Longitudinal Field Measurement Study of Infant and Toddler's Aggregate Exposure to Pesticides and Persistent Pollutants

Peer Reviewed Study Design

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LONGITUDINAL STUDY OF YOUNG CHILDREN'S EXPOSURES IN THEIR HOMES TO SELECTED PESTICIDES, PHTHALATES, BROMINATED FLAME RETARDANTS, AND PERFLUORINATED CHEMICALS (A CHILDREN'S ENVIRONMENTAL EXPOSURE RESEARCH STUDY - CHEERS)

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1.0 INTRODUCTION

1.1 Background

The U.S. Environmental Protection Agency (U.S. EPA) has pledged to increase its efforts to provide a safe and healthy environment for children by ensuring that all EPA regulations, standards, policies, and risk assessments take into account special childhood vulnerabilities to environmental toxicants.

In evaluating environmental health risks to children, it is important to understand that children are not little adults. Children's exposures to environmental contaminants and consumer products are expected to be different and, in many cases, much higher than older individuals. These differences in exposure are due to differences in physiological function, surface to volume ratio, and the ratio of food consumption to body weight. Children's behavior and the way they interact with their environment may have a profound effect on the magnitude of their chemical exposures. Children crawl, roll, and climb over contaminated surfaces, resulting in higher dermal contact than would be experienced by adults in the same environment. Children's mouthing activities (hand-to-mouth and object-to-mouth) will result in indirect ingestion of chemicals if their hands or objects are contaminated. Increased indirect ingestion of contaminants also occurs when children handle and eat foods that have come in contact with the floor or other contaminated surfaces.

In order to articulate the problems and research needs associated with children's exposure to environmental pollutants, the EPA Office of Research and Development (ORD) developed the *Strategy for Research on Environmental Risks to Children* (U.S. EPA, 2000). This strategy is centered on the child with the overall goal of improving risk assessments for children and reducing those risks. Within the Children's Risk Strategy three specific objectives have been formulated to (1) make use of existing information to develop improved risk assessment methods and models for children; (2) design and conduct research on exposure, effects, and dose-response that will answer questions about age-related differences in exposure and risks that will lead to better risk assessments for children; and, (3) explore opportunities for prevention and reduction of risks to children.

ORD also conducts research related to children's exposure in support of the Food Quality Protection Act (FQPA) of 1996. FQPA requires EPA to upgrade the risk assessment procedures for setting pesticide residue tolerances in food by considering the potential susceptibility of infants and children to both aggregate and cumulative exposures to pesticides. Aggregate exposures include exposures from all sources, routes and pathways for individual pesticides. Cumulative exposures include aggregate exposures to multiple pesticides with the same mode of action for toxicity. Very importantly, FQPA requires that risk assessments must be based on exposure data that are of high quality and high quantity or exposure models using factors that are based on existing, reliable data.

Currently, the data on children's exposures and exposure factors are limited and generally not adequate to assess residential exposures to consumer products and environmental contaminants. In 1998, a 10X Exposure Working Group was formed to evaluate approaches and data needs for implementing the Food Quality Protection Act (FQPA) with respect to exposure. In 1999, this workgroup produced the report, *Exposure Data Requirements for Assessing Risks from Pesticide Exposure of Children* (U.S. EPA, 1999). The report defined the components of a complete and reliable data set. The document also described why the components of a complete, reliable data set are currently not available. Critical elements that are missing include an understanding of the most important pathways of exposure for young children, approaches for evaluating exposure for critical pathways such as dermal and indirect ingestion exposure, protocols for generating the exposure data, and exposure factor data. Several general areas of research are needed to improve the quality and quantity of data available for exposure assessments for children. Appropriate age/developmental benchmarks for categorizing children in exposure assessments must be identified. The activity pattern data for children (especially young children) required to assess exposure by all routes need to be developed. Data are particularly lacking for infants and toddlers (younger than 3 years of age). Methods for measuring children's exposures need to be developed and improved. Finally, field studies are needed to develop ranges of exposure measurements and associated exposure factors.

1.2 NERL Children's Exposure Measurement Program

The Children's Exposure Research Program at the EPA National Exposure Research Laboratory (NERL) is designed to meet several research needs that have been identified in initial assessments of the adequacy of the data for estimating children's exposure to pesticides and environmental toxicants. A comprehensive approach is required to understand and adequately address all of the components of children's aggregate and cumulative exposure assessments for pesticides and other semi-volatile organic compounds. To develop NERL's research strategy and approach, factors influencing children's exposure to environmental contaminants were reviewed and the quality and quantity of available data associated with default assumptions for exposure factors were evaluated (Cohen Hubal et al., 2000a). A framework to systematically identify the important sources, routes, and pathways for exposure was developed (Cohen Hubal et al., 2000b). This framework is based upon the development of a conceptual model for aggregate exposure and provides the basis for developing a protocol to measure and assess aggregate exposures, as well as for developing sophisticated stochastic models. This framework also allows researchers to systematically identify the most critical research needs and data gaps associated with children's exposures to pesticides. NERL researchers identified four priority research areas that included the following:

- Pesticide use patterns – what, where, and how are pesticides used in children's microenvironments,
- Spatial and temporal distribution of pesticides in residential dwellings,
- Dermal and indirect ingestion – need to develop measurement approaches (microactivity or macroactivity approaches), and,

- Dietary exposure assessments, to include indirect ingestion due to the handling of food by children.

