the laboratory and field personnel, as described in the Standard Operating Procedures (SOPs). They will notify the TOL upon discovery of any quality-related problems or non-compliances.

2.2 Assessment Type

Formal or informal reviews and evaluation of the quality management system are critical to ensuring that the system is operating effectively in meeting desired quality objectives. At EPA, peer review of the study, its implementation, and its outputs are an important part of assuring the relevance, significance, quality, and scientific merit of the research. Internal peer review is a part of each step of the study, including the study design, QSIP, Task Orders, progress and final reports, and publications.

Battelle makes use of both informal and formal internal QA audits in order to ensure that technical quality is meeting stated requirements.

Informal QA Audits. Various QA responsibilities are defined for specific project staff members in the SOPs. Each will perform routine in-house QA audits on appropriate QA records and report to the TOL. These audits will be performed on a quarterly basis.

Errors will be sought in:

- Technician understanding of procedures
- Equipment performance
- Recording of data
- Compiling of data
- Analysis of data.

Procedures to search for errors include:

- Direct visual inspection
- Comparison of forms
- Statistical evaluation.

Formal internal QA Audits. These will be performed by the Battelle QA Officer. The QA audit will pertain to the specific QA requirements for the laboratory or field activities. Field audits will occur once each during the first 2 months of field activities in NC and OH. Laboratory and data audits will take place annually.

2.3 Assessment Usage

The QSIP, final report, and Battelle-generated draft manuscripts from this study will be reviewed by a senior staff member at Battelle and approved by the Project Manager prior to submission to the EPA TOPO. Typically, the EPA TOPO will review these documents and also send them to two reviewers for technical review. All of the review comments will be documented and returned to the TOL. Final versions of the final report and manuscripts will then be prepared based on the reviewers' comments. EPA-generated manuscripts will be treated according to NERL clearance procedures.

2.4 Assessment Criteria

Various types of external QA audits will be used by NERL to assess the quality of data from the CTEPP project. The Performance Evaluation Audit (PEA) is a quantitative evaluation of a measurement system, including data acquisition and reduction. This evaluation involves measuring or analyzing a reference material that is associated with a known value or composition. A Technical Systems Audit (TSA) is a qualitative on-site evaluation of a measurement system. The objective of the TSA is to assess and document all facilities, equipment, systems, record keeping, laboratory procedures, data validation, operations, maintenance, calibration procedures, reporting requirements, and QC procedures. An Audit of Data Quality (ADQ) involves assessing the methods used to collect, interpret, and report the information required to characterize data quality for the purpose of assessing data integrity. A Management Systems Review (MSR) is the review and evaluation of an organization's QA processes and structure and how well the organization is carrying out its QA program. All of the above audit types and associated assessment criteria will be employed by NERL to assess the quality of the data collected during the CTEPP project.

The QA Unit at Battelle has qualified scientists certified as QA reviewers. The QA Unit at Battelle is an independent department and QA Officers are not directly involved with the CTEPP study. They will perform formal audits on all aspects of the project. Documents that will be evaluated include this QSIP, all appendices, and all SOPs identified within this QSIP.

2.5 Assessment Documentation

At EPA, all reports, manuscripts, and other documents generated in the CTEPP study will be kept in the study file in the EPA TOPO's office, except that the files that link the results with individual participants will be kept in separate, secured and locked files that are accessible only to the principal investigators.

At Battelle, copies of all approved memoranda, letters, reports, and manuscripts generated in the course of the study will be kept in the study file in the TOL's office. Reports and manuscripts will also be submitted to the EPA TOPO for review. Review comments received from the EPA TOPO and other reviewers will also be kept in the study file. Results of QA audits and proposed corrective action in accordance with the SOPs, if needed, will be submitted in writing to the TOL. Documentation of the QA audits will reside with the TOL.

3.0 PROJECT IMPLEMENTATION

3.1 Project Responsibilities

The ultimate responsibility for the success of the project falls on the EPA Principal Investigator, Dr. Nancy K. Wilson, and the Battelle Task Order Leader, Ms. Jane Chuang. However, they cannot supervise such a large project alone. All project team members are responsible for immediately reporting problems to their direct supervisor. If the problems cannot be readily resolved, they are reported further up the chain of command. The solutions must be in conformance with all project documents. The project QA Officer can always be consulted for an outside perspective to resolve problems. Each supervisor is responsible to the TOL for a portion of the project. Figure 3.1 is an organization chart that summarizes the major tasks and the responsible key personnel for the CTEPP study. As shown in Figure 3.1, Dr. Marsha Morgan became the EPA PI and TOPO after Dr. Nancy Wilson, the CTEPP EPA PI and TOPO , retired from EPA in 2000.

Ms. Jane Chuang will serve as the Battelle TOL. She will have overall technical and administrative responsibility for the project support through the Task Order, including IRB and OMB (through EPA) approvals. She will also supervise and document the implementation of the study and population selection.
Day-to-day field operations in North Carolina and Ohio will be implemented and documented, and are the responsibility of the TOL and the respective Field Task Leaders (Christopher Lyu in NC; Patrick Callahan in OH). Day-to-day operations include:

- Changes in field study design will be made and documented by the TOL in conjunction with the TOPO..Changes in the Questionnaires will be made by the TOL in conjunction with the TOPO and in conformance with OMB regulations.
- Major changes in types of equipment used to sample a medium will be made and documented by the TOL.
- Minor substantive changes in field protocol implementation will be made and documented by the TOL and Field Task Leaders.
- Collection, preliminary sample preparation and stabilization, shipping and maintenance of samples, and questionnaires, surveys, and field collections will be the responsibility of the Data Coordinator.
- The Field Task Leaders are responsible for the post field transfer, storage, and shipment of all collected samples. These are to be performed according to the appropriate SOPs.
- The Field Task Leaders are responsible for maintaining and calibrating equipment during the field assessment.
- The Field Task Leaders are responsible for training, supervising, monitoring, evaluating, internal field audits, and enforcing all QA/QC requirements for their area, for conducting initial field audits, and for assigning tasks to all the field staff.

- The Field Task Leaders are responsible for the field and questionnaire data during the field activities and transferring all original data records to the data section.

Figure 3.1

Day-to-day laboratory operations will be implemented and documented in each of the responsible laboratories and are the responsibility of the individual Laboratory Supervisors. Day-to-day operations include:

- Major changes in laboratory methods, either in equipment used or procedures followed, will be recommended by the Laboratory Supervisors to the TOL, and decided and documented by them.
- Minor changes in laboratory protocol implementation will be made by the laboratory personnel and the Field Task Leaders, with documentation submitted to the TOL.
- The Laboratory Supervisors are responsible for the post field evaluation and preparation of all collected samples. These are to be performed according to the appropriate protocols, and include sample storage, shipment, and archiving.
- The Laboratory Supervisors are responsible for maintaining and calibrating support equipment for laboratory analysis and field assessment.
- The Laboratory Supervisors are responsible for training, supervising, monitoring, evaluating, internal laboratory audits, and adhering to all QA/QC requirements for their particular area and for assigning tasks to the other laboratory personnel.
- The Laboratory Supervisors are responsible for keeping laboratory data records and providing copies of all data records to the data section.

Day-to-day data processing operations will be implemented and documented for each of the relevant tasks. Day-to-day operations include:

- Major changes in data processing methods either in terms of equipment used or procedures followed, will be determined by the Data Manager and the TOL and documented by them.
- Minor substantive changes in data protocol implementation will be made by the Data Manager and TOL and documented by them.
- The Data Manager will provide EPA with the CTEPP data records in the format requested by EPA.

3.2 Project Design Criteria

3.2.1 Site Selection

Information and physical samples will be collected only from the participating day care centers and households in two states, North Carolina and Ohio. These day care centers and homes will be selected using a probability-based stratified survey sampling design (see Sections 1.5.3 and 1.5.4). Exclusionary criteria include: children who are older than 5, children who are being breast-fed, children who are not toilet-trained. Once a day care center or home is selected for monitoring, equipment will be located inside and outside each center or home to obtain specific exposure data.

3.2.2 Sample Types and Sample Collection Media

A summary of the types of samples that will be collected from each sample site (day care center or household) in the CTEPP study is given in Table 3.1. The samples include questionnaires, diaries, indoor air samples, outdoor air samples, floor dust samples, yard soil samples, floor surface wipe samples, food preparation surface wipe samples, duplicate-diet food samples, urine samples, and dermal wipe samples. If the sampling site has had a recent pesticide application (within the past seven days), PUF roller samples will also be collected. The sample collection media are also described in Table 3.1.

3.2.3 Sampling Time and Frequency

For the CTEPP study, the field monitoring period at each sample site is 48 hours. Thus, indoor and outdoor air samplers will be operated for 48 hours at each site. The sampling period for food, dermal wipe, and urine samples is also 48 hours. Due to the high unit costs, we will not perform repeat sampling at any sampling site at a different time.

3.2.4 Sample Collection

The field sample collection activities are summarized in Table 3.2. The sample collection procedures are described in the field sampling SOPs (CTEPP-SOP-2.10 through -2.29).

3.2.5 Sample Handling

All collected samples must be handled carefully to preserve identity and integrity. All samples will be appropriately labeled in the field. Prior to leaving the field, the field team leader will take a sample inventory. All labels will be checked and samples will be transported and stored in accordance with specifications described in the field sample handling SOPs (CTEPP-SOP-3.10 through -3.15).

3.2.7 Sample Custody

At the time of field sample collection, a sample custody form is completed for each sample. Chain-of-custody records will be utilized for all samples, as described in SOPs (CTEPP-SOP-2.30 and -4.11). The Field Task Leader and TOL will be responsible for making sure that sample custody and sample tracking procedures are followed.

The sample custody form will document all collection, shipment, receipt, analysis, processing, and handling steps which each sample undergoes as it passes from one individual to the next. This record will be initiated in the field by the responsible field staff member and will capture the original field collection of the sample, as well as all subsequent operations performed. Each sample custody record will contain as a minimum the following information: participant identification code (ID), sample ID, the operation performed on the sample (i.e., collection, processing, shipment, receipt, storage, laboratory procedure, disposal, etc.), initials of the person performing the operation (may also include his/her ID number), date on which the operation is

Table 3.1. Summary of Samples/Information to be Collected

Total Estimated Subjects		**256**	Total Estimated Day Care Centers		**28**	
Stay at Home		**128**	Est. No. of Children per Day Care Center		**4 - 6**	
Attend Day Care		**128**	Est. No. of Households Sampled per Day		**2**	
SAMPLES & DATA		**TOTAL (A)+(B)+(C)**	**CHILD STAY AT HOME**	**CHILD ATTEND DAY CARE**		
			(A) No./Household	**(B) No./Household**	**(C) No./Day Care Cr**	**Remarks**
1	Indoor Air - XAD/filter	312	1x128	1x128	2x28	48-Hour Air Sampling Method
2	Indoor Air - XAD/filter	312	1x128	1x128	2x28	48-Hour Air Sampling Method
3	Outdoor Air - XAD/filter	312	1x128	1x128	2x28	48-Hour Air Sampling Method
4	Outdoor Air - XAD/filter	312	1x128	1x128	2x28	48-Hour Air Sampling Method
5	Food: Duplicate plate for the child 1 Solid food container per child	312	(3 meals+snacks) for 2 days 1x128	(2 meals+snacks) for 2 days 1x128	(1 meal+snacks) for 2 days 2x28	For those children attending day care, some may have 2 meals (breakfast & lunch) at day care.
6	Food: Duplicate plate for the child 1 Liquid food container per child	312	(3 meals+snacks) for 2 days 1x128	(2 meals+snacks) for 2 days 1x128	(1 meal+snacks) for 2 days 2x28	For those children attending day care, some may have 2 meals (breakfast & lunch) at day care.* Drinking water sample will be stored in a separate container.
7	Food: Duplicate plate for the Adult 1 Solid Food container per adult	256	(3 meals+snacks) for 2 days 1x128	(2 meals+snacks) for 2 days 1x128	N/A	If both the child's parents work during the day, we will not ask the parent to collect the parent's lunch meal.
8	Food: Duplicate plate for the Adult 1 Liquid Food container per adult	256	(3 meals+snacks) for 2 days 1x128	(2 meals+snacks) for 2 days 1x128	N/A	If both the child's parents work during the day, we will not ask the parent to collect the parent's lunch meal. * Drinking water sample will be stored in a separate container.
9	Urine: Child	1,536	6 per child (3 per day for 2 days) 6x128	4 per child (2 per day for 2 days) 4x128	2 per child (1 per day for 2 days). [We will collect the sample in the after- noon-after lunch] 2x128	We will collect 3 samples per child per day [1 first morning void, 1 in the afternoon/after lunch, 1 in the evening/after dinner].

Table 3.1. Summary of Samples/Information to be Collected

Total Estimated Subjects		**256**	Total Estimated Day Care Centers		**28**	
Stay at Home		**128**	Est. No. of Children per Day Care Center		**4 - 6**	
Attend Day Care		**128**	Est. No. of Households Sampled per Day		**2**	
SAMPLES & DATA		**TOTAL (A)+(B)+(C)**	**CHILD STAY AT HOME**	**CHILD ATTEND DAY CARE**		
			(A) No./Household	**(B) No./Household**	**(C) No./Day Care Cr**	**Remarks**
10	Urine: Adult	1,280	6 per adult (3 per day for 2 days) 6x128	4 per adult (2 per day for 2 days). [We will not collect the sample in the after-noon.] 4x128	N/A	If the parent stays home with the child, we will collect 3 samples per day [1 first morning void, 1 in the afternoon/after lunch, 1 in the evening/after dinner]. If both the child's parents work during the day, we will collect only 2 samples per day [1 first morning void, 1 in the evening/after dinner].
11	Dermal-Hand Wipe: Child	1024	4 per child (2 per day for 2 days) 4x128	2 per child (1 per day for 2 days; before dinner) 2x128	2 per child (1 per day for 2 days; before lunch) 2x128	We will collect 2 samples per child per day (right before the child washes his/her hands for lunch/dinner).
12	Dermal-Hand Wipe: Adult	768	4 per adult (2 per day for 2 days) 4x128	2 per adult (1 per day for 2 days; before dinner) 2x128	N/A	If the parent stays home with the child, we will collect 2 samples per day [1 before lunch, 1 before dinner]. If both the child's parents work during the day, we will collect only 1 sample per day (before dinner).
13	Hard-Floor Wipe	284	1 per house (1 x 128)	1 per house (1 x 128)	1 per day care (1x28)	
14	Food-Preparation Surface Wipe	284	1 per house (1 x 128)	1 per house (1 x 128)	1 per day care (1x28)	
15	Dislodgeable Residues - PUF roller	284	1 per house (1 x 128)	1 per house (1 x 128)	1 per day care (1x28)	Total numbers of samples will be lower than 282 because only households/day care centers having a recent pesticide application will be sampled.

Table 3.1. Summary of Samples/Information to be Collected

Total Estimated Subjects		**256**	Total Estimated Day Care Centers		**28**	
Stay at Home		**128**	Est. No. of Children per Day Care Center		**4 - 6**	
Attend Day Care		**128**	Est. No. of Households Sampled per Day		**2**	
SAMPLES & DATA		**TOTAL (A)+(B)+(C)**	**CHILD STAY AT HOME**	**CHILD ATTEND DAY CARE**		
			(A) No./Household	**(B) No./Household**	**(C) No./Day Care Cr**	**Remarks**
16	Indoor Floor Dust	312	1 per household (child's most active room) 1x128	1 per household (child's most active room) 1x128	1 per classroom (est. 2 classrooms per day care) 2x28	Dust samples will be collected from the child's most active room at home and from the activity center in each classroom at day care.
17	Vacuum Bag	312	1 per household 1 x 128	1 per household 1 x 128	1 per day care center 1 x 128	
18	Soil	284	1 per household (child's usual outdoor play area) 1x128	1 per household (child's usual outdoor play area) 1x128	1 per day care (child's usual outdoor play area) 1x28	
19	Pre-Monitoring Interview	284	1 completed questionnaire per household 1x128	1 completed questionnaire per household 1x128	1 completed questionnaire per day care 1x28	We will interview parents at home and day care directors (or teachers) at the day care center.
20	Post-Monitoring Interview	312	1 completed questionnaire per household 1x128	1 completed questionnaire per household 1x128	1 completed questionnaire per classroom (est. 2 classrooms per day care) 2x28	We will interview parents at home and day care teachers at the day care centers.
21	House/Building Characteristics Observation Survey	284	1 completed survey per household 1x128	1 completed survey per household 1x128	1 completed survey per day care 1x28	This will be completed by project staff's observation and survey of the building and surroundings.
22	Child Activity/Food Diary	384	1 completed diary per child 1x128	1 completed diary per child 1x128	1 completed diary per child 1x128	The activity/food diary for each child will be completed by the child's parent at home and by the child's teacher at day care (if the child attends day care).

