Chapter 1
Introduction

1.1 Background

Young children, especially those of preschool age, are hypothesized to have greater exposures than do older children or adults to pesticides and semivolatile organic pollutants, 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.

Organochlorine (OC) and organophosphate (OP) pesticides, pyrethroid pesticides, acid herbicides, polycyclic aromatic hydrocarbons (PAHs), phthalates, phenols, and polychlorinated biphenyls (PCBs), are pollutants commonly found in multiple environmental media. Many of these compounds are persistent in the indoor and outdoor environments. Some have been shown to have deleterious effects on health, exhibiting not only acute toxicity, but also possible chronic effects at low levels. Many are sufficiently volatile or soluble to evaporate and condense, or to move otherwise through environmental media – air, water, and soil. They can enter indoor microenvironments through intrusion of outdoor air, inadvertent transport by people or pets, and other means (1-4). Additionally, there are many potential sources of these pollutants indoors, such as pesticides, home chemicals, environmental tobacco smoke, consumer products, and building materials.

With the passage of the Food Quality and Protection Act of 1996 (FQPA), new, more stringent standards for pesticide residues in foods were set, to provide increased emphasis on health protection for infants and children. The exposure component of the risk assessment for pesticides is now required to

- Consider the potentially greater susceptibility of children to pesticide exposure, compared to adults, 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. Because young children learn about their environment by exploring not only the appearance and texture of objects, but also their taste and smell, both dietary and indirect

ingestion can play an important role in their exposures. However, very little information on children's aggregate exposures is available at the present time, and the dominant pathways and media through which such exposures may take place are known uncertainly. The Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP) study provides some of this information.

In our previous work, methods to measure and estimate the exposures of preschool children in low-income families to PAHs were developed and evaluated (5,6). Preschool children's aggregate exposures to PAHs through three exposure routes including inhalation, dietary and indirect ingestion were estimated for 24 children (7). Further studies of an extensive suite of pollutants including OP and OC pesticides, acid herbicides, PAHs, phthalates, phenols, and PCBs concentrations in multiple media at nine child day care centers and of the aggregate exposures of nine preschool children to these pollutants were conducted (8-10). Results from these studies suggested that dietary and indirect ingestion could be important contributors to children's exposures. In addition, the children's potential absorbed doses resulting from their exposures could exceed those of adults living in the same households. This background work, along with the new requirements of the FQPA, led to the conceptualization, development, and realization of the CTEPP study.

1.2 Study Overview

The CTEPP study provides data on aggregate exposures of 257 children to pesticides and other persistent and non-persistent organic pollutants in several microenvironments, and has improved the methods for determining their exposures and the routes of exposure. The study results also allow identification of important hypotheses to be tested in future research. The following four major, specific goals were established for the CTEPP study:

1. To measure the environmental concentrations of pesticides and other persistent and non-persistent organic pollutants in multiple media at the homes and day care centers of 257 preschool children in six North Carolina and six Ohio counties,

2. To determine the distributions of child characteristics, activities, and locations that contributed to these children's exposures to the selected pollutants,

3. To estimate the exposures of the preschool children to these pollutants that they may encounter in their everyday environments, and

4. To apportion the exposures through the ingestion, inhalation, and dermal routes.

In meeting these goals, the following seven hypotheses were tested in the study:

1. Exposures of children to the target pollutants are similar at home and at day care.

2. Exposures of children to the target pollutants are similar for low-income households compared to those in other households.

3. Exposures of children to the target pollutants are similar for urban and rural households.

4. Routes of exposure and their relative importance are different for the different chemical classes of pesticides and other persistent and non-persistent organic pollutants.

5. Ingestion is a major route of exposure of the selected children and adults living in the same household.

6. Diet is a major contributor to children's ingestion exposures.

7. Children's exposures to the target pollutants (and the potential absorbed doses resulting therefrom) are significantly greater than those of adults living in the same household.