To address these research needs, targeted studies were designed and implemented. They included the following laboratory studies, small pilot field studies, and two large studies in which the EPA collaborated with other Federal agencies:

- Tests of the Feasibility of Using the Macroactivity Approach to Assess Dermal Exposure,
- Study to Identify Important Parameters for Characterizing Pesticide Residue Transfer Efficiencies,
- Use of Fluorescent Tracer Technology to Investigate Dermal Exposure,
- Study of Pets as Transfer Vehicles of Pesticide Residues Following Lawn Applications,
- Temporal and Spatial Distributions of Pesticides Following a Crack and Crevice Application in the EPA Test House,
- Children's Pesticide Exposure Measurements Following Crack and Crevice Applications,
- Characterizing Dietary Intake of Pesticides by Young Children,
- Development of Transfer Efficiencies of Pesticides from Household Surfaces to Foods,
- Coding the Activities of Preschool Children,
- First National Environmental Health Survey of Child Care Centers [Collaboration with the Department of Housing and Urban Development (HUD) and the Consumer Product Safety Commission (CPSC)], and,
- Characterizing Children's Pesticide Exposures in Jacksonville, FL [Collaboration with the Centers for Disease Control and Prevention (CDC) and the Duval County Health Department (DCHD)].

Research results from these studies have been used as input to the design of the study described in this document and for developing the *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by all Relevant Pathways* (U.S. EPA, 2002), described in the following subsection.

1.3 Draft Protocol for Children's Pesticide Exposure Measurements

A *Draft Protocol for Measuring Children's Non-Occupational Exposure to Pesticides by all Relevant Pathways* (hereafter referenced as the *Draft Protocol*) was developed by NERL researchers to provide guidance for generating data that can be used to improve exposure assessments for young children. Currently, standard protocols for conducting exposure field studies that provide data for measurement-based exposure assessments do not exist. Likewise, protocols for developing exposure factor data to be used for modeling assessments are not available. Although research on children's exposure to pesticides and other toxic chemicals is

being performed within EPA, academia, industry, and other research organizations, protocols that have been developed by individual researchers for specific studies do not always collect all of the data required for reliable exposure assessments. The *Draft Protocol* fills a critical need for standardization of the approaches and methods for collecting exposure concentration and exposure factor data. Use of this standardized protocol will facilitate comparison of data collected in children's exposure studies conducted by different groups in government, academia, and other research organizations.

The draft protocol provides approaches and methods that can be used for conducting field studies to collect exposure measurement data and to develop exposure factors. The protocol first provides a framework for conducting measurement studies for aggregate exposure assessments then describes the exposure algorithms developed to assess exposure by each route. The algorithms are used to determine *a priori* what data must be collected in field studies to quantify exposure; the protocol provides explicit data requirements for each route of exposure. The exposure algorithms and data requirements for each route of exposure are summarized in Table 1-1. The approaches for estimating exposure by each route (inhalation, dermal, dietary and indirect ingestion) are described and include discussions of the data requirements, general considerations related to data collection, measurement methods, collection of activity pattern information, and exposure factors. The use of activity diaries and questionnaires is discussed for each route of exposure.

Elements of the *Draft Protocol* were developed and evaluated, to a limited extent, in a set of small pilot studies performed by NERL researchers. However, the protocol has not been fully evaluated in a large field study. One of the objectives of this study is to evaluate the protocol for estimating exposure of young children to pesticides and to collect data that can be used to refine the protocol. Following this evaluation and refinement, the final protocol will serve as the primary protocol for conducting children's exposure assessments for pesticides and environmental contaminants.

1.4 References

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Table 1-1. Summary of the Algorithms and Data Collection Requirements by Exposure Route

Parameter	Measurement	How Collected	Units
Inhalation Exposure $E_{inh,me} = C_{me} \times T_{me,ma} \times IR_{ma}$			
C_{me}	Air concentration in me	Measured with active sorbent collection	µg/m³
$T_{me,ma}$	Time spent in each me/ma	Time-activity diary, questionnaire	h/d
IR_{ma}	Inhalation rate	Estimated from size, age, and activity data collected with diaries and questionnaires using reference values	m³/h
Dermal Exposure - Macroactivity Approach $E_{derm,ma} = C_{surf} \times TC_{derm,ma} \times AD_{me,ma}$			
C_{surf}	Surface loading (total or transferable) in each me	Measured by wipe, press, or roller methods	µg/cm²
$TC_{me,ma}$	Transfer coefficient[a]	Empirically determined for each me/ma from laboratory experiments or field studies	cm²/h
$AD_{me,ma}$	Activity duration for ma in a specific me	Time-activity diary, questionnaire	h/d

Parameter	Measurement	How Collected	Units
Dermal Exposure - Microactivity Approach $E_{dermal} = C_{surf} \times TE \times SA \times EF$			
C_{surf}	Surface loading (total or transferable) on surface	Measured by wipe, press, or roller method	µg/cm²
TE	Transfer efficiency*	Empirically determined from laboratory experiments	unitless
SA	Surface area contacted	Visual observation or videotape	cm²/event
EF	Frequency of contact events	Visual observation or videotape	events/d
Dietary Ingestion Exposure $E_F = \Sigma C_f W_f$			
C_f	Concentration of pesticide in the food item (s)	Measurement in individual food items or composite duplicate diet samples	µg/kg
W_f	Weight of food item consumed	Measured in duplicate diet sample	kg/d
Indirect Ingestion (Dietary and Non-Dietary) Exposure $E_{ingest} = C_x \times TE_x \times SA_x \times EF$			
C_{surf_x}	Surface loading (total or transferable) on object x	Measure by a wipe or press method	µg/cm²
TE_x	Transfer efficiency*	Empirically determined from laboratory experiments	unitless
SA_x	Surface area contacted	Visual observation or videotape	cm²/event
EF	Frequency of mouthing events	Visual observation or videotape	events/d