Table 3.1. Summary of Samples/Information to be Collected

Total Estimated Subjects		**256**	Total Estimated Day Care Centers		**28**	
Stay at Home		**128**	Est. No. of Children per Day Care Center		**4 - 6**	
Attend Day Care		**128**	Est. No. of Households Sampled per Day		**2**	
SAMPLES & DATA		**TOTAL (A)+(B)+(C)**	**CHILD STAY AT HOME**	**CHILD ATTEND DAY CARE**		
			(A) No./Household	**(B) No./Household**	**(C) No./Day Care Cr**	**Remarks**
23	Adult Food Diary	256	1 completed diary per adult per household 1x128	1 completed diary per adult per household 1x128	N/A	A pocket-size food diary will be developed for the child's parent to record the food data during the 48-hour monitoring period.
24	Day Care Food Menus	28	N/A	N/A	1x28	For each day care center, we will collect the day care center's food menus for the past 3 months.
25	Video Taping Selected Children's Activities	30	15 children will be selected from this group. 4 hours per day for 2 days (total of 8 hours per child)		Videotaping will be done at the day care center for ~10% of the child subjects.	
26	Recruitment Survey	320	Our goal is to obtain about 75% of eligible households to participate in the study. The estimated number of recruitment survey distributed is 170.	Our goal is to obtain about 86% of contacted parents to participate in the study. The estimated number of recruit- ment survey distri-buted is 150.	N/A	

Table 3.2. Summary of Field Data Collection and Sampling Activities

Sampling Day	Data Collection and Sampling Activity/Task
Day 1	▸ Obtain signed consent form ▸ Conduct Pre-Monitoring Interview ▸ Complete the Building Observation Survey ▸ Provide instructions on food sample collection, give food containers and cooler, ask if it's OK to store the food samples in the participant's refrigerator ▸ Remind parent and teacher--no vacuuming during the 48-hour period (sweeping with a broom is OK) ▸ Review the instructions for collecting urine and hand-wipe samples ▸ Give the sample collection supplies to the parent and teacher (e.g., urine and hand-wipe) ▸ Review instructions for recording in the Child Activity Diary ▸ Set up indoor air monitor, mark the location on the sketch, record air log ▸ Set up outdoor air monitor, mark the location on the sketch, record air log ▸ Take pictures of sampling activities. ***Note:*** *Each child's supplies (clean sample containers) are stored in a clean container with name labeled on top).*
Day 2	▸ Complete activities pending since Day 1, if any ▸ Check outdoor air monitor, record air log ▸ Check with the parent and teacher for questions about or problems with sampling activities ▸ Videotape child's activities, if randomly selected
Day 3	▸ Complete activities pending since Day 1, if any ▸ Unload indoor air samplers, record air log, remove air monitors ▸ Collect dust sample, vacuum the house (must unload the indoor air samplers first) ▸ Unload outdoor air samplers, record air log, remove air monitors ▸ Collect one soil sample (children's usual outdoor play area), mark the location on the sketch ▸ Collect hard-floor surface wipe sample ▸ Collect food preparation surface wipe sample ▸ Collect PUF roller sample for dislodgeable residues ▸ Pick up food samples, examine the samples, remove any non-edible materials ▸ Pick up urine and hand-wipe samples ▸ Pick up the Child Activity Diary ▸ Conduct Post-Monitoring Interview ▸ Present a *Certificate of Appreciation* to the parent and teacher ▸ Confirm the check mailing information with the parent and teacher ▸ Take pictures of sampling activities ▸ Videotape child's activities, if randomly selected

initiated, and any relevant remarks or comments pertaining to the sample. The sample custody form will be a hand-written paper record. In addition, a computer-based tracking system will be employed for all collected samples.

3.2.8 Sample Preparation and Sample Analysis

Samples will be prepared in accordance with written SOPs (CTEPP-SOP-5.10 through 5.23) developed for the laboratory evaluation of each sample type. Sample extracts or fractions will be analyzed by gas chromatography/mass spectrometry (GC/MS) according to Standard Operating Procedure CTEPP-SOP

3.3 Data Quality Indicators

Data Quality Indicators (DQIs) flow from the Project Quality Objectives. If the DQIs are met, the data are of consistently high quality. If DQIs are not met, then the data are not of sufficient quality to meet the stated objectives.

3.3.1 Accuracy, Precision, and Detection Limits

Because for some of CTEPP target analytes in multimedia samples, methods are being refined, thus the DQIs are set during the course of the study. The DQIs for accuracy, precision, and limits of detection for CTEPP samples are summarized in Table 3.3.

3.3.2 Completeness

Completeness is a measure of the amount of data obtained from a measurement process compared to the amount that was expected to be obtained under the conditions of the measurement. Completeness goals for the recruitment, field data collection, sample collection, and sample analysis are shown in Table 3.4

3.3.3 Comparability

Comparability is the confidence with which one data set can be compared with another. Data comparability will be achieved by using standard units of measure. For example, the unit of measure used for the concentration of target analyte in air is ng/m^3; in dust and soil, the unit of measure is ng/g and ng/m^2; in food, it is ng/g (or ppb); in wipes, it is ng/m^2; and in urine, it is ng/mL and µmole/mole of creatinine.

3.3.4 Sample Representativeness

Sample representativeness for the CTEPP study is discussed in detail in Experimental Design (see Section 1.5.5).

Table 3.3. Data Quality Indicators for the CTEPP Study

Sample Media	Accuracy[(a)]	Precision[(b)]	Estimated Detection Limit[(c)]
	% Recovery	% RSD	
Air	80 - 120%	± 20%	0.1 - 0.01 ng/m^3
Food	70 - 130%	± 30%	0.04 - 0.5 ppb
Dust/Soil	80 - 120%	± 20%	1-5 ppb
Urine	70 - 130%	± 30%	0.02-1 ppb
Dermal Wipe	80 - 120%	± 20%	0.5-5 ng/wipe
Surface Wipe	80 - 120%	± 20%	0.5-5 ng/wipe
PUF Roller	70 - 130%	± 30%	0.5-5 ng/PUF roller

(a) Accuracy is based on recovery data of the spiked samples.
(b) Precision is based on percent relative standard deviation (%RSD) of duplicate or split samples.
(c) Estimated detection limit is based on the results from pilot studies and is sample matrix dependent.

Table 3.4. Completeness Goals for the CTEPP Study

Task	% Completeness
Participant Completion for the Study	> 80
Field Data Collection	> 85
Field Sample Collection	> 85
Sample Analysis	> 95

4.0 DATA ACQUISITION

4.1 Data Recording

For valid study results, data have to be collected in a systematic and uniform way. One of the first assurances that data are being collected this way is to develop data collection forms that accurately record the data being sought, while at the same time allowing for enough flexibility to capture the unexpected. Data collection forms are often custom designed for each study to assist project investigators in successfully completing specific data collection efforts. For the CTEPP study, standardized questionnaires and other data collection forms will be used by field stations in North Carolina and Ohio. Information needed to interpret the chemical analyses will be collected through data collection forms that were developed for and used in the earlier pilot studies, and later modified for the CTEPP Study. The various steps and methodology used in assuring quality preparation of data collection forms are outlined below.

Quality control measures taken during preparation of data collection forms help to prevent problems during the data collection and processing stages. The key objectives of the quality control process for preparation of data collection forms are to:

- Produce data that are as error-free as possible.
- Collect data designed to answer specific research questions in a form amendable to computer data processing and analysis.
- Ensure that data collected measure what they are intended to measure.
- Produce data comparable to relevant research on the topic by employing standardized and proven questions and procedures whenever possible.

Table 4.1 briefly summarizes the recording methods used with the data collection forms. The CTEPP data collection forms are organized into 10 modules that are simple to administer and that collect information which can be related to the exposure, concentration, and biological measurements. The 10 modules are:

Form #1. Recruitment Survey: to identify individuals within the household for the purpose of participant recruitment based upon the stratification categories: (1) urban vs. rural, (2) low-income vs. middle-income, and (3) children who stay at home during the day vs. children who attend day care during the day.

Form #2. House/Building Characteristics Observation Survey: to further identify and inventory the presence of pollutant sources and to document the physical characteristics of the house/building (to be completed by project staff to minimize burden on respondents). The survey used for home (Form #2) is the same as the one used for the day care center (Form #3).

Form #3. Day Care Center/Building Characteristics Observation Survey: to further identify and inventory the presence of pollutant sources and to document the physical

Table 4.1. Data Recorded Methods

What is the data collection form?	How the data will be recorded?	Who will record the data?
Form #1. Recruitment Survey	For the Day Care Center Sample participants: Manually For the Telephone Sample participants: Computer Assisted Telephone Interview (CATI) System	For the Day Care Center Sample participants: Trained Participants For the Telephone Sample participants: Trained Interviewers
Form #2. House/Building Characteristics Observation Survey	Manually	Trained Field Staff
Form #3. Day Care Center/Building Characteristics Observation Survey	Manually	Trained Field Staff
Form #4. Parent Pre-Monitoring Questionnaire:	Manually	Trained Field Staff
Form #5. Day Care Center Pre-Monitoring Questionnaire	Manually	Trained Field Staff
Form #6. Parent Post-Monitoring Questionnaire	Manually	Trained Field Staff
Form #7. Day Care Center Post-Monitoring Questionnaire	Manually	Trained Field Staff
Form #8. Child Activity Diary [Children Who Don't Attend Day Care]	Manually	Trained Participants
Form #9. Child Activity Diary [Children Who Attend Day Care]	Manually	Trained Participants
Form #10. Child Activity Diary [Day Care Teacher]	Manually	Trained Participants

characteristics of the day care center/building (to be completed by project staff to minimize burden on respondents).

Form #4. Parent Pre-Monitoring Questionnaire: to identify individuals within the household and to describe the multiple environmental pathways and media through which they may be exposed.

Form #5. Day Care Center Pre-Monitoring Questionnaire: to identify individuals and classrooms within the day care center and to describe the multiple environmental pathways and media through which they may be exposed.

Form #6. Parent Post-Monitoring Questionnaire: to provide information on the child's activities and potential exposure during the 48-hour air sampling period, explain variation in the sample, and permit stratification for the monitoring results.

Form #7. Day Care Center Post-Monitoring Questionnaire: to provide information on the child's activities and potential exposure during the 48-hour air sampling period, explain variation in the sample, and permit stratification for the monitoring results.

Form #8. Child Activity Diary [Children Who Don't Attend Day Care]: to collect data on the child's activity patterns and information on food consumption patterns from the participant for use in estimating dietary exposure. Form #8 is designed for children who do not attend day care. It is very similar to Form #9.

Form #9. Child Activity Diary [Children Who Attend Day Care]: to collect data on the child's activity patterns and information on food consumption patterns from the participant for use in estimating dietary exposure. Form #9 is designed for children who attend day care.

Form #10. Child Activity Diary [Day Care Teacher]: to collect data on the child's activity patterns and information on food consumption patterns from the participant for use in estimating dietary exposure. This data collection form is designed to be used at the day care center.

In addition to the above steps and methodology used for assuring quality preparation of data collection forms, other key issues for high quality data acquisition include data recording, identification of data, control of erroneous data, data evaluation, and data validation.

All the completed data collection forms will be field edited to check for missing data or any potential problems. Manually recorded data will be double-entered into the computer with 100% data entry error verification.

4.2 Identification of Data

All CTEPP data will be clearly identifiable and traceable to the source from which the data were produced. Raw, reduced, and processed data will be identified and controlled to assure that only correct and acceptable items are used in the project.

Non-detects present a special data challenge. They are usually reported as "less than" some definitive number. We have a special symbol field in our data base which allows the data analyst to recode non-detects in a way that best suits that analysis. It also enables differentiation of non-detects from detection of low (but "real") values.

Drafts of reports, including calculations and supporting documentation for reviews, will be paginated and identified by author/preparer as to project number, draft, or revision number, date of preparation, and total number of pages.

All participants will be assigned a unique identification number (ID), which will provide privacy protection to the participants and at the same time identify the data source. The linkage between the ID numbers and the identification of participants will be maintained by Battelle and will be protected by a *Certificate of Confidentiality*. The participant ID numbering system is described below:

4.2.1 Participant ID

The participant ID will be a unique 6-digit number (e.g., ☐☐ - ☐☐☐ - ☐). The first two digits will be assigned to the day care centers. For NC day care participants, we will assign the numbers 01 to 39; for OH day care participants, the assigned numbers will be 40 to 79. For NC non-day care participants, we will assign the number 97; for OH non-day care participants, the assign number will be 98. We will assign the number 99 for field blanks.

The third, fourth, and fifth digits combined define the unique ID number for the participants. Valid ID numbers for participants are 001 to 899. However, we will assign "000" to samples collected from a day care center that are not linked directly to a specific individual (e.g., food, air, dust, and soil samples from a day care center are associated with all the children who attend that day care center). The last(i.e., the 6^{th}) digit in the ID number designates the sample as either a child or adult or day care sample. For samples collected at the child's home, we will assign a "1" to the child and a "2" to the parent. We will assign a "3" to the child's samples collected at the day care center.

Examples of participant ID numbers are as follows:

01-001-1 = NC day care#01, participant #001, child sample/data from home.

01-001-3 = NC day care#01, participant #001, child sample/data from day care.

01-001-2 = NC day care#01, participant #001, parent sample/data from home.

97-021-1 = NC non-day care, participant #021, child sample/data from home.

97-021-2 = NC non-day care, participant #021, parent sample/data from home.

40-001-1 = OH day care#40, participant #1, child sample/data from home.

40-001-3 = OH day care#40, participant #1, child sample/data from day care.

40-001-2 = OH day care#40, participant #1, parent sample/data from home.

98-141-1 = OH non-day care, participant #141, child sample/data from home.

98-141-2 = OH non-day care, participant #141, parent sample/data from home.

09-000-3 = NC day care#09, sample from day care.

51-000-3 = OH day care#51, sample from day care.

Note that a separate sample ID label will also be used together with the participant's ID for sample identification.

4.2.2 Sample ID

Unique sample identification codes will be assigned to all samples collected or produced in the CTEPP study to allow identification and tracking of samples. Bar code labels will be produced in the data management system and used whenever possible to identify samples in order to minimize human error during data entry. Because it can be used to code both alphabetical and numerical data, bar code 39 will be used to encode the sample identification codes. Bar code labels will be read using a charge coupled device (CCD) decoded scanner. The hand-held CCD will enable rapid, accurate scanning of labels – even those that have been crumpled, covered with cellophane tape (up to five layers), and/or affixed to curved surfaces.

The sample code assigned to each sample will consist of an 8-character code The first three characters will be alphabetical to identify the sample matrix type, and the next five numerical characters will uniquely identify the sample. No spaces, hyphens, or other separatory characters will be used in the sample coding scheme. All sample codes will be created in the following format:

AAA12345 with the following specifications:

AAA = the three-digit Sample Matrix Identification

AAA = Sample Matrix, with
IAN = Indoor Air Neutrals
IAA = Indoor Air Acids
OAN = Outdoor Air Neutrals
OAA = Outdoor Air Acids
SFC = Solid Food Child
LFC = Liquid Food Child
SFA = Solid Food Adult
LFA = Liquid Food Adult
DRW = Drinking Water

URC = Urine Child
URA = Urine Adult
DCN = Dermal Wipe At-Home Child Wipe #1 and #2, Neutrals
DCA = Dermal Wipe At-Home Child Wipe #3 and #4, Acids
DAN = Dermal Wipe At-Home Adult Wipe #1 and #2, Neutrals
DAA = Dermal Wipe At-Home Adult Wipe #3 and #4, Acids
DCH = Dermal Wipe Day-Care Child at Home Wipe #1 and #2, Neutrals or Acids
DCD = Dermal Wipe Day-Care Child at Day Care Wipe #1 and #2, Neutrals or Acids
DAH = Dermal Wipe Day-Care Adult at Home Wipe #1 and #2, Neutrals or Acids
IFD = Indoor Floor Dust
SOL = Soil
FSW = Floor Surface Wipe
FPW = Food Preparation Surface Wipe
PUF = PUF roller sample
BAG = Vacuum bag sample
12345 = Sample Number.

In order to minimize human transcription error, no sample numbers with contiguous same digits will be generated. Furthermore, a Field Sample ID Log will be used to document the ID labels assigned to each study subject.

4.3 Control of Erroneous Data

In spite of careful planning and implementation of quality control procedures, inaccurate and incomplete data and results may occur in data collection forms due to misunderstanding or confusion on the part of the respondent regarding the purpose of the question or format for response, unintentional skipping of all or parts of questions by the respondent, and/or data editing errors. The CTEPP study incorporates a number of controls to provide for the identification, documentation, evaluation, and disposition of erroneous data and, thus, maximize the accuracy and reliability of the data. These include:

- Using a tiered collection methodology to minimize the impact of non-responses
- Using standardized questionnaires and data forms for both field study sites
- Using pilot-tested questionnaires and data forms and improving the forms to meet the data collection needs of the CTEPP study
- Developing an attractive and easy-to-follow format for the self-administered data collection forms

- Updating the effective training materials for both the project staff and study participants based upon lessons learned from the pilot studies
- Using close-ended response categories whenever possible
- Using double-key entry to ensure 100% accuracy of the data entry
- Using automated checks for range, logic, and inconsistencies to assist in identifying potential errors and enhance the data quality.

All data collection forms will be developed using the latest computer desktop publishing technology. The data collection forms will be easy to use. Instructions for the participants will be printed on colored paper and with graphic illustrations. Photos of commonly used pesticides and household chemicals will be used to compile an illustration book to facilitate data collection during the interviews. The collected data will be processed using SAS programs or other comparable statistical software.

All completed data collection forms will be processed by trained data preparation staff. Prior to data entry, each form will be subjected to manual edit. Field staff will review the data for completeness and internal consistency in the field. If any missing data or errors are found, they will contact the participants immediately to collect the missing data or clarify any questions or problems. Experienced data preparation staff will review each data form for legibility. Senior project staff will develop edit specifications. Critical questions will be reviewed and problems resolved as specified. Any open-ended questions will be coded to numeric codes. Quality control activities during data preparation include 100% review of the first batch processed by each editor, and ongoing review of 10% of the batches. Specialist programmers will develop data entry computer programs to facilitate the keying of the data forms. A quality control computer program will be developed to check for data-entry errors. These checks reduce keying errors significantly, and operators can re-key incorrect entries without losing previously keyed valid entries.