CTEPP investigated the exposures of 257 preschool children and their adult care givers to a large number of persistent and non-persistent organic pollutants in their everyday surroundings. These exposures, through the dietary and indirect ingestion, inhalation, and dermal absorption routes, were measured in the participants' homes and child day care environments, in non-occupational settings. The target compounds include OP pesticides and metabolites, OC pesticides, pyrethroid pesticides and a metabolite, acid herbicides, PAHs, phthalates, phenols, PCBs, PAH metabolites, and atrazine. 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 commonly found in both indoor and outdoor environments.

To minimize selection bias, a population-based, multistaged stratified random sampling plan was devised for the CTEPP study (11). The target population for CTEPP was children between the ages of 18 months and five years. The study consisted of two separate field studies, one conducted in North Carolina (NC) and the other in Ohio (OH). Within each state, four urban and two rural counties were selected randomly according to population, distributed among three distinct geographical regions of each state to ensure a broad range of likely exposures. These regions were the mountains, the Piedmont, and the coastal plain of NC, and northern, central, and southern regions of OH. Two sampling frames, (1) the telephone component (households containing children who do not attend day care) and (2) the day care component (households containing children attending day care centers) were constructed within each state. For the telephone component, a list-assisted, random digit dialing telephone sampling in the selected counties was used. The calculated response rate for the telephone sample was 58% in NC and 57% in OH. For the day care component, 13 centers in the six chosen NC counties and 16 centers in the six chosen OH counties were recruited. Children were then selected randomly from classrooms having children in the eligible age group of two to five years, and their participation was recruited through their parents. The calculated response rates in NC were 53% for day care centers and 50% for day care parents. In OH, the response rates were 57% for OH

day care centers and 31% for OH day care parents. For ease of discussion, the participants from the telephone component are referred to as stay-at-home participants (children) and the participants from the day care component are referred to as day care participants (children) throughout the report

In NC, children and their caregivers in 130 households participated in the study, while in OH, 127 households participated. Approximately half of the children in each state attended day care centers (63 in NC and 58 in OH). About 84% of the NC participants and 87% of the OH participants lived in urban locations. Low-income households, classified according to federal guidelines for the Women, Infants, and Children (WIC) program (185% of the federal poverty level), comprised 46% of the sampled households in NC and 38% of those in OH.

Fifty Standard Operating Procedures (SOPs) were prepared for the CTEPP study, covering subject recruitment, field sampling, storing and shipping of samples, administering questionnaires, data processing, and laboratory procedures. All field activities, laboratory operations, and data handling were performed following these SOPs. The list of the CTEPP SOPs is given in Appendix A.

More than 5,000 discrete personal and environmental samples, including quality control samples, were collected in each state (NC and OH) and analyzed. Additionally, house/building characteristics observation surveys, pre- and post-monitoring questionnaires, day care food menus, and detailed child/adult time-activity and food diaries provided ancillary information necessary to estimate aggregate exposures and to aid in interpretation of the CTEPP data.

Field sampling for the participants from the day care component took place over a 48-h period at each participating child's day care center and simultaneously at his/her home. Field sampling for the participants from the telephone survey component took place over a 48-h period at each participant's home. Environmental and personal samples were collected at the participants homes and/or day care centers:

- to identify the sources of exposures in the participants' environments,
- to determine the important routes of exposure (inhalation, ingestion, and dermal absorption) and,
- to allow estimation of potential exposure and potential absorbed dose through multiple sample media

The environmental samples collected in this study included indoor and outdoor air, outdoor play area soil, and indoor floor (carpet) dust, or if no carpet, hard floor surface wipes. If a pesticide had been applied in the home or day care center in the seven days prior to sampling, transferable residues, hard floor surface wipes, and food preparation surface wipes were also collected. Personal samples collected in this study included drinking water, duplicates of all food and beverages that the participants ate or drank during the 48-h sampling period, hand wipes, and urine. In addition, approximately 10% of the children (26) in OH were videotaped for about 2 h at their homes. Note that the videotaped data are not presented in this report.