* This parameter must be calculated using the same surface loading measurement method as used to measure C_{surf}

2.0 OBJECTIVES AND STUDY OVERVIEW

A pilot study is planned to collect data that can be used for evaluation and refinement of the *Draft Protocol*, to improve our understanding of the important pathways of exposure for very young children, to evaluate the impact of developmental age and children's activities on exposure to pesticides in residences, and to evaluate the impact of residential exposures on young children's neurobehavioral development. The study will consist of a longitudinal field study

focusing on the collection of data on the exposures of infants and toddlers to pesticides and other persistent pollutants in residential dwellings. In addition, longitudinal data will also be collected on neurobehavioral development for this very young cohort. This pilot study will provide much needed longitudinal data such that hypotheses addressing contaminant exposures and neurobehavioral development can be formulated and tested in future field studies. To this end, the longitudinal field study has numerous goals and objectives.

2.1 Objectives

The objectives for the field verification study include the following:

- Evaluate the algorithms and approaches specified in the *DraftProtocol for Measuring Children's Non-Occupational Exposure to Pesticides by all Relevant Pathways*,
- Develop critical inputs for the models used in the regulatory process [eg., Stochastic Human Exposure and Dose Simulation model for pesticides (SHEDS-Pesticides), Cumulative and Aggregate Risk Evaluation System (CARES), Lifeline, Calendex, and others],
- Develop data on exposure factors as a function of age/developmental stage to test the Risk Assessment Forum (RAF) proposed age bins for children 0-3 years and to fill data gaps identified in the RAF report,
- Evaluate age and developmentally related differences in children's exposure to pesticides and other persistent pollutants in residential dwellings,
- Determine the impact of microenvironment and macroactivity on children's exposure to pesticides and other persistent pollutants in residential dwellings,
- Evaluate the utility of standardized data collection methods to obtain developmental data for assessing the interrelationships among development, demographics and potential exposures to environmental contaminants,
- Collect multimedia concentrations of pesticides in the residential environments of very young children (0 to 3 years of age), and
- Collect preliminary data on environmental concentrations of selected brominated flame retardants (polybrominated diphenyl ethers), other non-pesticide persistent organic compounds, and selected metals (e.g., arsenic, copper)

The first objective for this longitudinal field study is to evaluate the algorithms and approaches specified in the *DraftProtocol for Measuring Children's Non-Occupational Exposure to Pesticides by all Relevant Pathways*. The algorithms for inhalation, dermal, dietary, and indirect ingestion exposures require numerous data inputs, as specified in the *Draft Protocol*, and listed above in Table 1-1. Evaluation and refinement of the algorithms and approaches specified in the *Draft Protocol* are essential to ensure that children's non-occupational exposures are being accurately evaluated. The algorithms will be evaluated by comparing the exposures estimated using the algorithms with the predictions from the SHEDS model and the measured levels of urinary metabolites.

The second objective is to develop critical inputs for models used in the regulatory process [eg., Stochastic Human Exposure and Dose Simulation model for pesticides (SHEDS-Pesticides), Cumulative and Aggregate Risk Evaluation System (CARES), Lifeline, Calendex, and others]. These models require realistic input parameters in order to function as effective predictors of aggregate and cumulative exposures for cohorts of interest. The data to be collected and analyzed to meet this objective include the following:

- Pesticide use information (application method, active ingredient, amount of active ingredient, area treated, number of applications per year, total amount of active ingredient applied per year, interval between applications, and day of week use).
- Pre- and post-application pesticide concentrations in all relevant media in both treated and untreated rooms.
- Post-application decay profiles.
- Transfer coefficients, with estimates of intra- and inter-child variability and the influence of age, sex, activity level, surface-type, and season.
- Macroactivities (time spent in treated and untreated rooms, active play, quiet play, sleeping, and eating) with estimates of intra- and inter-child, day-of-week, and seasonal variabilities.
- Frequency of hand washing and bathing events.
- Dietary information (food and beverages).

The third objective is to develop data on exposure factors as a function of age/developmental stage to test the Risk Assessment Forum's (RAF) proposed age bins for children 0-3 years and to fill data gaps identified in the RAF report. Currently, there is little exposure factor data for children less than 1 year old. The longitudinal nature of this study will allow for the collection of environmental, biological, and personal measurements to fill a critical data gap at an age where developmental changes are occurring rapidly.

The next objective is to evaluate age and developmentally related differences in children's exposure to pesticides and other persistent pollutants in residential dwellings. Similar to objective 3, this objective will fill critical data gaps in exposure factors for very young children. In addition, the collection of environmental, biological, and personal measurements on the same children for 2 years will provide data on the developmental stages where the potential for exposure to contaminants is greatest based on children's activities.

Objective 5 is to determine the impact of microenvironment and macroactivity on very young children's exposure to pesticides and other persistent pollutants in residential dwellings. Locations where young children are spending time (i.e., their microenvironment) and the activities that they are engaged in (i.e., macroactivities), may significantly influence their exposures. As a result, the collection of activity pattern information in the form of questionnaires and videotape segments, combined with the use of the accelerometer data will enable the classification of the children based on activity level. Microenvironmental information will be collected through the use of questionnaires and videotape segments.