4.4 Data Evaluation

The survey questionnaires, child activity data, field sampling and analysis data, and statistical analysis data will be collected according to the study design by following the established SOPs. The data quality indicators, including accuracy, precision, and completeness, will be calculated and reported as part of data evaluation. Once master data bases are generated, including all survey, field and analytical data, 10% of the data will be randomly selected and compared against the questionnaires, field data forms, and laboratory record books as a QA measure. Furthermore, preliminary data evaluation tests will be performed to detect outliers. All studentized residuals in excess of three in absolute value will be considered to be tentative outliers. The concentration values or activity or physiological parameter values contributing to these extreme values will be reviewed in the basic data records for correctness. If errors are found, they will either be corrected or the outlier will be deleted. If no errors are found, the extreme responses will be considered to be natural variation and will be retained in the data set.

4.5 Data Validation

We will develop a data dictionary (or code book) for each data file generated in the CTEPP study. The data dictionary will evolve during data processing and become part of the documentation for the final data file delivered. It will include range (minimum, maximum) and type (numeric, alpha), checking, and missing value code (refusal, not applicable, unable to respond). In addition, it will also support the development of internal consistency checks by defining appropriate relationships among items in the questionnaire.

All field collection data will be 100% verified, that is, keyed twice. Any discrepancies between the first and second keying are detected by the verification program and will be corrected. Once the keyed data are in machine-readable form, we can perform more extensive and complex editing. Editing software will be developed to perform range checks within items, consistency checks among data items, and checks for properly followed routing patterns. The senior project staff will specify edits performed and review them after completion. The resulting edit report will document the current data values and verify that the records have passed all edit tests. The files will then be ready for data analysis, variable recording, and variable creation.

The analytical raw data generated from each instrument will be evaluated by qualified analysts for consistency of results within and among analytical sample runs and calibrations. The data will be scrutinized to identify unusual occurrences. The TOL will review all analytical data before import into the data base. If any anomalous results are observed in the data, every effort will be made to identify any problems in the sample collection, sample preparation, and/or analysis which could have contributed to the anomaly. If any problems occur, the data will be flagged, and corrective action will be taken. The reviewed raw data will then be electronically parsed into spreadsheet templates, pertinent data such as sample extraction weight and quality assurance codes are added, and the completed spreadsheet is electronically imported into the data base for final calculation of concentrations. For those data requiring calculation of results, a random subset (approximately 5%) of the raw data will be recalculated for validation.

5.0 DATA MANAGEMENT

All electronic sample custody, raw analytical, and calculated data will be stored in a networked, multi-user, relational data base. A data base manager will be assigned to coordinate and control all entries and access to the individual data files. The data base will be accessible to users via a 10baseT Ethernet local area network (LAN), in order to permit realistic data input to and output from a shared information source. Data base users will gain access to the data base through the use of a user account and password. Each user account will be configured with data file read/write permissions commensurate with the user's data input and/or review capabilities and needs.

To minimize human error, the data base will be programmed to prevent the direct or electronic entry of "nonsensical" data through the use of programmed input masks, validation rules, and referential integrity relationships. Examples of nonsensical data that will be automatically prevented from being entered into the data base include sample receipt dates that are earlier than sample collection dates, analytical information for sample identification numbers that do not exist, two or more different sample receipt dates for the same sample identification number, etc. Time-saving and error-minimizing techniques such as bar code labels/readers, drop-down lists, and auto-expanding fields will be used for keyboard data entry.

Sample collection and sample analysis data will be subjected to error-checking that includes, but is not limited to, out-of-range checks, outlier checks, duplication checks, and missing information checks. All calculations performed within the data base will be verified for accuracy. Appropriate flags will be assigned to data records to indicate any unusual or questionable condition of collection or analysis, and to those data that fall outside specified ranges.

The data base system will generate unique sample identification numbers that will be printed onto bar code labels and affixed to samples collected in the field, ensuring that each sample will be uniquely identified. Chain-of-custody information for each sample will be stored electronically and on signed hard copy chain-of-custody sheets.

The analytical results data will include the core analytical results data tables, corresponding QA/QC analytical data, and any ancillary data relevant to a particular sample type. These tables will be in the proper format such that they may be easily included in THERdbASE, the EPA's web-enabled repository of human exposure data.

The key personnel on the field sampling team will perform the first level of review, ensuring that all data have been validated. Questionnaire data will be validated against data dictionaries that are designed to draw out inconsistencies from the information provided by the respondent. When necessary, respondents will be contacted to explain questionnaire data discrepancies.

The data processing staff will check all collected field data (e.g., questionnaires, data forms, etc.) before they are entered into the data base or shipped to the laboratory for analysis. All paper records and data forms will be checked for completeness and missing information. All open-

ended data items (questions) will be coded and a code book will be developed. After the checks, the data will be entered into a computer data base. In order to produce data of maximum quality, all data will be verified, that is, keyed twice. Two staff members will enter the data into two separate files. A computer program will be developed specifically for checking the accuracy of the entered data. It will crosscheck every record in the two data bases. Any discrepancies will be detected by the verification program and will be corrected by the quality control staff.

Once the data are cleaned of keying errors, a more extensive and complex editing check will follow. An editing computer program will be developed to perform range checks within items; consistency checks among data items, and checks for properly followed routing patterns. The senior project personnel will specify edits performed and review them after completion. The resulting edit report will document the current data values and verify that the records have passed all edit tests. The files will then be ready for data analysis.

Data from the data base will not be released to the public and interested parties until the quality of all data has been verified; the data have been stripped of personal identifiers; and the data have been approved by EPA for public release.

6.0 RECORDS MANAGEMENT

6.1 Records Management System

The records management system establishes policies and standard operating procedures for handling the CTEPP study records. The TOL will determine and modify the system according to the needs of the project. The objectives of the records management system are: (1) to provide CTEPP records that are legible, identifiable, and retrievable; (2) to protect CTEPP records; and (3) to provide historical information needed for reviews, evaluation, and planning future research activities. The CTEPP records covered by the records management system include:

- Contract records
- Procurement records
- Training manuals
- Standard Operating Procedures (SOPs)
- Progress reports/meeting notes
- Field notebooks
- Shipping records
- Chain-of-custody records
- Data collection forms
- Informed consent forms
- Laboratory notebooks
- Sample analyses records
- Data files
- Final Reports.

The above records will be generated in electronic or paper documents. All the records will be clearly identified by a combination of study title, study ID number, participant ID number, and sample ID number. Written instructions and policies will be included in the appropriate SOPs and discussed in training. Sensitive, confidential records (such as participant identification data) will be stored in a locked file room, and the electronic files will be password-protected. Only authorized personnel will be allowed to access the study records. The unique records identification system will provide an efficient indexing system for records retrieval. A records retention policy has been established for the CTEPP records. Details are presented in the following sections.

6.2 Records Identification, Authentication, and Indexing

As described earlier in Section 4.2, all CTEPP data will be clearly identifiable and traceable to the source from which the data were produced by a unique participant ID number and a unique sample ID. Unique field sample ID numbers will be used to identify samples of air, food, dust, soil, urine, hand wipes, floor wipes, PUF roller, and food preparation surface wipes. Study title, study number, and purchase order numbers will be used to identify contract and procurement records. All of the electronic files or paper records will be clearly identified by a combination of study title, study ID number, participant ID number, sample ID number, and the record date.

The records will be sorted numerically for efficient indexing and retrieval. The electronic files will be stored in the main CTEPP folder. Sub-folders will be created and named after relevant project activities for easy retrieval (such as recruitment, field sampling, air samples, dust samples, etc.). Paper records will be stored in file cabinets. Every file folder will be clearly indexed and sorted either numerically or alphabetically for easy retrieval.

Authentication procedures include stamping, initialing, signing, dating, and transmittal statements. For example, all the data collection forms require the field staff's initials on the completed forms. The chain-of-custody records require the field staff as well as laboratory staff's signatures, date of receipt, and a description of the condition of the sample on arrival.

6.3 Records Distribution and Storage

The procedures for data records storage are described in the CTEPP data processing SOPs. All field data, physical forms, study documents, and analysis data will be stored and cataloged for at least three years from the end of the project. They will be stored in secure, dry, and locked storage containers on metal shelving or in metal file cabinets. All electronic data will be saved on "zip" disks, and the disks will be properly labeled and be stored in a secure and locked office. The TOL will retain summary information in the CTEPP study folder regarding records storage conditions, locations, and record tracking sheets. Access to all stored data record records will be controlled.

All field and sample analysis data will be transferred to CTEPP data bases in formats that are consistent with EPA data bases, such as TherdBase. The data bases will be provided to the EPA TOPO in hard copy and electronic form. The EPA TOPO will determine which groups at EPA and other interested parties will receive copies of the data.

6.4 Records Retrieval

The effectiveness and efficiency of records retrieval are determined by the records identification and indexing system. As described earlier, the CTEPP study has developed a comprehensive records identification system, which will ensure an effective and efficient indexing system. As a result, it will permit the efficient retrieval of study records. For example, all the completed data

collection forms will be labeled with participant ID numbers. The forms will be sorted (indexed) and stored in file folders and can be easily retrieved and verified.

6.5 Records Retention

All study records will be maintained in a secure office or storage room for at least three years after completion of the study. Then, the EPA TOPO will determine their ultimate disposition.

7.0 ROUTINE CONTROLS AND PROCEDURES

7.1 Control and Calibration of Measurement and Test Equipment

In general, laboratory checks and equipment calibration will be performed as each piece of equipment is returned from the field and before reuse in the field. Field checks and equipment calibration will be performed by the field technician when the equipment is installed in the field.

The air samplers will be operated at 4 ±0.4 L/min flow rate at each home or day care center sampled. Prior to each field sampling event, the air samplers will be calibrated using a calibrated (NIST-traceable) flow meter. If the flow rate is outside the target range 3.6 - 4.4 L/min, the sampler settings will be adjusted to give a flow rate within this range. At the end of the 48-hr sampling period, the sampler will be checked again to obtain the final flow rate. The initial and final flow rates, along with the sampler ID and sample cartridge ID, will be recorded in the field data logs. The procedures for calibration and field operation of the air samplers are described in the CTEPP SOPs.

The HVS3 vacuum unit will be used to collect house dust samples. The HVS3 will be operated according to the CTEPP SOP, which is based on the manufacturer's instructions and an ASTM standard procedure. The SOP describes the assembly, operation, and cleaning procedures for the HVS3. Briefly, the system is a high powered vacuum cleaner equipped with a sampling nozzle that can be adjusted to a specific static pressure within the nozzle, a cyclone to separate particles of 5 μm mean diameter or larger at a flow rate of 20 cfm (9.5 L/s), and a container to collect the sample.

The GC/MS systems used for sample analyses will be calibrated regularly with the calibration gas FC-43. Mass spectral intensities for FC-43 will be generated and these intensities will be used to verify that the mass tuning of the mass spectrometer has not varied significantly during analysis of the samples. The calibration results and GC/MS maintenance records will be kept in the GC/MS facility record books.

7.2 Procedures

7.2.1 Recruitment Procedures

The goal of the recruitment protocol is to successfully enroll 256 age-eligible children in North Carolina and Ohio (128 per state) into the CTEPP study. The recruitment procedures are illustrated in Figures 7.1, 7.2, and 7.3.

As shown in Figure 7.1, there are several tasks to be completed before the project staff can initiate any contact with potential study participants. Due to the nature of this study, some participants may have concerns about confidentiality. To ease their concerns and encourage participation, we will apply for a certificate of confidentiality from the Department of Health and Human Services. With this certificate, we will be able to give an honest and binding assurance

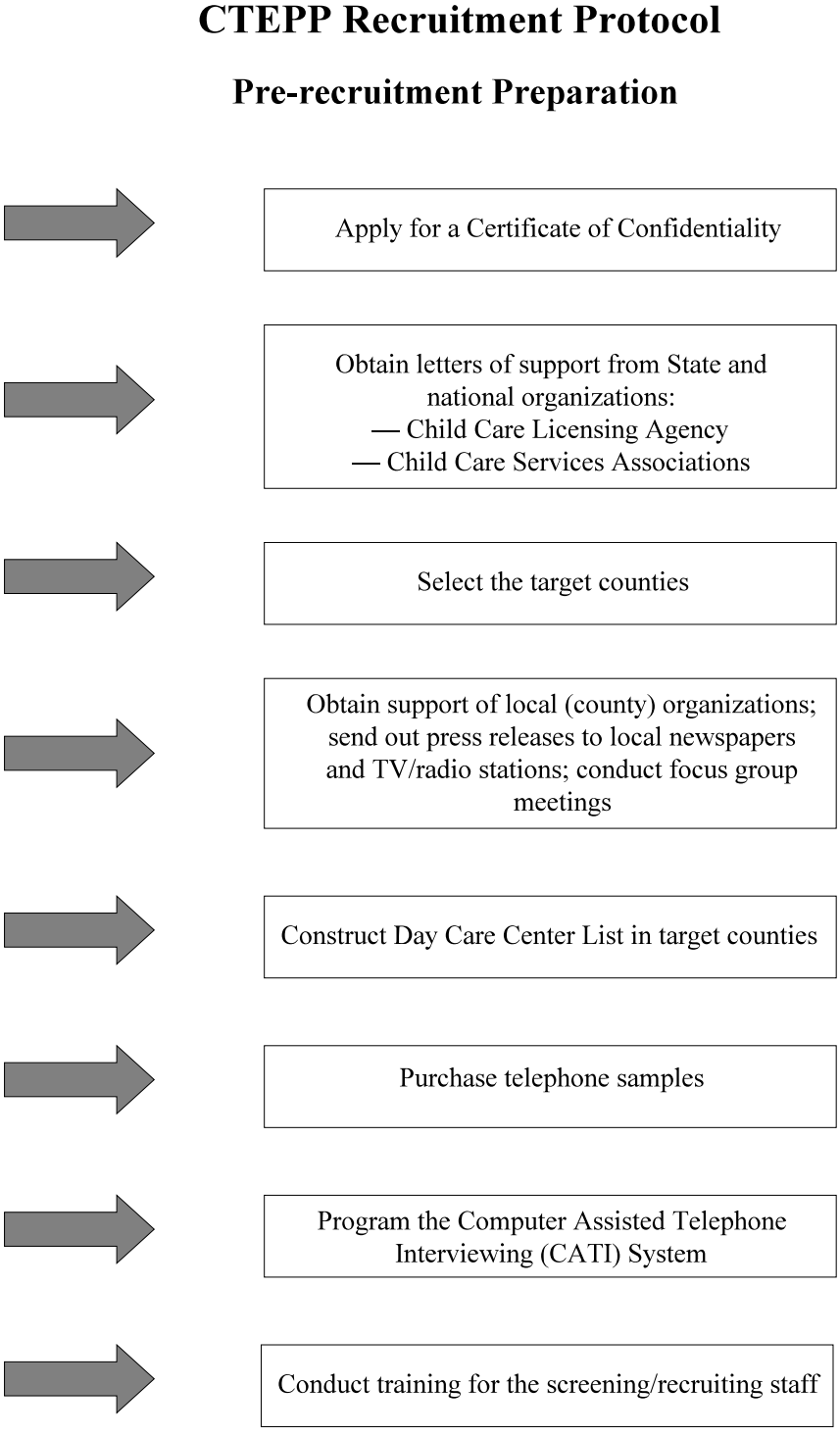

Figure 7.1. Summary of the Overall CTEPP Recruitment Protocol.
(a) Pre-recruitment Preparation

CTEPP Recruitment Protocol

Sample Component: Day Care Centers

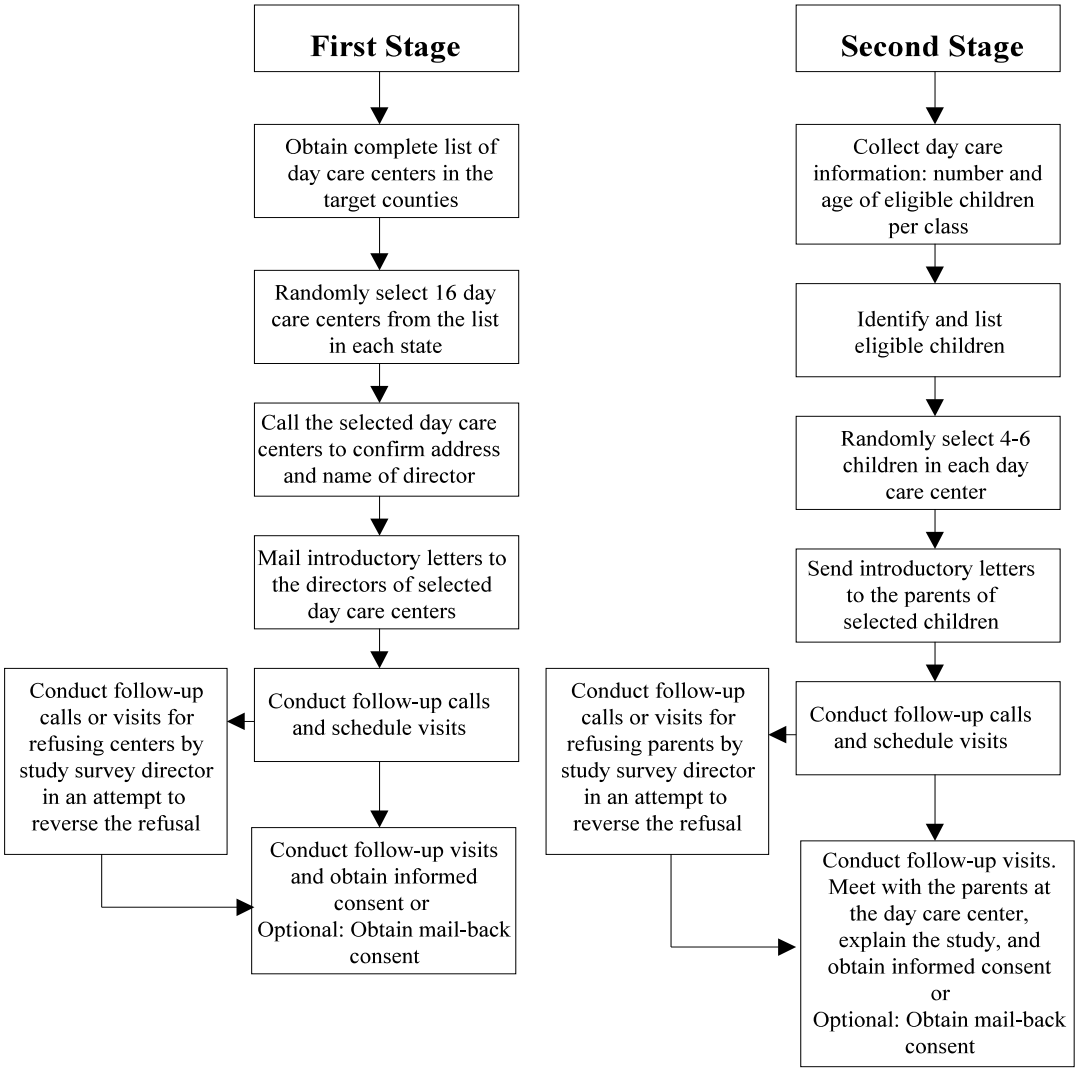

Figure 7.2. Summary of the Overall CTEPP Recruitment Protocol. Day Care Center Component