The collected field samples and field and laboratory quality control samples were extracted, then analyzed by gas chromatography/mass spectrometry for over 50 target compounds[1]. These compounds included the following:

- two OP pesticides: chlorpyrifos and diazinon;
- two OP metabolites: 2-isopropyl-6-methyl-4-pyrimidinol (IMP) and 3,5,6-trichloro-2-pyridinol (3,5,6-TCP);
- ten OC pesticides: aldrin, *alpha*-chlordane, *gamma*-chlordane, *p.p'*-DDE, *p,p'*-DDT, dieldrin, endrin, heptachlor, lindane, and pentachloronitrobenzene;
- three pyrethroid pesticides: cyfluthrin and *cis*- and *trans*-permethrin;
- one pyrethroid metabolite: 3-phenoxybenzoic acid (3-PBA);
- three acid herbicides: dicamba, 2,4-D, and 2,4,5-T;
- nine PAHs: benz[*a*]anthracene (BaA), benzo[*a*]pyrene (BaP), benzo[*b*]fluoranthene, benzo[*e*]pyrene, benzo[*ghi*]perylene, benzo[*k*]fluoranthene, chrysene, dibenz[*a,h*]anthracene, and indeno[1,2,3-*cd*]pyrene;
- six PAH metabolites: 1-hydroxybenz[*a*]anthracene, 1-hydroxypyrene, 3-hydroxybenz[*a*]anthracene, 3-hydroxybenz[*a*]pyrene, 3-hydroxychrysene, 6-hydroxyindeno[1,2,3-*cd*]pyrene, and 6-hydroxychrysene;
- two phthalates esters: benzylbutyl phthalate and di-*n*-butyl phthalate;
- three phenols: bisphenol-A, nonylphenol, and pentachlorophenol (PCP);
- 17 PCBs: PCBs 10, 15, 28, 44, 52, 70, 77, 95, 101, 105, 110, 118, 126, 138, 153, 169, and 180; and
- one triazine: atrazine.

These pollutants/metabolites, with the exception of atrazine, were analyzed in the multimedia samples. Atrazine was analyzed only in drinking water samples. Only one OP metabolite, 3,5,6-TCP, was analyzed in the NC multimedia samples, while both IMP and 3,5,6-TCP were measured in the OH environmental and personal samples. The NC urine samples were analyzed for the two OP metabolites, IMP and 3,5,6-TCP; 2,4-D; two hydroxy PAHs (1-hydroxybenz[*a*]anthracene and 3-hydroxychrysene); and PCP. The OH urine samples were analyzed for these same metabolites and/or parent compounds, in addition to five hydroxy PAHs (1-hydroxypyrene, 3-hydroxybenz[*a*]anthracene, 3-hydroxybenzo[*a*]pyrene, 6-hydroxychrysene, and 6-hydroxyindeno[1,2,3-*cd*]pyrene) and 3-PBA.

Two similarly formatted CTEPP databases were developed, one for the NC study and one for the OH study. Each database contained questionnaire data, analytical data, and metadata, and provide sufficient documentation to allow the data to be understood by a diverse set of users. Descriptive statistics were calculated for sample size, mean, standard deviation, percentage detected, minimum and maximum reported values, and selected percentiles (25^{th}, 50^{th}, 75^{th}, and

[1]Two carbamates, propoxur and bendicarb, were originally included on the list of target pollutants but were later removed due to the study's analytical methods being incompatible for these pollutants. Atrazine was only measured in drinking water because of co-eluting interference present in other sample media.

95th). The distributions of participant characteristics, activities, and locations that are important for exposure were quantified, based on the questionnaire data. Potential exposures and potential absorbed doses were estimated for selected target compounds, based on the percentage of samples that had detectable levels of these compounds, the measured concentrations, the participants' activity patterns, and assumed physiological parameters. Statistical analyses were performed on log-transformed data, using analysis of variance (ANOVA) models. The data summaries presented in this report represent only the children and their primary caregivers in NC and OH who participated in this study.

This report summarizes the recruitment, field sampling, chemical analyses, data analyses, and the study findings for both the NC and OH field studies.