Objectives 3 through 5 will be evaluated through the use of mixed-effects linear models, as described in Section 5.3.

The sixth objective listed above will provide information on functional developmental endpoints. A standardized data collection method will be used to obtain, from parents or other primary caregivers, information on developmental milestones over the course of the study. Resulting data will be evaluated in conjunction with demographic and exposure data to explore possible trends and correlations. The resulting information will be applied to the design of future studies. Information on an individual child's development relative to national norms as well as his/her individual development across the study period will be provided to the parent or caregiver. It will not be possible, based on overall study design, to project any casual relationship between development and exposure.

The seventh objective is to collect multimedia concentrations of pesticides in the residential environments of very young children (0 to 3 years of age). This data will be summarily collected as we meet the data needs of the other objectives.

A final objective is to collect preliminary environmental and exposure data for selected persistent organic pollutants, including three brominated flame retardants (BFRs) currently used in the U.S.. The final list of non-pesticide organic compounds to be measured in the study will be developed if additional funding is procured for the study. There are few data on the concentrations of BFRs in the indoor residential environment. Air samples and house dust samples will be collected in residences and analyzed for the BFRs. Additionally, environmental concentration data will be collected for selected metals (lead, arsenic, copper, and chromium), metals of concern to the Duval County Health Department and the U.S. EPA due to past use in the Jacksonville, FL area. Arsenic, chromium, and copper, in addition to having industrial use sources, have been used to treat wood used outdoors. Soil samples will be collected for analyses of the metals. Results of the analyses for the metals and the other persistent organic compounds will be used to assess the need for additional sampling and will assist in design of larger exposure studies addressing these environmental contaminants.

2.2 Study Overview

The proposed study will consist of a pilot two-year longitudinal study in which measurements will be made to estimate the aggregate exposures of approximately 80 to 100 infants/toddlers to current use pesticides applied in residences. The study participants will be in two cohorts: (1) infants recruited into the study soon after birth, and, (2) children recruited into the study at approximately one year of age. Participant recruitment will be performed at six Duval County Health Department clinics and at least three hospitals. Recruitment of participants at both clinics that serve lower income residents and at local hospitals will result in a study population with a range of socioeconomic status. The study will be performed in Jacksonville, FL, an area with year around pesticide use. A community-based approach will be used for the study. The Duval County Health Department (DCHD) will collaborate with the EPA and serve

as the liaison to the community. The goal will be to develop a study cohort with an active interest in the outcome of the study in order to ensure high participation and retention rates. The CDC will also collaborate with the EPA and DCHD on the study. The CDC will play a major role in the study by analyzing for biomarkers of pesticide exposure in urine samples collected in the study. The CDC, DCHD, and EPA previously collaborated on the study of "Pesticide Exposure in Children Living in Jacksonville, Florida," conducted in the summer of 2001. In that study, CDC collected urine samples from 200 children for biomarker analyses, the DCHD performed screening measurements at a subset of study participant homes, and the EPA measured multimedia concentrations at nine study participant homes to estimate aggregate exposure.

Participants will be recruited into the planned longitudinal study who report, in an initial eligibility questionnaire, that they have high pesticide use in their residence. A screening visit will then be made to the residence to collect additional information on the frequency and pattern of pesticide use in the residence, to perform a pesticide inventory, and to collect floor surface wipe samples as a screening measurement. If the results of the screening visit indicate that the residence is likely to have high pesticide use, the participant will be enrolled into the study. In addition, a limited number of individuals will be recruited who are known to have very low pesticide usage to serve as the study comparison population (less than 10% of the total number of participants recruited).

Monitoring visits will be performed at the study participant residences at selected time periods related to changes in children's development. Up to six visits will be made to the residences over the two-year period of the study. Monitoring will be performed prior to, and immediately following, a pesticide application by the resident or a pest control operator (PCO). Multimedia concentrations will be measured in the homes over a two-day period on each visit. Measurements will be performed to estimate inhalation, dermal, indirect ingestion, and dietary exposure (all routes and pathways of exposure), as described in the *Draft Protocol*. Multi-residue analysis methods will be used to quantify multiple active ingredients in the multi-media samples. The pesticides targeted for quantification will include the current indoor use pesticides (e.g., pyrethroids). Multi-media samples collected in the study will be handled and stored in such a way that additional analyses can be performed for other persistent organic pollutants if additional resources can be identified. During the study, participants will maintain a log of purchases and use of products for pest control in, and around, the home. Additionally, information will be collected from the study participants on use of antimicrobial products in the home. Biological samples (urine) will be collected from the children enrolled in the study and analyzed for selected pyrethroid and OP metabolites. Questionnaires and activity diaries will be used to assess the impact of the children's activities and the microenvironments on exposure. Information on the children's activities will also be obtained using accelerometers worn by the children and from videotape recordings collected by the study participant's caregivers and field technicians. Researchers in the EPA National Health & Environmental Effects Research Laboratory (NHEERL) will also participate in the study by collecting information to characterize the developmental milestones for the children participating in the study.

The general elements of the exposure scenario to be addressed in the study are presented in Table 2-1.

The Health Department has been active for many years in addressing environmental contamination in Duval County. In 1999, DCHD initiated a proactive Environmental Toxicology Program. The program has been instrumental in identifying potential hazardous substances from waste sites and other sources of pollution in the environment. The primary goal of the program is to prevent exposure and adverse human and environmental health effects that may diminish the quality of life of the County citizens. The DCHD has continuing interest in exposures to lead, arsenic, copper, chromium, and other metals. These metals may have originated from closed incinerator sites. There is also a concern by DCHD and the EPA about children's exposure to arsenic, copper, and chromium from CCA-treated wood used at residences. Therefore, as part of this study, soil samples and house dust samples will be collected during one of the initial visits to the participant residences will be analyzed by the EPA for metals.