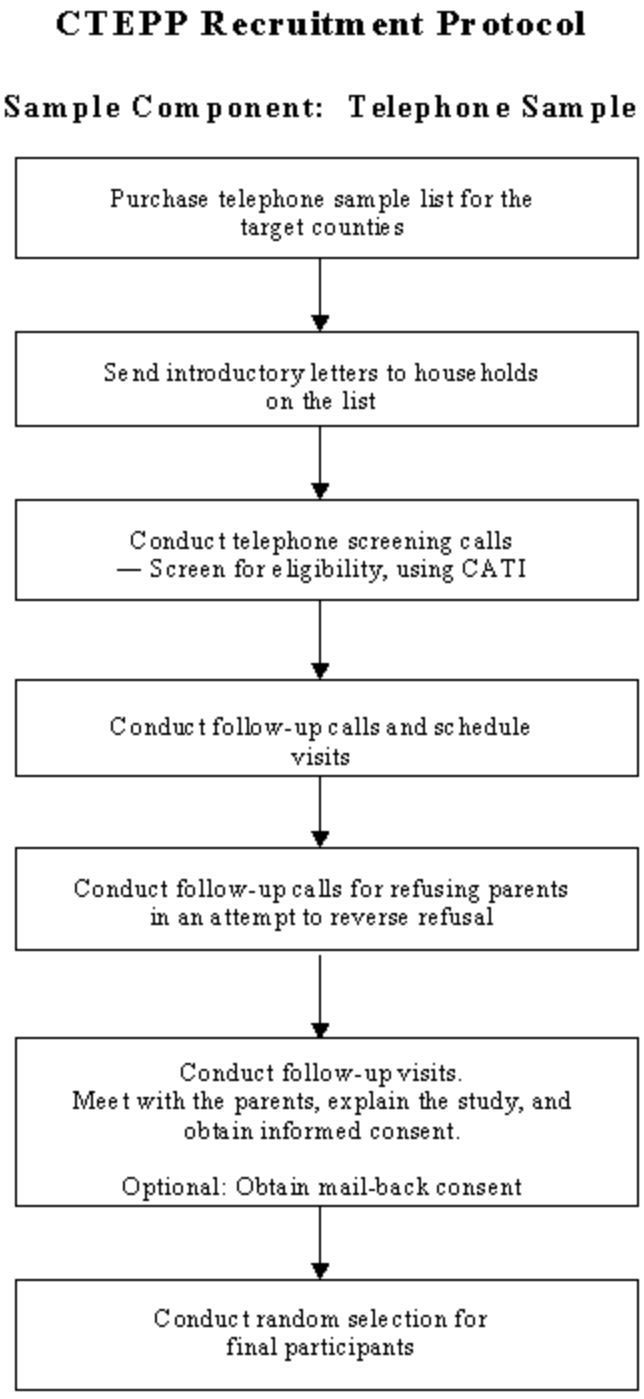

Figure 7.3. Summary of the Overall CTEPP Recruitment Protocol Telephone Sample Component

to study participants that any information they provide will not be disclosed without their consent (Public Health Service Act, 42 U.S.C. 241 (d)). We will ask the state licensing agencies for child care services and national and local child care associations to write a letter of support for the CTEPP study. To further enhance our understanding of the issues on study participation, we plan to invite a small group of potential participants for a focus group discussion. Finally, the project staff will prepare a press release describing the CTEPP study in layman's terms and distribute it to the local newspapers and TV/radio stations in the targeted areas before recruitment starts in order to raise public awareness.

During the pre-recruitment period, our sampling team will collect the latest state/county information and select the target counties in each state according to the sampling plan. Once the target counties are selected, we will contact the state licensing agencies and request a complete list of day care centers. We will also select a professional survey sampling firm and order the telephone sample list. Our programming team will develop the computer-assisted telephone interviewing (CATI) system for telephone screening. Finally, the recruitment/screening team will undergo extensive training. The topics that will be covered during training include study background, standard operating procedures for the CATI, and recruitment scripts.

The procedures for recruiting day care centers are illustrated in Figure 7.2. There are two stages to this phase of recruitment. The objective of the first stage is to enroll day care centers into the study. After we select the six target counties in each state using regional, urbanicity, and income guidelines, we will obtain a complete list of day care centers in each county and sort them by urbanicity and income. From these sorted lists, our sampling team then will randomly select 16 day care centers from each state.

The recruitment/screening team will call each selected day care center to confirm the address and name of the day care director. Once the address and name are confirmed, we will send an introductory letter and letters of support to each day care center director. To generate interest and raise the attention of the day care directors, the letters may be mailed using Federal Express or certified mail. About 2-3 days after the mailing of the letters, our senior project staff will make follow-up calls to each day care center director. As part of the effort to ensure participation of each center, we may also include follow-up visits to the center and direct contact by the Battelle TOL or the EPA TOPO. Finally, to complete the first stage recruitment activities, the project staff will obtain informed consent from each day care center.

The second stage recruitment activities begin with the collection of the day care center information on the number of age-eligible children in each classroom. The first names or initials of all age-eligible children will be obtained and a random number will be assigned to each child. Our sampling team will randomly select four to six children from each day care center.

Following the selection of the children, we will ask the day care director to distribute the introductory letters and letters of support to the parents of the selected children. In consultation with the day care center director, our project staff will set up appropriate times to meet with the parents at the day care center two to three days after the letters are sent to the parents.

During the initial meeting with the parents, our project staff will establish rapport with the parents and the child by giving a small gift to the child (e.g., a book, small toy, etc.). We will also emphasize the positive experience of the pilot study participants. Finally, we will obtain informed consent from the parents and ask the parents to complete the Recruitment Survey (Form #1). An initial sampling date will also be scheduled with each family.

The procedures for recruiting households by telephone sampling are illustrated in Figure 7.3. As soon as the target counties are selected, we will purchase a telephone sample list from a professional survey sampling firm. The list of sample households will include addresses, which we will use to send introductory letters prior to making the initial telephone contacts. The letters will be mailed in batches. Follow-up calls will begin about five days after the mailing of the letters. Standardized telephone scripts will be used. A CATI system will be developed to facilitate the recruitment process.

The initial telephone contact will include screening and a brief interview. To ensure participation of each eligible family, we will also include a follow-up visit and multiple follow-up calls. We expect to enroll more than 64 eligible telephone sample households in each state. The final participants will be randomly selected from all households that are willing to participate.

7.2.2 Surveys/Questionnaires

Standardized questionnaires and other data collection materials will be used by both field stations in NC and OH. Information needed to interpret the results of the chemical analyses will be collected through survey instruments that were developed for, and used in, the pilot studies [W1, W2, W6, W7, C10, C12, C13], and later modified for the CTEPP study. Statistical analyses will be performed to examine the association between personal/household information and measured pollutant concentrations.

Extensive information on housing characteristics will be obtained, including details on home interior, exterior, location, GPS coordinates, and surrounding areas. Each subject's age, weight, gender, and race or ethnicity will be recorded. The questionnaire includes questions regarding pesticide use, smoking habits, heating, cooking, and cleaning activities, income/education level of the household, and other information relevant to understanding the chemical measures, such as carpet and hard-surface floor area, location of residence and school, size of residence etc. Additionally, an activity log for the child and the adult, a diary of the foods eaten during the sampling period, and food logs or menus for the one month preceding sampling will be collected. Because active children breathe more, eat more, and move around more than those who are passive in a possibly polluted environment, the activity logs will include classification of the level of the child's activity.

Because the above information may include some sensitive information, or information that could conceivably be used to identify individual subjects, it is necessary to protect the privacy of the participants. A Certificate of Confidentiality will be obtained to protect the information from involuntary release. Additionally, researchers will not disclose any study information that can be

associated with individual participants without the participants' consent, and study data will be coded into the data base without individual identifying information.

7.2.3 Survey Instruments

Survey data will be collected by having field interviewers administer questionnaires and by having participants fill out questionnaires themselves. During training, field interviewers will learn what data are to be collected at each step, as well as what they must provide to the respondent for each questionnaire they complete. Each questionnaire and data sheet used in the collection will be labeled with a unique participant identification number. This number will link each data item to the respondent, and will be the only link to analytical data sets created.

The field interviewers will administer the pre- and post-monitoring questionnaires to both parents/caregivers and day care center teachers. All four surveys will consist of pre-coded, closed-ended questions that are designed to reduce the respondent burden and simplify the post processing and data reduction efforts. The field interviewers will train the respondents to correctly complete the child activity diary. The respondents will complete this document during the 48-hour sampling period. Data formats are simple, requiring minimal effort on the part of the respondent, and allow the monitoring team to quickly review the data and provide feedback to the respondent about missing items.

The monitoring team will complete the house/building characteristics observation survey. Respondents will be trained to collect food, urine, and hand-wipe samples. Personal and environmental samples will be collected and analyzed according to specific protocols. The procedures for subject recruitment are described in several subject recruitment SOPs (CTEPP SOP-1.1 to -1.5).

7.2.4 Sampling Methodology

For the CTEPP study, the media sampled will be indoor and outdoor air, house and classroom dust, play area soil, solid and liquid food, drinking water, hand and forearm skin surface, urine, hard-floor surface wipes, and wipes of the most-used food preparation surface. Dislodgeable residues will be collected using a polyurethane foam (PUF) roller in those households that have had pesticide applications indoors or outdoors in the seven days prior to sampling.

- *Indoor and outdoor air samples* will be collected by continuous sampling over 48 hours at 4 L/min, using a URG (University Research Glassware, Chapel Hill, NC) sampler with a 10 μm inlet and a cartridge containing a quartz fiber filter and XAD-2 resin or PUF [R3] in series.
- *Soil and dust samples* will be obtained at the conclusion of each 48-hour sampling period. Dust samples will be collected in the room that the child uses most, using an HVS3 vacuum sampler (Cascade Stack Sampling Systems, Bend OR) [L1, R3]. Participants will also be asked to donate a used vacuum cleaner bag containing the floor dust collected during the month prior to sampling. This will

be used to compare the spot dust sampling results with results for dust integrated over the entire dwelling for a longer period of time. Soil samples will be collected by scraping up the top 0.5 cm of soil in a 0.095 m^2 (1 ft^2) area in the middle of the child's play area [L1]. Dislodgeable residues will be collected using a PUF roller in those households that have had pesticide applications indoors or outdoors in the seven days prior to sampling.

- *Diet samples* will be obtained by the duplicate plate method [F1, N3], collecting duplicate servings of all foods that the child is served over the two-day period. In the post-monitoring visit, the caregiver will be asked to describe the food sample contents and confirm the food diary information. Solid food, liquid food, and drinking water will be collected separately in glass containers to avoid phthalate ester contamination likely with some food storage containers.
- *Hand wipe samples* will be collected prior to participants' washing their hands, just before lunch and just before supper on each of two days [G1]. The project staff will also measure the hand wipe surface area and record the information on the data form.
- *Urine samples* will be approximate 48-hour collections, collected as spot urine samples accumulated over the two-day sampling period. If the household has applied pesticides in the preceding seven days, the spot urine samples will be analyzed separately. Otherwise, the urine samples will be combined for each 48-hour period. Sampling methods are described in detail elsewhere [C10, C13, T2, W1, W2, W6, W7].
- *Hard-floor (smooth) surface wipes* will be collected in the area that is designated by the teacher or parent as the area where the child is most likely to spend time. Food preparation surface wipe samples will be collected from the most-used food preparation surface area.

Approximately 10% of the children will be videotaped by EPA/NERL staff for 3-4 hours each during the second day or the third day of the sampling period to supplement the activity logs. Subsequent videotape analysis and interpretation will be done by NERL staff, using published methods (F1, G2, L6, Z3). All field sampling procedures are described in field sampling SOPs (CTEPP SOP- 2.1 to -2.29).

7.2.5 Analytical Methods

Targeted chemicals for the CTEPP study include members of several compound classes: polycyclic aromatic hydrocarbons; phthalate esters; organochlorine, organophosphate, carbamate, triazine, and pyrethroid pesticides; phenols; acid herbicides; and polychlorinated biphenyls. Table 7.1. summarizes the target compounds and the reasons for their selection.

Methods for the chemical analysis of the targeted chemicals in the environmental and biological media of interest were developed previously and are available for use in this research [C10, C12, C13, H3, N5, N7, S4, S5]. These methods are summarized in Table 7.2.

Table 7.1. Targeted Chemicals

Target Compounds	Reason for Selection
Four-ring and larger polycyclic aromatic hydrocarbons (PAH), including benzo[a]pyrene*	Some probable human carcinogens (B2 Carcinogens), possible endocrine disrupters Ubiquitous combustion products
Butylbenzyl* and di-n-butyl phthalate	Possible endocrine disrupters, possible carcinogens Widely used plasticizers
Pentachlorophenol,* nonylphenols,* and bisphenol-A	Possible endocrine disrupters, teratogens, carcinogens Widely used wood preservative and pesticides; surfactants; plasticizers; Bisphenol-A in polycarbonate plastics, baby bottles, dental sealants, and coatings, US 1.6B lb/yr
Organochlorine pesticides: lindane,* aldrin,† α- and γ-chlordane,* DDT,*† DDE,*† dieldrin,† endrin,† and heptachlor†; pentachloronitrobenzene	Possible endocrine disrupters, toxicity, neurotoxicity, possible developmental neurotoxicity, some probable carcinogens Former widespread use, both indoors and outdoors; some still approved for specific uses, e.g. lindane in head lice shampoos
Penta-, hexa-, and hepta-chlorinated biphenyls (PCBs)*†	Possible endocrine disrupters, possible developmental neurotoxicity; coplanar PCBs are possible carcinogens Former widespread industrial use
Organophosphorus pesticides: diazinon, chlorpyrifos*	Possible endocrine disrupters, cholinesterase inhibitors Household insecticides, may persist indoors Dietary residues common
Acid herbicides: 2,4-diphenoxyacetic acid (2,4-D), dicamba, 2,4,5-T	Possible endocrine disrupters Home lawn herbicides
Triazine pesticide: atrazine	Carcinogenicity, possible endocrine disrupter Found extensively in drinking water in the midwest US
Carbamate pesticide: propoxur, bendiocarb	Neurotoxicity, possible endocrine disrupter
Pyrethrin pesticide: cis/trans permethrins, cyfluthrin	Neurotoxicity, possible endocrine disrupter
Urinary metabolites: pentachlorophenol; 2,4-D; chlorpyrifos metabolites trichloropyridinol (TCP); diazinon metabolite IMP; PAH metabolites, hydroxypyrene and other hydroxy-PAH; and permethrin metabolites, 3-phenoxybenzoic acid (3-PBA)	Improve exposure and dose estimates

* Denotes a compound or compound class currently under study as environmental potential endocrine disrupters in the Neuse River Basin, in cooperation between EPA/NERL, U.S. Geological Survey, EPA/National Human and Ecological Effects Laboratory (EPA/NHEERL), and North Carolina State University.

† Chemicals among those currently under consideration by approximately 120 nations for world-wide phase-out of production and use.

Table 7.2. Analysis Methods for the Targeted Chemicals

Medium	Targeted Chemicals	Summary of Method
Air	PAH, PCB, phenols (but not PCP), phthalates, organochlorine and organophosphate pesticides, pyrethrin pesticides, triazine pesticide, carbamate pesticide	Extract with dichloromethane, GC/MS analysis.
	Acid herbicides* and PCP (Requires dedicated sample)	Soxhlet extract with acetonitrile, split sample extract for silyation and methylate, GC/MS analysis.
Dust and Soil	PAH, PCB, phenols (but not PCP), phthalates, organochlorine and organophosphate pesticides, pyrethrin pesticides triazine pesticide, carbamate pesticide	Sonicate with 10% diethyl ether in hexane, Florisil SPE clean-up, GC/MS analysis.
	Acid herbicides	Acceleration solvent extraction (ASE) with acetone, clean-up, split sample extract for silyation and methylate, GC/MS analysis.
Drinking Water	Triazine pesticide	C18 SPE, GC/MS analysis.
Solid Food	PAH, PCB, phthalates, phenols, organochlorine and organophosphate pesticides, pyrethrin pesticides	Acceleration solvent extraction (ASE) with DCM, GPC clean-up, Florisil SPE clean-up, if needed, GC/MS analysis.
	Acid herbicides, PCP, 3,5,6-TCP, IMP	Acceleration solvent extraction (ASE) with methanol or liquid-liquid partitioning, clean-up, split sample extract for silyation and methylate, GC/MS analysis.
Liquid Food	PAH, PCB, phthalates, phenols, organochlorine and organophosphate pesticides, pyrethrin pesticides	Acceleration solvent extraction (ASE) with DCM, GPC clean-up, Florisil SPE clean-up, if needed, GC/MS analysis.
	Acid herbicides, PCP, 3,5,6-TCP, IMP	Acceleration solvent extraction (ASE) with methanol or liquid-liquid partitioning, clean-up, split sample extract for silyation and methylate, GC/MS analysis.
Wipes	PAH, PCB, phthalates, phenols, organochlorine and organophosphate pesticides, pyrethrin pesticides, triazine pesticide, carbamate pesticide	Soxhlet Extract with dichloromethane, Florisil SPE clean-up if needed, GC/MS analysis.
	Acid herbicides, PCP, 3,5,6-TCP, IMP	Acceleration solvent extraction (ASE) with acetonitrile, split sample extract for silyation and methylate, GC/MS analysis.
Urine	Hydroxy-PAH, PCP, 2,4-D, 3,5,6-TCP, and IMP	Hydrolysis, extraction, methylation and or silyation, Florisil SPE clean-up, GC/MS analysis.

* Acid herbicides include 2,4-D, 2,4,5-T, and dicamba.

The analytical laboratory will receive the samples and maintain sample custody records. The laboratory will provide completed sample custody records to EPA when analysis data for each sample are transmitted. Each analytical laboratory within Battelle will provide internal quality control and quality assurance, as specified in analytical protocols or SOPs (CTEPP-SOP-5.10 to -5.24). Sample analysis data will be electronically transferred into the appropriate data bases.

7.2.6 Calculation of Potential Daily Exposure

The exposure concentrations in the various media, along with activity patterns, dietary patterns, and various physiological and body size parameters will be combined using the EPA microenvironmental exposure model [E2] to derive estimates of daily exposures through the various pathways: inhalation, dietary and nondietary ingestion, and dermal absorption. The EPA microenvironmental exposure model is presented below.

The model converts exposure values (ng/day) for inhalation and ingestion (dietary and nondietary) to units of maximum potential (internal) dose by assuming 100% absorption in the lung and digestive tract and normalizing for body mass. Various factors can be found in the literature to account for physical, chemical, and/or physiological processes. For maximum estimates, this conversion gives upper limits on the amount of a pollutant available for delivery to target organs. In subsequent refinements of the exposure estimates, literature absorption factors for the targeted compounds will be used as they become available.

The potential daily dose of a target compound in ng/kg body mass per day will be estimated using the following equations, which together comprise the most commonly used micro-environmental exposure model (MEM):

$$D_{inh} = \frac{C_i * t_i + C_o * t_o}{t_i + t_o} * \frac{V}{W}$$

$$D_d = \frac{C_f * M_f * 1000}{W}$$

$$D_n = \frac{t_i * D_i + t_o * P_o}{t_i + t_o} * \frac{M \times 1000}{W}$$

where

D_{inh} = the estimated daily dose through inhalation, ng/kg/day
D_n = the estimated daily dose through nondietary exposure, ng/kg/day
D_d = the estimated daily dose through dietary exposure, ng/kg/day
W = the body weight of the subject, kg
C_i = indoor air concentration, ng/m^3
C_o = outdoor air concentration, ng/m^3
t_i = subject's time spent indoors, min
t_o = subject's time spent outdoors, min
V = subject's estimated daily ventilation rate, 15 or 20 m^3/day
D_i = target compound concentration in the floor dust, µg/g
P_o = target compound concentration in the play area soil, µg/g
M = subject's estimated daily dust/soil intake, 0.06 or 0.1 g/day
C_f = target compound concentration in the daily food samples, µg/kg/day
M_f = the daily mass of food intake, kg/day

For those target compounds that are likely to be absorbed through the skin surface, an additional increment to the total daily exposure may occur. As a first approximation, this can be estimated as:

$$D_{derm}=M_w \text{ x } A_{exp} / A_w \; F_{derm} / W$$

where

D_{derm} = the estimated daily dose through dermal absorption, ng/day
M_w = the mass of a target compound in the wipe sample, ng
A_{exp} = the exposed skin surface of the subject, m^2
A_w = the area of the skin from which the wipe sample was taken, m^2
F_{derm} = the fraction of the compound that can be absorbed through the skin.

Although exposure factors for children and adults are available in the literature for inhalation and soil ingestion [E2, B3, S3], and for dermal absorption of some compounds, there are uncertainties in these factors, which are especially large for the dermal and nondietary ingestion routes of exposure. It is commonly assumed that the ventilation rate is 20 m^3/day for adults and 15 m^3/day for children [B3, O6], and that the dust/soil ingestion rate is 0.06 g/day for adults and 0.1 g/day for children [L1, S3]. These factors will be used in the initial model. As refined estimates become available, they will be incorporated into the model.

The results of applying the potential daily dose model discussed above will be a vector of estimated daily component intake doses (ng/kg/day) for each subject via inhalation, dietary ingestion, nondietary ingestion, and dermal. The overall daily total dose is the sum of these component doses.

All of the target pollutant concentrations in multiple sample media (air, dust, soil, food, and wipe), activity patterns, food and beverage intake profiles, and physiological parameters specified

in the microenvironmental exposure model will be determined for each child in the study. Thus the comparisons of the children's total potential doses or component potential doses across pathways or across strata will be carried out based on the totality of pathways considered in the microenvironmental exposure model, namely inhalation of indoor and outdoor air, non-dietary ingestion from dust and soil through hand-to-mouth activity, dietary exposure, and dermal exposure through contact with the floor or other surfaces.

The comparisons of potential dose between children and their caregivers will also be addressed. In the households where the adult caregivers stay at home with the children (half the adults sampled, about 128), virtually the same suite of measurements and characteristics will be determined for the adults as for the children. This includes the target pollutant concentrations determined in the various media, food and beverage profile diaries, and urine biomarkers. The determinations for the caregivers are made with the same frequency and at the same times of day as for the children. The only difference in data collection is that activity profiles for the children are recorded in activity diaries, whereas those for adults are assessed in post-monitoring interviews. In the households where the child attends day care and the caregiver works outside the home during the day, the caregivers' activities, exposure, diet, and urine biomarkers are measured when the caregivers are at home, but not during the portion of the day when they are at work. The daily exposure information must thus be interpreted as the portion of exposure that can be attributed to the residential environment.

Therefore comparisons between exposures to children and their caregivers will be made separately within the day care and stay-at-home strata. The comparisons can be made based on the full set of media-specific responses, but for those adults who work outside the home, their exposures are interpreted as the residential component.

7.2.7 Adjustments for Cluster Sampling

The day care center portion of the sample selection will be based on a two-stage cluster sample. The sample size estimates are based on the assumption of 14 participating day care centers per state. From these 14 day care centers the 64 day care children within each state will be sampled (an average of 4.6 children per participating center). Each day care center may be considered a cluster, so the children sampled from the same day care center would be anticipated to have correlated responses. A substantial portion of the children's 24-hour daily exposures is obtained from the same day care center. The indoor and outdoor air concentrations, food concentrations, floor sample concentrations, and play soil concentrations obtained at the day care center would be the same for all these children. Furthermore, children attending the same day care center may live near each other and share similar living conditions. This would lead to correlated target compound concentrations at home.

The correlation in response among children in the same day care center will be estimated by incorporating day care center as a random effect in the analysis of variance model. This will lead to two components of variance, σ^2_{adc} and σ^2_{e}. The variance component σ^2_{adc} corresponds to

variation among day care centers. The variance component σ^2_e corresponds to the variance within day care centers. The correlation between two responses in the same day care center is $\rho = \sigma^2_{adc} / (\sigma^2_{adc} + \sigma^2_e)$. The correlation reflects the cluster design effects and will be incorporated into the analyses. Separate values of ρ will be calculated for each response and each target compound.
The analysis of variance model will also include the systematic factors (state, urban vs. rural, low vs. middle/upper income, day care vs. no day care) and possibly other important covariates that may be selected based on statistical criteria such as a step-wise regression procedure. Note that while a factor for state will be included in the model, no comparison between the two states will be performed. If results of the comparisons between urban and rural, low-income and middle/upper income, and/or day care and non-day-care are found to rely on the state, these comparisons will be made for each state separately.

7.2.8 Survey Weights and Weight Adjustments

Most of the statistical analyses will use weighted survey data. However, unweighted data will be used for the model development and validation parts of the analyses directed at analytical, model-based inferences rather than population-based inferences.

Survey weights will account for unequal sampling probabilities and reduce potential biases due to nonresponse. Sampling weights are needed for unbiased estimation under the sampling design. Nonresponse adjustments will force estimates based on participating children, for key characteristics, to match those of the entire sample or the entire universe of eligible children.

The first step in weighting the data is the computation of sampling weights that account for the varying probabilities of selection for different subgroups of children. Sampling weights will be computed separately for the two sample components (or frames). In each component, the probabilities of selection will be unequal due to stratification and disproportionate sampling (i.e., oversampling of certain strata). In addition, the day care sample weights may also need to reflect selection with probabilities proportional to size (PPS), a method that may be used for the first-stage sample of centers. Sampling weights will be computed as the reciprocal of the probabilities of selection at each sampling stage, and assigned to sample day care centers and children. The weights assigned to participating children will also be assigned to their parents and households. These weights will be used in analyses of measurement data collected on a parent- or household-level.

The next step in weighting consists of non-response adjustments. We plan to use weighting class (and/or post-stratification) adjustments that make use of class totals known either on a frame basis, that is, population cell totals; or on a sample basis, that is, for non-participating as well as for participating households. For example, weighting classes may be based on design strata, such as counties/states, income groupings and rural versus urban. Non-response adjustments, designed to reduce the potential bias of non-response, will force the weights for responding households to sum to known population totals within each cell (post-stratum, or weighting class).

7.2.9 Descriptive Statistics

Mean values and corresponding standard errors will be presented for each stratification factor level (for example, urban, middle/upper income) and for pairs of factors (for example, urban and middle/upper income), averaged over the remaining factors. The sample means will be weighted averages, using the survey weights as discussed in Section 7.2.8. Thus the sample averages will estimate the population averages within each stratum or combination of strata. The standard error estimate will account for the survey weights assigned to each observation, as well as the correlation among responses for children who attend the same day care center. Children who do not attend day care centers provide independent responses. Weighted averages will be based on the logarithms of the responses. Confidence intervals will be calculated about the logarithmic mean under the assumption that the weighted averages are approximately normally distributed. The weighted averages and associated confidence bounds will then be exponentiated to provide inferences in the domain of physical relevance.

7.2.10 Comparisons to Satisfy Primary Analysis Objective

The primary analysis objective is to compare estimated total exposure across one stratum at a time (except for state), averaging across the remaining strata, for example, total exposure for low income compared to total exposure for middle/upper income, averaging across urbanicity, and day care attendance status. Comparisons to satisfy the objective will be based on the doses calculated using the microenvironmental exposure model. A test of hypothesis of equality of average total doses between the two levels within the stratum will be carried out by comparing weighted averages and corresponding standard errors, using a two-sample, two-tailed t-test. If the goodness-of-fit test for normality and the normal probability plot based on the logarithmic transforms of the responses do not show serious departures from normal distribution assumptions, the comparison between levels will be based on weighted averages of the logarithmic responses within each stratum level and associated standard errors. The standard error calculation will account for weighting and for the correlated responses among children who attend the same day care center. If serious departures from normal distribution assumptions occur, the t-test comparisons between average values in the stratum levels will be based on a weighted mean of ranked responses within each stratum level and associated standard errors. The weights will be the same as those used with the logarithmic transformation, namely the survey weights. The estimated correlation among the children who attend the same day care center will need to be re-estimated, based on the rank transformation data.

Significance levels of the t-tests will be reported. If the t-test is based on the logarithmically transformed responses, the exponentiated mean difference (i.e., ratio of geometric means) and associated 95 percent two-sided t-statistic confidence interval bounds will be reported. If the t-test is based on rank transformed responses, only the exponentiated weighted logarithmic mean difference (i.e., ratio of geometric means) will be reported.

7.2.11 Comparisons to Satisfy Secondary Analysis Objectives

Secondary objectives pertain to comparing the components of total dose by pathway. This entails comparing the components of dose to one another, averaging across all the strata or assessing the interaction between components of dose and stratum level. For example, comparing the ratio of dose attributable to dietary ingestion with that attributable to nondietary ingestion, either averaged across all the strata or else comparing the ratio between rural and urban children.

Such comparisons will be carried out in a similar fashion to the primary comparisons. Let D_i, D_j denote the i^{th} and j^{th} pathway specific component of dose respectively, or alternatively let D_j denote the total dose, summed across pathways. Let $R_{ij} = D_i/D_j$, the ratio of D_i to D_j. If D_i and D_j are each approximately normally distributed and R_{ij} ranges from 0 to ∞, then X_{ij} may be approximately normally distributed. Suppose R_{ij} is bounded from above by u (e.g. if $D_j = D_{TOT}$ then u=1). In that event, transform R to $X = \log(\frac{R}{u-R})$. Then $-\infty < X < \infty$ and X may be more nearly normally distributed than is R. We will calculate a weighted average of the X's (if the X's are approximately normally distributed) or of the signed ranks of the X's (if the X's depart from normality) across the factor combinations. The weights will be the survey weights, as discussed in the section on weight adjustments. The standard error calculation will reflect the survey weights, as well as the correlation among the X's (or the signed ranks of the X's) for the children who are attending the same day care center. We will also calculate a two-sided t-statistic-based confidence interval based on the weighted average and its associated standard error. The transformation on the weighted average and on the upper and lower confidence bounds will be inverted to obtain an estimate of the weighted mean of the R's and associated confidence bounds in a physically meaningful scale.

For inferences about the two-factor interactions between relative doses in different exposure pathways and strata, we will compare the ratios of external pathway specific doses among strata. Let $R_{ij} \equiv D_i/D_j$ be as defined above. We wish to compare the average value of the R_{ij}'s between two strata. For example we may wish to compare the ratio of dietary dose to total dose between low income and middle/upper income children. We proceed as above, for the primary analysis objective, either parametrically or non-parametrically, depending on the approximate normality of $X_{ij} = \log(\frac{R_{ij}}{1 - R_{ij}})$. We calculate the weighted averages within each stratum, using survey weights as discussed above, and the corresponding standard errors of the mean. To compare the ratio of dietary external dose to total external dose between low income and middle/upper income children, we test the hypothesis H_0: $\mu_{lo} = \mu_{mu}$ versus H_1: $\mu_{lo} \neq \mu_{mu}$, where μ_{lo} and μ_{mu} are the population means of the X_{ij} within each stratum, by two-sample, two-sided t-tests.

7.2.12 Uses of CTEPP Data to Evaluate and Refine Currently Available Exposure Models

The CTEPP data set will include data from 256 children and their caregivers pertaining to concentrations of target compounds in indoor and outdoor air, dust, soil, and handwipe concentrations, food, beverage, and drinking water concentrations, activity diaries, food diaries,

and physiological information. These data used in combination can provide information to evaluate the performance of existing exposure models and to extend current exposure models to facilitate their more common use, and with a markedly reduced input data burden. Several examples of such applications of the CTEPP data are presented below.

Evaluate the EPA/OPP DEEM Dietary Exposure Evaluation Model. Each child's food concentration of each target compound may be estimated using the food consumption diaries and the EPA/OPP DEEM model. The predicted dietary residue concentrations can be directly compared to the measured concentration levels in the food, based on the duplicate plate analysis. It will be determined whether the results are significantly different. The questionnaire data can be used to determine whether are there environmental or home factors, such as cooking, washing and other practices that influence the residue levels found in the food samples. The questionnaire data can also be used to determine if the differences between observed and predicted levels vary by socio-economic status (SES) , housing, or measured indoor/outdoor environmental conditions. These and other similar questions will be addressed using the CTEPP measurements or the questionnaire and survey data. Deviations between the DEEM model and the measured dietary concentration data can be used to refine the model.