Table 2-1. General Elements of the Exposure Scenario to Be Addressed in the Study

Parameter	Description
Pesticide source	Any residential pesticide application (professional or self-application, if high use can be documented)
Exposed population	Children aged 0 to 3 years
Time frame for exposure	Short-term, episodic, 1 to 7 days following application
Microenvironments	Residential dwelling, indoors and outdoors
Microactivities	Active play, quiet play, sleeping, eating

The study will also provide the opportunity to collect data on environmental concentrations of selected brominated flame retardants, compounds of concern in the U.S.. There are few data available on BFR concentrations in environmental media. Air samples and house dust samples will be collected for analysis of three BFRs. Although the number of samples and scope of the measurement program will be small, the data will be useful in evaluating the need for additional measurements and in designing future exposure measurement studies for BFRs. Other persistent organic compounds will be measured in the study if additional funding becomes available. The study design will be amended as required to address additional study elements related to measurements of non-pesticide chemicals.

3.0 SURVEY DESIGN AND RECRUITMENT

3.1 Study Area

The proposed study will be conducted in Duval County, FL, a generally urban area in the northeastern part of Florida, near the Georgia border. Duval County was selected as the site for the proposed study because it (1) is located in a geographic region with a high likelihood of year-round indoor pesticide use, (2) a previous study has shown higher pesticide concentrations than in a city located in the Northeast, (3) data from the study conducted by Duval County, CDC, and EPA in the summer of 2001 are available to assist in planning the proposed study, (4) the Duval County Health Department is interested in continuing research on children's pesticides to assist in developing risk management programs in the County, and, (5) previous experience with the DCHD suggests that their participation will facilitate a community-based approach to the study, which is expected to improve response and retention rates. The following sections describe the demographics of the area and available information on pesticide use.

3.1.1 General Information and Demographics of Duval County and Jacksonville, FL

Duval County, FL, which includes the Jacksonville metropolitan statistical area (MSA), has a land area of 774 square miles. The County, with a population of 778,879 in the 2000 Census, includes the city of Jacksonville (population of 735,617), Atlantic Beach (13,368), Baldwin (1,634), Jacksonville Beach (20,990), and Neptune Beach (7,270). The population density is 1,006 persons per square mile. The 2000 Census reported 303,747 households in the County, of which 37% were with persons under 18. Median household income in the county was $35,883 compared to $32,877 for the state of Florida (model-based estimates) in 1997. The proportion of children living below the poverty level in Duval County in 1997 was estimated to be 18.8%, which is slightly lower than the figure of 21.8% estimated for the entire state. Duval County and the city of Jacksonville operate under a consolidated government. The population of the county is diverse, as shown in Table 3-1. Table 3-1 also shows that there are approximately 11,500 births in the County each year (i.e., approximately 1000 births per month), a number that should be sufficient for effective recruiting of children into the study.

3.1.2 Pesticide Use Information From Previous Studies

There have been two major studies conducted in Jacksonville that have addressed exposure to pesticides. The first study, a pioneering study on non-occupational exposure to pesticides in residences, was conducted by the EPA in 1986 to 1988 (Whitmore et al., 1994). The Non-Occupational Pesticide Exposure Study (NOPES) focused on measurements of inhalation exposures of adults to 32 pesticides and pesticide degradation products, although a limited number of measurements were also performed for water, food, and dermal routes of exposure. Measurements were performed in Jacksonville during summer 1986 (64 participants); spring 1987 (72 participants); and winter 1988 (71 participants). For comparison, measurements were performed in spring 1987 (49 participants) and winter 1988 (52 participants) in Springfield,

Table 3-1. Selected Demographic Information for Duval County

Population by Race	Number	Percent of total
Total	778,879	--
White alone	512,469	66
Black or African American alone	216,780	28
American Indian or Alaska Native alone	2,598	0.3
Asian alone	21,137	2.7
Native Hawaiian/Other Pacific Islander alone	446	0.1
Other race alone	10,170	1.3
Two or more races	15,259	2.0
Population by Age (number)	Male - number	Female - number
< 1 year	5,765	5,750
1 year	5,912	5,472
2 year	5,643	5,360
3 year	5,666	5,489

Massachusetts. The pesticides targeted for analysis in the study included pesticides in current use for indoor and outdoor applications at the time (e.g., chlorpyrifos, diazinon, carbaryl, malathion, atrazine) as well as persistent pesticides whose use had previously been banned or discontinued (e.g., aldrin, chlordane, DDT, DDD, DDE, heptachlor). There were 22 pesticides for which the estimated percentage detectable was at least 10% in at least one of the air sampling media in one site/season. The pesticide concentrations were generally higher in Jacksonville than in Springfield. For the most frequently detected compounds, levels tended to be highest in summer and lowest in winter. Chlordane, chlorpyrifos, diazinon, dichlorvos, heptachlor, ortho-phenylphenol, and propoxur had the highest mean concentrations in each season in Jacksonville for both indoor air and personal air samples. More recently, a collaborative study of children's exposure to pesticides was performed by the DCHD, the CDC, and the EPA. The objectives of the project were to (1) assess organophosphate (OP) and pyrethroid pesticide exposures in a group of 4-6 year old children from Jacksonville by measuring the urine metabolite levels of OPs and pyrethroids, (2) identify possible sources of these pesticides in homes by performing screening measurements and pesticide inventories, and, (3) examine the relationship between environmental levels of OP and pyrethroid pesticides and biological levels. For the study, the DCHD collected urine samples from 200 children visiting six public health clinics in Jacksonville, Florida. A questionnaire was administered at the clinic that focused on collection