Extend the EPA Microenvironmental Exposure Model. The EPA microenvironmental exposure model that is discussed in this section requires extensive monitoring inputs, both indoors and outdoors, personal activities, and detailed food consumption data. The CTEPP data set can be used to determine relations between indoor air and dust concentrations and outdoor concentrations which are much simpler and less costly to obtain, as well as activity patterns in the house. Potential models include:

$$C_I = \beta_o + \beta_1 PUA_7 + \beta_2 PUA_{14} + \beta_3 PUA_{30} + \beta_4 C_o + \beta_5 FREQ + \beta_6 PETS + \beta_7 FANS + \beta_8 AC + \beta_9 CLEAN + \beta_{10} COOKING + \beta_{11} INDSOURCES + ERROR$$

$$C_I = \beta_o + \beta_1 PUA_7 + \beta_2 PUA_{14} + \beta_3 PUA_{30} + \beta_4 C_o FREQ + \frac{1}{FREQ} \times \sum \beta_i X_i + ERROR$$

$C_h = \beta_o + \beta_1 f_s C_s + \beta_2 f_d C_d + ERROR$
where, (fs, fd = period of outdoor soil or indoor floor/surface dust contact time)

$$C_h = \beta_o + \beta_1 IDE_s C_s + \beta_2 IDE_d C_d + ERROR$$

$$C_d = \beta_o + \beta_1 C_s + ERROR$$

$$C_d = \beta_o + \frac{\beta_1 C_s}{FREQ} \times CLEAN + ERROR$$

These models relate indoor concentration values to outdoor concentrations and activity based variables. Incorporation of these relations into the microenvironmental model will simplify the burden of data collection considerably. An index of dermal exposure (IDE) will be calculated

using the reported level of the child's activity (high, medium, or low) in connection with potential contact with contaminated surfaces based on diary and/or videotape data. IDE scores will range at the minimum from 0 to 3, more likely from 0 to 6 depending on the range and type of activities noted or observed. Likewise, we will define an incidental ingestion exposure (IIE) score based on reported hand-to-mouth and object-to-mouth activities. A number of these variables will be used as class (indicator) or interaction variables in the predicted regression models. Pesticide use (PU) information will be coded by type and application history. Most recent application within a week will be denoted by the variable PU_7. Earlier applications more than a week but less than 2 weeks ago, and more than a month ago, will be denoted by the variables PU_{14} and PU_{30}, respectively. These variables will be used in the models. We define:

C_I	Indoor air concentration
C_o	Outdoor air concentration
C_d	Indoor dust concentration
C_s	Outdoor soil concentration
C_h	Handwipe concentration
FREQ	Frequency of window and door openings
PETS	Presence of pets in home (0, 1)
FANS	Use of ceiling fans (0, 1)
COOKING	Cooking source and type (0, 1, 2,...)
AC	Use of central air-conditioning and type (0, 1, 2,..)
INDSOURCE	Potential other non-cooking indoor sources
CLEAN	High, low, average amounts of cleaning activities or measures (e.g., doormats, shoes removed indoors, etc.)
PUA	PU x Area of pesticide applied

Evaluate Physical Dermal Exposure and Dose Models. Physical and mechanistic models of dermal exposure will be developed using the concentrations obtained in the CTEPP study and transfer coefficients (TC) either derived from the results of the CTEPP study or presently available either in the literature or in EPA Office of Pesticide Programs (EPA/OPP) SOPs. With CTEPP data we, therefore, have the opportunity of either: (1) developing these physical models, or (2) evaluating the models against the exposure data generated directly or indirectly during the study. Some examples of these model applications and evaluations are listed below. Note that the superscript "p" refers to predicted and "m" refers to measured exposure (E) or dose (D). ED donates exposure duration and C refers to dislodgeable surface or carpet concentrations. Again, time lags are denoted by subscripts. Since a multiplicative model is used in the prediction of dermal exposures, log transforms will be used to convert these equations to an additive regression model form.

$$E^p_{derm} = C \times TC \times ED \text{ (predicted dermal exposure or potential dose)}$$

$$C_h = \beta o + \beta_1 \ln C_d + \beta_2 \ln TC + \beta_3 ED + ERROR$$

$$D^m = D_{air} + D_{food/water} + D_{non\text{-}diet} + D_{dermal}$$

$$E^{m}_{dermal} = \alpha_{PBPK} (D^{m} - D_{air} - D_{food/water} - D_{non\text{-}diet})$$

where α_{PBPK} is the coefficient or function based on pharmacokinetic (PK) or physiologically-based pharmacokinetic (PBPK) modeling relating exposure to dose, and vice-versa.

$$D_{non\text{-}diet} = C_d \times IIE_d \times K_d + C_s \times IIE_s \times K_s$$

where K_s and K_d are the incidental soil or dust ingestion estimates used in the equations described earlier or obtained from literature.

$$\ln E^{m}_{dermal} = \beta_o + \beta_1 \ln C + \beta_2 \ln TC + \beta_3 ED + ERROR$$

Consequently, we can estimate TC also from:

$$TC = \exp(\ln E^{m}_{dermal} - \ln C - \ln ED)$$

or

$$TC = \exp(\ln C_h - \ln C - \ln ED)$$

Other pesticide application time lag models may be considered if these models prove to have acceptable predictive power.

Compare Exposures and Urinary Biomarker Data. Predicted total exposure/potential dose will be compared statistically to measured urinary biomarker data in order to evaluate the predictive power of the exposure models developed. Biological dose will be estimated using a PK-based average absorption and metabolic conversion rate, as well as in a few cases direct application of a PK model to the estimated exposure/dose profile (e.g., modeling trichloropyridinol (TCP) concentrations in urine associated with multimedia exposures to chlorpyrifos). Predicted route and pathway-specific exposures will be contrasted as well as summed over to estimate total potential exposures by different study sub-groups. Biomarker measurements will also be correlated with other behavioral and home and day care potential exposure factors. Use of pesticides in homes and day care centers, proximity to busy roadways, cooking, hobbies and cleaning activities which could result in higher indoor and consequently personal exposures will be examined statistically. Stepwise regression models or CART techniques will be used as exploratory models to examine the likelihood of various factors that could lead to elevated exposures and absorbed dose. Children's behavioral characteristics or activities, such as walking barefoot, digging in yard or playground soil with measurable or elevated pesticide levels, sleeping on the floor, low or high hand washing frequencies, habitual thumb sucking, etc., will be analyzed as part of this investigation.

Predict Intake Doses With Urinary Biomarker Concentrations. The environmental concentration measurements, activity diaries, and food consumption diaries are difficult, time-consuming, and expensive to obtain. These data however are needed to obtain estimates of the component

pathway external doses, and thereby, total external dose. In contrast, urinary biomarker concentrations are relatively quick, easy, and inexpensive to measure. They can be obtained for very much larger numbers of children and adults than can full suites of indoor and outdoor environmental measurements. The extent of the ability of the urinary biomarker information to serve as a surrogate indicator of the external component and total doses can be assessed based on the CTEPP data.

The correlation between urinary biomarker data and each of the component pathway doses or total aggregate dose can be assessed by a series of simple regression analyses. Let U_i, $D_{TOT, i}$ denote the urinary biomarker concentration and the total external dose, respectively, within the i^{th} combination of factors. We would like to determine how well U predicts D_{TOT}. We consider a succession of simple linear regression models

$$D_{TOT, i} = \beta_0 + \beta_1 U_i + e$$

$$D_{TOT, i} = \beta_{0i} + \beta_1 U_i + e$$

$$D_{TOT, i} = \beta_{0i} + \beta_{1i} U_i + e$$

to determine how well U can act as a surrogate for D_{TOT}, either within particular combinations of strata or across strata. These relations might also be expressed in terms of the logarithmic transformations of D_{TOT} and U. The coefficient of variation and the residual variation about the model indicate how precisely U can predict D_{TOT}. 95 percent 2-sided prediction intervals can be constructed to determine upper and lower prediction bounds on D_{TOT}, conditional on observing U.

Other factors contained in the activity and food diaries can be added to the predictive equations to determine whether they enhance the predictiveness of the relations. Several such factors discussed in the paragraph above, such as pesticide use or cleaning agent use, could enhance the total dose. Component doses can be substituted for D_{TOT} in the above relations to determine how well U can act as a surrogate for a component dose.

7.2.13 Additional Analyses

The above discussion on data summarization and the construction of tests of hypotheses and point and confidence interval estimates dealt with statistical displays and procedures designed specifically to address the primary and secondary statistical analysis objectives specified at the beginning of the section. The data set will be very rich and and will lend itself to many additional applications.

We will utilize the data (questionnaires, diaries, and POPs concentrations in multimedia) generated in the CTEPP study to evaluate and refine EPA SOPs for Residential Exposure Assessments (Draft Contract No. 68-W6-0030, Work Assignment No. 3385.102, prepared by The Residential Exposure Assessment Work Group: Office of Pesticide Programs, Health Effect Division, Versar, Inc. July 18, 1997). For example, the child activity diary data obtained from

the CTEPP study can be used to refine the parameters used in the SOP 2.3.2 "Postapplication Potential Dose Among Toddlers from Incidental Nondietary Ingestion of Pesticide Residue on Residential Lawns from Hand-to-mouth Transfer." We will convert all the collected data from the CTEPP study into EPA TherdBase format. The data will be easily accessible to EPA/OPP to evaluate and refine the SOPs for Residential Exposure Assessments.

7.3 Establishing the Adequacy of Technical Practices

The proposed procedures for recruiting, field sampling, and sample analysis in the CTEPP study are described in study-specific SOPs. These procedures have been tested and refined in previous small-scale pilot studies (W1, W2, W6, W7, C10, C12, C13, S4, S5, H3, N5, N7, T2). All EPA and Battelle CTEPP team members are well-trained and qualified for their respective tasks. The personnel qualifications and training required for CTEPP team members are described in Sections 1.6 and 1.7, respectively.

7.4 Maintenance of Equipment

Preventive maintenance will be performed on all instruments and equipment used according to the schedule defined in the appropriate SOPs. When applicable, the following information will be recorded:

- Results of performance tests
- Instrument calibration information and calibration checks
- Dates on which routine maintenance is performed and a detailed account of what was done
- Instances of instrument failure
- Record of all changes in location, instrument repairs, changes and modifications
- Description of any problems encountered and steps taken to rectify them.

7.5 Quality of Consumables

The quality of consumable products used are specified in each SOP, as appropriate. A visual inspection of all consumables will occur when received from the supplier and when used. A contaminant analysis of specific scientific consumables will be performed for one sample per each batch of consumables with the same lot number. Specific consumable materials to be tested include: filters, XAD-2, PUF, wipes, containers, bottles, vials, and reagents.

7.6 Labeling

Laboratory labels will be attached to all primary reagents. They will identify the material by composition, stability, storage requirements, safety handling requirements, safety hazards, and date of receipt. All secondary reagents (and those of subsequent generations) will have labels with materials identification, concentration, date of preparation, identification of preparer, and when appropriate, safety information and expiration date. Sample labels will be indelible and preprinted. Labels will be attached to all questionnaires and samples collected. Unlabeled materials will not be used. Unlabeled chemicals will be disposed of through the hazardous waste unit of the cooperating agency.

7.7 Acceptance of Equipment and Materials

All equipment and materials purchased will be evaluated to see if they meet critical specifications, as outlined in the project specifications. Changes in the specifications will not be permissible without the review and consent of the TOL. If changes in materials specifications are agreed to, they will be noted in writing and the specifications approved by the TOL.

7.8 Storage of Equipment and Materials

The storage of equipment and materials, will comply with manufacturer's recommendations. SOPs indicate storage requirements for each sample. These SOP specifications must be followed as some samples lose their integrity with time.

8.0 TECHNICAL ASSESSMENT AND RESPONSE

8.1 Assessment Procedures

For the CTEPP study, technical assessment procedures are classified in terms of pre-field assessment, field assessment, and laboratory assessment.

Pre-Field Assessment. Equipment will be calibrated in the laboratory prior to shipment to the field. Equipment must be able to maintain operating specifications during the course of operation. Equipment must be tested when it is set up and removed to assure that it performed to specifications, as defined in the relevant SOPs. All critical values associated with equipment operation must be independently validated by another field team member.

All SOPs must be field tested prior to project implementation. Field forms must be pretested. SOPs and filed forms that are found to be inadequate will be revised and finalized prior to entry into the field.

Field Assessment. Duplicates will be collected for 10% of all samples with the exception of dust, soil, food, urine, wipe, and PUF roller samples. These samples will be split in the laboratory (when possible) to provide QA split samples which will serve as field duplicates.

Field blanks and trip blanks will be used in conjunction with 10% of all samples collected. They will be prepared and analyzed using the same methods as study samples.

Questionnaire results obtained during field visits will undergo QC checks by technicians in the field and QA checks for completeness by the Field Team Leaders (or designees) acting as internal QA auditors for field forms.

Field Team Leaders (or designees) will routinely evaluate technicians as outlined in the appropriate training SOPs.

The QA Officer will perform periodic field audits as indicated in Section 2.2.

Laboratory Assessment. Field Team Leaders (or designees) will routinely evaluate technicians as outlined in the appropriate training SOPs.

Surrogate recovery standards will be used for all samples. NIST-traceable standards, if available, will be used in conjunction with all laboratory evaluations. Measurement deviations beyond acceptable limits described in the SOPs will be documented, investigated, and corrected. Any deviations in laboratory procedures will be corrected and documented.

All replicate, split, and blank samples (field and laboratory) will be treated as study samples and evaluated in accordance with pertinent SOPs. Values may vary from samples by some designated amount (see appropriate laboratory SOPs for value). Excessive deviation between samples will result in re-evaluation of the field and laboratory procedures. All implemented corrective actions will be dated and documented.

8.2 Assessment Evaluation

The QA Officer recognizes the need for project data to meet specific criteria for scientific validity and technical defensibility, and to be of defined precision and accuracy. The QA systems to be implemented provide a planned and systematic management approach of procedures and controls to ensure that personnel, equipment, activities, and documentation comply with EPA requirements. Battelle recognizes EPA's right to observe and perform additional QA audits at its discretion and welcomes these constructive efforts.

To assist in meeting these objectives, Battelle maintains a Qaulity Assurance Program to ensure that activities affecting the quality and integrity of data are appropriately planned and coordinated. The QA system audits will be used to assure that QA/QC plans are prepared, approved, and fully implemented, that QA/QC procedures are fully understood by field and laboratory personnel, and that data are reported in a manner reflecting the quality objectives of the project. To assist Field Team Leaders and Laboratory Supervisors in tracking critical QA issues, a QA Checklist will be developed for each aspect of sampling and analysis. These will be distributed to field and laboratory personnel with instructions.

QA performance audits will be used to assure compliance with the project plan. These audits will have the form of verification surveillances and will be performed by the QA Officer. These surveillances will be performed to ensure that a specific requirement is being met. The audits will include both real time observations during the work or analytical process to ensure that specific applicable procedures are being implemented, and traceability checks through data to ensure that project data can be tracked back through the analytical process, through sample handling and transportation, back to the date, location, staff member, and technique used to collect the sample. At least one QA surveillance audit will be performed for each of the following key activities: sampling, sample tracking from field to laboratory, analytical measurement, and data reporting.

8.3 Assessment Response and Follow-up

Field. Conditions that will have an adverse effect on quality, such as variances, unusual occurrences or abnormal conditions, and deviations from the SOPs or contractual requirements, will be identified promptly and corrected as soon as practicable. In the case of a significant adverse quality condition, the cause of the condition will be determined and measures taken to prevent a recurrence. The identification, cause, and corrective action for significant conditions

adverse to quality will be documented and reported to the appropriate levels of management. Follow-up action will be taken by the QA Officer to verify implementation of corrective action.

Laboratory and Data. The need for corrective action will be identified by the technical staff during the course of their work or review of the data. We expect that problems will be identified and corrected prior to QA audits, although this additional measure of oversight will provide further opportunity for identification of problems prior to data reporting. Each individual staff member performing laboratory or data processing activities will be sufficiently well trained in their operations that they will be responsible for notifying the appropriate supervisory personnel of any circumstance that would affect the quality or integrity of the data. Deviations from approved procedures that require corrective actions typically result from unforeseen circumstances. In the laboratory follow-up, all deviations will be documented in field or laboratory notebooks and will be dealt with as expeditiously as possible by the responsible task leader. For data issues, all corrective changes in the data bases must be approved by the Data Coordinator or Data Manager. All corrections will be noted on the appropriate "Data Change" form as outlined in the data SOPs.

9.0 REFERENCES

A1 M. C. R. Alavanja, D. P. Sandler, S. B. McMaster, S. H. Zahm, C. J. McDonnell, C. F. Lynch, M. Pennybacker, N. Rothman, M. Dosemeci, A. E. Bond, and A. Blair, "The Agricultural Health Study." *Environ. Health Perspec.*, **104**, 362-369 (1996).

A large prospective study of the exposures of farmers and farm families to agricultural pesticides.

B1 M. A. Bradman, M. E. Harnly, W. Draper, S. Seidel, S. Teran, D. Wakeham, and R. Neutra, "Pesticide Exposures to Children from California's Central Valley-- Results of a Pilot Study." *J. Expos. Anal. Environ. Epidem.*, **7**, 217-234 (1997).

Handwipe sampling for OP pesticides on 11 rural children detected 10 of 33 pesticides that were found in their house dust. Dust ingestion scenarios suggest that diazinon exposures could exceed the reference dose (9x10e-5 mg/kg/day).

B2 S. Bhatia and J. P. Neglia, "Epidemiology of Childhood Acute Myelogenous Leukemia." *J. Pediatric Hematol. Oncol.*, **17**, 94-100 (1995).

Environmental risk factors include association with parent and family member exposure to petroleum products and pesticides.

B3 Barclays Official California Code of Regulations (Barclays Law Publishers, South San Francisco, CA, 1996). "Level of exposure to carcinogens." Vol. 28, §12721

B4 T. J. Buckley, J. M. Waldman, R. Dhara, A. Greenberg, Z. Ouyang, and P. J. Lioy, "An Assessment of a Urinary Biomarker for Total Human Environmental Exposure to Benzo[a]pyrene (BaP)." *Int. Arch. Occup. Environ. Health*, **67**, 257-266 (1995).

B6 T. J. Buckley, J. D. Liddle, D. Ashley, V. Burse, D. Paschal, and G. Akland, "Measurements of Exposures and Biomarkers in the Lower Rio Grande Valley: Multimedia Results for Pesticides, Metals, PAH, and VOCs." *Environ. Int*. **23**, 705-732 (1997).

C1 J. C. Chuang, "Evaluation and Application of Methods for Estimating Children's Exposure to Persistent Organic Pollutants in Multiple Media." Progress report to USEPA for Contract 68-D4-0023, Work Assignment 2-01, September 1997.

C2 J. C. Chuang, M. A. Pollard, Y. Chou, R. G. Menton, and N. K. Wilson, "Evaluation of Enzyme-Linked Immunosorbent Assay for the Determination of Polycyclic Aromatic Hydrocarbons in House Dust and Soil." *Sci. Total Environ*., **224**, 189-199 (1998).

C3 J. C. Chuang, P. J. Callahan, R. G. Menton, S. M. Gordon, R. G. Lewis, and N. K. Wilson, "Monitoring Methods for Polycyclic Aromatic Hydrocarbons and their Distribution in House Dust and Track-In Soil." *Environ. Sci.Technol.,* **29**, 494-500 (1995).

C4 J. C. Chuang, M. R. Kuhlman, and N. K. Wilson, "Indoor Concentrations of Polycyclic Aromatic Hydrocarbons in Nonsmokers' Residences During Winter and Summer Seasons." *Measurement of Toxic and Related Air Pollutants: Proceedings of the 1991 EPA/AWMA International Symposium*, Pub. VIP-21, AWMA, Pittsburgh PA, 1991, pp. 1124-1140.

C5 M. D. Cheng, P. D. Hopke, and N. K. Wilson, "Receptor Modeling of Indoor Polynuclear Aromatic Hydrocarbons Collected in Columbus, Ohio." *Proceedings of the 1991 AWMA National Meeting*, AWMA, Pittsburgh PA, 1991.

C6 J. C. Chuang, P. J. Callahan, S. M. Gordon, N. K. Wilson, and R. G. Lewis, "Methods for Polycyclic Aromatic Hydrocarbons and Tobacco Smoke Markers in House Dust: Laboratory and Field Evaluation." *Measurement of Toxic and Related Air Pollutants: Proceedings of the 1993 EPA/AWMA International Symposium*, Pub. VIP-34, AWMA, Pittsburgh PA, 1993, pp. 88-93.

C7 J. C. Chuang, N. K. Wilson, and C. Lyu, "Summer Study of Field Methods for Estimating Exposure of Children in Low-Income Families to Polycyclic Aromatic Hydrocarbons." *Final Program, Annual Meeting of the Society for Risk Analysis and the International Society of Exposure Analysis*, Society for Risk Analysis, McLean VA, Paper P3.13, p.161.

C8 J. C. Chuang and N. K. Wilson, "Method Validation and Characterization of Phenols in House Dust and Soil." Presented at the 1997 EPA/AWMA International Symposium on Measurement of Toxic and Related Air Pollutants, Research Triangle Park NC, May 1997, Paper P-1.

C9 J. C. Chuang, M. G. Nishioka, and N. K. Wilson, "Evaluation of Enzyme-Linked Inmmunosorbent Assays for Polycyclic Aromatic Hydrocarbons, Pentachlorophenol, and 2,4-D Herbicide in House Dust and Soil." Invited paper presented in the

Immunochemistry Summit VI symposium at the national meeting of the American Chemical Society, Las Vegas NV, September 1997.

C10 J. C. Chuang, P. J. Callahan, C. W. Lyu, Y.-L. Chou, and R. G. Menton, "Characterization of Polycyclic Aromatic Hydrocarbons Exposure Among Children of Low-Income Families from Inner Cities and Rural Areas." Final report on Cooperative Agreement CR822073, EPA 600/R-98/163a, 163b, and 163c (1998).

C11 J. C. Chuang, Y. L. Chou, M. Nishioka, K. Andrews, M. Pollard, and R. Menton, "Field Evaluation of Screening Techniques for Polycyclic Aromatic Hydrocarbons, 2,4-Diphenoxyacetic Acid, and Pentachlorophenol in Air, House Dust, Soil, and Total Diet." Final Report, Contract 68-D4-0023, WA 1-04. EPA 600/R-97/109, 1997.

C12 J. C. Chuang, P. J. Callahan, C. W. Lyu, and N. K. Wilson, "Polycyclic Aromatic Hydrocarbon Exposures of Children in Low-Income Families." *J. Expos. Anal. Environ. Epidem.*, **2**, 85-98 (1999).

C13 J. C. Chuang, C. Lyu, Y-L Chou, P. J. Callahan, M. Nishioka, K. Andrews, M. A. Pollard, L. Brackney, C. Hines, D. B. Davis, and R. Menton, "Evaluation and Application of Methods for Estimating Children's Exposure to Persistent Organic Pollutants in Multiple Media." Report, Contract 68-D4-0023, EPA 600/R-98/164a, 164b, and 164c (1998).

C14 D. E. Camann, H. J. Harding, C. L. Stone, and R. G. Lewis, "Comparison of PM2.5 and Open-Face Inlets for Sampling Aerosolized Pesticides on Filtered Polyurethane Foam." *Measurement of Toxic and Related Air Pollutants: Proceedings of the EPA/AWMA International Symposium*, Air & Waste Management Association, Pittsburgh, PA, Publication VIP-39, 1994, pp. 838-843, ASTM Standard Practice D 4861.

C15 D. A. Crain, L. J. Guilette, A. A. Rooney, and D. B. Pickford, "Alterations in Steroidogenesis in Alligators *(Alligator Mississippiensis)* Exposed Naturally and Experimentally to Environmental Contaminants." *Environ. Health Perspect.,* **105**, 528-533 (1997).

Studies of the effects of pesticides as EDCs in juvenile alligators showed no effects of vinclozilin or 2,4-D, but showed an ED effect of atrazine, as measured by plasma testosterone, aromatase, and gonadal histopathology.

C16 *Chemical and Engineering News*, June 8, 1998, p. 11.

C17 E. A. Cohen-Hubal, L. S. Sheldon, T. R. McCurdy, M. L. Rigas, J. M. Burke, V. G. Zartarian, and N. C. G. Freeman, "Children's Exposure Assessment: A Review of Factors Influencing Children's Exposures and the Data Available to Characterize and Assess that Exposure." Submitted for publication to *Environmental Health Perspectives,* July 1999.

D1 J. R. Davis, R. C. Brownson, R. Garcis, B. J. Bentz, and A. Turner, "Family Pesticide Use and Childhood Brain Cancer." *Arch. Environ. Contam. Toxicol.*, **24**, 87-92 (1993).

Significant positive associations were found with child brain cancer for use of pesticides in the home -- pest strips, termiticides, flea collars, garden diazinon, and herbicides, comp to non-cancer controls. Associations were significant compared to other cancers for pest bombs, termiticides, flea collars, insecticides in the garden, carbaryl in the garden, and herbicides. (Done by survey; no physical measurements were made.)

D2 J. L. Daniels, A. F. Olshan, and D. A. Savitz, "Pesticides and Childhood Cancers." *Environ. Health Perspect.*, **105,** 1068-1077 (1997).

Epidemiological studies published between 1970 and 1996 were reviewed. Reported relative risk estimates were modest. Frequent occupational exposure to pesticides or home pesticide use was related to increased risk of childhood cancer, especially leukemia and brain cancer. Residence on a farm was associated with increased risk.

D3 I. R. Danse, R. J. Jaeger, R. Kava, M. Kroger, W. M. London, F. C. Lu, R. P. Maickel, J. J. McKetta, G. W. Newell, S. Shindell, F. J. Stare, and E. M. Whelan, "Position Paper of the American Council on Science and Health – Public Health Concerns about Environmental Polychlorinated Biphenyls (PCBs)." *Ecotoxicol. Environ. Safety*, **38**, 71-84 (1997).

A review of the scientific literature on PCBs in the environment and their potential risk. Studies of workers exposed to high doses of PCBs over long periods of time have not demonstrated an increased cancer risk. Recent studies implicating prenatal PCB exposure in neurodevelopmental toxicity have methodological deficiencies. No conclusive evidence exists at this time that PCB levels in the population are causing *in utero* intellectual deterioration. Evidence for estrogenic effects of environmental PCBs remains weak and circumstantial. Thus more study is needed.

D4 C. DeRosa, P. Richter, H. Pohl, and D. J. Jones, "Environmental Exposures that Affect the Endocrine System: Public Health Implications." *J. Toxicol. Environ. Health*, Part B, **1**, 3-16 (1998).

An overview of the chemicals that have been implicated as endocrine disrupters. Approximately one-fourth are the persistent and lipophilic organochlorine compounds, such as DDT and PCBs.

E1 Environmental Working Group, "Overexposed: Organophosphate Insecticides in Children's Food." Report, Environmental Working Group, Washington, DC, 1998.

Reports analyses of data from the 80,000 food samples tested by USDA and FDA and dietary records collected for 4000 children by USDA. Concludes that unsafe levels of OP exist in baby food and other foods eaten by children, especially apples, peaches, and grapes. Calls for ban on all home and structural uses of OP pesticides and on commodities that end up in baby food.

E2 *Exposure Factors Handbook*, U.S. EPA Office of Health and Environmental Assessment (1996). Washington, DC.

F1 T. Field and E. Ignatoff, "Videotaping Effects on the Behaviors of Low Income Mothers and Their Infants During Floor-Play Interactions." *J. Appl. Developmental Psych.*, **2**, 227-235 (1981).

Videotaping initially affects the behavior of mothers interacting with their children, but repeated sessions or more lengthy exposures reduce the observer effect.

G1 P. W. Geno, D. E. Camann, H. J. Harding, K. Villalobos, and R. G. Lewis, "Handwipe Sampling and Analysis Procedure for the Measurement of Dermal Contact with Pesticides." *Arch. Environ. Contam. Toxicol.*, **30**, 132-138 (1996).

Cellulose sponges wet with isopropyl alcohol were used to wipe children's hands, with quantitative removal of chlorpyrifos and pyrethrin. Applicability to 29 other pesticides is suggested, including acid herbicides.

G2 D. Gross, "Issues Related to Validity of Videotaped Observational Data." *Western J. Nursing*, **13**, 658-663 (1991).

A review of strategies for obtaining useful videotaped observational data.

H1 M. Heil, B. Schiller, A. C. Huggett, and F. Haschke, "Toxicological Aspects of Food for Infants and Children." *Monatsschrift Kinderheilkunde*, **144** Suppl. 2, S224-S229 (1996).

The author estimates exposure to pesticide residues in food from food analyses and the estimated diet of a 4-mo old child.

H2 P. T. C. Harrison, P. Holmes, and C. D. N. Humfrey, "Reproductive Health in Humans and Wildlife – Are Adverse Trends Associated with Environmental Chemical Exposure." *Sci. Total Environ*., **205**, 97-106 (1997).

Trends in the incidences of testicular and breast cancer, and concern about reduced semen quality, cryptorchidism, hypospadias, and polycystic ovaries may be associated with endocrine disruptors. Suspected compounds include naturally occurring steroids, phyto- and myco-estrogens, synthetic hormones, organotins, organochlorine pesticides, polychlorinated biphenyls, dioxins, alkylphenols, polyethoxylates, phthalates, and bisphenol-A. However, there is no direct causal evidence in humans.

H3 J. P. Hsu, H. G. Wheeler, Jr., H. J. Schattenberg, III, D. E. Camann, R. G. Lewis, and A. E. Bond. "Analytical Methods for Determining Nonoccupational Exposures to Pesticides," *J. Chromatogr. Sci.* ***26***, 181-189 (1988).

K1 W. R. Kelce and E. M. Wilson, "Environmental Antiandrogens – Developmental Effects, Molecular Mechanisms, and Clinical Implications." *J. Molec. Medicine*., **75**, 198-207 (1997).

A review of the mechanism of toxicity and clinical implications of environmental chemicals that inhibit androgen-mediated sex development. These EDCs include the fungicide vinclozilin and the pesticide DDT and its metabolite DDE.

K2 R. J. Kavlock, G. P. Daston, C. DeRosa, P. Fennercrisp, L. E. Gray, S. Kaattari, G. Lucier, M. Luster, M. J. Mac, C. Maczka, R. Miller, J. Moore, R. Rolland, G. Scott, D. M. Sheehan, T. Sinks, and H. A. Tilson, "Research needs for the risk assessment of health and environmental effects of endocrine disruptors–a report of the U. S. EPA-sponsored workshop." *Environ. Health Perspect.*, **104** (Suppl.4), 715-740 (1996).

A review of research needs in endocrine disrupter risk assessment.

K3 W. Karmaus and N. Wolf, "Reduced Birthweight and Length in the Offspring of Females Exposed to PCDFs, PCP, and Lindane." *Environ. Health Perspect.*, **103**, 1120-1125.

The newborn infants of 221 teachers who had been exposed to pentachlorophenol (PCP) and lindane in wood panels and chlorinated dibenzo-p-dioxin and chlorinated dibenzofurans in indoor air were compared to the infants of 189 teachers who had not been exposed. The median difference was 175 g birth weight and 2 cm birth length. The reductions in birth weight and birth length were significant at the $p = 0.04$ and $p = 0.02$ level, respectively.

K4 R. A. Kulka, "The Use of Incentives to Survey 'Hard-to-Reach' Respondents: A Brief Review of Empirical Research and Current Practice." Proceedings of the Seminar on New Directions in Statistical Methodology, Council of Professional Associations on Federal Statistics (COPAFS), Bethesda, MD, May 1994.

L1 R. G. Lewis, R. C. Fortmann, and D. E. Camann, "Evaluation of Methods for the Monitoring of the Potential Exposure of Small Children to Pesticides in the Residential Environment." *Arch. Environ. Contam. Toxicol.*, **26**, 37-46 (1994). HIPES study.

L2 J. K. Leiss and D. A. Savitz, "Home Pesticide Use and Childhood Cancer--A Case-Control Study." *Amer. J. Publ. Health*, **85**, 249-252 (1995).

For 252 child cases and 232 controls, yard treatment was associated with soft tissue sarcomas (odds ratio ~4.0). Home pest strip use was associated with leukemia (OR ~1.7-3.0). The findings suggest that the use of home pesticides is associated with some types of childhood cancer.

L3 M. P. Longnecker, W. J. Rogan, and G. Lucier, "The Human Health Effects of DDT (Dichlorodiphenyltrichloroethane) and PCBs (Polychlorinated Biphenyls) and an Overview of Organochlorine in Public Health." *Ann. Revw. Public Health*, **18**, 211-244 (1997).

Many organochlorines are EDCs in experimental assays. High-level exposures to some OC compounds appear to cause abnormalities of liver function, skin, and the nervous system. Neonatal hypotonia or hyporeflexia has been associated with PCB exposure. Epidemiological data is not convincing that OC compounds cause cancer. However, if animal data is included, a recent risk estimate of 10 (exp-4) per year for chlorinated dioxins and some PCBs has been suggested.

L4 C. Loewenherz, R. A. Fenske, N. J. Simcox, G. Bellamy, and D. Kalman, "Biological Monitoring of Organophosphorus Pesticide Exposure Among Children of Agricultural Workers in Washington State." *Environ. Health Perspect.*, **105**, 1344-1353 (1997).

Children up to 6 yr old who lived with pesticide applicators were monitored for OP pesticide exposure, by measuring the urinary metabolite dimethylthiophosphate (DMTP). Of 88 children, 47% of applicators' children and 27% of non-applicators' children had detectable levels of DMTP. Younger children and those who lived less than 200 feet from an orchard had higher levels.

L5 C. S. Lu and R. A. Fenske, "Air and Surface Chlorpyrifos Residues following Residential Broadcast and Aerosol Pesticide Applications." *Environ. Sci. Technol.*, **32**, 1386-1390 (1998).

Ambient air and surface chlorpyrifos residues were measured for seven days following broadcast (Dursban) and total release aerosol (K-RID) chlorpyrifos applications for flea control in dormitory rooms. Broadcast applications resulted in 7.5 times more total deposited chlorpyrifos on carpets than aerosol applications; dislodgeable residues on carpets were 2 times greater. Residues on nontarget surfaces such as furniture were 140-150 times greater from aerosol applications than from broadcast applications. However, the estimated total absorbed doses (12-33 μg/kg) were near the no observable effect level (NOEL 30 μg/kg) on the first day, and lower on following days.

L6 A. Lohaus, "The Effect of Videotaping on Preschool and Primary School Children." *Zeitschrift Pedagogische Psychologie,* **1**, 131-140 (1987).

Videotaping improved the performance of 105 children ages 5-11 on tasks requiring convergent and divergent thinking. The results were independent of the children's ages.

M1 L. S. Miller, D. B. Davis, C. S. Preven, J. C. Chuang, J. C. Johnson, J. M. Van Emon, and N. K. Wilson. "Analysis of Soil and Dust Samples for Polychlorinated Biphenyls by ELISA." Presented in the Immunochemistry Summit VI symposium at the national meeting of the American Chemical Society, Las Vegas NV, September 1997.

M2 R. Meinert, P. Kaatsch, U. Kaletsch, F. Krummenauer, A. Meisner, and J. Michaelis, "Childhood Leukemia and Exposure to Pesticides--Results of a Case-Control Study in Northern Germany." *Europ. J. Cancer*, **32A**, 1943-1948 (1996).

For 219 cases of childhood leukemia, there was a significant association with pesticide use in home gardens. Parental agriculture-related exposure was not significant.

M3 D. Mukerjee *et al.*, "Assessment of risk from Multimedia Exposures of Children to Environmental Chemicals." 28th Annual Critical Review*, J. Air & Waste Manage. Assoc.,* **48**, 483-501 (1998).