of information on recent and planned pesticide use in the participant's residences. Urine was collected from August to October, 2001, during months with relatively high pesticide use in Florida. The CDC is performing analyses of the urine samples for OP and pyrethroid pesticide metabolites. In a second component of the study, DCHD staff collected environmental screening samples at approximately 25% of these children's homes. The visits for collection of screening samples also included collection of an additional urine sample, collection of time-activity data for the 24-hr period prior to urine collection, and performance of a pesticide inventory at the residence. The third component of the study, performed by the EPA with assistance from DCHD, involved a detailed aggregate exposure assessment at nine of the study homes. The assessment involved collection of surface wipes, transferable residues, air, duplicate diet, cotton garment samples, and urine samples. Children's activities were recorded in time-activity diaries. The field sampling has been completed and sample analysis is ongoing.

Data have been analyzed from the questionnaire administered to 203 participants at the clinics at the time of collection of the urine sample. Results of the pesticide inventories performed at 43 homes have also been analyzed. The responses to questions about recent and planned pesticide use suggest that many of the participants may be frequent users of pesticides in the residence. Table 3-2 summarizes the responses to selected questions. As shown in the Table, 50% of the participants had applied pesticides indoors in the last month and 48% were planning to apply pesticides in the next month. Thirty-five percent of the participants reported that a professional service had performed the last pesticide application. Results of the pesticide inventory in the 43 homes screened by DCHD showed that synthetic pyrethroids were the primary pesticides used in the residences in addition to gels and baits containing hydramethylnon and fipronil (Table 3-3). Chlorpyrifos and diazinon, two OPs whose use indoors has been discontinued, were also identified in the pesticide inventory. Initial results from environmental samples collected in the nine-home aggregate exposure study indicate measurable pesticide concentrations in a number of air samples and many of the floor surface wipe samples. The samples are currently being analyzed. Data will be available to serve as input to the final design of the proposed field study described in this document.

3.2 Study Population

The proposed study will follow two cohorts. One cohort will consist of children (infants) recruited into the study soon after birth. The second cohort will consist of children recruited at an age of 10 to 14 months. Both cohorts will be established at the same time. The use of two age groups monitored over two years will allow for more efficient field sampling and expand the age range that can be studied. It will also double the size of the population studied during the period of 1 to 2 years of age, a period with substantial developmental changes in children that may affect exposure. The longitudinal study approach will facilitate a better evaluation of the impact of developmental age on exposure for the same children over the two-year period because intra-child variability in macroactivities is expected to be lower than inter-child variability.

The study will be limited to measurements of exposure in residential environments.

Measurements will not be performed in child care centers or other locations that the child may occupy, although information will be collected to estimate the amount of time the child spends away from the home.

Table 3-2. Responses to Selected Questions in the Jacksonville Study

When was the last you or someone else sprayed pesticides inside your home for the control of fleas, roaches, ants, spiders, flying insects, or other bugs inside your home?	Percent of responses
(1) Less than 7 days	20
(2) 8-14 days ago	11
(3) 2-4 weeks ago	19
(4) Greater than 1 month ago	34
(5) Other response	5
(99) Do not know	10
Who applied the pesticide?	
(1) Self	30
(2) Professional service	35
(3) Family member; Specify	12
(4) Other; Specify	12
(99) Don't know	11
Are you going to apply pesticides in your home or have pesticides applied in your home in the future?	
(1) Yes – in the next week	10
(2) Yes – in the next 2 weeks	8
(3) Yes – in the next month	30
(4) No – not planning of future application	39
(5) Don't know	4

Table 3-3. Pesticides Identified in the Pesticide Inventories at 43 Residences in Jacksonville

Pyrethroids	
Allethrin	Fenpropathrin
Bifenthrin	Imiprothrin
Bioallethrin	Permethrins
Cyfluthrin	Pyrethrins
Cypermethrin	Tetramethrin
Esfenvalerate	Tralomethrin
Organophosphates	**Other**
Chlorpyrifos	Fipronil
Diazinon	Hydramethylnon
	Piperonyl butoxide
	DEET

3.2.1 Eligibility Criteria

To meet the objectives of the study, it is critical that a high proportion of both environmental and biological samples have measurable levels of pesticides. A high frequency of detection is important, for example, to evaluate the factors that affect exposure. Therefore, the study will be performed in residences expected to have high pesticide use based on pesticide frequency and patterns of use as reported by the participants and results of a screening visit to the potential participant's home. It should be recognized that it is difficult to define high pesticide use for either the general population or the population targeted for inclusion in this study. There are few data that can be used for that purpose. However, the data from the study performed by EPA/CDC/DCHD in Jacksonville in the summer of 2001 will be available prior to recruiting and will be analyzed to develop an initial definition of high pesticide use for the study participants. Criteria for eligibility in the study will include the following:

- Age of the child at time of recruitment: newborn or one-year old,
- High pesticide use in the residence,
- Participant child will not attend day care outside of the home,
- Participant lives in a permanent residence (not transient housing),
- Participant is willing to advise field measurement team of planned pesticide applications,
- Participant will collect urine samples and diet samples, and,

- Participant is willing to participate in the study for two years.