A review of the adverse effects observed in children associated with exposure to environmental chemicals. Exposure factors and equations for estimating total exposures and potential doses through the various environmental pathways are presented. Extensive references.

N1 M. G. Nishioka and K. D. Andrews, "Method Validation and Application for Semivolatile Organic Compounds in Dust and Soil: Pesticides and PCBs." Final Report, Contract 68-D4-0023, WA 1-08, Task 3. EPA 600/R-97/141 (1997).

N2 National Academy of Sciences, Committee on Risk Assessment of Hazardous Air Pollutants, "Science and Judgment in Risk Assessment." National Academy Press, Washington DC, 1994.

N3 National Academy of Sciences, "Pesticides in the Diets of Infants and Children." National Academy Press, Washington DC, 1993.

N4 Nonoccupational Pesticide Exposure Study (NOPES), Final Report, Atmospheric Research and Exposure Assessment Laboratory, U. S. Environmental Protection Agency, Research Triangle Park NC, 1990. EPA/600/3-90/003.

N5 M. G. Nishioka, H. M. Burkholder, M. C. Brinkman, S. M. Gordon, and R. G. Lewis, "Measuring Transport of Lawn-Applied Herbicide Acids from Turf to Home--Correlation of Dislodgeable Turf Residues with Carpet Distribution and Carpet Surface Residues." *Environ. Sci. Technol.*, **30**, 3313-3320 (1996).

A study of the track-in of 2,4-D and dicamba from lawn pesticide applications.

N6 National Exposure Research Laboratory, Research Strategy, 1997 draft.

N7 *Development of Analytical Methods for Lawn-Applied Pesticides in House Dust*, Report No. 600/R-97/110, US Environmental Protection Agency, Research Triangle Park, NC, November 1997.

N8 M. C. Brinkman, J. E. Sawchuk, and S. M. Gordon. "Sample Management and Reporting of Results Using Data Base Software." Presented at the 7th Annual Meeting of the International Society of Exposure Analysis, Research Triangle Park, North Carolina, November 1997.

O1 W. R. Ott, "Human Exposure Assessment: The Birth of a New Science." *J. Expos. Anal. Environ. Epidem.*, **5**, 449-472 (1995).

O2 W. R. Ott and J. W. Roberts, "Everyday Exposure to Toxic Pollutants." *Scientific American*, February 1998, pp. 86-91.

O3 Office of Research and Development, Strategic Plan, U. S. Environmental Protection Agency, EPA/600/R-96/059, May 1996; updated 1997, EPA/600/R-97/015.

O4 Office of Research and Development, U. S. Environmental Protection Agency, Children's Risk Strategy, draft document, June 1997.

O5 M. O'Malley, "Clinical Evaluation of Pesticide Exposure and Poisoning." *Lancet*, **349**, 1161-1166 (1997).

Pesticide exposure effects range from skin irritation, acute toxicity to complex systemic illness as a result of cholinesterase inhibition, e.g. from OP exposure. Possible links to asthma from exposure to OP pesticide contaminants.

O6 ORETG, Occupational and Residential Exposure Test Guidelines (1994, 1997). U.S. Environmental Protection Agency Office of Prevention, Pesticides, and Toxic Substances, Washington, DC, Series 875.

O7 N. Olea, P. Pazos, and J. Exposito, "Inadvertent Exposure to Xenoestrogens." *Eur. J. Cancer Prevention*, **7**, Suppl 1, S17-S23 (1998).

Defines endocrine disruptor (EDC) as an exogenous substance that causes adverse health effects in an intact organism or its progeny, secondary to changes in endocrine function. The following anthropogenic compounds are identified as EDCs: o,p-DDT, kepone, methoxychlor, phenolic derivatives, and PCBs. Also toxaphene, dieldrin, endosulfan, t-

butylhydroxyanisole, benzylbutylphthalate, 4-hydroxy alkyl phenols, and bisphenol-A. However, evidence for ED by these compounds in humans is meager or nonexistent.

O8 W. R. Ott, *Environmental Statistics and Data Analysis*, CRC Press, Boca Raton, FL, 1995.

P1 F. D. Perera, "Environment and Cancer: Who Are Susceptible?" *Science*, **278**, 1068-1073 (1977).

Physiological factors associated with the decreased detoxification capability, DNA repair, and immune function in the elderly and in the very young make these groups more susceptible to environmental insults. There is a hormonal association with deregulation of growth and differentiation through receptor binding.

P2 J. M. Pogoda and S. Preston-Martin, "Household Pesticides and Risk of Pediatric Brain Tumors." *Environ. Health Perspect.*, **105**, 1214-1220 (1997).

An investigation of the risk of household pesticide use from pregnancy to diagnosis in mothers of 224 children with brain tumors and 218 controls. Risk was significantly elevated for prenatal exposure to flea/tick pesticides (OR 1.7). Sprays and foggers were the only products significantly related to risk (OR 10.8). Elevated risk was not observed for termite or lice treatments, pesticides for nuisance pests, or yard and garden insecticides, fungicides, herbicides, or snail killer.

P3 F. D. Perera, R. M. Wyatt, W. Jedrychowski, V. Rauh, D. Manchester, R. M. Santella, and R. Ottman, "Recent Developments in Molecular Epidemiology – Study of the Effects of Environmental Polycyclic Aromatic Hydrocarbons on Birth Outcomes in Poland." *Amer. J. Epidem.*, **147**, 309-314 (1998).

Biomarkers of PAH exposure (DNA adducts) and physical characteristics of newborns from a heavily industrialized city and a rural town in which coal heating is predominant were compared. Infants with high levels of DNA adducts had significantly decreased birth weight, length, and head circumference. Cotinine (a marker for environmental tobacco smoke exposure) was also significantly associated with decreased birth weight and length.

R1 J. W. Roberts and P. Dickey, "Exposure of Children to Pollutants in House Dust and Indoor Air." *Rev. Environ. Contam. Toxicol.*, **143**, 59-78 (1995).

R2 D. C. Rice, "Neurotoxicity Produced by Developmental Exposure to PCBs." *Mental Retardation Developmental Disabilities Res.*, **3**, 223-229 (1997).

Prospective studies suggest decreased reflexes, retarded psychomotor development in early childhood associated with PCB exposure. Decreased IQ and reading ability were evidenced at age 11. Animal models reveal changes in activity and cognitive function with developmental exposures to PCBs.

R3 J. W. Roberts, W. T. Budd, M. G. Ruby, A. E. Bond, R. G. Lewis, R. W. Wiener, and D. E. Camann, "Development and Field Testing of a High Volume Sampler for Pesticides and Toxics in Dust." *J. Expos. Anal. Environ. Epidem.* **1**, 143-155 (1991), ASTM Standard Practice D 5438

R4 N. C. Rawlings, S. J. Cook, and D. Waldbillig, "Effects of the Pesticides Carbofuran, Chlorpyrifos, Dimethoate, Lindane, Triallate, Trifluralin, 2,4-D, and Pentachlorophenol on the Metabolic Endocrine and Reproductive Endocrine System in Ewes." *J. Toxicol. Environ. Health,* **54**, 21-36 (1998).

Carbofuran caused a significant increase in serum concentrations of thyroxine, the major secretory product of the thyroid and a principal regulator of metabolism; all other pesticides except trifluralin caused a decrease in thyroxine. Serum concentrations of cortisol were increased by trifluralin and chlorpyrifos. Insulin concentrations were increased by dimethoate, lindane, trifluralin, triallate, and pentachlorophenol. Estradiol concentrations were increased by lindane and trifluralin. Luteinizing hormone (LH) was decreased by trifluralin, lindane, and dimethoate, but increased by triallate. Pentachlorophenol and triallate caused increased severity of oviductal intraepithelial cysts.

R5 R. A. Rudel, S. J. Melly, P. W. Geno, G. Sun, and J. G. Brody, "Identification of Alkylphenols and Other Estrogenic Phenolic compounds in Wastewater, Septage, and Groundwater on Cape Cod, Massachusetts." *Environ. Sci. Technol.,* **32**, 861-869 (1998).

The potential EDCs nonylphenol, octylphenol, and their ethoxylates, bisphenol-A, nonylphenol, and phenylphenol were analyzed in wastewater, septic effluent, and wells. Nonylphenol was detected in all septage samples. Phenylphenol and bisphenol-A were detected in septage and wastewater. Bisphenol-A and some ethoxylates were detected in several drinking water wells.

R6 J. R. Reigart *et al.*, "Report of the Children's Health Protection Advisory Committee to the U. S. Environmental Protection Agency Regarding the Selection of Five Regulations for Re-Evaluation," Children's Health Advisory Committee, May 28, 1998.

The committee recommends re-evaluation of five regulations in the light of recent data and the fact that protection of children was not adequately considered in the original regulations. The five regulations are Mercury, Farm Worker Protection Standard, Triazine Pesticides, Organophosphates and Carbamates, and Air Quality and Asthma. Of the triazines, atrazine is identified specifically because of its carcinogenicity and potential for causing hormonal developmental effects, and because it has been detected in drinking water throughout the Midwest and other parts of the nation. Of the organophosphates and carbamates, methyl parathion, dimethoate, and chlorpyrifos are identified specifically because they represent the bulk of the dietary risk of neurotoxicity.

S1 D. B. Shealy, M. A. Bonin, J. V. Wooten, D. L. Ashley, L.L. Needham, and A. E. Bond, "Application of an Improved Method for the Analysis of Pesticides and their Metabolites in the Urine of Farmer Applicators and their Families." *Environ. Int.*, **22**, 661-665 (1996).

S2 N. J. Simcox, R. A. Fenske, S. A. Wolz, I. C. Lee, and D. A. Kalman, "Pesticides in Household Dust and Soil--Exposure Pathways for Children of Agricultural Families." *Environ. Health Perspect.*, **103**, 1126-1134 (1995).

OP pesticides were higher in dust in farm homes than in non-farm homes for 59 residences in WA. Tested pesticides included azinphosmethyl, chlorpyrifos, parathion, and phosmet. Dust concentrations were greater than soil concentrations.

S3 E. J. Stanek, III and E. J. Calabrese, *Human and Ecological Risk Assessment*, **1**, 133 (1995).

S4 L. S. Sheldon, J. Keever, J. Beech, J. M. Roberds, and P. Gross, "Manual of Analytical Methods for Determination of Selected Environmental Contaminants in Composite Food Samples." Final Report, Contract 68-C2-0103, U.S. Environmental Protection Agency, Cincinnati, OH.

S5 L. S. Sheldon, J. T. Keever, J. M. Roberds, J. B. Beach, and J. N. Morgan, "Methods for Measuring Base/Neutral and Carbamate Pesticides in Composite Dietary Samples." *J. Expos. Anal. Environ. Epidem.*, **7,** 37-60 (1997).

S6 M. D. Shelby, R. R. Newbold, D. B. Tully, K. Chae, and V. L. Davis, "Assessing Environmental Chemicals for Estrogenicity Using a Combination of *in vitro* and *in vivo* Assays." *Environ. Health Perspect*., **104**, 1296-1300 (1996).

Suspected or known EDCs studied include 17-beta-estradiol, diethylstilbestrol, tamoxifen, 4-hydroxytamoxifen, methoxychlor, the methoxychlor metabolite 2,2-bis(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE), endosulfan, nonylphenol, o,p'-DDT, and kepone.

S7 J. D. Sherman, "Chlorpyrifos (Dursban)-Associated Birth Defects: A Proposed Syndrome, Report of Four Cases, and Discussion of the Toxicology." *Int. J. Occup. Med. Toxicol.,* **4**, 417-431 (1995).

It is suggested that four cases of unusual birth defects are associated with maternal exposure to Dursban.

T1 R. D. Thomas, "Age-Specific Carcinogenesis–Environmental Exposure and Susceptibility." *Environ. Health Perspect.*, **103**, 45-48 (1995).

Emphasizes the importance of dietary exposure of children relative to cancer risk.

T2 K. W. Thomas, L. S. Sheldon, E. D. Pellizzari, R. W. Handy, J. M.. Roberds, and M. R. Berry, "Testing Duplicate Diet Sample Collection Methods for Measuring Personal Dietary Exposures to Chemical Contaminants." *J. Expos. Anal. Environ. Epidem.*, **7**, 17-36 (1997).

U1 U. S. Environmental Protection Agency, *Proceedings of the Science to Achieve Results (STAR) Program Workshop on Children's Exposure to Pesticides*, Washington, DC, April 1998.

U2 U. S. EPA Standard Operation Procedures (SOPs) for Residential Exposure Assessments, Draft, Contract 68-D4-W6-0030, Work Assignment 3385.102, Versar, Inc., prepared for the Residential Exposure Assessment Work Group, Office of Pesticide Programs, Health Effects Division, Washington, DC, July 1997.

V1 T. Vial, B. Nicolas, and F. Descotes, "Clinical Immunotoxicity of Pesticides." *J. Toxicol. Environ. Health*, **48**, 215-229 (1996).

Author suggests potential risk, especially during chronic exposure or to immunocompromised persons such as those who are old, malnourished or young, but evidence is scarce.

W1 N. K. Wilson, J. C. Chuang, and C. Lyu, "Multimedia Concentrations of PAH in Several Day Care Centers." *Polycyclic Aromatic Compounds,* in press (1999).

W2 N. K. Wilson, J. C. Chuang, and C. Lyu, "Exposures of Nine Children Who Attend Day Care to Persistent Pesticides and Other Organic Pollutants." *J. Expos. Anal. Environ. Epidem.* (1999), to be submitted for publication.

W3 N. K. Wilson, J. C. Chuang, and M. R. Kuhlman, "Sampling Polycyclic Aromatic Hydrocarbons and Other Semivolatile Organic Compounds in Indoor Air." *Indoor Air,* **4**, 513-521 (1991).

W4 N. K. Wilson and J. C. Chuang, "Indoor Levels of PAH and Related Compounds in an Eight-Home Pilot Study." In M. J. Cooke, K. Loening, and J. Merritt, Eds., *Polynuclear Aromatic Hydrocarbons: Measurements, Means, and Metabolism*, Battelle Press, Columbus OH, 1991, pp. 1037-1052.

W5 N. K. Wilson, J. C. Chuang, and C. Lyu, "Evaluation of Field Methods for Estimating Exposure of Children in Low-Income Families to Polycyclic Aromatic Hydrocarbons." *Measurement of Toxic and Related Air Pollutants: Proceedings of the 1996 EPA/AWMA International Symposium*, Pub. VIP-64, AWMA, Pittsburgh PA, 1996, pp. 797-802.

W6 N. K. Wilson, J. C. Chuang, and C. Lyu, "Measurements of Persistent Organic Chemicals in Several Day Care Centers." Presented at the 1997 annual meeting of the International Society of Exposure Analysis, Research Triangle Park NC, November 1997.

W7 N. K. Wilson, J. C. Chuang, and C. Lyu, "Multimedia Microenvironmental Concentrations of PAH in Day Care Centers." Presented at the 16th International Symposium on Polycyclic Aromatic Compounds, Charlotte NC, November 1997.

W8 R. W. Whitmore, F. W. Immerman, D. E. Camaan, A. E. Bond, and R. G. Lewis, "Nonoccupational Exposure to Pesticides for Residents of Two U. S. Cities." *Arch. Environ. Contam. Toxicol.*, **26**, 47-59 (1994).

W9 L. A. Wallace, "Human Exposure to Environmental Pollutants: A Decade of Experience." *Clin. Exper. Allergy*, **25**, 4-9 (1995).

W10 B. Weiss, "Pesticides as a Source of Developmental Disabilities." *Mental Retardation Developmental Disabilities Res.*, **3**, 246-257 (1997).

Organochlorine pesticides have been linked with developmental neurotoxicity; the evidence for organophosphate pesticides is ambiguous.

W11 N. K. Wilson, J. C. Chuang, and C. Lyu, "Persistent Pesticides and Other Organic Pollutants in Multiple Environmental Media in Nine Day Care Centers." Journal article to be submitted for publication.

W12 R. S. Whiton, C. Witherspoon, and T. J. Buckley, "A Modified HPLC Method for Determination of Polycyclic Aromatic Hydrocarbon Metabolites in Human Urine." *J. Chromatog.*, **B 665**, 390-394 (1995).

Z1 S. H. Zahm and S. S. Devesa, "Childhood Cancer--Overview of Incidence, Trends, and Environmental Carcinogens." *Environ. Health Perspect.*, **103**, 177-184 (1995).

8000 child cancers occur annually in the US. There is a well-established link with one EDC (diethylstilbestrol). Some pesticides are possibly EDCs and some data suggest higher susceptibility in children.

Z2 S. H. Zahm and M. H. Ward, "Pesticides and Childhood Cancer," *Environ. Health Perspect.*, in press (1998). Presented at the U. S. Environmental Protection Agency Conference on Avoidable Causes of Childhood Cancer, Arlington VA, September 1997.

Z3 V. G. Zartarian, J. Streicker, A. Rivera, C. S. Cornejo, S. Molina, O. F. Valadez, and J. O. Leckie, "A Pilot Study to Collect Micro-Activity Data of Two- to Four-Year-Old Farm Labor Children in Salinas Valley, California." *J. Expos. Anal. Environ. Epidem.*, **5**, 21-34 (1995).

Methods were developed to videotape activity patterns of children. Four children in farm labor families were studied. Questionnaires the day after taping and comparison with the videos tested the hypothesis that recall is inadequate for specifying children's activity patterns. However, the presence of the observers did alter the children's behaviors to some extent.