In addition, a limited number of individuals (less than 10% of the total participants) will be recruited who are known to have very low pesticide usage. This group will serve as the study comparison group.

It is recognized that some children may be enrolled into day care programs outside of their residence during the two-year study even though the parent indicated that the child would not attend day care. If this occurs, the participant will be retained in the study. A data collection contingency protocol will be developed to address this situation should it occur. The first step of the contingency protocol is to attempt to schedule monitoring visits on weekends or days the child does not attend a day care outside their residence. If this can not be accomplished, an attempt will be made to sample at the child care center. Sample collection will be restricted to collection of a surface wipe sample in the primary room where the child spends time, collection of a duplicate diet sample, and use of a questionnaire administered to the day care manager/operator to collect information on pesticide use at the day care center.

3.3 Sample Size

Two cohorts will be established for the study, one consisting of infants recruited into the study soon after birth, and the second consisting of children approximately one year old at the time of recruitment. The cohorts will be a convenience sample drawn from the DCHD clinics and the three participating hospitals. The target sample size is 40 to 50 participants in each cohort for the two-year duration of the study. Initially, 60 children will be recruited into each cohort to allow for attrition during the study. The final sample size will be based on available resources. This is not a random sample. It will not be possible to draw inferences to a larger population from the results of the study. When samples are not drawn at random and the sample size is based more on budget constraints than the probability of detecting a significance (i.e. power of test), then the inference space is limited to the exact levels of the observed effect.

3.4 Participant Identification, Recruiting, and Scheduling

Participants for the study will be recruited from six Duval County Health Department clinics and three local hospitals. The recruitment of participants from clinics and hospitals will facilitate implementation of the community-based study. It will also utilize the DCHD capabilities for establishing a study population with a community linkage and interest in the potential health effects of pesticides used in the home. The use of both the clinics and local hospitals will facilitate recruitment of a population with some diversity with respect to socioeconomic status (SES).

The six DCHD health centers (also referred to as clinics by the DCHD) to be used in the

study are the following:

- Beaches Family Health Center
- Center for Women and Children
- Marietta Family Health Center
- South Jacksonville Family Health Center
- Westconnet Family Health Center
- West Jacksonville Family Health Center

The location of the centers is depicted in Figure 3-1. There is limited demographic information for these clinics. Although all Duval County citizens are eligible to use the centers, they primarily serve individuals with lower incomes. In the year 2000, seventy five percent of the users of the clinics for pregnancy issues were at or below the poverty level. Only 1.8% of the users were above two times the poverty level. The DCHD reported that there 1924 children under one year of age and 3090 children age 0 to 1 year that used the clinic in the year 2000.

The three hospitals that have discussed the study with the DCHD and indicated a willingness to participate are Shands Jacksonville, St. Vincents, and Memorial hospitals. Demographic information for these hospitals is shown in Table 3-4. Comparison of the two columns on the right side of the table shows that the percentage of births to individuals classified as black in the U.S. Census is higher at these three hospitals than for the County as a whole (as represented by the seven major hospitals). Also indicated in the table is the fact that St. Vincents and Memorial hospitals have a higher percentage of births from mothers with higher education levels (college or graduate school). Including St. Vincents and Memorial hospitals will provide a more diverse study population than use of the DCHD clinics and Shands hospital alone.

The goal is to have approximately 80 to 100 subjects participate during the two-year longitudinal study. Every attempt will be made to recruit and retain subjects who will participate over the entire period of the study. If required, a limited number of individuals will be recruited as replacements for participants who may drop out before all the field monitoring is completed. In addition, a limited number of individuals will be recruited who are known to have very low pesticide usage to serve as the study comparison population (less than 10% of the total number of participants recruited).

Recruitment of newborns (~0-3 months in age) and young children (~12 months in age) into the study will be performed by trained recruiters at the DCHD clinics and the three hospitals. Promotional materials describing the study and benefits of participation will be prepared and distributed at the clinics and hospitals prior to initiating recruitment. The primary method of recruiting study participants will be by use of recruiters on-site at the DCHD clinics and the participating hospitals. Recruiters will work with the DCHD liaison to facilitate effective and efficient recruiting. Informed consent to fully participate in the study will be obtained at the time

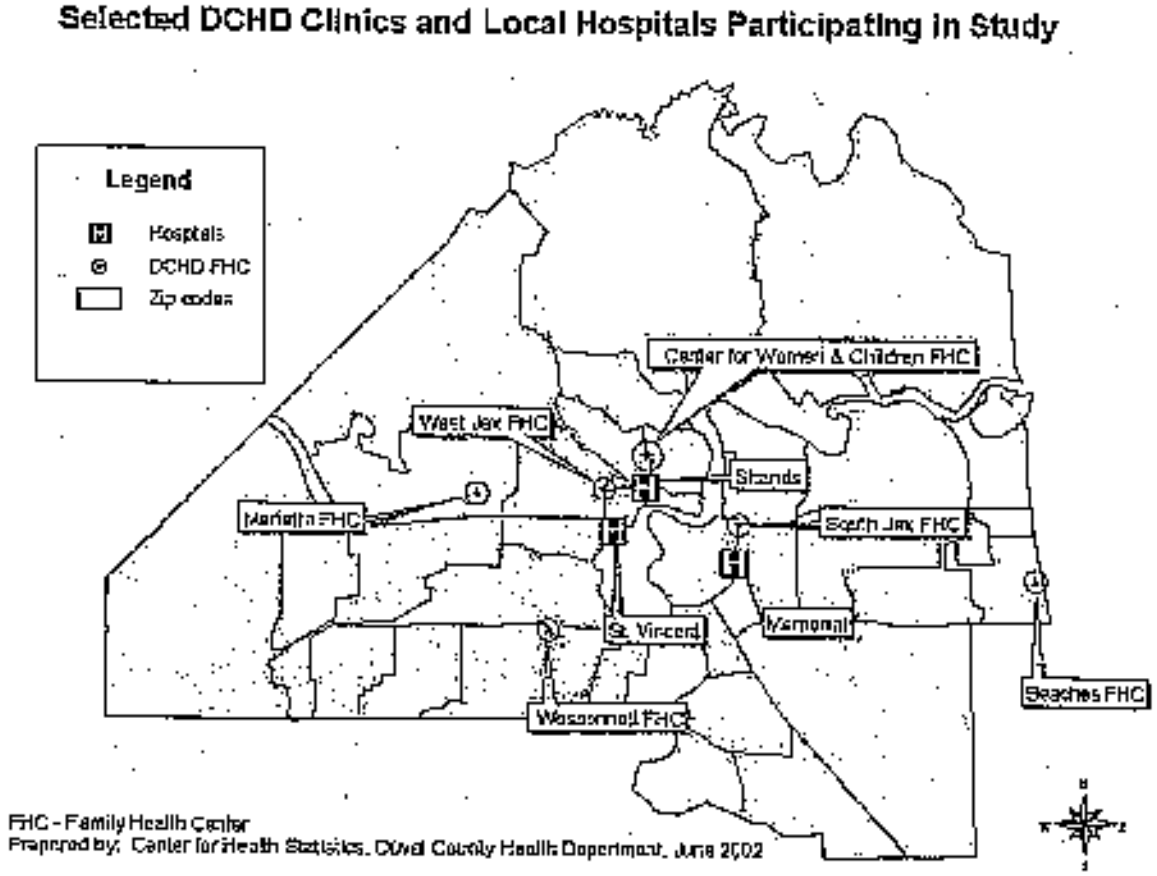

Figure 3-1. Map of Duval County indicating locations of participating hospitals and DCHD Health Centers (Clinics)

Table 3-4. Demographic Information for Three Hospitals in Jacksonville

Number of Births at Three Hospitals in 2001			
	Shands	St. Vincent's	Memorial
Births/yr	2842	1781	1868
Births/mo	237	148	156
% of all births	25%	16%	16%

Number of Births per Year by Race				Number subtotal for the 3 hospitals	% of total births at the 3 hospitals	% of total births for the 7 major hospitals in Duval County
	Shands	St. Vincent's	Memorial			
Other Asian	42	27	66	135	2.1	2.2
White	908	1058	1208	3174	48.9	60.2
Black	1868	668	548	3084	47.5	35.7
Nat. Am.		4	7	11	0.2	0.3
Chinese	3		4	7	0.1	0.1
Japanese	2	1	3	6	0.1	0.1
Hawaiian	1	1	0	2	0.0	0.0
Other nonwhite	2	1	4	7	0.1	0.1
Filipino	16	20	25	61	0.9	1.3
Unknown	0	1	3	4	0.1	0.1
Total	2842	1781	1868	6491	100	100

Percent of Births by Mother's Education Level						
	Shands	St. Vincent's	Memorial			
Elementary	6.7	2.0	2.3			
Secondary	75.0	51.6	50.8			
1-4 yrs college	12.5	39.0	39.0			
5+ yrs college	0.8	7.3	7.4			
Unknown	4.9	0.1	0.5			

of recruitment. This consent will indicate that the participants voluntarily agree to take part in the study, can withdraw at any time, and will receive a modest compensation for their time and effort.

As described in the following sections, a screening visit will be conducted at the potential participant's home following the initial determination of eligibility. This visit will provide the necessary information to determine final eligibility as a participant.

Following the analysis of the results from the screening visits, participants will be selected for the full study. Upon final selection into the study, informed consent will be obtained for the full monitoring study. The field measurements coordinator and DCHD liaison will visit the participant's home to complete the informed consent, to provide the log sheets used to collect information on pesticide purchases and use, and to provide training on study procedures including those for contacting the study team when a pesticide application is planned.

3.5 Participant Compensation

Reimbursements will be made to study participants to compensate them for their collection of samples during the study. Two types of reimbursements will be given: monetary and material (i.e., videotape equipment). During the study, each participant's caregiver will be asked to make a short videotape his/her child during specific types of behaviors. The participant will be given a video camera to use during the study to collect the video samples. If the participant remains in the study for the entire duration and collects all the video samples, then the participant will be given the video camera, blank tapes, and a VCR as partial compensation.

The monetary reimbursements will be sufficient to cover the costs for collection of the diet and urine samples, plus completion of the activity time line and questionnaires, and the monthly pesticide inventories.

To ensure retention of the participants in the study, a tiered approach will be used, with increasing amounts of compensation as the duration of their participation in the study increases. The proposed schedule of reimbursements is consistent with those offered in other longitudinal studies involving collection of diet samples and biological (urine) samples (e.g., the National Human Exposure and Assessment Survey). The schedule for participant reimbursements is as follows:

- First visit - screening to determine eligibility: $20
- First monitoring visit: $50
- Second monitoring visit: $50
- Third monitoring visit: $75
- Fourth monitoring visit: $75
- Fifth monitoring visit: $100
- Sixth monitoring visit: $100